Author's response to reviews

Title: Outcome of gastric emptying and gastrointestinal symptoms after liver transplantation for hereditary transthyretin amyloidosis

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Author's response to reviews: see over
Dear Dr Roshandel,

Thank you for the constructive comments on our manuscript titled “Outcome of gastric emptying and gastrointestinal symptoms after liver transplantation for hereditary transthyretin amyloidosis”. Please pass on our gratitude and appreciation to the referees for their work on our manuscript.

We have now revised the manuscript according to the concerns raised by you and the referees. Changes in the manuscript are highlighted in yellow. Please find below point-to-point answers to the reviewers' comments.

We believe that the suggested revisions significantly strengthen our work and hope that the improved manuscript is now acceptable for publication in BMC Gastroenterology.

Sincerely,

Jonas Wixner,
MD, PhD
Reviewer 1

Comment 1. The major problem with this report is the claim to describe a course in a group of patients for at least 5 years, when only less than a third of those included from the beginning are followed all the way. (Figure 2). This opposition is supported by the fact that in the part of the study where drop outs are less prevalent (Figure 3), the results are different. This problem could easily be solved by restricting the analysis to the patients that were followed during the whole study period.

Response: This is a valid concern. However, it is not possible for us to influence the inflow of patients since we work at a tertiary referral center, with most of our patients coming from other regions of Sweden. A large proportion of the dropouts were patients who had not been referred to us for follow-up and, consequently, this is the best available material. We chose to report the entire material to give a picture of the dropout rates and to provide a more holistic description. We have separately described the outcome of the GI function at the first follow-up after LTx in order to assess a potential deterioration while waiting for transplantation. As regards the main analyses (i.e. Fig 2 and 3 and Table 2), however, only patients who had completed the evaluations at all three time-points were included. This has now been clarified in the Results and Discussion sections of the manuscript. We have also performed additional outcome analyses only including the patients who had completed the scintigraphies at all three time-points, and no different outcome was found either for mBMI or for GI symptom scores.

Comment 2. The observation that there is a relation between the use of loperamide and the Lower GI score (Tab 3) should not be interpreted as loperamide being the cause of the intestinal symptoms, but the opposite.

Response: We fully agree and we have now added a comment in the Discussion section to clarify this.
Reviewer 2

Comment 1. When we evaluate the “T50” measurements separately before and after scintigraphic software differences is there any difference between the results?

Response: We have not performed a direct comparison of the T50 results from before and after the software update since this is not an easy task to do. In general terms, the risk of error is probably greater with the new software, since the number of data points had been reduced in this version. However, we have tried to minimize the differences between the measurements by the manual assessment of T50 (by a single reviewer), and by adding the variable retention at 90 min, which can be electronically calculated from the curves generated by both the old and the new software. It should be noted that, apart from the software update, the scintigraphic acquisition procedure remained unchanged. We have now clarified this in the Methods section.

Comment 2. Although we do not expect a significant symptomatic amelioration after transplantation and evaluation of symptoms is a subjective thing, the comparison of symptoms in accordance different time periods will increase the subjectivity of your comment.

Response: This is a valid concern. We have addressed this problem in the Limitations section and tried to minimize the error by using the same validated questionnaire at all three time-points and by asking the patients to state their current (last week's) symptoms at each time-point.

Comment 3. I noticed that not all the patients responded the survey and it is possible that patients with complaints are more prone to respond the survey.

Response: We agree that this is a potential problem. However, as much as 84% of the patients responded the questionnaires, which is usually considered to be a high response rate (Evans SJ. Good surveys guide. BMJ. 1991 Feb 9;302(6772):302-3). Furthermore, we found no difference in patient characteristics or GI function between the patients who had responded the questionnaires and those who had not (Table 1), and we therefore don't believe that there are any significant differences between the groups. We have now tried to clarify this in the manuscript.

Comment 4. On the other hand it is not clear how a person can get 4 and 6 points from lower GI symptoms which consists of from three symptoms (192-193)

Response: We apologize if this hasn't been explained clearly enough. Since each GI symptom was assessed with a 10-point rating scale (from 0-10), and since the lower GI symptom category consists of three different symptoms, the possible score for this specific category ranges from 0-30. In this case the median score was 4 and 6 points, respectively. Please see the revised Methods section and Figure 3 for details.