Thank you for considering our paper for publication in World Journal of Gastroenterology. We have addressed the pertinent comments from the peer reviewers and revised our paper as suggested. We believe that the changes have improved the quality of our work.

Kind regards,

Agnete Riedel

Point to point response to:

Development and predictive validity of the Cirrhosis-associated Ascites Symptom Scale: A cohort study of 103 patients

Reviewer 1:

Comments for ESPS Manuscript NO 37323 ⑴ General comments: The study is interesting, and the contents would give some useful information. ⑵ Specific comments a) Major comments：Cirrhosis, if severe enough, can cause many different complications. Such complications may have an impact on many dimensions of health-related quality of life (HRQL), and the impact may be substantial. I wonder how the authors excluded the influence of such complications affecting CAS scale scores. b) Minor comments: The language needs to be improved.

Reply:

a) We agree that decompensated cirrhosis is a multi-facetted disease and several factors influence the quality of life in these patients. We therefore included a control group consisting of participants with cirrhosis and two groups of patients with mild/moderate and severe ascites (known group comparison). Our findings suggest that our scale reflects dimensions of HRQOL associated with ascites rather than cirrhosis. This is now highlighted in the results and discussion (please also see table 1). As now highlighted in the discussion, we need additional evidence to test the applicability of the scale in different settings.

b) We have revised the language in the manuscript.

Reviewer 2: 0

In the current manuscript, the authors developed a questionnaire to scale the symptoms related to liver cirrhosis associated with ascites and to access its affects on the quality of life of patients. The authors also validated this scale in a group of patients. The study is interesting and would be helpful to evaluate cirrhotic ascites associated impairment of quality of life. However, the authors should clarify the following question: Did this CAS scale have any significance between severe/tense ascites and moderate/mild ascites? I wonder if this CAS scale was effective in discriminating severe ascites and mild ascites. If not, the authors should make some comments in the Discussion.

Reply:

The CAS scale was able to discriminate between mild/moderate and severe ascites, see Results section, Discriminant Validity and Figure 2. We have elaborated on this in the Discussion, first paragraph.

Reviewer 3:

The manuscript written by Riedel et al. describes that the authors developed a CAS scale and the scale is effective in discriminating between various severities of ascites. Although there are some other scales evaluating the QOL in chronic liver disease, the scale is specified to evaluate the impact of ascites severity on the QOL in patients with chronic liver diseases. The data are interesting and important, but there are some concerns that need to be addressed.

Major points. 1. CAS scale scores could be affected not only by ascites severity but also other physical conditions such as severity of liver cirrhosis, treatment, anemia, or complication of hepatocellular carcinoma. It is unclear how the authors excluded the influence of those factors affecting the score.

2. How do the scores change after reduction of ascites by diuretics treatment?

3. It is still unclear how the CAS scales are superior to CLDQ or SF-36 in evaluating QOL and total management of in patients with chronic liver disease.

Reply:

1) **We agree with the severity of cirrhosis and comorbidities are important factors, which may affects the HRQOL. As shown in our description of patient characteristics, we included three groups of patients with ascites and found that the scale is able to differentiate between patients with mild/moderate or tense ascites as well as patients with cirrhosis who do not have ascites (we did not include patients with malignant ascites).**
2) **We agree that it is important to evaluate if the CAS scale reflects changes in the HRQOL after treatment and are planning to use the scale for this purpose in future (ongoing) trials.**
3) **Unlike the CLDQ, our scale is developed and validated specifically with this purpose. The CAS scale is therefore more sensitive towards changes in the amount of ascites than the CLDQ. The SF-36 is a generic scale, which is helpful in the comparison of different groups of patients (including groups with different diseases). The SF-36 does not reflect changes in HRQOL associated with ascites. This may explain why previous studies found that ascites had little impact on HRQOL when evaluated using the SF-36. This is now clarified in the introduction and discussion. In addition, we would like to underline that the CAS comprises of only 14 questions taking less than 5 minutes to complete.**

Reviewer 4:

Dear sir, thank you to select me for reviewer of paper: Riedel AN. Development and predictive validity of the Cirrhosis-associated Ascites Symptom Scale: A cohort study of 103 patients. Authors designed a Cirrhosis-associated Ascites Symptom (CAS) scale. The final scale included 14 items describing symptoms with a potential detrimental impact on HRQL. 14 questions in CAS are accurately selected, they reflected real-life problems in the group of patients with cirrhosis and ascites. Authors found a strong correlation between the total CAS and CLDQ score (Liver specific QoL questionnaire) and a moderate correlation between the CAS and the EQ-5D-5L score (general QoL questionnaire) and between CAS and some CLDQ individual subscale parameters. Paper is well written, methodology, statistical analysis and discussion are adequate.

Only minor changes are needed: 1) Please, add Ethic committee approval.

2) Please explain in discussion, why CAS is better correlated with total CLDQ score than with all CLDQ individual subscale parameters (fatigue, activity, systemic symptoms, abdominal symptoms, emotional function and worry).

3) Please correct data in table 2. Data about creatinine levels are missing, data about Na levels are written in line creatinine, and data about potassium are written in line Natrium.

Reply:

1) We have added our approval number.

2) We found a strong correlation between the CAS and the CLDQ total score (Spearmans rho = 0.82, P<0.001) as well as the CLDQ subscores, Fatigue (0.78, P<0.001), Activity (0.81, P<0,001) and Systemic symptoms (0.77, P<0.001). The CLDQ subscore Abdominal symptoms was not associated to CAS. The total CLDQ was better correlated with CAS than each subparameter. This may be due to the impact of low quality of life affecting all aspects of life, allowing a total low score higher statistical significance. We have revised the discussion page 8 accordingly.

3) Thank you pointing this out. We have revised the table accordingly.

Reviewer 5:

Please make clear the advantage of the CAS scale over current scales in Discussion section.

Reply:

We have revised the discussion to point out the aspect more clearly.