Boechout 09-07-2015
To the Editor
World Journal of Hepatology
Letter of response
Revision 18692-manuscript

Dear colleague,

We are happy to send you the revised version of our article. We thank the reviewer's fort heir positive comments, which helped to improve the manuscript. In the following of this letter you'll find our detailed point-by-point answers and changes in the manuscript. We followed the requested re-submission procedure as indicated in the editors' mail, except for step 4 of the procedure. We did not subject the manuscript to the suggested CrossCheck analysis and the final title to Google Scholar search. This is a paying service for which the money is not provided by our institution. As authors we would like to stress that this is an invited review by the World Journal Gastroenterology (WJG), which they suggested to be published in WJH. We accepted this change of journal within your publishing group, but do not think we need to pay additional costs for an invited article. However, when WJH like to subject the manuscript to a CrossCheck analysis, we would be happy to adapt the manuscript if any problems need to be changed on this basis.

We count upon that, with the requested changes, the manuscript will be accepted for publication in WJH, and thank you for understanding our point of view concerning the resubmission procedure.

Sincere regards,

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Response to the reviewer's comments

Revision 18692-manuscript

We thank the reviewer's for their constructive comments and give our point-by-point responses in following:

Nice review. Only few queries:

Ad 1. Thank you for positive comment

Is there a role for CDT (Carbohydrate Deficient Transferrin) for monitoring alcohol use? This topic should be addressed and discussed in paragraph 5.

Ad 2. We have changed paragraph 5 elaborating more on the topic of biomarkers, including CDT and their value in detecting alcohol use:

Traditional alcohol biomarkers such as gamma-glutamyltransferase (GGT) are not recommended in ALD patients because they will be elevated as a result of the liver damage itself. They could provide some information in post-transplant patients, however, as also within non-ALD alcohol patients,, they have low sensitivity (30-60%) and specificity (60-95%). Other often-used biomarkers in blood (MCV, ALT, and AST) also have low sensitivity (<50%) and specificity (60 to 95%), and are also confounded by liver damage itself [48, 49]

Carbohydrate-Deficient Transferrin (CDT) is more specific for heavy (from 5 to 6 standard drinks per day for several days) alcohol use and will be elevated for about two weeks after the drinking bout. However, in pre-transplant ALD patients, CDT lacks specificity. However, as a post-transplant measure it has value as an indicator of heavy alcohol use. In comparison with other biomarkers, CDT would be a biomarker that is less affected by false positive results due to liver disease [50, 51].

Recently, several recent studies suggest a promising role for using ethylglucuronide in hair samples (hEtG) as a biomarker for alcohol use detection.

How should be assembled the addiction team? Which specialists must be present in an ideal addiction team? This topic should be addressed.

Ad 3. This is an important suggestion. We have changed the text paragraph 7 to specify:

Given the complexity and diversity of the core services to be provided, as described infra, ideally this work is taken on by a multidisciplinary addiction specialist team. Although economic barriers and possibilities may differ widely between countries, team composition should at least contain a psychiatrist, psychologist-psychotherapist, and social worker, all trained in addiction work. Their services need to be offered as an integrated part of the transplant program[11].

It is arguable that during the waiting list data from monitoring should not be shared with members of transplant team...

Ad. 4 Important point well taken. This is a difficult issue were complex interests need to be balanced carefully. We have introduced a discussion on this item in paragraph 7.1.

Both within the screening-assessment procedures as to the monitoring during waiting list periods, one of the most challenging questions remains how and how much information is shared between the addiction team and the transplant team. Indeed, a high level of confidentiality is needed in the relation between the addiction specialist and the patients, facilitating an open sharing, necessary for treatment and growth of motivation. On the other hand, when relapse risks are high some information needs to be communicated allowing a balanced discussion between transplant and addiction team on very difficult questions of candidacy for transplantation. As yet no clear-cut solution for this dilemma is at hand. However, it is of utmost importance that it is very transparent for the patient and family what is communicated and what the consequences can be.

At the end, in case of higher risk of relapse who is empowered to decide if the patient earns to be transplanted or not? The addiction team? The transplant team? Both? In the latter case information about the patient should be necessarily shared... (see point 3)

Ad 5. See Ad 4

Remarks of the editor included within the manuscript:

Title should be no more than 12 words.:

Ad 6. Title has been changed into:

The addiction specialist's role in liver transplantation procedures for alcoholic liver disease.

Please write a summary of no more than 100 words to present the core content of your manuscript, highlighting the most innovative and important findings and/or arguments. The purpose of the Core Tip is to attract readers' interest for reading the full version of your article and increasing the impact of your article in your field of study.

Ad 7. We included a Core tip
Liver transplantation is performed increasingly for patients with end-stage alcoholic liver disease. Assessment of a patients risk on relapse in alcohol use after transplantation and helping patients to achieve and maintain abstinence are crucial within this process. The addiction specialist's input is essential and needs to be integrated within the transplantation team. Ideally a multidisciplinary approach is offered to the patients including addiction psychiatrist, behavioral therapist and social worker following up the patient before and after transplantation.

Please put the reference numbers in square brackets in superscript at the end of ciatation content or after the cited author's name.
Please check across the text.

Ad 8. We changed reference style accordingly