

January 27, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript NO: 7385-edited.doc).

Title: Diagnosis of Alcoholic Liver Disease

Author: Cara Torruellas, Samuel W. French, Valentina Medici

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 7385

The manuscript has been improved according to the suggestions of the reviewers. We appreciate the reviewer's comments and we have addressed each specific concern as follows:

Concern #1: At least 50% of the patients with alcoholic liver disease have increased hepatic iron content, which may lead to a diagnostic confusion with hereditary hemochromatosis. The differential diagnosis of hemochromatosis and increased iron indexes in alcoholic liver disease should be discussed in detail.

We agree with the reviewer's comment regarding the overlap in iron metabolism changes between hemochromatosis and alcoholic liver disease. We commented on this issue providing additional details on the diagnosis of hemochromatosis (page 11, lines 13-23) and provided additional references (#78-#81).

Concern #2: What is the current status of alcoholic steatohepatitis and alcoholic hepatitis in the spectrum of alcoholic liver disease? There is a need for an evaluation of these two concepts, whether they represent same conditions or not.

We agree with the reviewer that there is some potential confusion between the two terms and our literature search was not conclusive. Therefore, we believe there is still a gap in these definitions. Our response to the reviewer's concern is addressed on page 22, lines 21-25.

Concern #3: Another question that arises is that; what is value of liver biopsy in discrimination of alcoholic simple steatosis and alcoholic steatohepatitis?

Liver biopsy can facilitate the differentiation between simple steatosis and steatohepatitis based on distinct histological features. This differentiation is of clinical significance in that it provides important prognostic information for the patient. We added an additional comment about the value of a liver biopsy in this setting on page 16, lines 10-13.

Concern #4: Are there non-invasive methods or markers other than liver biopsy to differentiate those two conditions (alcoholic simple steatosis and alcoholic steatohepatitis)?

Our literature search was not conclusive in identifying markers that could differentiate between these two conditions. However, we expanded our search to biomarkers for nonalcoholic steatohepatitis which could be potentially applied to the alcoholic variant and provided some additional references (#117-#119) as well as additional comments in the main text (page 13, lines 16-23).

We hope that our review will be considered of sufficient quality for publication in *World Journal of Gastroenterology*.

Kind regards,

A handwritten signature in black ink that reads "Valentina Medici". The script is cursive and fluid, with the first name and last name clearly distinguishable.

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