

Independent Review Report

Reviewer #1:

1. I advise that the work be systematized again. Despite the detailed approach, the text is quite difficult to follow, especially due to the large number of abbreviations (which are often similar).

Response: Thanks for your valuable comments and advice. The manuscript has been carefully checked and revised accordingly, especially, unnecessary abbreviations have been deleted.

2. I advise the authors to point out the definitions that they consider to be the most adequate, it can also be in the form of a table.

Response: Thanks for your valuable comments and advice. A table (Table 2) has been added to the revised manuscript to show the brief definition of each clinical type of AoCLD and their respective diagnostic criteria.

3. I advise to briefly describe Acute liver failure, as well as its differential diagnosis in relation to acute on chronic liver failure with respect

Response: Thanks for your valuable comments and advice. The main difference between acute on chronic liver failure (ACLF) and acute liver failure (ALF) or subacute liver failure (SALF) is that whether liver failure occurs on the basis of chronic liver injury or not. The following sentences have been added to the text.

“In the diagnosis of ACLF, attention should be given to discriminating ACLF from acute liver failure (ALF) or subacute liver failure (SALF) in which liver failure develops within 2 or 26 weeks, respectively, in patients without pre-existing chronic liver injury[36]. Therefore, the difference between ACLF and ALF/SALF mainly lies in the presence or absence of underlying chronic liver injury.”

Reviewer #2:

1.The article did not add to the existing data about this condition in the literature.

Response: To date, the definition of AoCLD is still vague, and a consensus concept of the clinical classification is lacking. This review aimed to define the concept and clinical types of AoCLD based on related studies and the literature. The latest literature related to the concept and clinical types of AoCLD has been added to the revised manuscript.

2.the flow of the article is somewhat confusing to readers like this statement (At this point, the disease has progressed to severe hepatitis, decompensated cirrhosis, and even acute-on-chronic liver failure (ACLF) characterized by high short-term mortality [4, 5], The main clinical types of CLD are chronic hepatitis, liver fibrosis, and liver cirrhosis [17])). It has several definitions that are not well organized and unclear in different parts of the article. In some parts of the article, the author is confusing the histological classification of liver disease to the clinical classification. This is very clear under the clinical classification section that mainly addresses the histological classifications for liver disease.

Response: Thanks for your valuable comments and advice. We are sorry for the inappropriate expression in the clinical classification section. The manuscript has been carefully checked and revised accordingly, to make the classification and definition clearer.

3. On the other hand in the section on ACLF the author suddenly and for unclear reason jumped from ACLF to a discussion of chronic hepatitis B, this is very clear on pages 6-7.

Response: Because HBV infection is the main cause of ACLF, and the natural history HBV infection is complex, it is sometimes difficult to distinguish HBV-ACLF from ALF. The following sentences have been added to the text.

“In the diagnosis of ACLF, attention should be given to discriminating ACLF from acute liver failure (ALF) or subacute liver failure (SALF) in which liver failure develops within 2 or 26 weeks, respectively, in patients without pre-existing chronic liver injury[36]. Therefore, the difference between ACLF and ALF/SALF mainly lies in the presence or absence of underlying chronic liver injury. HBV infection is the main cause of ACLF[37].”

4. On page 7. Another confusing point on page 7 about the use of fibroscan, first the tool is named transient elastography because other similar machines to the fibroscan are available in the market. Second transient elastography using fibroscan is not meant to assess the degree of inflammation, rather on the contrary it is not indicated in patients with acute hepatitis or exacerbation as it will give misleading results. (, dynamic monitoring of ALT/AST levels and FibroScan will facilitate the assessment of liver inflammatory activity and fibrosis, which is helpful in distinguishing ALF from ACLF [42, 44].)

Response: Thanks for your valuable comments and advice. The phrase “FibroScan” has been replaced with “liver stiffness”. We agree with you that patients with acute hepatitis or deterioration will have misleading results on liver stiffness. However, for patients with chronic HBV infection without obvious symptoms and signs of active hepatitis, dynamic monitoring of the ALT/AST

levels and liver stiffness could facilitate the assessment of liver inflammatory activity and fibrosis, respectively, which is helpful to identify an underlying chronic liver disease.

5. In addition to the article need some language polishing

Response: Thanks for your valuable comments and advice. The revised manuscript has been polished again by a language editor from AJE.

2 Editorial Office's comments

Science Editor: This manuscript summarizes the concept and clinical classification of AoCLD based on relevant research and literature. The full text should be supplemented when the abbreviation appears for the first time. The logic of the manuscript is a little confused. Please re sort out the logic for better display.

Response: Thanks for your valuable comments and advice. The manuscript has been carefully checked and revised accordingly, especially for the abbreviations and the internal logic.

Round 2:

Comment: The authors have placed a very good effort in revising the article making to be more reader friendly. However I still think that it will be difficult for a reader who is not expert in the field to follow all those definitions. I would suggest to the author to summarize all those definitions in a table form;

Response:1. Definitions relevant to AoCLD, including CLD, C-LC, D-LC, have been added to Table 2 (Modifications are marked in red) . 2. A decomposable figure of Fig. 1 has been provided and uploaded as requested. 3. We agree with the Copyright License, and accepted in F6publishing system. 4. The file "72876 auto-edited" has been checked and revised (Modifications are marked in red) .