

Reviewer number 03509551

Conclusion: Rejection

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

REVIEWER: Thank you for allowing me to review this manuscript. It is a very important topic in liver transplantation. While many topics are highlighted in this manuscript, it is not comprehensive enough.

ANSWER: It is not a review about liver transplantation. The paper is about diagnosis and screening of hepatocellular carcinoma and consequently there is no information about liver transplantation in our paper.

Language Quality: This paper has been written in Spanish and translated to English by Dr. Planells (co-author), who is a native speaker of English

Reviewer number 02520738

Conclusion: Minor revision

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

REVIEWER: A representative figure should be created for this review. - The role of care manager should be discussed. Please consider and discuss the paper from Ciccone MM et al. Vasc Health Risk Manag. 2010 May 6;6:297-305.

ANSWER: The reviewer did not explain the role and the objective of a representative figure in our paper and we did not know how to do it.

The proposed article to be cited and discussed is about the role of a care manager in primary health care system for patients with heart failure and diabetes (a paper from Ciccone MM et al. Vasc Health Risk Manag. 2010 May), but this paper has no relationship with our topic and we do not understand the intention of the author. We have not included this paper in our review.

Reviewer number 03358964

Conclusion: Minor revision

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

REVIEWER: The authors should shorten the paragraph IMAGING DIAGNOSIS, introducing some tables, for examples, to summarize the typical pattern of HCC; but they should mention as well the atypical features of HCC. Moreover, they should emphasize the role of HEPATOSPECIFIC CONTRAST AGENTS, adding more recent and up to date references to this topic. MRI with HEPATOSPECIFIC CONTRAST is nowadays considered, as they only briefly mentioned, the most accurate diagnostic tool in imaging diagnosis of HCC. I strongly suggest supporting the text with additional table. 2. Minor language polishing is needed.

ANSWER: The "imaging diagnosis" paragraph has been shortened and 2 new tables have been added in order to clarify typical and atypical patterns of HCC, as the reviewer suggested. However, we have not changed the role of hepatospecific agents, because in our environment and in our revision we don't conclude that they are the most accurate diagnostic tool in imaging diagnosis of HCC as the reviewer suggests. We would appreciate if you can give us more information about it with references.

Reviewer number 02992582

Conclusion: Minor revision

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

REVIEWER:

1) I would stress much more the importance of screening in NAFLD population, which is becoming more and more relevant. What are the main limitation of diagnostic techniques? What would be the target? Only patients with cirrhosis or also those with advanced fibrosis? If yes, what would be the best way to diagnosis advanced fibrosis?

2) I think it's very important to underline the need of continuing HCC surveillance in patients with HCV cirrhosis after the achievement of SVR

3) I would probably quote the studies that showed an increased incidence of non neoplastic portal vein thrombosis in HCC patients (see for example Zanetto 2017), and the need of make a differential diagnosis between neoplastic and non-neoplastic portal vein thrombosis in patients with HCC

4) Please describe a bit more the biomarkers and their clinical use

ANSWER:

- 1) The approach to HCC in NAFLD population has been improved.
- 2) The need of continuing HCC surveillance has been expressed.
- 3) The relevance of making a differential diagnosis between neoplastic and non-neoplastic portal vein thrombosis has been made and the suggested paper has been quoted.
- 4) The biomarkers have been described a bit more, although the usefulness of most of them has not been described.

Reviewer number 02860516

Conclusion: Minor revision

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

REVIEWER:

N 1 Authors should insert abbreviations throughout the manuscript starting from the Abstract session

N 2 Page 5 last line and page 6 lines 1-13 : Authors should specify in a flow charts how many articles have been analyzed in both the topics considered (i.e diagnosis and screening). In particular, they should specify the articles included and excluded from analysis according to the type (i.e. Case reports, meta-analysis, and reviews)

N 3 Page 6 line 18: Authors should give more details on the number of patients analyzed in the two manuscripts.

N 4 Page 6 line 41: authors wrote "...A recent meta-analysis of studies published between 1990 and 2014, including abstracts presented in congresses from 2009 to 2012, identified a total of 45 articles that included in total 15158 patients with HCC, of which 41% had been diagnosed in screening programs.." This is related to what previously underlined in the previous question (N 3) regarding the type of products included in the study (original studies, meta-analysis etc.). Furthermore, authors

should give information on the geographic provenience of the studies and the aetiologies of patients included in the analysis

N 5 Page 7 line 4: The sentence is too long and deserves English revision

N 6 page 7 line 35: Authors should specify the criteria used to consider the relevance of the studies included in Table 1

N 7 Page 8 line 38 Authors should specify that US is an operator-dependent technique

N8 Page 13 line 1: Authors should also cite the EASL indications for HCC screening in the different categories of HBV patients.

N9 Page 14 line 15: Authors should include the diagnostic algorithm for hepatic <1 cm nodules as stated by the EASL.

N 10 Page 17 line 11: Authors should give more details on the use of CEUS particularly in patients with contraindications to perform MRI or CT

ANSWER:

N 1 Abbreviations have been included in the text

N 2 Page 5 last line and page 6 lines 1-13: More details about bibliography selection have been given

N 3 Page 6 line 18: More details about the number of patients analyzed in the two manuscripts have been listed.

N 4 Page 6 line 41: More information about the geographic provenience of the studies and other characteristics have been provided.

N 5 Page 7 line 4: The sentence has been changed

N 6 page 7 line 35: The specify criteria used to consider the studies included in Table 1 has been detailed.

N 7 Page 8 line 38: The sentence US is an operator-dependent technique has been included

N8 Page 13 line 1: EASL indications for HCC screening in HBV patients has been added.

N9 Page 14 line 15: The EASL diagnostic algorithm for <1 cm hepatic nodules has been included.

N 10 Page 17 line 11: Details regarding the uses of CEUS in patients with contraindications to perform MRI or CT have been included.