

ANSWERING REVIEWERS



January 15, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2429-review.doc).

Title: Management of small hepatocellular carcinoma in cirrhosis: focus on portal hypertension

Author: Virginia Hernandez-Gea, Fanny Turon, Annalisa Berzigotti, Augusto Villanueva

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 1431

The manuscript has been improved according to the suggestions of reviewers.

Here you have a point by point response to every reviewer's comment:

[We would like to thank the reviewers for their review and comments to our article.](#)

[We have modified the manuscript accordingly and below please find enclosed our answers to the points arose by the reviewers.](#)

The manuscript is interesting because it is a review of an important issue in clinical management of HCC. The manuscript is well written but it should be improved in some parts before publication.

1. On page 4 the authors described the role of liver resection in patients with portal hypertension. Even if the Authors reported in table several publications they should describe more clearly the role of liver resection in patients with portal hypertension. Several clinical studies included into the table did not contraindicated surgery for patients with portal hypertension.

[This point has been better clarified in the text now. In summary, data presented in Table 1 show that even if the presence of clinically significant portal hypertension \(CSPH\) is not an absolute contraindication for performing liver resection for HCC, it clearly increases the risk of post-operative complications and death, suggesting that other available options such as liver transplantation should be considered in this subgroup of patients](#)

2. The Authors should describe the risk of surgical resection in presence of portal hypertension in terms of postoperative complications and long term results.

[Accurate information regarding this point is difficult to describe as many studies did not evaluated HVPG and only portal hypertension related complications, underestimating the number of patients with CSPG. However the main survival in the studies described in table 1 was in mean 59% \(ranging 45-71%\) in patients with clinical signs of portal hypertension, while it increased to 72% \(62-81%\) in patients without any clinical sign of the syndrome. These data support that idea that that even if the presence of CSPH is not an absolute contraindication for performing liver resection for HCC, it clearly increases the risk of post-operative complications and death, suggesting that other available options such as liver transplantation should be considered in this subgroup of patients. Hence, the best candidates for surgical resection are patients with solitary tumors, preserved liver function and absence of CSPH. Consequently, the European and American Associations for the study of the Liver \(EASL⁹ and AASLD¹⁰\) guidelines for HCC management recommend surgical resection as the first-line option in patients with small HCC without CSPH or liver dysfunction.](#)

3. On page 4 the Authors should consider the statement that liver transplantation is the treatment of choice for BCLC 0.

We have better explained now in the text that, liver transplantation is the best option for patients in BCLC stage 0/A, CSPH and absence of other medical conditions that contraindicate this procedure. However when BCLC stage 0/A patients do not have CSPH, surgical resection becomes the more suitable therapeutic option.

4. On page 4 the Authors reviewed the results of RFA compared to Surgery, they should analyze the controversial results of the trials reported in the table.

Although further evidence will be needed to appropriately address this issue, we have collected information of the available RCT evaluating face-to-face surgery and local ablation. See page 5 of the MS: “Although resection remains the first-line option for patients without CSPH, well-preserved liver function and solitary tumors less than 2 cm, there is an increasing debate as to whether ablative therapies (particularly RFA) could be a competitive option in these patients. Theoretically, in these solitary small tumors RFA could be as effective as surgery in terms of oncological results, and avoid all the possible complications related to the surgical procedure. However, available evidence is still limited as the few RCT available evaluating face-to-face both therapeutic options show controversial results (**Table 2**). In addition, there are several methodological issues that preclude reaching any robust conclusion from these trials (e.g., treatment allocation, patient selection criteria, trial implementation, short follow-up, etc.). In fact, none of them was specifically design to only include patients with HCC less than 2 cm. Replacement of resection by RFA as first line therapy in patients with early HCC cannot be recommended at this point.”

5. The authors should add to the manuscript a part with clinical consideration in order to guide the treatment selection for patients with small HCC.

Although all the therapeutic approaches available for the management of patients with small HCC have been reviewed in this MS, giving therapeutic recommendations is out of the scope of this review. Updated and high-quality guidelines specifically evaluating this issue are available (EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. *J Hepatol* **56**, 908-943 (2012) and Bruix, J. & Sherman, M. Management of hepatocellular carcinoma: an update. *Hepatology* **53**, 1020-1022.)