

Replies to Reviewers and Editor

Reviewer #1:

R: The manuscript review by Fancellu et al. constitutes an important critical state-of-the-art revision on the effects of the COVID19 pandemics in the treatment of patients with hepatocellular carcinoma (HCC). The review is extremely well-written, well-structured and summarizes the pivotal information on the field that are of great usefulness for the medical community.

A: We thank our reviewer for pointing out the significance of this review on the recommendations on the treatment of HCC in the COVID era.

A: I only have small concerns that might be addressed before the final publication:

- A table or a figure showing the % of patients with HCC undergoing surgery before and after the COVID pandemics would be useful to support the findings displayed in the main text.

R: Unfortunately, very few studies have reported the percentages of patients who underwent surgery for HCC before and after the pandemic. However, we resumed in a new table (Table 2), the main data from studies reporting on the surgical treatment of HCC in the pre-COVID and COVID era.

- In the section “The effects of SARS-CoV2 on liver diseases and HCC, the authors might want to correct the expression in which they mention that patients with cancer are at high risk for infection. This might not be true since the risk of infection might be the same, when compared with general population. The population of patients with cancer in fact present a higher risk to develop severe disease.

A: the reviewer raised a good point here. In the section “The effects of SARS-CoV2 on liver diseases and HCC” the first paragraph was modified as follows:

~~Strong evidence indicates that, in general, patients with cancer are at a higher risk of COVID-19 infection, progression to severe disease, admission to the intensive care unit, and death than patients without cancer[1,10,20-22].~~ Several studies underscored that patients with cancer affected from COVID-19 may be at higher risk of progression to severe disease, admission to intensive care unit, and death compared with patients without cancer[1,10,20-22].

- Et al. should be in italics.- In the section “Transarterial bridging therapies” please correct the typo in cytoreduction.

A: corrections have been made

- Nothing is discussed regarding asymptomatic COVID19 patients with liver cancer. Are these patients treated normally, they might follow the regular therapeutic regimens?

A: We agree with our reviewer. A new paragraph titled “Management of HCC patients with covid-19 infection” was added to pointing out the recommendations for the treatment of HCC in this subgroup.

Management of HCC in patients with SARS-CoV-2 infection

The management of HCC patients who develop a COVID-19 infection remains ill defined, and also depends on the underlying liver disease. In fact, cirrhotic patients with COVID-19 infection may have a poor outcome for either respiratory complications or liver failure^[38]. Management also varies between symptomatic and asymptomatic patients. In patients with symptomatic SARS-CoV-2 infection, the intensive treatment of the coronavirus infection overweighs that of any co-existing hepatic disease. There is a general agreement that patients with HCC and asymptomatic COVID-19 infection should postpone their surgical treatment of HCC until COVID-19 test becomes negative. Patients with suspected HCC who require tumour biopsy should postpone the procedure until at least 14 days after the onset of symptoms and when fever or respiratory symptoms have been absent for at least 3 days^[28]. Also endoscopic procedures, usually performed in the preoperative work up of patients with HCC, should be postponed because spreading of virus-containing droplets can occur. Indications for endoscopic procedures in patients with COVID-19 should be limited to emergencies such as gastrointestinal bleeding, bacterial cholangitis or other life-threatening conditions^[48].

Reviewer #2:

R: I have read with great interest the manuscript entitled 'Surgical treatment of hepatocellular carcinoma in the era of COVID-19 pandemic. A comprehensive review of current recommendations', submitted to the World Journal of Gastroenterology. In this manuscript, the authors present a comprehensive review of hepatocellular carcinoma (HCC) management during the COVID-19 pandemic. While the review article concludes that the treatment of HCC —especially surgical— should not be compromised due to the risk of disease progression, it advocates that treatment guidelines must be adapted to respond to the pandemic emergency. The manuscript is written well, and the topic is relevant on these pandemic days. Despite a review article, it summarises the most updated review on available recommendations on the surgical treatment of HCC.

A: We thank our reviewer for the comments and for highlighting the usefulness of the present review.

R: MINOR COMMENTS- The manuscript would benefit from proofreading as minor language corrections are pending (few incorrect prepositions and inappropriate articles)

A: Also to respond to the request of the Editor, a professional English language editing was made. The certificate of editing was submitted.

Editorial Office's comments

I found the language classification was grade D. Please visit the following website for the professional English language editing companies we recommend:

<https://www.wjgnet.com/bpg/gerinfo/240>; and (2) Authors should not cite their own unrelated

published articles. Please check and remove any references not relevant to this study.6 Re-Review: Required.7 Recommendation: Conditionally accepted.

A: The manuscript was sent for a professional English language editing. A certificate ...was downloaded along with the manuscript.

As for citations of authors' published articles, reference # 6 was eliminated. Please note that references # 5 (In-Hospital Mortality in COVID-19 Patients); # 8 (liver resection); # 44 (laparoscopic resection of HCC); # 56 (percutaneous microwave ablation of HCC); # 57 (percutaneous cryoablation of HBP malignancies); # 60 (De-escalating cancer treatments during COVID 19 pandemic) are relevant to this study.