

RESPONSE TO REVIEWER'S COMMENTS – Manuscript 67007 – Jul 2021

Dear Professor Lian-Sheng Ma,

Thank you for considering publication of our manuscript (67007) entitled “Hepatocellular Carcinoma Surveillance and Quantile Regression for Determinants of Underutilisation in At-Risk Australian Patients” in the World Journal of Gastrointestinal Oncology. We are grateful for the time of the editors and reviewers to our initial manuscript. Our point-by-point response is outlined below.

Reviewer 1

Comment: This is a retrospective study aiming to assess the adherence to HCC surveillance in a high-risk cohort in Australian tertiary centre where also liver transplantation is performed. This is a well-presented and well-conducted study. The authors have confirmed that, even in a good health care system, adherence to HCC surveillance is still not satisfactory and they have identified some factors which are associated with it. The limitations of the study are well underlined in the discussion.

Response: Thank you for your comment.

Comment: It would be of interest to add in the methodology section a brief comment on how the pathway of HCC surveillance is done in your centre. For instance, if a patient with cirrhosis is diagnosed in another clinic/department, is then referred to yourselves? In addition, after deemed one patient as high-risk for HCC (cirrhosis, HCV etc) how are the next screenings booked?

Response: We have described the pathway for HCC surveillance in the ‘Methods’ section, subsection 2.1 ‘Study Design’ on page 7, lines 6-9. As mentioned here, referrals from other departments or from external providers (e.g. primary care physicians) were received and patients assessed in specialty clinics. Patients meeting criteria for HCC screening according to AASLD guidelines, had regular review in clinic and USS organised as part of routine clinical care.

Comment: What is the decision-making process to refer a patient to a nurse-led clinic or specialist hepatologist? This seems to be important as, interestingly, nurse-led clinics have had high percentages of surveillance. I believe these highlights would help the reader's to better understand the whole process behind the results.

Response: We have now described the decision-making process in the ‘Methods’ section, subsection 2.1 ‘Study Design’ on page 7, lines 9-14.

Comment: How many of these patients were in the transplant waiting list during the study period? Adherence to surveillance in this cohort should be close to 100%. I couldn't find this variable in the manuscript. The authors only mentioned that 16.3% of patients were FU in pre-transplant clinics. This is a reasonable amount and if numbers permit, a subgroup analysis of these patients would be of interest.

Response: A total of 126/775 (16.3%) of patients in our cohort were followed-up in pre-transplant liver clinics, with their median PTUDS of 97.4% as stated in the ‘Results’ section. Of these 126 patients, 36 were active on the transplant waitlist (28.6%). While a subgroup analysis would be of interest, the current numbers do not permit meaningful analysis.

Comment: NESB can be misinterpreted in my opinion, as it might seem that these patient did not speak english at all. I believe this is not the case, as patients would probably speak english as second language and indeed in the text the authors mentioned several times "primary language spoken", so I would probably be more specific and possibly change "NESB" with "non native english speaking background".

Response: We have modified the wording to the term 'CALD', for those of culturally and linguistically diverse background, in the following sections to avoid misinterpretation:

- Abbreviations (page 2, line 19)
- Abstract (page 3, line 22-24)
- Results (page 12, line 5-6)
- Discussion (page 12, line 15; page 14, line 9; page 15, line 24)
- Table 2 (row 5, column 3)
- Table 3 (row 6, column 1)

Comment: Table 1: I believe the "MELD score 9" should be under the column of Mean (SD)

Response: In Table 1, the MELD score of 9 was a median value, given the asymmetric distributional spread of data values. However, we acknowledge that further clarity is required, and have thus created a new column of Table 1 to better display this.

Reviewer 2

Comment: This a nice study that reflects daily practice in HCC surveillance in Australia. The number of patients is remarkable. This paper showed a fragile subgroup of patients in which the surveillance shown to be weaker, thus stressing a problem. At regards it could be nice to report in the study if there are any solutions to suggest.

Response: Factors contributing to poorer surveillance adherence with HCC screening have been considered throughout the 'Discussion' section. While potential solutions to these limiting factors are valuable, extensive evaluation was outside the scope of this manuscript. However, widening the care providers directing HCC surveillance (e.g. through nurse-led clinics), the use of tailored resources for non-native English-speakers, and targeted provider education to improve screening in non-cirrhotics were discussed (page 13, lines 18-20; page 14, lines 5-15; page 13, lines 25-27).

Reviewer 3

Comment: This article is well written, highly original.

Response: Thank you for your comment.