

Dear Editors

Thank you so much for your elegant comments and a chance to improve our manuscript (No 82280 entitled 'Acoustic radiation force impulse predicts long-term outcomes in a large-scale cohort: high liver cancer but low comorbidity in the HBV group').

Point to point response to comments are list below:

Reviewer #1:

1, The author analysed the patients mainly enrolled from 2011 to 2018. However, whether the statistics of patients enrolled in recent years (i.e. 2020-2022) existed? I think it would be more solid. 2, Regarding the cancer registration data link and mortality data link, the authors linked these database up to 2020. Why not link these database with more recent data?

*Thank you for these comments. Both cancer registration and mortality databases are handled by our Big Data Department. We asked our Big Data department immediately after we received these comments. They replied that the mortality data of 2022 will be available after July 2023. This means that we can get additional one year's data only. Since the request to update our outcome will require a new IRB application. We start the application process, but it will take several months to get permission. Therefore, it is difficult for us to add data into this analysis. We will report our data in a future study.*

Reviewer #2: The study assesses a current, timely topic in HCC. We recommend some changes: - We believe this article is suitable for publication in the journal although major revisions are needed. The main strengths of this paper are that it addresses an interesting and very timely question and provides a clear answer, with some limitations. Certainly, the study is limited to an Asian population, and authors should further express this point. -

*We are very appreciative for the support of our concept. We agree that the high comorbidity was observed in East Asian only. We point out this limitation in the discussion.*

The background of the changing scenario of medical treatment in HCC should be better discussed, and some recent papers regarding this topic should be included (PMID: 32684988; PMID: 36368251; PMID: 34431725 ; PMID: 34976841 ; ). Major changes are necessary.

*We made a brief discussion in the limitation section. We did not evaluate the therapeutic response of HCC in this study. There is a significant improvement of HCC immunotherapy*

*recently. New predictive biomarker study will be needed in the future study. Two new references concerning these points are added.*

Reviewer #3: minor revise

*Thank you for the suggestion. We made changes according to the first reviewer.*

Best regards

Dar-In Tai

CGMH