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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 76322

Title: Hepatocellular carcinoma, decompensation, and mortality based on hepatitis C treatment: A prospective cohort study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00032020
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Professor
Reviewer's Country/Territory: Japan
Author's Country/Territory: South Korea

Manuscript submission date: 2022-03-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-13 23:55

Reviewer performed review: 2022-03-14 03:25

Review time: 3 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Manuscript NO: 76322 Title: Hepatocellular Carcinoma, Decompensation, and Mortality Based on Hepatitis C Treatment: A Prospective Cohort Study Manuscript Type: Observational Study Results of the present study were reasonable, and confirmed the previous studies. A few new findings were added in the present long followed-up observation. First, guideline has recommended only DAA therapy since 2015. So, there were several differences in supporting liver therapies, imaging modalities for HCC between IBT and DAA groups. The time of patient enrollment into to study should be added Table 1. Also, authors had better add limitations in details. Page 10; Follow-up evaluations At baseline of patients treated with IBT or DAA was not clear. The initiation of anti-viral therapy or the end of the therapy or others? Authors should clearly mention the start of observation in each group; untreated, IBT, and DAA. How about outcome of non-SVR patients? Were there any differences between untreated, IBT, and DAA? Comparisons of outcome between IBT and DAA were interesting. Figure 1 showed that 147 of 186 untreated patients died during observational period. This was high mortality. Cause of death should be shown in results; add data describing at least the hepatic or extrahepatic. Finally, the HCV elimination campaign is going by WHO. Why were 619 patients observed without anti-HCV therapies for 3.4-8.2 years? Some comments had better be added in Discussion. Minor; Page 8; METHODS, Study subjects Patients who met any of the following criteria were excluded: None of the patients had a history of HCC. These sentences were misread. Authors had better revise them.

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Reviewer's code: 04970307
Position: Peer Reviewer
Academic degree: MMed

Professional title: Associate Chief Physician, Surgeon, Surgical Oncologist

Reviewer's Country/Territory: China

Author's Country/Territory: South Korea

Manuscript submission date: 2022-03-12

Reviewer chosen by: AI Technique

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Review time: 3 Days and 6 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors explored the associations between the long-term outcomes for patients with chronic HCV infection and treatment with IBT or DAA, and outcome-determining factors after SVR. The design and methods used in this study are basically reasonable. Only several minor points needs to be revised. 1. In the entire cohort, 619 (30.1%) patients were left untreated, but the authors did not explain why they did not receive treatment, for ethical principle, they should be explained. 2. If the patients did not receive treatment because of contraindications, these contraindications must be taken into consideration, as they also lead to poor prognosis. 3. For accuracy, throughout the manuscript, “chronic HCV” should be “chronic HCV infection”. 4. In the first sentence of the second paragraph in Introduction, “HCC” may be “HCV”. 5. In the section “Follow-up evaluations”, “unless there were no contraindications” should be “unless there were contraindications”. 6. One-way analysis of variance (ANOVA) was also used for categorical variables, is that reasonable?

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Title: Hepatocellular carcinoma, decompensation, and mortality based on hepatitis C treatment: A prospective cohort study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04737423
Position: Peer Reviewer
Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Poland

Author's Country/Territory: South Korea

Manuscript submission date: 2022-03-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-14 19:20

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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The Authors of the paper "Hepatocellular carcinoma, decompensation, and mortality based on hepatitis C treatment: a prospective cohort study" performed a prospective analysis of the long-term outcomes for patients with chronic hepatitis C infection untreated and treated with antiviral therapy, IFN- or DAA- based. The manuscript is well-written and provides valuable data from clinical practice. It should be emphasized that the observed population consists of patients with different degrees of severity of liver disease at baseline, which increases its value. However, below I present some questions and critical comments to the paper. There is information in the "Methods" about the exclusion of 62 patients with positive HBV serology from the analysis. What tests are they about? HBsAg(+) only? Or anti-HBc(+) also? Since 62/2485 gives only 2,5% and the analysis concerns the Asian population with high endemicity of HBV infection (according to reference cited below the rate of HBsAg(+) among the population in South Korea was 3%), I assume that the Authors mean HBsAg positivity only (doi: 10.3904/kjim.2019.007.). Therefore, I have a question about the percentage of patients with positive anti-HBc antibodies. Was it assessed? How many anti-HBc positive patients were diagnosed with liver cirrhosis? Did they receive nucleos(t)ide analogues as prophylaxis of HBV reactivation? Were they monitored for the HBV reactivation during treatment and follow-up period? It is known that the risk of HBV reactivation following antiviral therapy in HBsAg(-)/anti-HBc(+) patients, exists and cannot be omitted especially in cirrhotics. It is a very important issue due to the impact of HBV reactivation on the risk of HCC, decompensation, death, and liver transplantation in HCV-infected patients with liver cirrhosis, especially but not only, in DAA treated patients. This issue

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should be included and discussed in the manuscript (doi: 10.1007/s12072-019-09988-7.). If this parameter has not been analyzed, it should be listed among limitations in "Discussion". The second question is about fatty liver disease. Have patients been assessed for this condition and its impact on the long-term outcomes? And the last comment concerns the other studies evaluating long-term outcomes in HCV-infected patients. I suggest discussing paper reporting the most prolonged follow-up in a DAA-cured real-world population observed for 5 years after treatment (doi: 10.3390/cancers13153694.) and manuscript on the long-term outcomes in a population of two clinical trials TOPAZ-I and TOPAZ-II after treatment with O/P/r/D±RBV (doi: 10.1111/jvh.13261.).