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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 72516

Title: The assessment of fibroblast growth factor 19 as a non-invasive serum marker for hepatocellular carcinoma

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05393032
Position: Peer Reviewer
Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Egypt

Manuscript submission date: 2021-10-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-19 04:13

Reviewer performed review: 2021-10-20 14:28

Review time: 1 Day and 10 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish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
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] 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

The authors investigated the diagnostic utility of FGF-19 in HCC and demonstrated that the HCC group showed a higher level of FGF-19 than the healthy control and cirrhotic groups. Therefore, they concluded that FGF-19 could be a novel biomarker of HCC. The subject of this study is interesting, but there are some problems. Comments to the authors are described as follows. 1. Sample size is small. There are some similar studies which have larger samples. (N=300. Maeda T, et al. BMC Cancer 2019;19:1088). Therefor, I cannot accept your article to this journal. 2. HCC group includes a lot of C-P class B and C (83.4%), while cirrhotic group includes only 40%. As you know, the stronger cirrhosis is, the more frequently HCC occurs. So I concern that the higher level of FGF-19 in your study reflects just the degree of cirrhosis. Indeed, Table 4 shows that the FGF-19 levels are not different between the low tumor volume group and the high tumor volume group (<2cm. vs 2-3cm. vs >5cm, single. vs 2-3. vs multiple, and PVT negative. vs PVT postitive). It confuses me very much, and I guess FGF-19 is less useful for the monitoring HCC. 3. The percentage of advanced HCC seems to be very high in your study (Tumor size > 5cm: 33.3%, Multiple tumors: 36.7%, PVT positive: 30%). I think early detection is the key factor for improving the prognosis of HCC. However, your study cohort probably has a small number of early staged HCC. You should evaluate more cases of early stage. 4. The definition of cirrhosis should be described in more detail in the Material & Methods section. Your comment about cirrhosis is too concise. 5. You should insert the underlying liver diseases (HBV/HCV/nonBnonC) and the alcoholic consumption into Table 1, and compare them between the groups. 6. I believe that the box plot is better than the bar plot to express the distributions of FGF-19 level in each

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group in Figure 1. 7. I want to know the FGF-19 levels of the HCC group after treatment. If possible, you mention them in the manuscript.

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Title: The assessment of fibroblast growth factor 19 as a non-invasive serum marker for hepatocellular carcinoma

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00070760
Position: Peer Reviewer
Academic degree: MD

Professional title: Full Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Egypt

Manuscript submission date: 2021-10-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-24 09:00

Reviewer performed review: 2021-10-30 15:26

Review time: 6 Days and 6 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] 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
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Tumour markers for HCC with high sensitivity and specificity are necessary. This manuscript demonstrated that FGF-19 can be a possible novel non-invasive marker for HCC. It may enhance the prognosis of HCC patients due to its usefulness in several aspects of HCC detection and management. Further studies are needed to evaluate the clinical applications of the current results. There are still some limitations fo this study. 1. This manuscript illustrated the function and concentration of FGF-19 in HCC, but there has no demonstration about the expression pattern of FGF-19 in other malignant cancers such as cholangiocarcinoma. It is important to further explain the application value of FGF-19 in HCC. 2. This manuscript has listed a series of study of FGF-19 in HCC, but the authors have no elucidate the difference and innovation of this study compared with other similar observations. 3. AFP may remain in the normal range not only in the early stages, but also in the advanced stages of HCC. What's the expression pattern of FGF-19 in different stage of HCC? It would be better to carry out a stratified research.