OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

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- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "Evaluation of Liver Fibrosis and Portal Hypertension in Chronic Hepatitis B Patients by Acoustic Radiation Force Impulse Elastography"

Author(s): Yu-Li Zhu, Ding Hong, Tian-Tian Fu, Shi-Yao Chen, Jian-Jun Luo, Chen Xu, Yuan Zhuang, Wen-Ping Wang

Review Timeline:

Submit Date: 19 Jul 2018
Revised Date: 9 Aug 2019
Accepted Date: 11 Dec 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 18 Sep 2018

Dear AE,

1- The authors mentioned: “patients with liver neoplasm who were referred for surgery were included.” Did all of these patients have chronic liver disease due to viral hepatitis? Please describe the clinical condition of patients and their reason for chronic liver disease in detail.

2- The authors mentioned: “Liver function was confirmed to be normal or almost normal” the authors should define a normal or near-normal liver function in the paper.

3- Please write the paper based on the latest version of the STARD guideline.

4- What is the meaning of “oral informed consent”? The patients should sign an informed consent. Please correct.

5- The authors should explain how did two radiologists assess the patients and mix their evaluations? By consensus? Or each one assessed independently part of patients and the data were combined together? Please explain this point in the paper.

6- If two radiologists assessed the patients and performed ARFI, we need to know what were their interobserver and intraobserver reliability for ARFI assessment.

7- Please add a brief of the HVPG method in the paper.

8-there are two pathologists in the study. similar to questions 5, we need to know how did they assess and combine the liver assessment results together and their reliabilities in pathologic assessments.

9- Please define advanced cirrhosis in the paper.

10- It is better the authors mention the cut-off points that yielded a sensitivity of 100% and specificity of 100% in diagnosis cirrhosis [S0-3 vs. S4] [may be two cuts off points]. The other diagnostic indices of table 3 should be mentioned in these cut off points. [It is important that performing such analysis for determining portal hypertension in advanced cirrhosis patients would be useful but according to the ROC curves in figure 3, I am not sure that such analysis would be useful. It is recommended to the authors mention such an analysis in the paper if the results are useful and applied].

11- Please compare the mean of LSM, ARFI, SSM, and spleen index between different liver fibrosis stages and mention P-value and compare different subgroups by post hoc or other appropriate statistical methods. performing such analysis in different inflammatory liver grades would be useful.

12- It is better to mention 95% CI for diagnostic indices [sen, spec, PPV, and NPV and accuracy] mentioned in table 3.

13- Determining advanced cirrhosis patients could be an interesting point in this study. this could be done by LSM and ARFI. Could the authors perform such ROC analyses? Please add in the paper. Please note that we can perform such analysis among all patients and among the S4 subgroup only. I am not sure which one is better [or both of them??] It seems the clinical application of this analysis in the S4 subgroup is evident: when a patient is grouped in S4, he/she will progress into the severe fibrosis and cirrhosis; in this case, we need a follow-up measurement for monitoring the patient and his/her progression to severe cirrhosis. ARFI and LSM could play such a role. Thus, I recommend the author at least evaluate the feasibility of such ROC analysis [ROC of ARFI and LSM for differentiating severe cirrhosis patients among S4 patients] and add the data to the paper.

14- Please compare the mean of ARFI, LSM, and SSM between severe cirrhosis and other patients of the S4 subgroup.

15- The authors mentioned: “From February 2012 to September 2015, patients with liver neoplasm who were referred for surgery were included. Patients with advanced cirrhosis without tumors who would undergo HVPG measurement in our hospital at the same time were also recruited.” The first question is that what is the liver neoplasm? Is it HCC due to CHB? Please explain. The second question is that if the patients have positive for HBV and their neoplasm are due to complications of HBV ant its chronic hepatic disease, why some of the patients are S0 and S1? These are the first stages of fibrosis and the probability of HCC due to HBV chronic liver disease is low in such cases? Please explain.

16- The authors have recruited only patients with liver neoplasm. These are could be different from other chronic liver disease patients regarding their value of RAFI and LSM. So the results of this study could be non-generalizable to all chronic liver disease cases. Please discuss this point in the paper and mention it as a potential limitation of the study. [especially, the results could be totally different for infiltrative chronic liver diseases such as hemochromatosis. Please discuss this point in the paper].

17 -As the authors have added intentionally the extreme cases of severe cirrhosis in the study, this could accentuate the differences between subgroups and increase the AUC of the ROC curve and diagnostic indices falsely. Please discuss this point in the paper.

Thanks.

REFEREE: Reviewer | **Revision** (0) 12 Oct 2018

Dear AE,
Thanks the author for submitting the manuscript in our journal. The manuscript could be accepted for publication in our journal.
But is too long. Please omit some unnecessary dates.
Thanks.

REFEREE: Reviewer | **Revision** (0) 16 Dec 2018

Dear AE,
I have read the article about Evaluation of liver fibrosis and portal hypertension in chronic hepatitis B patients by acoustic radiation force impulse elastography. The article has a clear title, good methodology, proper English writing,, good interpretation of results, and discussion. Although there is no strict need for liver biopsy in every patient this method was interesting and seems to be accurate for the diagnosis of liver fibrosis. The results were comprehensive, The English writing of discussion needs some revision.
Thanks

REFEREE: Associate Editor | **Revision** (0) 25 Dec 2018

Dear EIC,
In my point of view the article needs a minor revision because of some drawbacks as below:
1- The author should clarify the etiology of underlying chronic liver disease in patients with liver neoplasm who the candidate for surgery. What was the percentage of CLD due to viral hepatitis?
2- The authors should define the criteria of normal or near-normal liver function in detail.
3- The article should be written based on the latest version of the STARD guideline.
4- Oral informed consent is meaningless? The patients should sign an informed consent. It should be corrected.
5- The method of inter-observer agreement between two radiologists and mixing them should be explained.
With Respect

REFEREE: EIC | **Revision** (0) 25 Dec 2018

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs major revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Editors and Reviewers:

Thanks for your careful reviewing. We've earnestly read your comments and have been inspired with enthusiasm for your positive comments on our revised manuscript entitled " Evaluation of liver fibrosis and portal hypertension in chronic hepatitis B patients by acoustic radiation force impulse elastography" (Manuscript ID: 82396). However, the article was not satisfactory enough for you. We agreed with all of the comments you had raised and we had tried our best to make correction which we hope would meet with approval. Sometimes we failed to find an appropriate solution because it was just a preliminary study, we would do further research on it. The main corrections in the paper and the responds to the editors and reviewer's comments are as following:

Responds to the reviewers' comments:

Reviewer 1:

1-the authors mentioned: "patients with liver neoplasm who were referred for surgery were included." Did all of these patients have chronic liver disease due to viral hepatitis? Please describe the clinical condition of patients and their reason of chronic liver disease in detail.

Reply:

Thank you for your careful reviewing. In our study, all of the patients had chronic liver disease due to viral hepatitis B, which was verified with serologic testing. Our patients were 196 consecutive CHB patients who underwent partial hepatectomy and 64 advanced cirrhosis patients who underwent HVPG measurement. Liver function was confirmed to be normal or almost normal (within the normal range or increased no more than twice the normal value). We have added this and marked in red in our revised manuscript.

2-the authors mentioned: "Liver function was confirmed to be normal or almost normal" the authors should define normal or near normal liver function in the paper.

Reply:

Thank you for your review. “Liver function was confirmed to be normal or almost normal” means the index of liver function was within the normal range or increased no more than twice the normal value.We have added this and marked in red in our revised manuscript.

3-please write the paper based on the latest version of STARD guideline.

Reply:

Thanks for your comments.We have rewrote the paper based on the lasted version of STARD guideline. And here we did not list the changes but marked in red in our revised manuscript. We hope that the correction will meet with approval. Special thanks to you for your comments.

3-what is the meaning of “oral informed consent”? The patients should sign inform consent. Please correct.

Reply:

We thank the reviewer very much for the careful reading of our manuscript. We are sorry for our typographical errors and have corrected the errors. The patients have signed informed consent.

4-the authors should explain how did two radiologists assess the patients and mix their evaluations? By consensus? Or each one assessed independently part of patients and the data were combined together? Please explain about this point in paper.

Reply:

Thanks for your comments. Two radiologists in our study assessed independently part of the patients and the data were combined together. We have added this and marked in red in our revised manuscript.

5-if two radiologists assessed the patients and performed ARFI, we need to know what were their interobserver and intraobserver reliability for ARFI assessment.

Reply:

Thanks for your comments. In our study, two radiologists assessed independently part of the patients and the data were combined together. In our previous study, we have compared the interobserver and intraobserver reliability of ARFI assessment with intraclass correlation coefficient (ICC) and Bland-Altman method. We foud the ICC of ARFI measurements was relatively high (ICC=0.87) and the differences between the two experienced observers were no statistical significance. So in our study, two radiologists assessed independently part of the patients and the data were combined together.

6-please add a brief of HVPG method in the paper.

Reply:

Thank you for your review. We have added a brief introduction of HVPG method and marked in red in our revised manuscript.

7-there are two pathologists in the study. similar to questions 5, we need to know how did they assess and combine the liver assessment results together and their reliabilities in pathologic assessments.

Reply:

Thank you for your review. All specimens in our study were analyzed according to the Scheuer scoring system by two pathologists by consensus, each of them with 20 and 10 years of experience, respectively. They were blind to serological ,ultrasound and ARFI data. They were all full of experience in diagnosing and staging fibrosis.

8-please define advanced cirrhosis in the paper.

Reply:

Thanks for your comments. The diagnosis of advanced cirrhosis was established on progressive chronic liver disease due to hepatitis B with laboratory and sonographic evidence of portal hypertension or the presence of portal hypertension complications such as ascites and variceal bleeding. The sonographic signs of portal hypertension were evaluated according to EFSUMB recommendations: dilatation of the portal vein ≥13 mm, reduction of portal vein

velocity < 13 cm/s, dilatation of the splenic vein and superior mesenteric vein ≥11 mm, splenomegaly > 12 cm, increased resistive index of the hepatic artery > 0.78, and presence of portosystemic shunts. We have added this and marked in red in our revised manuscript.

9-it is better the authors mention the cut off points that yielded sensitivity of 100% and specificity of 100% in diagnosis cirrhosis [S0-3 vs. S4] [may be two cut off points]. The other diagnostic indices of table 3 should be mentioned in these cut off points. [It is important that performing such analysis for determining portal hypertension in advanced cirrhosis patients would be useful but according to the ROC curves in figure 3, I am not sure that such analysis would be useful. It is recommended to the authors mention such analysis in paper if the results are useful and applied].

Reply:

Thank you for your careful reviewing. We agreed with your comments and have mentioned the cut off points that yielded sensitivity of 100% and specificity of 100% in diagnosis cirrhosis and HVPG ≥12 mm Hg. We thought these cut off points may be help to rule in and rule out cirrhosis or HVPG ≥12 mm Hg. However, its clinical application may be limited. Our study was just a preliminary study, we will do more research on this aspect to make it more suitable for clinical application.

10-please compare mean of LSM, ARFI, SSM and spleen index between different liver fibrosis stages and mention P-value and compare different subgroups by post hoc or other appropriate statistical methods. performing such analysis in different inflammatory liver grades would be useful.

Reply:

Thank you for your careful reviewing. We greatly appreciate the insightful comments from you. In our study, the SSM and spleen index were performed only in 64 patients who underwent HVPG measurement with a diagnosis of advanced cirrhosis, so we could not perform such analysis in different inflammatory liver grades. We will do more research on this in the future.

11-it is better to mention 95% CI for diagnostic indices [sen, spec, PPV and NPV and accuracy] mentioned in table 3.

Reply:

Thank you for your review. We have added 95% CI for diagnostic indices mentioned in table 3.

12-determining advanced cirrhosis patients could be an interesting point in this study. this could be done by LSM and ARFI. Could the authors perform such ROC analyses? Please add in the paper. Please note that we can perform such analysis among all patients and among S4 subgroup only. I am not sure which one is better [or both of them??] It seems the clinical application of this analysis in the S4 subgroup is evident: when a patient are grouped in S4, he/she will progress into the severe fibrosis and cirrhosis; in this case, we need a follow up measurement for monitoring the patient and his/her progression to severe cirrhosis. ARFI and LSM could play such role. Thus, I recommend the author at least evaluate feasibility of such ROC analysis [ROC of ARFI and LSM for differentiating severe cirrhosis patients among S4 patients] and add the data to paper.

Reply:

We greatly appreciate the insightful comments from the reviewer. Advanced cirrhosis patients was a clinical diagnosis, we agree with you that when a patient are grouped in S4, he/she will progress into the severe fibrosis and cirrhosis; in this case, we need a follow up measurement for monitoring the patient and his/her progression to severe cirrhosis and the ROC analysis [ROC of ARFI and LSM for differentiating severe cirrhosis patients among S4 patients] will be useful for clinical. However, no all of the S4 subgroup underwent HVPG measurement, In fact, only a few of them (n=64) has performed HVPG, so we could not estimate the severity of cirrhosis in all the S4 subgroup. The staging of cirrhosis in our study were analyzed on patients who underwent HVPG measurement with a diagnosis of advanced cirrhosis in the gastroenterology department in our hospital (n=64). We aimed to get some simple conclusion about the feasibility of estimating the severity of cirrhosis based on portal hypertension in

CHB patients. In our future research with more patients, we will do research on this aspect. Your comments are extremely valuable for our future research work.

14-please compare the mean of ARFI, LSM and SSM between severe cirrhosis and other patients of S4 subgroup.

Reply:

Thank you for your careful reviewing. LSM and SSM were all ARFI measurements. The SSM measurement were only conducted on those patients who would undergo HVPG (the severe cirrhosis patients). We compared the LSM between advanced cirrhosis and other patients of S4 subgroup. The mean LSM was 2.08 m/s in all S4 subgroup. The mean LSM was 1.99 m/s in advanced cirrhosis while the mean LSM was 2.12 m/s in other patients of S4 subgroup (those with liver neoplasm who were referred for surgery). There is not statistical significance between them.

15-the authors mentioned: “From February 2012 to September 2015, patients with liver neoplasm who were referred for surgery were included. Patients with advanced cirrhosis without tumors who would undergo HVPG measurement in our hospital in the same time were also recruited.” The first question is that what is the liver neoplasm? Is it HCC due to CHB? Please explain. The second question is that if the patients have positive for HBV and their neoplasm are due to complications of HBV ant its chronic hepatic disease, why some of the patients are S0 and S1? These are first stages of fibrosis and probability of HCC due to HBV chronic liver disease is low in such cases? Please explain.

Reply:

Thank you for your careful reviewing. Most of the liver neoplasm in our study group were HCC, However, there were some liver hemangioma, hepatic focal nodular hyperplasia(FNH), Inflammatory pseudotumor and some other. We included those patients who were referred for surgery and had chronic liver disease due to viral hepatitis B, verified with serologic testing. So there are some patients S0 and S1.

16-the authors have recruited only the patients with liver neoplasm. These are could be different from other chronic liver diseases patients regarding their value of RAFI and LSM. So the results of this study could be non-generalizable to all chronic liver disease cases. Please discuss this point in the paper and mention as a potential limitation of the study. [especially, the results could be totally different for infiltrative chronic liver diseases such as hemochromatosis. Please discuss this point in the paper].

Reply:

Thanks for your comments. As suggested, we had explained to the authors and added this as a limitation of our research in the revised manuscript.

17-as the authors have added intentionally the extreme cases of severe cirrhosis in the study, this could accentuate the differences between subgroups and increase the AUC of ROC curve and diagnostic indices falsely. Please discuss this point in the paper.

Reply:

Thanks for your comments. The comment you had raised went straight to the heart of the weakness of the article. We had explained to the authors and added this as a limitation of our research in the revised manuscript.

Thanks for your relevant comments. We agreed with all comments but we couldn't find solutions for all problems. It was just a preliminary study and we just aimed to get some simple conclusions. And in the future study we will do more researches on it. Your comments are extremely valuable for our future research work.

Reviewer 2:

Dear author

thank you for submitting your manuscript in our journal . The manuscript could be accepted for publication in our journal .

But is too long . Please omit some unnecessary date.

Reply:

Thank you for your careful reviewing. We've earnestly read your comments and have been inspired with enthusiasm for your positive comments on our manuscript. As suggested, we have omitted some unnecessary data.

Reviewer 3:

I have read your article about Evaluation of liver fibrosis and portal hypertension in chronic hepatitis B patients by acoustic radiation force impulse elastography.The article has clear title,good methodology,proper English writing,,good interpretation of results and discussion. Although there is no strict need for liver biopsy in every patient but this method was interesting and seems to be accurate for diagnosis of liver fibrosis.the results were comprehensive,The English writing of discussion need some revise.

Reply:

Thank you for your careful reviewing. We've earnestly read your comments and have been inspired with enthusiasm for your positive comments on our manuscript. We have carefully checked and the manuscript has been edited by English native speaker. Wish the expression of discussion will be better than before.

Associate Editor's Comments:

Associate Editor 1:

Dear Editor-in – chief

In my point of view the article needs a minor revision because of some drawbacks as below:

1- The author should clarify the etiology of underlying chronic liver disease in patients with liver neoplasm who candidate for surgery. What was the percentage of CLD due to viral hepatitis?

Reply:

Thank you for your careful reviewing. In our study, all of the patients had chronic liver disease due to viral hepatitis B, which was verified with serologic testing. We have added this and marked in red in our revised manuscript.

2-The authors should define criteria of normal or near normal liver function in detail.

Reply:

Thank you for your review. “Liver function was confirmed to be normal or almost normal” means the index of liver function was within the normal range or increased no more than twice the normal value.We have added this and marked in red in our revised manuscript.

3-The article should be written based on the latest version of STARD guideline.

Reply:

Thanks for your comments.We have rewrote the paper based on the lasted version of STARD guideline. And here we did not list the changes but marked in red in our revised manuscript. We hope that the correction will meet with approval. Special thanks to you for your comments.

4- Oral informed consent is meaningless? The patients should sign inform consent. It should be corrected.

Reply:

Thanks for your comments. We are sorry for our typographical errors and have corrected the errors. The patients have signed informed consent.

5- The method of inter observer agreement between two radiologist and mixing them should be explained.

Reply:

Thanks for your comments. Two radiologists in our study assessed independently part of the patients and the data were combined together. In our previous study, we have compared the interobserver and intraobserver reliability of ARFI assessment. the ICC of ARFI measurements was relatively high and the differences between the two experienced observers were no statistical significance. So in our study, two radiologists assessed independently part of the patients and the data were combined together.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) 3 May 2019

Dear AE,
Thanks to the author for submitting the manuscript in our journal. Requested changes were made and the manuscript could be accepted for publication.
Thanks.

REFEREE: Reviewer | **Revision** (1) 17 May 2019

Dear AE,
The author has corrected the manuscript properly in a well-written format.
Thanks.

REFEREE: Reviewer | **Revision** (1) 1 Jun 2019

Dear AE,
The authors have responded to many points. They have mentioned some points in response to a question that I think it is better to add the data in the paper. Here is what they mentioned that is better to add in the paper:
Most of the liver neoplasm in our study group were HCC, However, there were some liver hemangioma, hepatic focal nodular hyperplasia (FNH), Inflammatory pseudotumor and some other. We included those patients who were referred for surgery and had chronic liver disease due to viral hepatitis B, verified with serologic testing. So there are some patients S0 and S1" in addition, it is better they mention how many HCC, FNH hemangioma and other diagnoses were enrolled in the study. This point seems to be included in the method section and patients enrollment. I recommend they mention these data and any other similar data that have not been mentioned in the current version of the manuscript [but could be informative and useful] to the paper.
Thanks.

REFEREE: Associate Editor | **Revision** (1) 20 Jul 2019

Dear EIC,
The authors were done the corrections regarding reviewers' comments so that only some minor changes should be performed as below:
- Please clarify how many HCC, FNH hemangioma, and other diagnoses were enrolled in

the study. It seems to be included in the method section and patients enrollment. I recommend adding them and any other similar data that have not been mentioned in the current version of the manuscript as they are very informative for the paper.
Thanks.

REFEREE: EIC | **Revision (1)**

21 Jul 2019

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript " Evaluation of liver fibrosis and portal hypertension in chronic hepatitis B patients by acoustic radiation force impulse elastography" (Manuscript ID: 82396). We've earnestly read your comments and have been inspired with enthusiasm for your positive comments on our revised manuscript.We agreed with all of the comments you had raised and we had tried our best to make correction which we hope would meet with approval. Those comments are all valuable and very helpful for improving our paper. The main corrections in the paper and the responds to the editors and reviewer's comments are as following:

Reviewers' Comments:

Reviewer 1:

Thank you for submitting your manuscript in our journal . Requested changes was made and the manuscript could be accepted for publication.

Reply:

Thank you for your careful reviewing. We've earnestly read your comments and have been inspired with enthusiasm for your positive comments on our revised manuscript.

Reviewer 2:

the authors have responded many points. they have mentioned some points in response to a question that i think it is better to add the data in paper. Here is what they mentioned that is better to add in paper:

"Most of the liver neoplasm in our study group were HCC, However, there were some liver hemangioma, hepatic focal nodular hyperplasia(FNH), Inflammatory pseudotumor and some other. We included those patients who were referred for surgery and had chronic liver disease due to viral hepatitis B, verified with serologic testing. So there are some patients S0 and S1" in addition, it is better they mention how many HCC, FNH hemangoioma and other diagnoses were enrolled in study. this point seems to be included in method section and patients enrollment. I recommend they mention these data and any other similar data that have not been mentioned in

the current version of manuscript [but could be informative and useful] to the paper.

Reply:

We thank the reviewer very much for the careful reading of our manuscript. We agreed with your comments and have mentioned the data of the liver neoplasm of our patients and other similar data we thought could be informative and useful in our our revised manuscript. We hope the correction would meet with approval.

Reviewer 3:

The author has corrected the manuscript properly.

Reply:

Thank you for your reviewing. We've earnestly read your comments and have been inspired with enthusiasm for your positive comments on our revised manuscript.

Associate Editor's Comments:

Associate Editor 1:

The authors were done the corrections regarding reviewers comments, so that only some minor changes should be performed as below:

• Please clarify how many HCC, FNH hemangoioma and other diagnoses were enrolled in study. It seems to be included in method section and patients enrollment. I recommend to add them and any other similar data that have not been mentioned in the current version of manuscript as they are very informative for the paper.

Reply:

Thank you for your careful reviewing. We have clarified the data of the liver neoplasm of patients in our study and added other similar data we thought could be informative and useful which were marked in red in our revised manuscript.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Mehranoosh Dolatshahi: Associate Editor | **Revision** (2) 11 Dec 2019

Dear EIC
The reviewer(s) have recommended publication.
Kind regards,
Associate Editor

Kavous Firouznia: EIC | **Revision** (2) 11 Dec 2019

Dear Authors,
According to the reviewers' comments, your article is acceptable for publication in IJR.
Regards.