

A point-by-point response letter

Mar 18, 2020

To editor and reviewers

Manuscript NO.: 54521

Title of manuscript: A systematic review and meta-analysis of computed tomography in evaluating esophageal varices in cirrhotic patients comparing with liver stiffness measurement and magnetic resonance

Dear editor and reviewers,

On behalf of all co-authors, I would like to thank the reviewers and the editor for your well-considered and critical comments on our manuscript. The addition and modification of the manuscript is highlighted in yellow. With regard to the reviewers' comments and suggestions, we wish to reply as follows:

Reviewer #1:

This is an interesting systematic review aimed to determine the overall accuracy and sensitivity of 3 non-invasive methods to diagnose esophageal varices and the risk of bleeding in patients with liver cirrhosis. The study is appropriate and timely. To determine with a non-invasive method the risk for bleeding of esophageal varices might have important clinical applications in daily practice. The study gives an overall view of the problem, and for sure does give clinical details which could be useful in making decisions in everyday practice. I have some points to address, which may help to give the paper a more significant clinical application.

Minor Points

Comments 1. The title is quite complex and difficult to understand.

Response: Thank you very much for the consideration and suggestion. I agree with you. The title was changed as follows "A systematic review and meta-analysis of computed tomography in evaluating esophageal varices in cirrhotic patients

comparing with liver stiffness measurement and magnetic resonance”.

Comments 2. The Authors should underline the fact that there was no direct comparison between the 3 non-invasive methods. The comparison was merely determined indirectly by the difference in accuracy in comparison to endoscopy for each method. This indirect comparison inevitably brings to a significant statistical bias.

Response: Thanks for the helpful suggestion. I agree that direct comparison between the 3 non-invasive methods will make the results more reliable. The main limitation of this manuscript was no direct comparison between CT, MRI and Fibroscan. We've appended the following sentence to the discussion of the manuscript: We regarded endoscopy currently as the “gold standard” for diagnosing EV and HREV, nevertheless, there was no head-to-head controlled study of the above-mentioned non-invasive diagnostic methods in the same series of patients. This indirect comparison bring to a statistical bias, thus might attribute to study heterogeneity.

In this systematic review and meta-analysis paper, included the article “Lipp MJ, et al. Detection of esophageal varices using CT and MRI. Dig Dis Sci 2011; 56: 2696-2700” found that CT is a superior imaging modality to MRI by directly evaluating the ability of CT and MRI to detect EV.

Major Points

Comments 1. Very few papers were included into the study in comparison to the many published papers on this subject. The reasons why some papers were included and others excluded should be more clearly specified.

Response: Thanks for your suggestions. We have specified the reasons why some papers were excluded or included in Figure 1, the flow chart of the search and selection of articles.

Comments 2. The paper should give a better definition of the criteria used to assess the risk of bleeding at least for CT scan examination This could be a valuable practical clinical point. It is possible that different criteria were used in the reported studies about CT scan.

Response: Thanks for the valuable and helpful suggestion. We have added the

definition of high bleeding risk esophageal varices in the materials and methods. The criteria to diagnose high bleeding risk esophageal varices for CT imaging in the included articles and the cut-off value is listed in the table 2.

Comments 3. Bleeding of esophageal varices is quite a "generalized definition". At least for the papers describing the accuracy of CT scan, it may be convenient to specify the interval between CT scan and bleeding and somehow to define the entity of the bleeding and the clinical outcome. There is a significant difference between a minor bleeding self-resolving and an uncontrolled bleeding leading to death Future Perspectives. The study is very important and interesting with significant practical applications. I suggest to include in a specific session papers which compared the 3 non-invasive methods (they are few but they exist). At the same time, it could be interesting to analyze (or at least to mention in the paper) the possibility to identify in a multidimensional statistical method the simultaneous measurement of Liver Stiffness (by CT scan) and characteristics of esophageal varices by CT scan. There is the possibility that combining the results of these two measurements by CT scan, we could have a better idea of the overall risk for bleeding. CT scan of the esophageal varices may give a morphological evidence of a local risk, liver stiffness could give a general idea of the general conditions of the liver function, including an indirect evaluation of the probability of a valid coagulation system. All these observations of mine could transform the paper from a mere virtual observation into a practical guideline useful in everyday practice.

Response: Thanks for your kindly comments and suggestions. I agree with you. The results of this manuscript is useful for clinicians in practice. However, more clinical issues need further research

Reviewer #2

Comments 1. I suggest to add that endoscopic can demonstrate associated gastroesophageal lesions, that increase the risk of varices to bleed. MR or CT angiographies cab be useful to a complete study of the entire portal vein system, to discover ectopic varices, and also to get information about the intra-hepatic venous

system.

Response: Thank you for suggestions. We have added the following comments and corresponding references to the discussion section in the text. “There is no doubt that endoscopy is irreplaceable. It can diagnose esophageal and gastric varices as well as other lesions that cause upper gastrointestinal bleeding, such as peptic ulcer. Combined with the ultrasound probe, it was applied to probe the blood vessels around the wall of the esophagus. MR and CT imaging can clearly show the portal vein system and collateral circulation and they can be used for the diagnosis of other complications including hepatocellular carcinoma”.

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