Author's response to reviews

Title: Diagnostic performance of alpha-fetoprotein, Lens culinaris agglutinin-reactive alpha-fetoprotein, des-gamma carboxyprothrombin, and glypican-3 for the detection of hepatocellular carcinoma: a systematic review and meta-analysis

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David Moher, Paul G Shekelle, and Lesley A Stewart
Editors-in-Chief
Systematic Reviews

Dear Editors-in-Chief:

We sincerely thank to the editors and reviewers who spent precious time reviewing our manuscript and gave constructive comments. With this mail, we are re-submitting our manuscript entitled “Diagnostic performance of alpha-fetoprotein, Lens culinaris agglutinin-reactive alpha-fetoprotein, des-gamma carboxyprothrombin, and glypican-3 for the detection of hepatocellular carcinoma: a systematic review and meta-analysis” for publication in Systematic Reviews as a Protocol (Manuscript ID: 1774457763937076).

The major revisions of the original manuscript are accounted in the following:

Major compulsory revisions
Reviewer’s comment 1:

We agreed with the reviewer’s comment and revised the Rationale section.

Indeed, we think these biomarkers may serve as the add-on role in clinical practice. In this study, we may be able to evaluate the diagnostic performance of these biomarkers. As for there roles in clinical practice, it is another issue and
could not be answered in this review. The decision for resection, liver transplantation, or radiofrequency ablation depends on liver function, associated diseases, and cancer staging of the patients. Surgical resection is indicated for patients with single tumor and without portal hypertension. Liver transplantation is indicated for patients with single tumor and portal hypertension, or patients with 3 modules < 3 cm in diameter, whereas radiofrequency ablation is justified for patients with portal hypertension and associated diseases.

Reviewer’s comment 2:

We agreed with the reviewer’s comment on this issue. We had added one paragraph (Multiple index tests) in the Background section for clarification. Also, we corrected the Objectives to assess this hypothesis.

Reviewer’s comment 3:

We agreed with the reviewer’s comment and deleted that sentence.

Discretionary Revisions

Reviewer’s comment 4:

We agreed with the reviewer’s comment and corrected it.

Reviewer’s comment 5:

Only AFP will be potential as part of the reference standard in the earlier version of the guidelines (tumor > 2cm, AFP # 400ng/ml, CT/MRI/Angiography for EASL guidelines 2001, and tumor > 2cm, AFP > 200ng/ml, dynamic CT/MRI for AASLD guidelines 2005). DCP and glypican should not be part of the reference standard.

Reviewer’s comment 6:

We agreed with the reviewer’s comment and deleted the sentences.

In fact, there is little chance that one study incorporates AFP as part of the reference standard for all recruited patients. The Sensitivity analyses section have described our planning for AFP as part of the reference standard.

Reviewer’s comment 7:

We agreed with the reviewer’s comment and corrected it for consistency.

We hope the editor and reviewer now find the manuscript of great interest and significance to the community, and suitable for publication in the Systematic Reviews.

Thank you in advance for your editing efforts.
Best regards,

Sincerely,

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