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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 81402

Title: Better performance of serum protein induced by vitamin K absence or antagonist-II for detecting hepatocellular carcinoma in patients with chronic liver disease with normal serum total bilirubin

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02936529
Position: Editorial Board
Academic degree: FRCS (Hon), MD, PhD
Professional title: Professor, Surgical Oncologist
Reviewer's Country/Territory: Brazil
Author's Country/Territory: China

Manuscript submission date: 2022-11-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-17 11:02

Reviewer performed review: 2022-11-26 12:32

Review time: 9 Days and 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

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

SPECIFIC COMMENTS TO AUTHORS

This manuscript is highly important for guiding health care profissionals in HCC management. The early diagnoses has major impact on these patients survival, and PIVKA-2 can improve the detection of HCC in CLD scenario. The methodology is impecable and the discussion is concise and updated. The charts and tables are well displayed. Congratulations for the authors.

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Peer-review model: Single blind

Reviewer's code: 03805961
Position: Peer Reviewer
Academic degree: MD
Professional title: Assistant Professor, Instructor, Lecturer
Reviewer's Country/Territory: Thailand
Author's Country/Territory: China

Manuscript submission date: 2022-11-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-19 07:25

Reviewer performed review: 2022-11-28 15:29

Review time: 9 Days and 8 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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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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Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Qian et al. studied the role of PIVKA-II in patients with CLD compared with HCC in a large cohort. The authors found that PIVKA-II may have a role in HCC surveillance in terms of the highest performance of detecting early-stage HCC, particularly in patients with bilirubin ≤ 1×ULN. However, some issues need to be clarified. Major: 1. It is essential to know the reason for the exclusion of varices from the study. 2. Currently, the BCLC system has been widely used for guiding prognosis and treatment in patients with HCC. Could the authors analyze by stratifying the BCLC stages? Minor: 1. Could the authors provide the IRB number in the ethical part of the manuscript? 2. There were varied in the cutoff level of PIVKA-II. Please cite the reference of the cutoff in the manuscript. 3. Table 1: Could the authors describe the proportion of cirrhosis in percentage?

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Peer-review model: Single blind

Reviewer's code: 06394964
Position: Peer Reviewer
Academic degree: MD
Professional title: Associate Chief Physician, Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2022-11-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-19 08:59

Reviewer performed review: 2022-11-29 13:03

Review time: 10 Days and 4 Hours

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
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection

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

SPECIFIC COMMENTS TO AUTHORS

More than half of patients present with advanced stages when diagnosed as HCC，AFP combined with ultrasound is the most commonly used screening method. However, we have been looking for novel and reliable diagnostic biomarkers. The paper presents the relationship between PIVKA-II levels with diagnosis of HCC，At the same time, this article describes the impaction of different etiology, liver function on diagnostic effectiveness Serum PIVKA-II in a subgroup of TBIL ≤ 1×ULN had the highest AUCs and the best performance in detecting early-stage HCC .It is a topic interested to researchers in the related areas. The author should explain questions as follows: 1、AFP is a biomarker widely accepted in the world, while PIVKA-II is not commonly used in the western countries, although it is increasing used in China, Japan and Korea. Whether the specificity and sensitivity of PIVKA-II are superior to AFP in this population？ 2、Several methods are applied to PIVKA-II detection, including chemiluminescence and ELISA detection. Please provide detection methods and reagents. If multiple methods are used, how to keep the consistency in the quantitative results. Whether the detection results may differ with other studies？