Peer Review File

Article information:

Reviewer A

The article describes a new possibility for defining high-risk patients with coronary artery disease. As the authors conclude, this tool may have a beneficial effect on reducing the incidence of MACE. Despite some limitations, it should find a place in imaging diagnostics in cardiology. However, the CEUS value should be compared with existing predictors, for example, carotid plaque. I have three minor comments:

1) By the latest guidelines, I recommend changing the nomenclature: coronary artery disease (CAD) instead of coronary heart disease (CHD) and chronic coronary syndrome (CCS) instead of stable CHD.
Reply 1: We have changed the relevant expressions in the entire text.

2) If possible, the characteristics of the groups should be supplemented with the results of laboratory tests and medications taken.
Reply 2: We have added some laboratory test and medications taken data in the revised version. See the revised table 1.

3) The first paragraph of the discussion repeated the information contained in the introduction and the results; I recommend deleting this fragment.
Reply 3: We have deleted it.

Reviewer B

Nicely written article, however, I have some small remarks:
1) hypertension => arterial or pulmonary?
Reply 1: Arterial hypertension. We have revised it.

2) contrast=> what was the trade name of contrast media, dose, place of infusion, amount, how it was calculated? Were there any intolerance, allergiic reactions?
Reply 2: We have added in the methods. See page 4, line 93-102.

3) How do you define coronary lesions?
Reply 3: It was coronary artery stenosis. Coronary angiography was used to determine if there is coronary artery stenosis.
Changes in text: None

4) Do you use CEUS in clinical practice in your centre?
Reply 4: The CEUS was commonly used in our centre. No changes was made in the text.
Changes in text: None

5) What is the value of CEUS on contrary to angio-CT, sct oraz ECG treadmill test?

Reply 5: We have added it in the discussion. See page 6, line 171-173.

6) Would you introduce this test in your centre as a follow-up method over ECG treadmill test and standard TTE?

Reply 6: CEUS is a supplement to other examinations, but cannot replace them. No changes was made in the text.

Changes in text: None

Reviewer C

I found the manuscript by Li et al. regarding the effect of contrast-enhanced ultrasound on prognosis in patients with stable coronary artery disease quite intriguing. Its topic is innovative and highly engaging. Additionally, the authors should be commended for their extensive follow-up of many cases over a significant duration.

Regrettably, the most significant limitation of this paper is the lack of refinement.

Major comments

Comment 1

A comprehensive restructuring of the paper's presentation is essential, referring to previous manuscripts. The Results section appears confusing due to excessive paragraphs, and I wonder if the limitations section thoroughly explained its limitations in the current description.

The Introduction also falls short of adequately explaining the significance of this study to readers. Since readers are likely familiar with CHD and MACE, I suggest emphasizing CEUS-related information more instead of describing the basics of CHD.

Reply 1: We have revised it. For example. The page 6, line 162-175.

Comment 2

The inspection method is difficult to understand. The authors should recognize that not all readers are experts in contrast-enhanced echocardiography. Please consider incorporating more figures and providing explanations that make the methodology and CEUS-parameters understandable to non-specialists. In particular, detailed explanations about the "Platform stage" and "microbubble reperfusion" are necessary for result interpretation.

Reply 2: We have revised the expression. See page 4, line 93-102.

Minor Comment:

Comment 1

"From January 2016 to December 2017, 473 patients with stable CHD were continuously retrospectively collected and followed up for five years at Yueyang People's Hospital." (Line 29 and 78)

This should be rephrased to avoid confusion, as it might be misinterpreted as 2,017,473 patients.

Reply 1: We have revised it as "From January 2016 to December 2017, a total of 473 patients"

Comment 2
Line 134, "were" is underlined. Do the authors want to emphasize the word?
Reply 2: It was a mistake. We have deleted the underline.

Comment 3
I recommend including page numbers in your manuscript.
Reply 3: We have added.