Author’s response to reviews

Title: Low Expression of PRMT5 in Peripheral Blood May Serve as a Potential Independent Risk Factor in Assessments of the Risk of Stable CAD and AMI

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A

Reply to reviewer 1 Jacek Bil, MD, PhD, FESC (Reviewer 1): The papers assessed whether the expression levels of the PRMT5 gene in peripheral blood could be used as a biomarker for predicting the risk of Acute Myocardial Infarction (AMI).

1. As is visible the manuscript was edited by the professional company. But I would suggest some further changes such as: not ‘obviously lower’ but ‘significantly lower’; not ‘uniform definition of MI’, but ‘universal definition of MI’.

page 2, line 25-26: I have corrected these errors according to your suggestions.
I have corrected these errors according to your suggestions.

2. AMI patients were only patients with STEMI or also with NSTEMI?

AMI patients were not only patients with STEMI but also patients with NSTEMI.

3. Gensini score should be briefly described in the Methods section.

I have added the score descriptions into the manuscript (the coronary artery score equals the sum of all of the segment scores [each segment score equals the segment for multiple weighting based on a severity score]). The severity scores that were assigned to the specific percentage luminal diameter reductions of the coronary artery segments are 32 for 100%, 16 for 99%, 8 for 90%, 4 for 75%, 2 for 50%, and 1 for 25%.

3. In Table 2 PCI means the history of PCI, not at the event of AMI?

I apologize for the confusion. In Table 2, PCI indicates the number of people who were treated with PCI in the event of AMI. Additionally, we recalibrated our data.

4. I think authors should add the control group (healthy subjects) to add the value of the paper and show the real significance of the PRMT5 measurements.

We agree with you. It would be better if we could add healthy subjects for a comparison. We also have the results of the PRMT5 gene expression levels of 11 healthy people. Levels of PRMT5 gene expression in healthy people were compared with those levels in patients with
AMI; there was an upward trend in these levels (higher average and higher median). However, it is possible that the sample size is small, thus indicating that there is no difference between the groups (p=0.135). However, the topic of this study was based on the results of our previous gene chip study. The gene chip results showed that there was a difference in the PRMT5 gene expression levels between the stable CAD patients and the AMI patients. There was no difference in the PRMT5 gene expression levels between the stable CAD patients and the healthy subjects. Therefore, our advice is to not add healthy subjects for a comparison.

B

Reply to reviewer 2

Alexandre Stewart (Reviewer 2): The manuscript by Tan et al. titled "Low Expression of PRMT5 in Peripheral Blood May Serve as a Potential Independent Risk Factor in Assessments of the Risk of Stable CAD and AMI" found that PRMT5 mRNA and protein levels in peripheral blood are markedly reduced in individual who have had an acute myocardial infarction as compared to individuals who have stable and clinically significant coronary artery disease. The authors go on to suggest that low levels of PRMT5 predict myocardial infarction by the ability of this marker to adjust the receiver operating characteristic (ROC) curve. The problem with their approach is that they use the same sample of patients to look at "prediction" of MI as they used to originally identify the association. This is a "self-fulfilling" prophecy. The authors need to test their marker in an independent sample of cases and "controls" to demonstrate its ability to predict events.

Unless an additional naive cohort is tested, the predictive section of the results and ROC curves should deleted.

A key question is whether this "biomarker" is better able to predict myocardial infarction than the current standard. The other question is what is the clinical relevance of this marker to therapy?

The PDF manuscript I reviewed was formatted as a "track changes" papers, making reading tedious and difficult. Please do not submit manuscripts in this format in future.
Unless an additional naive cohort is tested, the predictive section of the results and ROC curves should be deleted.

A key question is whether this "biomarker" is better able to predict myocardial infarction than the current standard.

Thank you for your question. From our results, we have observed that the PRMT5 gene may serve as a marker for predicting the occurrence of acute myocardial infarction. Risk factors that can predict the occurrence of acute myocardial infarction generally include increased TC, increased TG, increased LDL-C, decreased HDL-C, hypertension, diabetes/GIGT, age, sex, BMI, genetic factors, and so on. Our study showed that patients who have lower PRMT5 gene expression levels in the peripheral blood are 5.472 times more likely to suffer from AMI than other stable CAD patients. In this study, other factors were not found to be independent risk factors for the progression of stable CAD into AMI.

The other question is what is the clinical relevance of this marker to therapy?

This is a great question. Further research is needed to confirm whether there was a change in PRMT5 gene expression levels after treatment. Whether the differential expression of the PRMT5 gene can serve as a therapeutic marker for acute myocardial infarction has not been confirmed in this study, and the use of this gene as a marker requires new experiments for verification. However, in this study, PRMT5 gene expression may serve as a marker for predicting the occurrence of AMI in stable CAD patients. This may be useful in the diagnosis of disease, and it may even provide a molecular target for early interventions of AMI.