Author’s response to reviews

Title: Use of magnetic resonance imaging combined with gene analysis for the diagnosis of fetal congenital heart disease

Authors:
Lishun Wang (tmcqjs9@163.com)
Hongyan Nie (tmcqjs@163.com)
Qichen Wang (uofgiw@163.com)
Guoliang Zhang (dwsclh4@163.com)
Gang Li (knwjwn1@163.com)
Liwei Bai (cjreng4@163.com)
Tianshu Hua (umalux3@163.com)
Shuzhang Wei (dfbbms@163.com)

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Author’s response to reviews:

BMIM-D-18-00130

Title: Use of magnetic resonance imaging combined with gene analysis for the diagnosis of fetal congenital heart disease

Authors: Lishun Wang; Hongyan Nie; Qichen Wang; Guoliang Zhang; Gang Li; Liwei Bai; Tianshu Hua; Shuzhang Wei

Journal: BMC Medical Imaging

Dear Editor,

Our manuscript "Use of magnetic resonance imaging combined with gene analysis for the diagnosis of fetal congenital heart disease" (BMIM-D-18-00130) has been revised according to the reviewers’ comments. We are sorry for our late reply. We have considered every suggestion
thoroughly and made corrections carefully. Please check our “point-by-point response to the comments” listed below.

Technical Comments:

--Please include the email addresses for all authors on the title page. The corresponding author should still be indicated. Please also ensure these email addresses match the email addresses provided in the editorial manager system.
Response: We have added the email addresses for all authors on the title page.

--The abstract must include the following separate sections:
Background: the context and purpose of the study
Methods: how the study was performed and statistical tests used
Results: the main findings
Conclusions: brief summary and potential implications
Response: We have divided the abstract into four parts: background, methods, results and conclusions.

--Please represent authors' names using their full initials, not their full name, in the Authors’ Contributions section. For example, the initials of John Smith would be ‘JS’. If there are any duplicated initials, please differentiate them to make it clear that the initials refer to separate authors, for example, by adding their middle name initial.
Response: We have changed the authors’ full name to their initials.

--Please list all abbreviations used in your manuscript under the heading "Abbreviations" after the conclusions section. If no abbreviations are used in the manuscript, please state "Not applicable" in this section.
Response: We have listed the abbreviations after the conclusions section and hear. Please check. Thanks.
Magnetic resonance imaging (MRI)
computed tomography (CT)
Array comparative genome hybridization (aCGH)
Fluorescence in situ hybridization (FISH)
bacterial artificial chromosome (BAC)

Editor Comments:

Please carefully address the comments and then get back the reviewers.

Response: Please check our response to reviewers’ comments below.

Reviewer reports:

Lin Li (Reviewer 1): Wang et al. presented a study with the combination of MRI and gene methods in the diagnosis of fetal congenital heart disease. This study aims to propose an improved diagnostic solution that has a higher diagnostic specificity and sensitivity, comparing to the MRI or gene method alone. I like this idea very much. The research of multi-modality prognosis approach is on the top flow of clinical-relevant study and have been shown to have significant improvement of the accuracy. The current study also provided a reasonable sample size (n=78) with a well-matched control subject (n=78), making this study with a reliable statistical power. However, I saw several critical issues in the presented manuscript, which need to be fixed before this manuscript to be published.

1. The first issue is the lack of information about the MRI. Neither the scanning parameters nor the data analysis has presented. The authors should provide very detailed information about the MRI scan hardware and software setup. The authors also should give detailed imaging processing steps, as well as the imaging screening process. I am also wondering which parameters were used to generate the diagnostic rate in Figure 1 and Table 2, for the MRI session?

Response: We added some information about MRI, image processing and diagnosis procedure (see 2.3 section). Diagnosis of congenial heart diseases was made by an experienced radiologist based on T2-hypotensities in the left ventricular free wall and left atrium. This yielded the data in Figure 1 and Table 2.
I assume Figure 1 is to demonstrate the suspected case of fetal congenital heart disease. However, a more detailed description in the figure legend and the context should be included. Please also present an example image with health control.

In both MRI and gene analysis, the measurement values (for MRI, such as the size and location of malformation areas; for the gene, such as the 17q12 signaling) should be presented quantitatively, with descriptive statistics.

Response: We have added suggested images from healthy control in Fig.1C. We have also added description in the figure legend. We appreciate the reviewer’s recommendation to include some measured values in MRI and gene expression. However, the present study focuses on diagnostic rates made by MRI and gene mutation. MRI diagnosis was made by a radiologist, who gave positive or negative diagnosis. We acknowledge that the size and location of malformation areas are valuable information for diagnosis of congenital heart disease, which however was not essential in the present study. Detection of gene mutation also gave “positive” or “negative” values. We would consider including the suggested analyses in our future studies.

2. The second issue is that it lacks the information of how to distinguish Pulmonary stenosis and Arterial stenosis (which has been shown in table 2). Both MRI and gene analysis did not provide enough information about this part.

Response: The present study didn’t involve differentiation between Pulmonary stenosis and Arterial stenosis. Table 2 is to present how many patients with Pulmonary stenosis and Arterial stenosis were accurately diagnosed with MRI, gene analysis, or the combination, based on prior knowledge.

3. In table 1, by reading the description, it seems like the HR is observed from the mother, which is abnormally high than usual. Please double check this data.

Response: We have corrected this mistake.

4. There is a typo in line 40, please correct.

Response: We have corrected this typo.
Fengmei Lu, Ph.D. (Reviewer 2): The aim of the study was to investigate the effectiveness of MRI in combination with gene analysis for the diagnosis of fetal congenital heart disease. The results demonstrated that the combination of MRI and gene analysis resulted in significantly improved diagnostic accuracy, sensitivity and specificity for fetal congenital heart disease compared with either method alone. I don’t have so many suggestions but just some small issues as following:

1. In the abstract part, the "(" on line 40 should be deleted.

Response: We made the correction accordingly.

2. In the Introduction part, the 21-three body syndrome on line 52 is not a professional description, the Down's Syndrome may be more appropriate

Response: We have corrected it to Down’s syndrome.

We look forward to hearing from you.

Sincerely yours,

Wang Lishun