Author’s response to reviews

Title: Changes in the levels of inflammatory markers after transthoracic device closure of ventricular septal defects in pediatric patients

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Dear Editor and reviewers:

Thank you for your decision letter on our MS(ID JCTS-D-2019-000001 entitled "Changes in the levels of inflammatory markers after transthoracic device closure of ventricular septal defects in pediatric patients"). We studied the reviewer's comments thoughtfully and found that all these comments are very constructive for revising the manuscript. We have revised the manuscript according to the comments and send it to you again.

To reviewer #1:

Thank you very much for your positive comments, we must say sorry for our poor English. We had revised our MS with the help of AJE.

To reviewer #2:

1. We added the details of the indications for VSD closure in the revision. The inclusion criteria were: not accompanied by other intracardiac malformation and or organ disease, a significant hemodynamic left to right shunt, and/or chamber enlargement and capacity overload, and/or mild to moderate pulmonary hypertension, no aortic regurgitation. The exclusion criteria were: age below 9 months, weight below 6 kg, pulmonary or other organ infection, severe pulmonary hypertension or Eisenmenger syndrome.
2.(a) The patients were divided into two groups according to the different VSD closure procedures. The 38 patients with isolated and restrictive VSD (the size of VSD was ranged from 4-6 mm) in group A underwent transthoracic device closure. The rest of 47 patients in group B underwent surgical repair under CPB. This part of patients included: nonrestrictive or misaligned VSD, failed to complete or refused device closure, and those were not suitable for device closure. In this group, 21 patients were selected to receive a right infra-axillary incision, and 26 patients were selected to receive a median incision, based on their individual situation. (b) We added the definition of infection in detail in the article which including: 1, body temperature higher than 38.5℃. 2, chest radiography indicated pulmonary infection. 3, pulmonary auscultation can detect obvious moist rales. 4, the expectorated sputum is clear purulent sputum. 5, bacteria appeared in sputum culture and blood culture. All the above data were recorded in detail in the medical records. The final diagnosis of infection was made by two experts independently, and a third researcher evaluated whether included of excluded this case. The purpose of this paper is to explore the changes of inflammatory factors related to the different treatments for VSD closure. The postoperative pulmonary infection may affect the change of inflammatory indicators, then affect the judgment of the result. So we need exclude those patients with infection. (c) None of the patients in group A needed blood transfusion, while 32 patients in group B needed blood transfusion. (plasma and/or erythrocyte)

3.(a) We added mean ± standard deviation in table 3. (the original table 3 and table 4 were merged into one) (b) All patients had data in each time point. (c) In this paper, pulmonary arterial pressure refers to the mean pulmonary arterial pressure (mPAP).

4.In the revision, we removed some superfluous content to make the discussion part more concise. (a) Although transthoracic approach does not need CPB, the inflammatory markers go up the same as surgical repair. The reasons may include the following aspects: the pericardium still needs to be opened, and the puncture of the right ventricle and the embedded occluder may directly lead to myocardial injury. In addition, the blood flow through the occluder may also cause inflammatory response. But it is still necessary to further study the relevant factors for the increase of inflammatory factors after device approach. (b) The device closure group is superior in clinical data. But it had no advantage in terms of postoperative changes in inflammatory factors.

To reviewer #3:

1.In our previous experience and reports, underwent transthoracic device approach in patients with less than 9 months may increase the probability of conduction block. So we used the indication in our center.

2.In this study, all patients were used a patch for VSD closure in surgical group. In some other patients with small VSD, direct closure also can be performed. But we have not counted this part of patients in this study.

3.There are many incision options in surgical repair for VSD. We performed the median incision and the infra-axillary incision. We made the comparison to show that the different incision may
have no effect on the outcome of the surgical result, excluding the impact of the incision on the study results.

4. Thanks to the reviewer’s correction. We retrieved and learned the definitions of systemic inflammatory response and systemic inflammatory response syndrome. In the revision, we used systemic inflammatory response instead of SIRS according the reviewer’s opinion.

5. We added the comparison between the levels of inflammatory factors in these two groups at any period after treatment in the revised table.

6. Only isolated perimembranous VSD was included in this study. We didn’t count in other types of VSDs.

7. These indicators are routinely used in our clinical practice, but the frequency of examination is not so much. In order to study the relation between the closure treatments and the systemic inflammatory response, we appropriately added observation points.

Thanks

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