Author’s response to reviews

Title: N-terminal pro-brain natriuretic peptide levels in patients with anomalous left coronary artery from pulmonary artery

Authors:

Yunfei Ling (Lingyunfei1988113@126.com)
Qiang Fan (m13541221953@126.com)
Yue Wang (wangyuehuaxi@outlook.com)
Yongjun Qian (qianyongjun@scu.edu.cn)

Version: 1 Date: 21 Dec 2019

Author’s response to reviews:

Dear editor reviewers,

Thanks very much for your pertinent comments and suggestions. And all people in our team think that these comments and suggestions would be of great value to our work. We have revised the manuscript according to the comments and suggestions of reviewers and editors, and responded, point by point, to the comments as listed below.

Replies to the REVIEW COMMENTS:

Reviewer reports:

Reviewer #1: Lin g et al revealed the age and LVEF negatively correlate with high levels of NT-pro-BNP in ALCAPA patients and no correlation with age and LVEF in patients with NT-pro-BNP &lt;300 pg/mL and a negative correlation with age and LVEF when NT-pro-BNP above 300 pg/mL in a small series of 23 ALCAPA patients. The research is interesting and worth publishing, however there are necessary revisions needed:

1. The authors revealed the negative correlation was shown between NT-pro-BNP and LVEF, Blood samples were obtained from each patient on admission, however when the echo was performed was not mentioned.
   Answer: The echo was performed on admission and LVEF, MR grade were gained at that time

2. All the patients included are associated with other heart diseases which may affect the level of NT-pro-BNP.
   Answer: All the patients included are associated with different grade of MR and who were with other heart diseases were excluded.
3. The Materials and methods was too simple and need to be re-written. 
Answer: We have added the content in the “Materials and methods”: Continuous variables were analyzed with a Wilcoxon rank-sum test, as assumptions of normality could not always be satisfied. Dichotomous outcomes were analyzed using Fisher’s exact test.

4. Physiological NT-proBNP levels are different (in healthy subjects) at different ages: is this a bias of your observation? 
Answer: In pediatric patients, we should take variability associated with both physiology and methodology into consideration in order to use NT-pro-BNP as a clinical biomarker effectively. In healthy populations, NT-pro-BNP is very high in the first 4 days of life, and then decrease quickly through the first week, followed by a slow progressive decline for up to the first month of life.

5. Why has a cutoff of 300 pg/mL been quoted? 
Answer: Previous studies have indicated that it is reasonable to use 300 pg/mL as cutoff value to “rule out” HF. When interpreting NT-pro-BNP values in ALCAPA patients, the NT-pro-BNP cutoff point (300 pg/mL) may provide quick information about the severity of myocardial ischemia and LV dysfunction.

6. English style requires significant improvement. 
Answer: We have got the help from a professional English editor to revise our manuscript, grammatical mistakes and incorrect words were corrected.

Reviewer #2: ALCAPA is a rare congenital heart disease which is associated with adult sudden death and early infant mortality. The most effective treatment is surgical coronary artery rebuilding and the result is perfect. However, few serum indexes were used to indicates the severity of ALCAPA. NT-pro-BNP has also been indicated as a strong independent prognostic factor in patients with various CHD. The authors tried to show the relationship between NT-pro-BNP and LVEF, Mitral regurgitation (grade). Finally, in patients with ALCAPA, NT-pro-BNP levels showed a negative correlation with age and LVEF when NT-pro-BNP above 300 pg/mL and no correlation with age and LVEF when NT-pro-BNP under 300 pg/ml. The article is interesting. However there are some concerns regarding the case report.

1. The paper need a native English speaker to revise the manuscript. 
Answer: We have got the help from a professional English editor to revise our manuscript, grammatical mistakes and incorrect words were corrected.

2. Heart failure is not the KEY WORD. 
Answer: We have excluded Heart failure from the KEY WORD.

3. Patient presenting early will be expected to have increased BNP and in late presentation the BNP could be normal. What is the clinical question or hypothesis is this study trying to answer?
Answer: Patients who developed extensive coronary collaterals could stay asymptomatic before diagnosed with ALCAPA by physical examination in adolescence or adulthood, with little subclinical myocardial ischemia and lower NT-pro-BNP levels. Those who were diagnosed with ALCAPA in infancy or childhood are mostly symptomatic and have higher NT-pro-BNP levels.

4. Details about the study design, duration need to be provided. Details about the statistical methods used have not been provided.
Answer: We have added the content in the “Materials and methods”: Continuous variables were analyzed with a Wilcoxon rank-sum test, as assumptions of normality could not always be satisfied. Dichotomous outcomes were analyzed using Fisher’s exact test.

5. Why you selected 300 as NT-pro-BNP cutoff value?
Answer: Previous studies have indicated that it is reasonable to use 300 pg/mL as cutoff value to “rule out” HF. When interpreting NT-pro-BNP values in ALCAPA patients, the NT-pro-BNP cutoff point (300 pg/mL) may provide quick information about the severity of myocardial ischemia and LV dysfunction.