Author's response to reviews

Title: Etiology of pulmonary venous aneurysm diagnosed by a combination of echocardiography and contrast-enhanced computed tomography: a case report

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Author's response to reviews: see over
Re: Manuscript # 1072807666126944

Dear Dr. Zamvar, Dr. Taggart and The Journal of Cardiothoracic Surgery Editorial Team:

Thank you very much for your review of our manuscript, “Etiology of pulmonary venous aneurysm diagnosed by a combination of echocardiography and contrast-enhanced computed tomography: a case report,” which we are resubmitting after making the suggested revisions.

We hope the manuscript is now suitable for publication in Journal of Cardiothoracic Surgery, and we look forward to hearing from you at your earliest convenience.

Yours sincerely,

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Response to editor’s comments:
1. Please include the Ethnicity of the patient in the Abstract and Case presentation sections.
   Thank you for your comment. We added “Chinese” in the Abstract and Case presentation section to state the Ethnicity of the patient.

2. Please include a list of abbreviations used in the manuscript and their meanings after the Conclusions section
   Thank you for your comment. We provided a list of abbreviations used in the manuscript and their meanings after Conclusion section: PVA, Pulmonary venous aneurysm; CT, computed tomography; LA, left atrium; MV, mitral valve; RIPV, right inferior pulmonary vein.
Other revisions are as follows:
On page 1 lines 7-15, we reorganized the sentences about the authors’ information to conform to the journal style as follows: 1Department of Ultrasound and 2Department of Cardiothoracic Surgery, The First Affiliated Hospital, College of Medicine, Zhejiang University, #79 Qingchun Road, Hangzhou, China
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On page 2 lines 20-23, we revised the sentence “We present a case with strong evidence that the pulmonary venous aneurysm was secondary to severe mitral valve regurgitation by a combination of echocardiography and contrast-enhanced computed tomography.” to “We present a case of pulmonary venous aneurysm diagnosed using a combination of echocardiography and contrast-enhanced computed tomography with strong evidence for an etiology of severe mitral valve regurgitation.”

On page 2 line 27, we revised “gave” to “provided”.

On page 3 line 36, “……and is commonly secondary to arteriovenous malformation” was revised to “with arteriovenous malformation being the most common cause”

On page 3 line 40, “We present a case with strong evidence that the PVA was secondary to severe mitral valve regurgitation.” was revised to “We present a case of PVA with strong evidence for an etiology of severe mitral valve regurgitation.”

On page 3 line 44, “previously’ was changed to “earlier”.

On page 3 line 45, “……infectious endocarditis with vegetation in the mitral valve, and mitral valve insufficiency.” was revised to “infectious endocarditis with mitral valve vegetations and insufficiency.”

On page 3 line 46, we added “Chest x-ray was normal at that time and three years prior to presentation.” to supplement the patient’s history.
On page 3 line 48, we revised “no severe lower extremity edema” to “mild lower extremity edema”.

On page 3 line 54, we added “To study the case more carefully” before “we performed repeat echocardiography” to explain why we took echocardiography for the second time.

On page 3 line 55, “showed a severe mitral valve regurgitation jet extending to a giant right inferior pulmonary vein, which was filled with a high-velocity, turbulent jet in systole” was revised to “revealed severe mitral regurgitation with a turbulent high-velocity jet extending to a giant right inferior pulmonary vein during systole.”

On page 4 line 57, “showed” was revised to “enabled”.

On page 4 lines 59-60, “Transesophageal echocardiography showed only mild residual mitral regurgitation after surgery.” was revised to “Transesophageal echocardiography showed mitral regurgitation remained.”

On page 4 lines 60-61, we added “The patient underwent contrast-enhanced CT and echocardiography 3 months postoperatively, which showed that the aneurysm had decreased in size”.

On page 4 lines 62-63, “DeBoer et al. surgically corrected a PVA by pulmonary lobectomy and its corresponding pulmonary vein system” was revised to “DeBoer et al. performed pulmonary lobectomy and excision of the corresponding pulmonary venous system for surgical correction of a PVA”.

On page 4 lines 64-66, “The pathological findings were nonspecific, including focal interruptions in the elastic lamina and areas complete absence of elastic lamina, and the etiology of the PVA was unclear.” was revised to “The pathological findings were nonspecific. These included focal interruptions in the elastic lamina and areas complete absence of elastic lamina, but the etiology of the PVA was unclear.”

On page 4 lines 73-75, “We report a case of PVA caused by severe mitral regurgitation with relative conclusive evidence using a combination of echocardiography and contrast-enhanced chest CT” was revised to “We report
a case of PVA diagnosed using a combination of echocardiography and contrast-enhanced chest CT, which provided strong evidence for an etiology of severe mitral regurgitation.”

On page 5 line 75, we added “In this case, we excluded the possibility of congenital PVA on the basis of previous x-ray examinations.”

On page 5 line 81, “not” was revised to “rather than”.

On page 5 line 82, we added “The patient’s 3-month follow-up results confirmed our hypothesis.”

On page 5 line 95, we cited a new reference “9: Br Heart J 1993,70:297-300.” here to support this point of review. The study revealed that complication rates of diagnostic catheterization are low but neither negligible nor irreducible, and that catheter- or guidewire-related thromboembolism may cause cerebrovascular accidents, transient ischemic attacks, or amaurosis fugax, or other complications such as arrhythmia, hemodynamic collapse.

On page 5 line 96, we deleted the words “less financial burden” because it may be right in China but we are not certain how much these examinations cost in other countries. We revised the sentence to “We found the combination of echocardiography and contrast CT to facilitate accurate and safe diagnosis of PVA.”

On page 5 line 99, we revised “Contrast CT scan and echocardiography enabled correct diagnosis of PVA” to “The combination of contrast-enhanced CT scan and echocardiography facilitated the diagnosis of PVA.”

On page 8 lines 142-145, we added a new reference NO.9 as we mentioned before.

We added the contrast enhanced CT image taken 3 months postoperatively in the Figure 1. It showed the right inferior PVA decreased in size. The figure legend was also revised as: Figure 1 Comparison of the right inferior PVA pre and postoperatively. (A) The PVA is 5.14 cm in diameter preoperatively. (B) Three months postoperatively, the PVA is decreased in size. PVA, pulmonary venous aneurysm.
Responses to Reviewer Comments

Reviewer: Dong Kyu Lee
- Major Compulsory Revisions

Page 4 line 87: 'Echocardiography was repeated to … ', you should describe why you repeated TTE.

Thank you very much for your comment. The PVR was observed on contrast-enhanced chest CT, and after studying the CT images, we felt echocardiography would be able to reveal its structure. However, the PVR was not seen on echocardiogram. To study the case more carefully, we repeated TTE. We added this information to the manuscript as follows:

To study the case more carefully, we performed repeat echocardiography, which revealed severe mitral regurgitation with a turbulent high-velocity jet extending to a giant right inferior pulmonary vein during systole.

Page 5 line 106: You did not describe how you excluded the possibility of congenital PVR.

Thank you for your comment. We should have described how we excluded the possibility of congenital PVR. Fifteen years earlier, when the patient was diagnosed with infectious endocarditis, a chest x-ray was normal and no mediastinal mass was seen. A chest x-ray performed 3 years prior to admission also did not reveal a mass. We therefore concluded that the PVA was not congenital. This conclusion was confirmed on the 3-month follow-up examination, when contrast-enhanced CT and echocardiography showed that the aneurysm was decreased in size.

We added the information in the manuscript as follows:

On page 3 line 46, Chest x-ray was normal at that time and three years prior to presentation.

On page 4 line 75, In this case, we excluded the possibility of congenital PVA on the basis of previous x-ray examinations.

On page 5 line 82, The patient’s 3-month follow-up results confirmed our hypothesis.

Page 5 line 109, 110: MR jet was reached to all 4 pulmonary veins? You also
mentioned ‘were not reached by the jet.’
We appreciate this comment regarding the confusing language in this section. The MR jet did not reach all four pulmonary veins; it reached only the right inferior pulmonary vein. We have revised the manuscript to reflect this. “The vein was filled with high-velocity turbulence downstream and was much larger than the right superior pulmonary vein, left inferior pulmonary vein, and left superior pulmonary vein. The latter three veins were not reached by the jet.”

Page 6 line 124,125: Need a reference.
We cited the following reference: De Bono D, The Joint Audit Committee of the British Cardiac Society and Royal College of Physicians of London: Complications of diagnostic cardiac catheterisation: results from 34,041 patients in the United Kingdom confidential enquiry into cardiac catheter complications. Br Heart J 1993, 70:297-300. The study revealed that complication rates of diagnostic catheterization are low but neither negligible nor irreducible, and that catheter- or guidewire-related thromboembolism may cause cerebrovascular accidents, transient ischemic attacks, or amaurosis fugax, or other complications such as arrhythmia, hemodynamic collapse.

Page 6 line 126,127: provide the evidence of ‘less financial burden’.
Thank you for this suggestion. Venography of four pulmonary veins costs more than 5,000 CNY in our province, whereas one contrast-enhanced chest CT costs about 1,000 CNY and one echocardiogram costs 120 CNY. Based on this, we concluded that there was less financial burden, but we are not certain how much these examinations cost in other countries. We have therefore deleted this text from the manuscript.

- Minor Essential Revisions
Page 4 line 69: Some words missed? Recommend ‘the most common cause of PVR is….’
Thank you very much. We have revised the manuscript in accordance with your suggestion. “Pulmonary venous aneurysm (PVA) is rare, often presenting as a mediastinal mass [1-3], with arteriovenous malformation being the most common cause.”
Page 4 line 71,72: Please rephrase to be grammatically correct

Thank you for your comment. We have made a revision that makes the sentence clearer. “Some studies have shown that acquired aneurysms are the result of an increase in left atrial pressure and mitral regurgitation.”

Page 4 line 83,84: You can delete the words “The patient’s” and ‘a perforation… in size’ could be changed to ‘an 1 cm sized perforation’

Thank you for this comment. We have changed the sentence to “Severe mitral valve regurgitation was caused by an approximately 1 cm sized perforation in the A3 segment of the anterior leaflet”

Page 4 line 88: you can delete ‘valve’, ‘the’ instead of ‘a giant right …’

Thank you very much. We have revised this in accordance with your suggestion.

Page 5 line 89: Completely separate the sentences instead of ‘,’

Thank you very much for this suggestion. We have completely separate the sentences.

Page 5 line 92: ‘mild mitral regurgitation remained’

We appreciate this comment and have revised the sentence to “Transesophageal echocardiography showed mild mitral regurgitation remained.”

Page 5 line 94, 95 and 99,100: Need reorganization of the sentence

Thank you for pointing this out. We have reorganized the sentences as you suggest:

“The pathological findings were nonspecific. These included focal interruptions in the elastic lamina and areas of complete absence of elastic lamina. But the etiology of the PVA was unclear.”

“In a report by Erkanli et al. [4], atriotomy revealed a left inferior PVA with an enlarged left atrium, with the aneurysm located opposite the mitral valve.”

Reviewer: Yanli Guo

Reviewer's report:

Discretionary Revisions

Transesophageal echocardiography showed only mild residual mitral
regurgitation after the patient underwent mitral valvuloplasty, but no surgical intervention for the aneurysm was performed. Did the patient have follow-up examination of echocardiography or contrast-enhanced CT after operation? And did the follow-up imaging show whether the morphology and size of pulmonary venous aneurysm changed or not?

Thank you very much for your comment. We checked the patient 3 months after the operation. Echocardiography and contrast-enhanced CT showed that the right inferior pulmonary vein had decreased in size, but there was persistent mild mitral regurgitation. We added this information to the manuscript, as follows: “The patient underwent contrast-enhanced CT and echocardiography 3 months postoperatively, which showed that the aneurysm had decreased in size (Figure 1).” We also added the postoperative CT image in the Figure 1.

Reviewer: Jinwook Hwang

Major Compulsory Revisions

Comment 1: MV regurgitation was well known etiology for PVA in the references, which authors cited. I think that your evidences were weak for the brand new evidence of relationship of MV regurgitation and PVA. Please suggest the stronger evidence. How about the postoperative chest CT scan, which shows reduced PVA size?

Thank you for mentioning this. We checked the patient 3 months after the operation. Echocardiography and contrast-enhanced CT showed that the right inferior pulmonary vein had decreased in size. Mild mitral regurgitation remained. We added this information in the manuscript, as follows: “The patient underwent contrast-enhanced CT and echocardiography 3 months postoperatively, which showed that the aneurysm had decreased in size (Figure 1).”

Comment 2: An asymptomatic pulmonary venous aneurysm might be misdiagnosed as posterior mediastinal mass. But, if mitral regurgitation could develop symptom and murmur, researchers were able to notice an abnormal dilatation of pulmonary venous structure by echocardiography and chest CT scan. So I think that the echocardiography and chest CT scan were basically currently practiced combination. I don’t think that 3D echocardiography is needed to diagnose PVA. Please tell us the needs for 3D echocardiography.

We agree that the combination of echocardiography and chest CT scan is currently performed. However, 3D echocardiography provided a stereoscopic view of the aneurysm, and we feel this provides another
option in the diagnosis of PVA.