Author’s response to reviews

Title: Case Presentation: Implantation of Cardiac Resynchronization Therapy Pacemaker via the Coronary Sinus in a Patient with Triple Valve Replacement

Authors:

cheng zheng (793601136@qq.com)
Weiqian Lin (373806983@qq.com)
Yuanzheng Lin (408811608@qq.com)
Hao Lian (184900642@qq.com)
Zhirui Liu (410034577@qq.com)
Jiahui Chen (jiahuits@qq.com)
jia-feng Lin (linjiafeng_wzmcfey@163.com)

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Author’s response to reviews:

Dear editor,

We really thanks the reviewers for the useful comments to improve the paper. We have done significant revisions according to the suggestions from the reviewers, all changes to the manuscript were indicated in the text by highlighting, meanwhile, we included a cover letter with a point-by-point response to the comments.

Response to reviewer1

- The quality of written English is not suitable for publication and should be improved.

Answer: Dear reviewer, we have invited a professor good at English writing to help us revise the language, after the language revision, the quality of written English has been largely improved. We hope it can satisfy you.

- Data about anticoagulation during the CRT-P implantation in this patient should be added.

Answer: Dear reviewer, thanks for your suggestion. We have added the data about anticoagulation during CRT-P implantation. We detailed described in article as follow: After full consideration of the patient’s basic situations, the CRT-P via two pacing leads in cardiac venous system to provide dual-site ventricular pacing was primarily planned. The instant blood test prior
to operation showed a PT-INR of 2.42s. The intravenous unfractionated heparin was used during the procedure to keep an activated clotting time (ACT) range between 250 and 300s. Electric surgical knives were applied to stop bleeding of the incision during the whole procedure.

- Authors report "It has been confirmed that a wide QRS complex in patients with heart failure reflecting left-sided intraventricular conduction delay is associated with worse LV function, poorer prognosis and a higher all-cause mortality rate compared with patients with a narrow QRS complex". Their 42 year-old female patients had a 65% ejection fraction and a moderate prosthetic tricuspid valve stenosis. Signs of right heart failure could be secondary to tricuspid valve stenosis more than to ventricular dyssynchrony. Moreover, to clarify if a dual ventricular lead implantation was necessary, it would be interesting to see the cardiac mechanics (tissue Doppler imaging, myocardial strain imaging, etc.) during single lead quadripolar pacing (as reported in several case reports) and using the vector from the proximal tip of the quadripolar lead to the coil of bipolar lead in MCV (vector P4-MCV, as described in the paper). Please provide this data and images/videos. Moreover, data on functional capacity (6 minute walking test, cardiopulmonary exercise test) and laboratory tests (NT-proBNP) should also be provided to confirm the correct indication to dual lead instead of single lead implantation.

Answer: Dear reviewer, thanks for your suggestion. In the revised article, we added the data on 6 minute walking test and laboratory tests (NT-proBNP) of the patients. Meanwhile, we supplied a table in revised manuscript described the left ventricular systolic function measured with Simpson method by transthoracic echocardiography during single the single-site pacing and dual-site pacing. We found the ventricular dual-site pacing achieved by two pacing leads in coronary sinus brought an obvious acute hemodynamic improvement over single-site pacing (LVEF: ventricular dual-site pacing 71.5±0.96% vs ventricular single-site pacing 62.9±2.38%), and the best left ventricular systolic function was obtained by ventricular dual-site pacing of P4 combined with MCV. These data further supported the correct indication to dual lead instead of single lead implantation. In the revised manuscript, we declared that by our method of ventricular dual-site pacing with two pacing leads in coronary sinus, increased left ventricular electrical and mechanical synchronization was achieved, long-term follow up also showed a good clinical outcome.

- Atrial rhythm is not reported. Is the device in VVI pacing mode (no atrial lead is visible in the chest radiography)? What about atrio-ventricular dyssynchrony as possible cause of heart failure? Please comment on that.

Answer: Dear reviewer, in the last manuscript, we forgot to provide the significant information respect to the heart rhythm of the patient. In the revised manuscript, we supplied the this information. The patient has a history of rheumatic heart valvular disease with a permanent atrial fibrillation rhythm. For the patient was in the permanent atrial fibrillation rhythm, the atrial lead placement was abandoned due to the inability to achieve an atrioventricular synchrony.

- Pacing thresholds of 1.75 V at 1.0 msec are not excellent and may cause early battery consumption. What about battery length in this patient? Please comment on that.
Answer: Dear reviewer, we found the pacing thresholds of both pacing lead decreased obviously 2 months later. We thought the initial high pacing threshold maybe related to the swelling of cardiomyocyte caused by the procedure of lead implantation. In last follow-up one month ago, the pacemaker showed a left battery length of six and half years.

Response to Reviewer 2

I just would like to call attention to a point that needs further clarification: in addition to the study of Noheria et al, that you reported, discussing the different approaches that you considered for your patient, it would be interesting to include also the consideration proposed by Boriani et al in the B-LEFT HF trial [1]. Furthermore Pu and colleagues [2] proposed the use of echocardiography to optimize the A-V (right atrio-LV) delay using an RAAVD algorithm, comparing left univentricular pacing pacing versus standard biventricular pacing.

Please discuss these points, expressing your opinion about it.

Answer: Dear reviewer, thank you for your suggestion. B-LEFT HF trial indicated that Left ventricular-only pacing is noninferior to BiV pacing in a 6-month follow-up with regard to clinical and echocardiographic responses while Noheria et al. revealed that long-term coronary sinus single-site pacing resulted in an inferior left ventricular systolic function compared with standard cardiac resynchronization therapy, in addition, in Noheria’s study, a patient of long-term coronary sinus single-site ventricular pacing was found developing pacing mediated cardiomyopathy with progressive decline in LVEF. We thought the different clinical outcome may related to duration of follow-up. Different from B-LEFT HF trial followed the patients for 6-month, Noheria et al. followed the patients with 5.3±2.8-years.

What more, in this special patient of complete AV block, if single pacing lead in coronary sinus was selected, in the event of coronary sinus lead dislodgement or malfunction, the underlying complete AVB may be life-threatening. Based on these considerations, we still recommended the dual pacing leads in coronary sinus. In addition, we found there was an exactly increased left ventricle electrical and mechanical synchronization by this method.

Otherwise, for this patients of rheumatic heart valvular disease was in a permanent atrial fibrillation rhythm, the left univentricular (LUV) pacing using a rate-adaptive atrioventricular delay (RAAVD) algorithm could not be achieved.

Thanks sincerely,

Jia-feng.