Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

The title reflects the main subject of the manuscript. The abstract summarizes and reflects the work described in the manuscript. The key words reflect the focus of the manuscript. The background is well described. The results are clear but the discussion lacks some issues. Illustrations and tables are of good quality. In the paper "Cryoballoon pulmonary vein isolation and left atrial appendage occlusion prior to atrial septal defect closure: a case report", authors describe a very singular case where a single pathology (i.e. interatrial septal defect) and its consequences (i.e. atrial fibrillation and cloth formation in left atrial appendage – LAA-) have been treated simultaneously and percutaneously.

1. The moot point is the indication to LAA closure and pulmonary vein isolation (PVI) in a patient with first diagnosis of atrial fibrillation and no contraindication to anticoagulation. The closure of interatrial defect is mandatory but the other two procedures as first approach are, at least, questionable.

Response: The patient had a history of atrial fibrillation for 2 years, which was not the first diagnosis. He had previously diagnosed atrial fibrillation and still had recurrent episodes after drug treatment. The patient had no contraindication of anticoagulation, but the patient refused to take anticoagulants for a long time. This case wants to express that this 3-in-1 operation is feasible, but it is not recommended as a routine.

2. The PVI has been performed as first strategy treatment of atrial fibrillation; the patient was not symptomatic for atrial fibrillation and no antiarrhythmic or rate control drugs have been tested before the procedure. The justification to PVI is the maintenance of sinus rhythm and the consequent atrial remodeling but no drugs were tested before the procedure. Moreover, even after a procedure of pulmonary veins isolation the indication to anticoagulation is still present. The justification to the LAA closure is the refusal of the patient to the anticoagulation but he has taken the anticoagulation after the procedure for three months.

Response: The patient had paroxysmal palpitation, which was considered to be caused by atrial fibrillation. The patient had previously diagnosed atrial fibrillation and still had recurrent attacks after drug treatment, so PVI was selected this time. We agreed with the anticoagulant indication after PVI. According to the consensus of Chinese experts, after 3 months of anticoagulation combined with antiplatelet therapy, patients after left atrial appendage occlusion can be changed to long-term antiplatelet therapy instead of anticoagulants. The patient refused to take anticoagulants for a long time, so according to the consensus, he can change to long-term antiplatelet therapy after anticoagulation for three months.

3. Theoretically, the PVI and LAA closure have been performed as first approach before the septal defect closure because of the complexity to perform a transseptal puncture

thought a device but this it is feasible (Transseptal Puncture Through an Amplatzer Atrial Septal Occluder for Edge-to-Edge Repair With MitraClip NTr System. Villablanca PA, Lee J, Wang DD, Frisoli T, So CY, Kang G, O'Neill WW, Eng MH.Cardiovasc Revasc Med. 2020 Nov;21(11S):63-64: one of several examples). This mean that it should have been performed the interatrial defect closure and reserve the other to invasive procedures after the failure of the medical therapy. For sure the case report is singular but should better explicated by authors the reasons to perform three complex and expensive procedures in one shot giving no chance to medical therapy.

Response: The patient had a history of atrial fibrillation for 2 years, which was not the first diagnosis. He had previously diagnosed atrial fibrillation and still had recurrent episodes after drug treatment. It is feasible to perform a transseptal puncture thought a device, but it would be relatively more complex and risky. As the attempt of drug treatment failed, and he was unable to tolerate long-term oral anticoagulants, the patient agreed to complete the 3-in-1 operation.

Moreover, authors should stress the fact that even if something is feasible it does not means that it must be do or it is the best for the patient. Thank you for the opportunity to revise this paper.

Response: Indeed, this is not a must, nor is it the best. What this case wants to express is that this 3-in-1 operation is feasible, but it is not recommended as a routine. We have stressed the fact in the case.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

Peer review: Authors present a case where cryoballoon PVI, LAA occlusion and ASD closure were performed in a patient at the same instance.

Major comments:

Language: Overall language grade D (please use help of native English speaker to refine the language of the manuscript or English editing services).

Response: We have used the editorial services recommended by your journal.

Final diagnosis: “atrial fibrillation, ASD, CAD, DM” how does any of that explain the shortness of breath in the patient? Did the patient have acute pulmonary edema? Pulmonary hypertension? All these diagnoses identified do not warrant a triple procedure in the same setting. Authors need to justify the reason behind performing the procedure.

Response: The patient had elevated BNP and cardiac insufficiency. At the same time, the onset of atrial fibrillation exacerbated the symptoms of shortness of breath. The patient had a history of atrial fibrillation for 2 years, which was not the first diagnosis. He had

previously diagnosed atrial fibrillation and still had recurrent episodes after drug treatment. As the attempt of drug treatment failed, and he was unable to tolerate long-term oral anticoagulants, the patient agreed to complete the 3-in-1 operation. This case wants to express that this 3-in-1 operation is feasible, but it is not recommended as a routine.

Treatment: This section appears like an "operative note". Instead of providing the steps of procedure, authors need to clearly justify the need for each procedure. Indications/ risks/ benefits/timing etc.

Response: The indications and benefits of atrial septal occlusion are clear. For PVI and LAAO, the patient had recurrent atrial fibrillation and poor control of antiarrhythmic drugs, so PVI was tried to cure atrial fibrillation. In addition, the patient needed anticoagulant therapy, but refused to take oral anticoagulants for a long time, so LAAO was selected. We have made supplements in the treatment section.

Conclusion: What are the final recommendations from the authors? Do they suggest performing this "3 in 1" procedure routinely? What would be the factors for patient selection?

Response: This case wants to express that this 3-in-1 operation is feasible, but it is not recommended as a routine. For patients with atrial septal defect complicated with poorly controlled atrial fibrillation and unable to tolerate long-term oral anticoagulants, this "3 in 1" procedure can be considered.