Author’s response to reviews

Title: Exercise-Induced Left Bundle Branch Block and Subsequent Mechanical Left Ventricular Dyssynchrony -Resolved with Pharmacological Therapy-

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Author’s response to reviews: see over
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Eugenio Picano, MD, PhD.
Editor-In-Chief
Cardiovascular Ultrasound

RE: MS ID 5265329075065861 “Exercise-Induced Left Bundle Branch Block and Subsequent Mechanical Left Ventricular Dyssynchrony -Resolved with Pharmacological Therapy-”

Dear Prof. Dr. Picano,

We are delighted with your interest in publishing our manuscript and submit a revised version of this manuscript to the Cardiovascular Ultrasound. We found your reviewer’s comments very helpful and have revised it accordingly. To make our changes easier to follow, the reviewer and editor’s comments appear in bold type, followed by our responses in non-bold type in the cover letter, indicating how our manuscript was revised.

Responses to Reviewer (Quirino Ciampi):

The authors are thankful to this reviewer for his or her thoughtful and constructive comments. This individual clearly has a high level of expertise and experience in this topic, and his or her insight for improving this manuscript is greatly appreciated.

1. The authors should include a table with 3 columns (baseline, follow-up and p value) with resting echocardiographic characteristics of the patient (left atrial and left ventricular diameters, thickness of interventricular septum and posterior wall).

As you suggested, we created Table 1. We are sorry but p-value was not added because this study included only one subject.

2. The authors should include a table with 5 columns (rest and peak stress at baseline and after pharmacological therapy during follow-up and p value) with the clinical parameters (heart rate and blood pressure and double product at rest and at peak stress) and echocardiographic parameters (LV end-diastolic and end systolic volumes, ejection fraction, transmitral pattern, E/E’ and radial strain at rest and at peak stress).

As you suggested, we created Table 2. P-value was not added for aforementioned reason.

3. The authors should provide the dosage of carvedilol and candesartan during follow-up.

As you suggested, we added the dosage of carvedilol and candesartan during follow-up. Revised to Page 5: “The patient was treated with final daily dosages of 20mg carvedilol and 4mg candesartan for depressed LV systolic function.”
Responses to Reviewer (Rosa Sicari):

The authors are thankful to this reviewer for his or her thoughtful and constructive comments. This individual clearly has a high level of expertise and experience in this topic, and his or her insight for improving this manuscript is greatly appreciated.

1. The onset of LBBB is heart rate related. Medical therapy simply shifted the heart rate at which LBBB ensues.

As you suggested, following sentence has been added to the Discussion.

Added to Page 7: “While the precise reason for the effect of pharmacological therapy on exercise-induced LBBB remains unknown, such therapy may simply shift the heart rate at which LBBB ensues because the onset of LBBB is heart rate related.”

2. It is not clear the advantage of strain assessment in this patients and for what aim

As you suggested, we addressed the advantage of the quantitative assessment of LV dyssynchrony by echocardiography in the Discussion.

Added to Page 7: “LV dyssynchrony impairs LV diastolic, right ventricular and left atrial function as well as LV ejection efficiency. LV dyssynchrony has therefore emerged as an important mechanisms contributing to the progression of heart failure and ventricular remodeling, and appears to play a major pathophysiologic role in heart failure. Since roughly one-third of heart failure patients with a wide QRS width do not show significant LV dyssynchrony[8, 12], the quantification of LV dyssynchrony by means of echocardiography could be important for assessment of heart failure patients.”


3. The conclusions of the case are not supported by the results: on what basis authors state that exercise-induced dyssynchrony is ominous?

We agree with your suggestion. The following sentence has been added to the Discussion.

Added to Page 7: “In our case, the patient’s symptom appeared during treadmill exercise, and LBBB with LV dyssynchrony during the activity impaired his LV function (Table 2). Thus, exercise-induced LV dyssynchrony might constitute a warning for this patient.”

4. The conclusions of the case are largely hypothetical

As you suggested, the conclusions have been revised.

Revised Page 8: “Exercise-induced LBBB with significant mechanical LV dyssynchrony may constitute an important prognostic finding for patients with heart failure. Moreover, pharmacological therapy using drugs such as carvedilol and candesartan may be useful for the treatment of exercise-induced LBBB. Because ours was an isolated case, further clinical studies are required to validate this finding.”
5. Furthermore, the imaging aspect of this case report is limited to typical asynchrony imaging. As you suggested, the following sentence has been added to the Discussion. 
Added to Page 8: “Because this phenomenon was observed only in a case with a typical LV dyssynchrony pattern, the presence of this phenomenon needs to be confirmed in a case without LV dyssynchrony.”

6. The English language should be extensively revised. We appreciate this comment, and have revised errors that we found.

Thank you for this kind consideration,

Sincerely,

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