

Dear editor,

Thank you for your email regarding on our manuscript titled “**Left bundle branch pacing in a ventricular pacing-dependent patient with heart failure: A case report and literature review**” numbered 74101. We appreciate the comments of the reviewers and your kind offer of revision. We have carefully studied the comments and addressed all of the issues raised by the reviewers and editor with necessary revisions. We have made all of these changes in the revised version, and a point-by-point response is also given below.

### **Point-by-point response**

**Reviewer #1: The authors describe a case on an interesting and upcoming area of intervention in cardiac pacing and electrophysiology. The case is well written. The title ,abstract, key words and introduction are well written. The discussion enumerates the various aspects of His bundle and LBB pacing also. The study adds to the emerging body of evidence in support of LBB pacing over past decade. A few comments are noted.**

We thank the reviewer for appreciating our effort and his/her very helpful comments to improve the manuscript and render it more concise and complete. According to his/her suggestions, we addressed all comments.

**1. "A single-chamber pacemaker with left bundle branch pacing (LBBP) was selected, with the plan to take amiodarone and upgrade to dual-chamber ICD or CRT-D at an appropriate time"- How can you upgrade a LBB pacing lead to an Dual chamber ICD or CRT-D? The statement is erroneous and need to reframed!**

Our description in the article is ambiguous. We explained it in the revised version:

A single-chamber pacemaker with left bundle branch pacing (LBBP) was selected, with the plan to take amiodarone and upgrade to dual-chamber ICD or CRT-D at an appropriate time. We will still use the LBB electrode as the right ventricular pacing electrode and place the defibrillation electrode on the right ventricular apex with only the defibrillation function applied as the dual-chamber ICD. Similarly, we will use the LBB electrode combined with the right ventricular defibrillation electrode and the traditional left ventricular electrode as CRT-D, which comprises the left bundle branch optimized CRT-D (LOT-CRTD) that we are performing a lot currently.

**2. Ventricular bigeminy may be added to ECG findings at admission.**

We followed the reviewer's suggestion. We changed the ECG of Figure 1. with III° AVB and ventricular bigeminy.

**3. "In the 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy, CRT-P is highly recommended for patients with heart failure and high-degree atrioventricular block to reduce morbidity, whether patients have atrial fibrillation or not". The statement needs clarity as pacing in Sinus Rhythm is a class I indication while in AF it is Class II. Hence , they cannot be clubbed together especially in absence of RCT in AF patients with need for CRT.**

We apologize and revised:

In the 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy, CRT-P is highly recommended for patients with heart failure and high-degree atrioventricular block to reduce morbidity, including patients with atrial fibrillation.

**Reviewer #2: Overall clearly written manuscript. It is intriguing as LB pacing is not common practice in USA. I have few suggestions that will make manuscript interesting to readers.**

We thank the reviewer for his/her very helpful comments to improve the manuscript and render it more concise and complete.

**1. The premise of article is cost benefit with Left bundle pacing in this patients but authors have not included cost difference between CRT and LB pacing including follow up and if there are any studies on recurrent CHF hospitalization among these two group of patients.**

In the revised version of the manuscript, we addressed these issues:

However, due to the local insurance policy, the reimbursement ratio of pacemaker implantation is very low, and the cost of a CRT pacemaker is much more expensive than that of a single-chamber pacemaker. The patient was worried about the financial burden.

In 2020, Wu et al. revealed that LBBP produced significantly greater reductions in QRS duration and resulted in significant improvements in the function of the left ventricle and clinical response compared to biventricular pacing (BVP) in heart failure patients with typical

LBBB.<sup>[15]</sup> Subsequently, a number of studies have shown that in heart failure with LBBB, LBBP-related complications and adverse clinical outcomes, including heart failure hospitalization and mortality, were not significantly different compared to CRT.<sup>[16]</sup> However, whether LBBP is an ideal choice for heart failure patients with high-degree atrioventricular block lacks evidence.

**2. Though manuscript beginning seemed like patient improved a lot, authors have short term follow up on this patient with very small improvement in ECHO parameters so it should be noted in manuscript accordingly.**

As suggested, we noted the small improvement in ECHO parameters in the revised version: During the follow-up at 3 months after LBBP, the patient showed an improvement in cardiac function with slightly improvement in echocardiography parameters, and the NYHA functional class was maintained at I.

**3. Authors should include a paragraph on general procedural technicalities and complications (short term and long term) of traditional right Ventricular pacing, LB pacing and CRT including few citation of available literature.**

In the revised version of our manuscript, we include a paragraph on general procedural technicalities and complications (short term and long term) of traditional right ventricular pacing, LB pacing and CRT:

To date, cardiac pacing is the only effective treatment for patients with symptomatic bradycardia. Traditional right ventricular apical pacing (RVAP) has been widely used for more than half a century, although it has been proven to lead to electrical and mechanical asynchrony, which increases the risk of atrial fibrillation, heart failure and even death.<sup>[17]</sup> In addition, other ventricular pacing sites, such as the right ventricular septum and right ventricular outflow tract, have been developed and applied to minimize the above potential adverse consequences. However, their long-term results have not been proven to be better than those of RVAP. Cardiac resynchronization therapy through BVP is another pacing method for the treatment of heart failure. Clinical studies have shown that CRT can promote left ventricular reverse remodeling and exercise tolerance and reduce the incidence rate and mortality of heart failure patients.<sup>[6]</sup> Although the benefits of CRT have been fully demonstrated, the nonresponse rate of this therapy is very high (30-40%). In addition, BVP is a nonphysiological method that requires two

leads to activate the ventricular myocardium rather than a specialized conduction system. Therefore, the physiological pacing technology of directly activating the conduction system has become the focus of attention. LBBP is achieved through the transventricular septal approach, which can directly excite the left bundle branch area, and the QRS duration is narrowed due to the rapid activation of the left ventricle. At present, this method has been extended to treat some patients with heart failure and ventricular dyssynchrony caused by LBBB. According to the current research, with the increase in clinical application, the clinical development of LBBP is in an early but encouraging stage. However, there is a need to develop standardized procedures with improved delivery tools and pacing leads, as well as long-term efficacy and safety studies.[18]

**4. In core tip authors claim in LBBB and pacemaker induced cardiomyopathy, left bundle pacing is ideal choice seems very much out of norm of current guidance from major profession societies, so wording like cheaper alternative with potential for similar outcomes might be more appropriate unless authors can cite major studies showing comparable outcomes and lesser complications.**

We changed our description in the revised version:

Left bundle branch area pacing (LBBP) is a new and prospective pacing technique that is a promising alternative with potential for similar outcomes in patients with complete left bundle branch block who need cardiac resynchronization therapy (CRT) or for patients with pacemaker-induced cardiomyopathy.

**Reviewer #3: I read with interest the article "Left bundle branch pacing in a ventricular pacing-dependent patient with heart failure: A case report and literature review". The article is interesting and instructive for a wide readership, although there are very similar articles in recent literature (eg Zhang D, Huang X. Treatment of atrial fibrillation with third-degree atrioventricular block by pacing His bundle and left bundle branch: Case report. *Medicine (Baltimore)* 2020 Aug 14; 99 (33): e21097. The biggest complaint is of a technical nature - the text attached as a "Manuscript file" is a working version of the text, that is, probably the one edited by an English language lecturer, which should not happen when sending to a serious medical journal!**

We are thankful that the reviewer thinks that our manuscript is interesting and instructive for a wide readership. We appreciate his/her very helpful and precise suggestions to further improve the manuscript.

**1. I advise to enclose another ECG or Holter record where it is clearer that in addition to atrial fibrillation, it is also a total AV block!**

We enclosed another ECG with III° AVB and ventricular bigeminy as Figure 1. However, due to the basic heart rhythm of the patient, we could not find another clearer ECG with atrial fibrillation and total AV block.

**2. I advise to attach additional ECHO material where severe MR is seen and its reduction after pacing treatment!**

It would be perfect that we could attach additional ECHO material where severe MR is seen and its reduction after pacing treatment. However, for technical reasons, we are lacking ECHO images during follow-up, and the patient cannot come back for follow-up recently.

**3. Why do the authors believe that the patient is at high risk of sudden death and that there is an indication for ICD implantation with LVEF 38%, then 51%?**

First, we apologize for a clerical error in Table 1. that we wrote 41% to 51%, we have corrected it in revise version.

Beside atrial fibrillation with third-degree atrioventricular block, the patient was also with frequent multifocal ventricular premature beats, Ron-T and ventricular tachycardia. That was a complex ventricular arrhythmia. Meanwhile, the patient's heart was enlarged, and it is easy to induce ventricular tachycardia or ventricular fibrillation. Therefore, ICD implantation was a better choice for patient.

**4. What was the level of NTproBNP before pacemaker implantation and later in the control period?**

In our hospital, only BNP level is measured. We added the BNP level before pacemaker implantation and later in the control period in paragraph of laboratory examinations and follow-up and outcomes.

**4. It is necessary to specify the drug therapy with which the patient was treated in connection with CHF!**

We clarified the drug therapy in the revised version:

An optimal medical therapy with rivaroxaban, diuretic, sacubitril valsartan and dapagliflozin was chosen.

I believe you will find that the revisions have greatly improved the quality of this manuscript and hope it meet the high standards of **World Journal of Clinical Cases**.

Sincerely yours,

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