Dear Editor,

Please find enclosed the revised manuscript as per the comments from the reviewers.

Title: A comparison of echocardiography and device based algorithm for atrio-ventricular delay optimization in heart block patients.

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The manuscript has been improved according to the suggestions of reviewer. The point wise clarification about reviewer's comments are as follows:-

Reviewer 1 comments:-

The manuscript deals with the comparison of two methods, namely echocardiography and intra-cardiac electrocardiogram based QuickOpt algorithm, for atrio-ventricular delay optimization in 20 CHB patients. The issue has a clinical importance since a good optimization provides better haemodynamic outcomes in patients. The study lacks clarifications on some important issues, and the manuscript should be revised in a few sessions, as stated below: 1) This study did not consider repeatability. This issue is relevant to the study of method comparison because the repeatabilities of the two methods of measurement limit the amount of agreement which is possible. If one of the two method has considerable variation in repeated measurements on the same subject, the agreement between the two methods is bound to be poor too. If both methods have poor repeatability, the problem is even worse. Repeated measurements on a series of subjects should be taken and the coefficient of variation discussed to strengthen the importance of data presented.

The question of repeatability has been addressed in the study by taking an average of the three measurements of the EA duration (at different AV/PV delay) and LVOT VTI (at the optimum AV/PV delay) both during echocardiography and IEGM optimisation. This has been done according to the guidelines issued by the American Society of Echocardiography (ASE)/ European Association of Echocardiography (EAE) and has been clearly mentioned in the "Methods" section of the manuscript.

2) It not clear to me what does it mean that two variables are in agreement but do not correlate. I can understand the opposite, since two parameters can show a linear relationship (correlation) but exhibit a bias, and thus not to be interchangeable.

Our results show that there is a good agreement and poor correlation between the optimum AV/PV delay measured by the echocardiography and the IEGM method. This means that the value of optimum AV/PV delay given by echocardiography and IEGM method was not different by more than 20 milliseconds in 80% patients (16/20 patients for both AV and PV delay). However, poor correlation between optimum AV/PV delay measured by the two techniques means that if the optimum AV delay measured by echocardiography in one patient is more than it doesn't mean that the delay measured by IEGM method will also be more, it may even be less, but the absolute value is more likely (80%) to be within 20 milliseconds.

3) As recognized by the authors, the small sample size may represent a limitation, especially considering that for an other class of patients, namely those with cardiac resynchronization therapy, has been demonstrated a poor agreement between the optimal AV and VV interval values determined by the two optimization techniques (echocardiography and QuickOpt algorithm) (ref 2 of the manuscript). Minor comments: Several typos and /or errors have to be addressed

We agree that the sample size is small. This is a pilot study and a larger sample size is required to validate the results, as mentioned in limitation of the study.   The typographical errors has been corrected.

Reviewer 2 Comments:-

  The authors stated that optimization of sensed and paced atrio-ventricular (AV/PV) delay is required for better hemodynamics in patients with complete heart block (CHB). They studied the AV/PV delay optimization usisng echocardiography and intra-cardiac electrocardiogram (IEGM) based QuickOpt algorithm in 20 CHB patients. The results revealed a good agreement between optimal AV and PV delay determined by the two methods. Authors concluded that the automated programmer based IEGM method is a quick, easier and reliable alternative to echocardiography for the optimization of atrio-ventricular (AV/PV) delay in CHB patients subjected for dual chamber pacemaker. The tables and figures are presented appropriately. However, I have several comments: 1. This study did not provide with new concept or findings compare with many previously published articles. Twenty cases are not enough for convincing a special issue. I would suggest to increase the numbers for at least 30 cases before considering acceptance of this manuscript.

We agree that the sample size is small and the study needs to be validated on a bigger sample size. However, we would like to disagree that our study did not provide any new concept/finding as compared to previous studies as the other studies were done in dilated cardiomyopathy patients receiving Cardiac resynchronization therapy (CRT). Ours is probably the first study to demonstrate the IEGM algorithm use in patients with CHB subjected for dual chamber pacemaker.

2. In the " AV delay Optimization Methods Section", authors have not described the definition of "optimal AV delay" and "optimal PV delay". These terms should be mentioned.

Optimal AV delay has been described in the "AV delay optimization methods" and is quoted as "The optimal AV interval on echocardiography was the AV interval at which the maximum transmitral inflow duration was documented without the interruption of the A wave". The optimal PV delay was not mentioned and this sentence has been rephrased in the manuscript as "The optimal AV/PV interval on echocardiography was the AV/PV interval at which the maximum transmitral inflow duration was documented without the interruption of the A wave". "Optimal AV interval was determined in DVI pacing

mode, while optimal PV interval was measured in VDD pacing mode. To pace atria in DVI mode, the atrial rate was increased by 10 beats per minute over the baseline atrial rate".

3. In References Section, there was no "No. 5" reference. Authors should not have this mistake.
The missing reference mistake is regretted and has been rectified.

Kindly inform for any further clarification to be made in the manuscript. The minor language editing is also completed in the manuscript.
I hope the editor will find it suitable for publication.

Sincerely yours,

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