# Clinical Benefit of Biventricular and Bifocal Right Ventricular Pacing in Heart Failure Patients, With or Without Atrial Fibrillation

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## Summary

*The clinical benefit of cardiac resynchronization therapy for patients with severe heart failure, left bundle-branch block, and sinus rhythm (SR) has been proven in numerous studies. It is still under debate to what extent heart failure patients with atrial fibrillation (AF) benefit from cardiac resynchronization therapy, and whether right ventricular bifocal pacing is an acceptable alternative to biventricular pacing. Among 49 patients, (69 ± 10 years old, 36 male, NYHA class III – IV, left ventricular ejection fraction ≤ 35%, QRS width ≥ 150 ms, AF 24, SR 25), biventricular (AF 21, SR 22) and bifocal right ventricular (AF 3, SR 3) pacing was performed. The NYHA class, QRS width, ejection fraction, and mitral insufficiency class were determined pre- and postoperatively (20 ± 11 months). The patients with SR as well as those suffering from AF showed significant (p-value < 0.005) improvements in NYHA class, ejection fraction, and mitral insufficiency class as well as a reduced QRS width after the implantation of a biventricular pacemaker system. Bifocal pacing shows similar improvements in NYHA class and ejection fraction compared to achievements with biventricular pacing, but due to the small number of patients, no significance can be shown. Heart failure patients with SR and AF benefit significantly from biventricular pacing. The differences between the SR and AF group are insignificant. Initial results indicate that bifocal right ventricular pacing shows benefits comparable to those achieved through biventricular pacing.*

## Key Words

Congestive heart failure, cardiac resynchronization therapy (CRT), atrial fibrillation, bifocal pacing

## Introduction

The clinical benefit of cardiac resynchronization therapy (CRT) with respect to hemodynamics, quality of life, and mortality in patients with heart failure (HF) and left bundle-branch block has been proven in numerous randomized studies [1-17]. The MUSTIC (Multisite Stimulation in Cardiomyopathies) study showed, among other things, that the above statement not only applies to patients with sinus rhythm (SR), but also to those with atrial fibrillation (AF) [17-20]. It is still under debate to what extent CRT in patients with AF leads to a reversal [11,12] of the remodeling process of the failing ventricle (despite missing atrioventricular synchronicity) and additionally to a reversal of the remodeling process in the fibrillating atria. In this context, we previously reported the case of a patient with permanent AF who spontaneously returned to the SR due to CRT [21]. Despite considerable progress in implantation technology, in approx. 10% of HF patients who could benefit from CRT, the coronary sinus lead cannot be successfully positioned due to anatomical circumstances of the cardiac veins. Problems arising in this situation are as follows: the coronary sinus ostium cannot be intubated, the pacemaker lead cannot be positioned in the cardiac veins with sufficient stability, or a position with an acceptable threshold cannot be found.

Pachon, et al. [22,23] report successful results of right ventricular bifocal pacing and propose this therapy as an alternative to biventricular pacing for patients in whom no coronary sinus lead can be positioned.

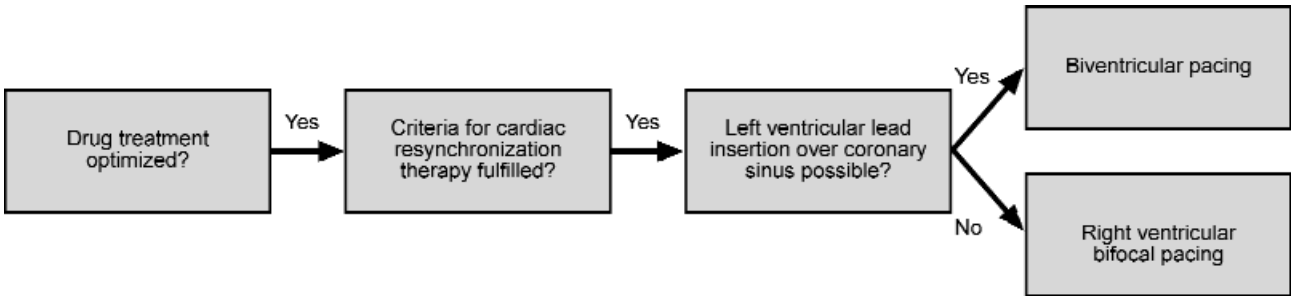


*Figure 1. Therapy concept.*

During right ventricular bifocal pacing, the second ventricular lead is fixated in the right ventricular outflow tract (RVOT) or in the upper septum in order to simultaneously pace the apex and RVOT from the upper septum. This article presents a therapy concept which is based on the above idea and discusses clinical experiences gathered from patients with or without AF.

## Material and Methods

*Therapy Concept*

Patients with HF were first treated with medication according to current guidelines [24]. A patient was considered for the implantation of a biventricular pacemaker system (Figure 1) under the following circumstances: existence of moderate to severe NYHA class III – IV HF despite optimal medication, left ventricular dysfunction with ejection fractions below 35%, and left bundle-branch block with a QRS complex of more than 150 ms for patients with intrinsic rhythm, or a QRS complex width of more than 200 ms in pacemaker-dependent patients during right ventricular apical pacing (displayed on the surface ECG). If anatomical circumstances made the intubation of the coronary sinus impossible, or if no stable position with an acceptable pacing threshold for the left ventricular lead could be found, the second chamber lead was alternatively fixated in the right ventricle in the upper septum or the RVOT.

*Patients*

Forty-nine patients with drug-refractory heart failure were treated according to the above-described therapy concept. Twenty-four of the patients displayed permanent AF. In Table 1, both patient groups with SR and permanent AF respectively are compared based on number, age, gender, other pacemaker and/or ICD indications, and the type of dilatative cardiomyopathy (DCM). In each of the two groups three patients were implanted with a right ventricular bifocal system instead of a biventricular system due to the above mentioned complications during the positioning of the coronary sinus lead.

| | Sinus rhythm | Permanent atrial fibrillation |
|---|---|---|
| **General information** | | |
| No. of patients | 25 | 24 |
| Male | 16 (64%) | 20 (83%) |
| Age (years) | 68.9 ± 8.3 | 68.3 ± 11.3 |
| **Pacemaker indication** | | |
| Sinus node disease | 1 (4%) | - |
| Binodal disease | 4 (16%) | - |
| Atrioventricular block | 6 (24%) | 5 (21%) |
| No conventional pacemaker indication | 14 (56%) | - |
| **ICD indication** | 6 (24%) | 2 (8%) |
| **Dilated cardiomyopathy (DCM)** | | |
| Primary DCM | 4 (16%) | 5 (21%) |
| Secondary DCM and coronary heart disease | 11 (44%) | 15 (62%) |
| Secondary DCM and hypertension | 8 (32%) | 4 (17%) |
| Others* | 2 (8%) | - |
| **Pacing mode** | | |
| Biventricular | 22 (88%) | 21 (88%) |
| Bifocal | 3 (12%) | 3 (12%) |

*Table 1: Composition of the patient groups with and without atrial fibrillation. *secondary dilated cardiomyopathy in the presence of Cor pulmonale, heart failure in the presence of myocardial infarction.*

*Follow-up*

The follow-up was performed 4 weeks and 3 months after the implantation, and then in quarterly increments. In addition to the usual inspection of the pacemaker system, the following procedures were performed: determination of the NYHA class, echo cardiography to determine the left ventricular ejection fraction and the mitral insufficiency class, and a surface ECG. The baseline values of these parameters were also determined preoperatively in order to evaluate the success of the therapy. The following values refer only to the results of the 1-, 3-, 6-, and 12-month follow-up.

*Data Evaluation*

Three patient groups were observed separately in order to compare the impact of the therapy on SR and AF patients who underwent biventricular and right ventricular bifocal pacing. The three groups were: biventricular paced patients with SR (n = 22), biventricular paced patients with AF (n = 21), and right ventricular bifocal paced patients with and without AF (n = 6, gathered into one group due to the small number of patients). In each patient group, the postoperative results from the 1-, 3-, 6-, and 12-month follow-up were compared to the baseline values of the preoperative measurements using a Student t-test and tested for significance (p-value < 0.005).

## Results

According to Figures 2 – 5, both the SR and the AF patients show a significant postoperative improvement of NYHA class (change at 12-month follow-up compared to the preoperative values: –1.1 ± 0.5), the ejection fraction (+15% ± 9%), and the mitral insufficiency class (–1.2 ± 0.5). They also showed a decrease in QRS width (–29 ms ± 26 ms). These changes remained stable during the observation period compared to the preoperative values. The preoperative and postoperative values of SR patients did not show significant differences compared to the corresponding values of the AF patients.

In the case of the bifocally paced patients, these changes in parameters did not reach the significance level due to the small number of patients. However, improvements tendentially similar to biventricularly paced patients with respect to the NYHA class (Figure 2) and the ejection fraction (Figure 4) could be observed. The bifocally paced patients already displayed a relatively low preoperative mitral insufficiency class (Figure 5). Therefore, an improvement can hardly be observed, even if the postoperative values in the mitral insufficiency class do not differ significantly from the postoperative values of the biventricularly paced patients. No effect of bifocal pacing can be determined with respect to the QRS width (Figure 3). During the first

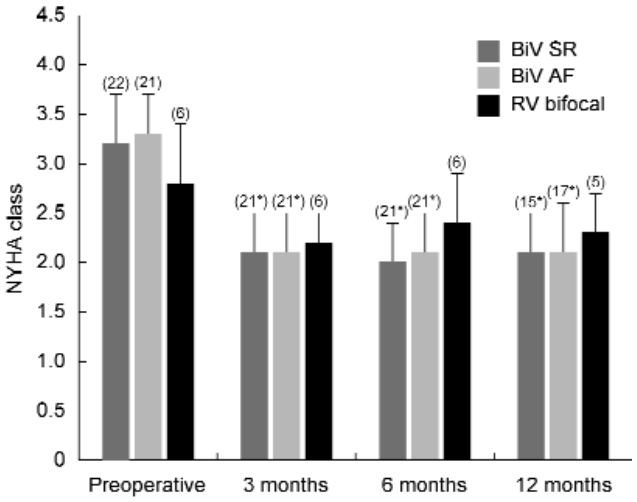


*Figure 2. Reduction of NYHA classification; *p < 0.001 compared to preoperative values. A total of 11 patients died over the course of the 12-month follow-up. BiV SR = biventricular pacing in patients with sinus rhythm, BiV AF = biventricular pacing in patients with atrial fibrillation; RV bifocal = right ventricular bifocal pacing.*

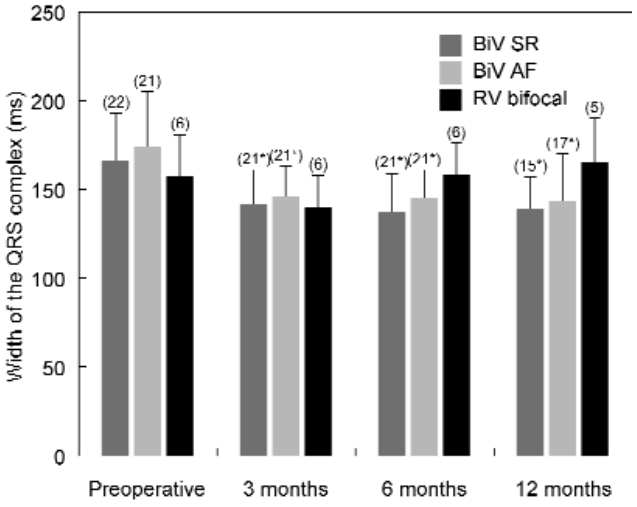


*Figure 3. Decrease of the QRS complex width; *p < 0.005 compared to preoperative values. See legend of Figure 2.*

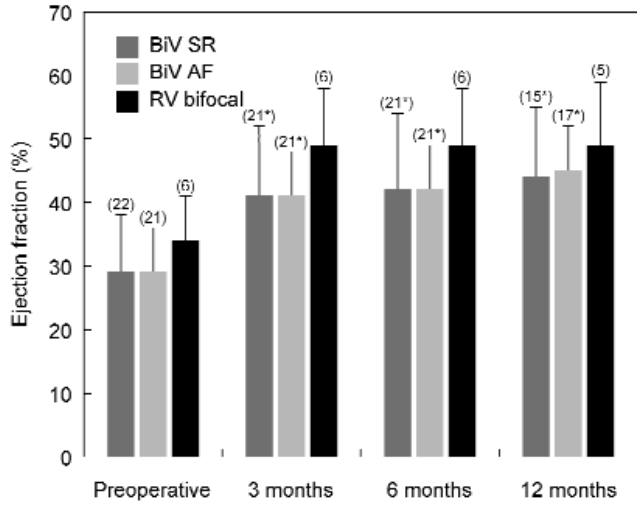


*Figure 4. Increase of the ejection fraction; *p < 0.005 compared to preoperative values. See legend of Figure 2.*

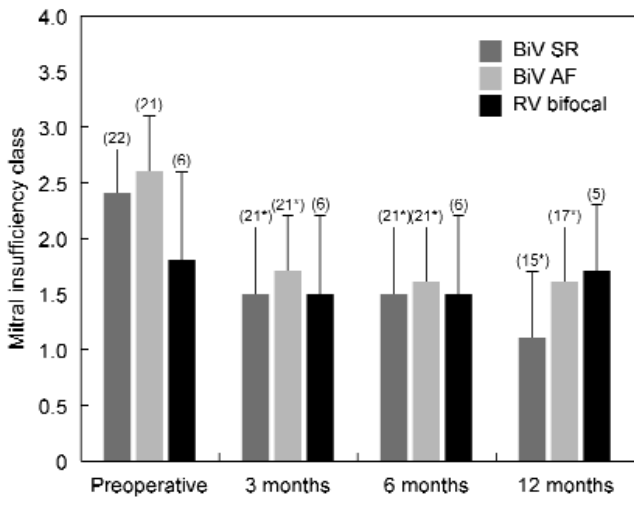


*Figure 5. Decrease of the mitral insufficiency class; *p < 0.001 compared to preoperative values. See legend of Figure 2.*

postoperative year, seven patients of the biventricularly paced SR group died due to:

- non-cardiac-related cause of death (1),
- myogenic failure (3),
- sudden cardiac death (1), and
- unknown cause (2).

In the biventricularly paced AF group, four patients died due to:

- non-cardiac-related cause of death (2), or
- myogenic failure (2).

## Discussion

The expected clinical benefit of CRT was obvious in patients with SR. A comparable effect was also observed in patients suffering from AF. This suggests that biventricular pacing acts mainly via the synchronization of both chambers, and that the optimization of the AV delay merely plays a secondary role [19]. The success of the therapy becomes apparent after a few weeks and is maintained throughout the entire observation period of 12 months. Three patients were converted from permanent AF to SR via biventricular pacing.

Due to the comparable success of CRT in patients with or without AF, the bifocally paced patients with and without AF were observed in one group. Further studies might be necessary to determine to what extent the generalization between results of biventricular pacing and right ventricular bifocal pacing is permissible. Patients who underwent right ventricular bifocal pacing showed improvements in NYHA class and ejection fraction comparable to those who underwent biventricular pacing. However, due to the small number of patients, these improvements were not significant.

Contrary to biventricular pacing, patients undergoing bifocal pacing did not exhibit a noteworthy reduction of the QRS width and the mitral insufficiency class, which might be due to the low mitral insufficiency of bifocally paced patients preoperatively. However, the postoperative values of the mitral insufficiency class of bifocally paced patients are easily comparable to those of biventricularly paced patients. Pachon et al. [23] report a 25% reduction of the QRS width and a 32% reduction of the mitral regurgitation area with right ventricular bifocal pacing compared to pure right ventricular apical pacing.

The preliminary experiences of the presented therapy concept are promising. Further studies are planned for a final assessment of the clinical benefits of bifocal pacing. Among the 11 deceased patients, eight suffered from severe heart failure preoperatively, with an NYHA classification higher than III. The patient who died of sudden cardiac arrest might have been saved with a preventively implanted ICD. We hope that due to the results of the COMPANION Study [13,14], the indications for ICDs will be expanded in the future.

## Conclusion

HF patients with or without AF benefit significantly from CRT. Preliminary clinical research indicates that right ventricular bifocal pacing represents a satisfying alternative to biventricular pacing, if positioning the left ventricular lead via the coronary sinus is impossible due to the anatomical conditions of the cardiac veins. Further studies must be done before this thesis can be fully confirmed.

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