

Original article

# Cardiac resynchronization therapy allows the optimization of medical treatment in heart failure patients

*La resynchronisation cardiaque permet l'optimisation du traitement médical dans l'insuffisance cardiaque*

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## Abstract

**Aim.** – Cardiac resynchronization therapy (CRT) is recommended for selected patients with advanced heart failure (HF) despite optimal medical treatment. However, the doses of pharmaceuticals in this population are often limited by adverse effects. We compared the drug regimens of 21 patients before and 6 months after they underwent the implantation CRT systems.

**Methods.** – We studied 17 men and four women (mean age =  $63.4 \pm 11$  years) presenting in New York Heart Association HF classes III-IV, and with a left ventricular ejection fraction (LVEF)  $\leq 35\%$  and cardiac dyssynchrony, who underwent implantation of CRT systems.

**Results.** – At baseline, 52% of patients were treated with  $\beta$ -adrenergic blockers ( $\beta$ -B), though in optimal doses in only 19%. The introduction of ( $\beta$ -B) was complicated by cardiogenic shock in three patients. At baseline, all patients were treated with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB), of whom 76% received optimal doses. After 6 months of CRT,  $\beta$ -B were administered to 76% of patients, in optimal doses of ACE or ARB but 75% of them were receiving maximal doses. After 6 months of CRT,  $\beta$  blockers have been introduced in 72% of patients and maximal doses have been achieved in 60% of them. Maximal doses of ACE or ARB were reached in 95% of the study population. We noticed that systolic blood pressure was higher after implantation. There was also a significant improvement in functional status and left ventricular ejection fraction compared to baseline.

**Conclusion.** – CRT is an efficacious adjunctive device therapy to standard medical therapy for patients with heart failure and cardiac dyssynchrony. Its benefits are in addition to those afforded by standard pharmacological therapy. Achieving maximal doses of medical treatment and the possibility of introducing  $\beta$  blockers after CRT prove that CRT and pharmacological treatment are complementary strategies and should not be considered as competitive.

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**Keywords:** Heart failure; Cardiac resynchronization therapy; Medical treatment;  $\beta$  blockers; ACE; ARB

## Résumé

**Introduction.** – La resynchronisation cardiaque (RC) est indiquée chez les patients insuffisants cardiaques qui restent symptomatiques malgré un traitement médical optimal. Cependant, l'atteinte des doses optimales du traitement médical dans cette population est souvent limitée par l'hypotension et la bradycardie.

**Objectif.** – L'objectif de ce travail est de comparer le traitement médical avant et après resynchronisation cardiaque.

**Méthodes.** – Vingt et un patients (17 hommes et quatre femmes, âge =  $63,4 \pm 11$  ans) en insuffisance cardiaque stade III-IV NYHA avec une FE VG  $\leq 35\%$  et asynchronisme cardiaque ont bénéficié d'une stimulation biventriculaire.

**Résultats.** – À l'état de base, 50 % des patients étaient sous  $\beta$  bloquants mais que 20 % étaient sous doses maximales. L'introduction des  $\beta$  bloquants a été émaillée par la survenue d'un état de choc dans trois cas. Tous les patients étaient sous IEC ou ARA II mais 75 % parmi eux

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recevaient un traitement maximal. Après six mois de RC, les  $\beta$  bloquants ont pu être introduits chez 72 % des patients et des doses maximales ont été atteintes dans 60 % des cas. Des doses maximales d'IEC et d'ARA II ont été atteintes chez 95 % de la population. On a remarqué que la pression artérielle systolique était plus élevée après l'implantation. On a noté également une amélioration du statut fonctionnel et de la FE VG par rapport à l'état de base.

**Conclusion.** – La RC est un traitement adjuvant efficace au traitement médical standard chez les insuffisants cardiaques dysynchronisés. Ces bénéfices sont supplémentaires à ceux qui sont obtenus par le traitement médical standard. L'atteinte de doses maximales de traitement médical et la possibilité d'introduire les  $\beta$  bloquants après RC démontrent que la RC et le traitement pharmacologique sont des stratégies complémentaires et ne devraient pas être considérées comme compétitives.

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**Mots clés :** Insuffisance cardiaque ; Resynchronisation cardiaque ; Traitement médical ;  $\beta$  bloquants ; IEC ; ARA II

## 1. Introduction

Cardiac resynchronization therapy (CRT) is an established efficacious adjunctive therapy in patients with systolic heart failure (HF) and ventricular dyssynchrony refractory to optimal medical treatment [1,2]. The use of the optimized medical therapy in recent randomized trials of heart failure ranges from 30 to 60% essentially due to bradycardia, hypotension and worsening heart failure; factors that could be controlled by CRT. Optimization of medical treatment after CRT has not been systematically studied, as in most of CRT trials no change in heart failure treatment was permitted between the time of inclusion and the end of the study. The aim of this study is to compare medical treatment before and after 6 months of CRT.

## 2. Methods

### 2.1. Inclusion criteria

This prospective study included consecutive patients between 2004 and 2006 presenting in New York Heart Association (NYHA) HF classes III or IV despite optimal medical treatment, a LV ejection fraction (EF)  $\leq 35\%$ , left ventricular (LV) end-diastolic diameter  $\geq 55$  mm, and intraventricular dyssynchrony ascertained by echocardiography, who underwent successful biventricular stimulation and survived up to 6 months of implantation of the CRT system.

### 2.2. Exclusion criteria

We excluded the following patients: those having ischemic cardiomyopathy and programmed for revascularization and patients who were revascularized within 6 months before the inclusion.

### 2.3. Medical treatment

Concomitant medication use was recorded. The use of angiotensin-converting enzyme (ACE) or angiotensin receptor blockers (ARB) and  $\beta$  blockers was evaluated before and after implantation. Optimal medical treatment dose was defined as at least half target doses recommended by studies. We considered optimized medical treatment the association of ACE or ARB and  $\beta$  blockers at optimal doses.

### 2.4. Echocardiographic study

Evaluation of left ventricular ejection fraction (LVEF) was based on a Simpson's biplane calculation.

Echocardiographic criteria of asynchronism were studied [3]. Intra-left ventricular delays were studied using TM mode. Basal LV septum, lateral, inferior and anterior walls were evaluated. The longest delay reflecting the maximal systolic wall thickening was studied and was compared to the end of the out flow ejection time both measured with respect to the QRS onset. Intra-ventricular asynchronism was present if the longest delay was greater than 40 ms or in case of diastolic contraction.

The interventricular electromechanical delay was the time difference between the aortic and pulmonary pre-ejection time intervals. Interventricular asynchrony was considered when the interventricular electromechanical delay was 40 ms. The total diastolic time was measured and correlated with respect to the complete cardiac cycle. A value  $< 50\%$  defined atrioventricular dyssynchrony.

### 2.5. Implantation procedure

The transvenous approach for permanent LV resynchronization pacing was used. The LV lead was placed in a lateral or a posterolateral coronary vein where the pacing threshold was considered adequate without diaphragmatic contraction. The atrial lead was positioned in the right atrial appendage. The right lead was positioned on the septum or in the apex. Atrioventricular delay was individually programmed before discharge using the mitral inflow method according to previous published data [4].

### 2.6. Follow-up

At each follow-up visits data concerning functional status, medical treatments, LV ejection fraction and dimensions at echocardiography and pacemaker check up were collected.

### 2.7. Statistical analysis

Analysis of data was done on SPSS version 11.5 software. Differences between patient groups were assessed by using Student's *t* test for quantitative variable and Fisher's test of exact probability or Chi-square test for qualitative variables. A probability value of  $P < 0.05$  was considered significant.

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