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Cardiac Resynchronization Therapy in Heart Failure in Sub-Saharan Africa Environment: Experience of the Principal Hospital of Dakar (Senegal)

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Abstract

Background: Heart failure is a major public health challenge in sub-Saharan Africa. In patients with chronic Heart Failure and cardiac desynchrony, studies have suggested that cardiac resynchronization, can improve cardiac function and the quality of life of patients. However, in Sub-Saharan Africa, very few studies have been done on cardiac resynchronization which is in its infancy. The aim of this study is to report the local data from our hospital. **Method:** It was a transversal, descriptive and analytical study conducted from November 2019 to September 2022 at the Cardiology Department of the Principal Hospital of Dakar. **Results:** Twelve patients were implanted for Cardiac Resynchronization Therapy (CRT). The sex ratio was 8 males/4 females. The average age was 67 ± 11 years. Ten patients had non-ischemic heart disease and the two others had ischemic one. All of them had NYHA III or IV scores before CRT. The Quality of Life (QOL) was judged as poor by all of the patients. The average duration of QRS was 156 ± 9 ms. 27.9% ± 5% was the mean Left Ventricular ejection fraction (LVEF). Complications occur in 3/12 patients (25%). It was one CS vein dissection, one micro LV lead dislodgement and one phrenic nerve stimulation. Nine patients, who were considered as responders, had an improvement of QOL and NYHA, the LVEF increased and the end-diastolic dimension, and the duration of the QRS interval all decreased. Two patients do not respond and one (1) who had permanent atrial fibrillation, was a secondary responder after an atrioventricular junction ablation. **Conclusion:** Cardiac resynchronization is a therapy that improves the QOL of patients, the LVEF and reduces the duration of the QRS interval. However, this procedure is not without risk of complications. In

sub-Saharan Africa, the major challenge is to improve the financial accessibility of this therapy for the population.

Keywords

Cardiac Resynchronization Therapy, CRT, Heart Failure, Biventricular Pacing, Sub-Saharan Africa

1. Introduction

Heart failure (HF) is a major public health challenge, accounting for significant morbidity and premature mortality globally, including in Sub-Saharan Africa [1]. Owing to high prevalence and poor clinical outcomes, HF is associated with recurrent hospitalizations and substantial healthcare expenditure. In patients with chronic Heart Failure, the disease process not only depresses cardiac contractility but also affects the conduction pathways by causing a delay in the onset of right or left ventricular systole [2]. Such desynchrony is apparent on the electrocardiogram as a QRS interval lasting more than 120 msec. Devices that make use of atrial-synchronized biventricular pacing to coordinate right and left ventricular (LV) contraction have been developed, and studies have suggested that short- and long-term cardiac resynchronization can improve cardiac function and enhance functional capacity and the quality of life [3] [4] [5]. In sub-Saharan Africa, cardiac resynchronization (or biventricular pacing) is in its infancy and very few studies have been done on this therapy [6]. This explains why there is very little data on this therapy in our low-income countries where economic conditions and technical facilities are different from those in developed countries. The aim of this study is to report the local data from our hospital by describing the epidemiological, clinical and follow-up evolution aspects of the patients who underwent cardiac resynchronization.

2. Methods

We report the results of a retrospective cross-sectional study conducted in the Cardiology Department of the Principal Hospital of Dakar from November 2019 to September 2022, on patients who underwent cardiac resynchronization. The aim of this study was to describe the epidemiological, clinical and follow-up evolution aspects of the implanted patients with moderate-to-severe Heart Failure and a prolonged QRS interval. Patients were eligible for the study if they had moderate or severe New York Heart Association (NYHA) functional class III or IV chronic HF due to either ischemic or non-ischemic cardiomyopathy. All patients had a Left Ventricular Ejection Fraction (LVEF) of 35 percent or less, and a QRS interval of 130 ms or more. Patients received all appropriate treatments for HF, which included a diuretic, an angiotensin converting-enzyme inhibitor or an angiotensin-receptor blocker, and a beta-blocker.

2.1. Study Design

Patients meeting the criteria for entry underwent the following evaluations at baseline:

- NYHA class,
- Quality-of-life (QOL) (judged on the patient's appreciation in three ways: good, fair, poor),
- A two-dimensional Doppler-flow echocardiography (to assess the LVEF and the LV internal dimensions),
- QRS interval (from a 12-lead electrocardiogram).

After this initial evaluation, patients underwent implantation of a cardiac-resynchronization device along with three pacing leads: a standard right atrial lead, a standard right ventricular lead, and a specialized left ventricular lead, which was placed into a distal cardiac vein by way of the coronary sinus through a guiding catheter. Medications for HF were to be kept constant. Baseline variables were reevaluated at one, three, six and twelve months after Cardiac Resynchronization Therapy (CRT).

2.2. Statistical Analysis

The study had endpoints: The NYHA class, the patient's assessment of QOL, the LV ejection fraction and the LV diastolic and systolic dimensions, the duration of QRS interval, and clinical response, which assigns patients to one of three response groups (improved, unchanged, worsened) as the major efficacy variables for the study. In addition, the protocol specified an analysis of death or worsening HF. All endpoints were analyzed. Comparisons of changes from baseline to the first, third, sixth- and twelfth-month visits were evaluated. Only patients for whom data were available at baseline and at the sixth months were included in these analyses. The data have been entered and analyzed in Excel of Office 2016 pack. The qualitative data were expressed in percent (%), and the quantitative data in averages of the plus or minus standard deviations.

3. Results

Between November 2019 and September 2022, twelve (12) patients were implanted for CRT in our hospital, which corresponded to 5.8% of all pacemakers implanted in our hospital. Indeed, during the same period, 196 patients were successfully implanted with mono and dual-chamber pacemakers. The characteristics of patients who underwent CRT at entry are provided in Table 1. The sex ratio was 8 males/4 females. The average age was 67 ± 11 years (range 54 - 76 years). There was one up-grading of a dual-chamber pacemaker. Most of the patients had non-ischemic heart disease (ten patients) and the others (two patients) had ischemic heart disease. All of them had NYHA III or IV score. The QOL was judged as poor by all of the patients. The average duration of QRS was 156 ± 9 ms (between 140 and 180 ms) before cardiac resynchronization. The Doppler-flow echocardiography assessed 27.9% ± 5% as the mean LV ejection

Table 1. Baseline characteristics of the study patients.

Characteristics	Patients (N = 12)
Age (year)	67 ± 11
Sex (nb)	
Male	8
Female	4
Ischemia (nb)	2
Non ischemia (nb)	10
NYHA functional class (nb)	
III	4
IV	8
QOL according to the patients	
Poor	12
Good	0
Duration of the QRS interval (msec)	156 ± 9
Left ventricular ejection fraction (%)	27.9 ± 5
Left ventricular end-diastolic dimension (mm)	62 ± 6
Left ventricular systolic dimension (mm)	49 ± 8

fraction from 20% to 35%. The LV diastolic dimensions ranged between 52 mm and 71 mm. The systolic LV diameter was on average 49 ± 8 mm (between 38 mm and 58 mm).

For all of these patients, the decision of CRT-P implantation was taken. The implantations were scheduled in our rhythmologic unit with an operating room in which asepsis was ensured.

The price of one new CRT-P device was $6500. All patients paid also for the operating room and four days of hospitalization approximately $750. The total cost of CRT-P was then about $7250 for each patient. All CRT-P's devices were new, there were no reused ones.

All patients received antibiotic prophylaxis before implantation, local anesthesia with Lidocaine and a Left sub-clavian vein approach. The right ventricular lead position was apical in eleven patients and septal in one patient. The LV lead was quadripolar and in a lateral vein position for all our patients. We used routinely steerable electrophysiology catheters to guide coronary sinus (CS) and facilitate coronary sinus cannulation. The mean operation time was 141 minutes (between 90 minutes and 210 minutes). We had success in implanting the system in 11/12 patients (success of 92%). One failure of the implant was due to the difficulty of LV lead implantation with CS vein dissection. This patient was reimplanted successfully one month later.

Besides the CS vein dissection, complications occur in 2/12 patients. That is to say a frequency of complications of 3/12 (25%). Early postoperative complications occurred in one patient with a micro LV lead dislodgement with an elevated LV pacing threshold but there were continuous and effective biventricular stimulation. Because of the possible infectious risk of lead repositioning and the

biventricular pacing percentage which was effective (95%), we did not replace this LV lead. With another patient, an unwanted phrenic nerve stimulation was identified during the first month of the scheduled follow-up visit. It was solved by programming another LV pacing vector. After the resynchronization, the duration of the QRS interval was decreased on average by 131 ± 5 msec which means a decrease of 16% from the baseline.

Of the 12 patients, eleven (11) completed the follow-up. One died one day after the implantation of progressive hypotension and acute HF. All patients continued to receive medications.

The follow-up was between 6 and 40 months (21 ± 11 months). Nine patients of the eleven had improvements in the QOL assessment and in the NYHA class (Table 2); Three patients one month after implantation, five patients after three months, and nine patients after six months.

At six months, we noticed an improvement in NYHA of 2 classes in 6/11 patients, and of 1 class for 3/11 patients. For the two other patients who were considered non-responders, clinical conditions were judged by the patient as the same as before CRT implantation.

At the end of six months, nine of the eleven successfully implanted patients, who were considered as responders, had an improvement of QOL and NYHA which were maintained without attenuation for the entire study period. Furthermore, the LV ejection fraction increased and the end-diastolic dimension, and the duration of the QRS interval all decreased in resynchronized patients (Table 2). So, the condition of our patients was considered to have improved (81 percent) but was considered as unchanged in two patients (19%), who had otherwise an ischemic heart disease. These two patients received consultations several times after resynchronization for acute HF. For one of them, one hospitalization with intravenous diuretic treatment was required. He presented permanent atrial fibrillation at the device's check with the programmer with a biventricular

Table 2. Effects of cardiac resynchronization on different parameters in follow-up.

Parameters	1 month	3 months	6 months	12 months
Change in patient's view of progress of QOL				
Improved	3	5	9	10
No change	8	6	2	1
Worse	0	0	0	0
Change in NYHA functional class				
Improved by two or more classes	0	3	6	6
Improved by one class	1	6	3	4
No change	10	2	2	1
Worsened	0	0	0	0
Mean Interval QRS duration (msec)	131 ± 5	-	130 ± 12	130 ± 9
Mean LV ejection fraction (%)	-	29 ± 3	36 ± 3	40 ± 3
Mean LV end-diastolic dimension (mm)	61 ± 3	59 ± 8	57 ± 13	56 ± 6
Mean LV systolic dimension (mm)	44 ± 15	42 ± 8	37 ± 4	35 ± 7

stimulation of 85%. Despite an attempt at a pharmacological ratecontrol, he remains with severely symptomatic atrial fibrillation. Finally, after an atrioventricular junction ablation, the biventricular stimulation grew up to 97% and both NYHA and QOL were improved. The second patient continued to suffer from acute Heart Failure, despite optimal medical treatment. This condition required an increase in the dose of oral diuretics. He presented neither arrhythmia nor ventricular ectopy and inappropriate lead position either during implant or through lead migration. Up to 96% of Biventricular pacing remained satisfied and the LVEF was unchanged from 29% to 30%, despite the shortened duration of QRS intervals from 140 to 120 ms after twelve months of checking.

4. Discussion

CRT implantation is a complex procedure with several limitations and hazards. First, the implantation success rate is reduced compared to conventional procedures. In our series, the overall success-rate of CRT was 92%. This is similar to or even better than experience in the CARE-HF trial (95% success-rate, [7]) and the MUSTIC, MIRACLE and COMPANION trials (92%, 92% and 90% success-rate, respectively [8] [9] [10]). The reasons for no success were mostly due to an inability to locate the coronary sinus ostium.

In our study complications occurs in three patients 3/12 (25%) (one CS dissection, one LV lead dislodgment and one phrenic nerve stimulation). A review of the literature in context to our data showed that these events can amount to about 10% - 15% [11] [12] [13] [14]. Major complications with consequences were CS lead dislodgements (due to a non-availability of active CS lead fixation) or intolerable phrenic nerve stimulation. According to this, it is of interest that non-tolerable phrenic nerve stimulation sometimes occurred. Fortunately, the worst case (intra-operative death) did not occur in our series. Others also reported a very low operative mortality rate of 0% [9] or 0.25% - 1/409 pts [7], respectively. Nevertheless, apart from these complications which can occur, the beneficial effects of cardiac resynchronization are considerable [4] [5] [7] [13] [14]. The results of the present study indicate that cardiac resynchronization therapy improves a broad range of measures of cardiac function and clinical status in patients with moderate-to-severe heart failure and a prolonged QRS interval. Cardiac resynchronization reduced the degree of ventricular desynchrony (as evidenced by a shortened duration of the QRS interval), and this effect was accompanied by both an increase in the LV ejection fraction and a decrease in the LV end-diastolic dimension [4] [5] [13] [15]. In the Cardiac Resynchronization—Heart Failure (CARE-HF) trial, LVEF increased by an absolute 3.7% at 3 months and 6.9% at 18 months from a baseline of 25% in the CRT group when compared with medical therapy [7] [17]. In the Multicenter InSync Randomized Clinical Evaluation (MIRACLE) trial, significant improvement in LVEF (absolute 3.6% vs 0.4%) was seen in patients treated with CRT compared with medical therapy [7] [18]. As a result, patients who underwent cardiac resynchronization

had significant improvements in functional capacity, clinical status, and QOL. Our findings are consistent with the results of studies that reported both hemodynamic and symptomatic improvement after cardiac resynchronization [3] [4] [5] [9] [12] [13] [14] [15]. Finally, cardiac resynchronization had a highly favorable effect on the clinical HF score. CRT not only increased the likelihood of clinical improvement but also reduced the risk of clinical deterioration during the course of follow-up. Furthermore, cardiac resynchronization was associated with fewer admissions to the hospital and fewer days in the hospital for the treatment of HF [13] [14] [15] [16] [17].

Our study suffers from limitations; we evaluated only a small number of patients. This situation is explained by the low purchasing power of the majority of our patients who cannot afford these expensive devices. The monthly income in Senegal is $119. Few people can easily pay $7250 for a CRT.

Most of our patients were able to buy the device after that several family members contributed. Statistical analysis is impossible with such a small number of patients. However, our results suggest a beneficial effect of CRT on our patients.

Another problem we faced in our study was the presence of non-responders to this therapy. Indeed, two of the eleven patients who were followed up, almost 20%, were not clinically and hemodynamically improved by cardiac resynchronization. The benefit of CRT is not seen equally in all patient groups, and there is a group of patients called "non-responders" who do not improve or might even worsen with CRT. The "non-response" rate to CRT ranges between 20 and 40% depending on the response criteria and definition used [6] [17] [19].

There are specific characteristics that have been associated with poor responses from CRT. Analysis from the CARE-HF study showed that end-stage heart failure patients, particularly those who are inotropic drug-dependent, appear to have a lesser response rate [10] [17]. Heart failure from ischemic etiology (as it is the case for our non-responders patients) has also been observed to have a worse response to CRT presumably because scar tissue can result in ineffective LV pacing and inadequate LV synchronization [18]. Insufficient conduction delay at baseline may also contribute to CRT non-response; QRS duration of 120 - 140 ms portends a lower likelihood to achieve an improved outcome as defined by reduced LVEF, rate of hospitalizations, or overall mortality. This is consistent with the idea that a shorter QRS would be expected to exhibit less mechanical **dyssynchrony** and so derive less benefit from CRT. The PROSPECT study however did not prove any specific dyssynchrony measurements to be useful for specifically predicting CRT response [19]. Finally, sinus rhythm or the presence of atrial tachyarrhythmias and/or ventricular ectopic beats may reduce the efficacy of CRT by preventive effective LV capture and synchronization; Among the reasons for non-response, atrial fibrillation (AF) plays a prominent role. AF limits the degree of biventricular pacing during CRT, not only when the ventricular rate is fast and highly irregular, but also during periods of relatively constant

rate, by causing fusion and pseudo-fusion complexes. Importantly, achievement of nearly 100% biventricular pacing is necessary to derive benefit from CRT. One of our patients who were at first non-responder was secondary greater improved after we did an AV junction ablation with a better degree of biventricular pacing [20] [21].

Non-response to CRT remains the Achilles heel of this highly beneficial treatment strategy for drug-refractory heart failure. Therefore, the prevention of CRT non-response is of utmost importance. A standardized protocol to avoid CRT non-response encompasses careful patient selection, optimal device implantation, and post-implant device programming with long-term device monitoring.

A problem we face in our country and in most of the countries in sub-Saharan Africa is the lack of health insurance and coverage or subsidy by governments for CRT devices as well as single and dual chamber pacemaker devices. This would certainly increase the population's access to these beneficial procedures and thus increased the number of implantations.

5. Conclusion

Cardiac resynchronization is a therapy that improves the quality of life of patients, the ejection fraction of the left ventricle and reduces the duration of the QRS interval. Improvements with CRT were greater in patients with a no-ischemic versus ischemic cause of Heart Failure. However, this procedure carries the risk of the possible occurrence of coronary sinus dissection, dislodgment of the LV lead and unwanted phrenic nerve stimulation by the LV lead. In sub-Saharan Africa, the major challenge is to improve the accessibility of this therapy for the population by setting up health coverage, health insurance or a subsidy by the states on the price of the devices which are very expensive.

Limitation of the Study

Low patients' number, very poor access of patients to cardiac resynchronization therapy.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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