

Impact of Cardiac Resynchronization Therapy on Heart Failure Patients: Experience from One Center

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Abstract

Background: Cardiac Resynchronization Therapy (CRT) has been proposed as a treatment of patients with idiopathic as well as ischemic left ventricular dysfunction with drug refractory heart failure and intra or inter ventricular conduction delay. CRT improves heart failure, reduces the risk of death and improves the status of LV dysfunction.

Objective: To detect the long term effect of CRT on clinical outcome in patients with heart failure.

Patients and Methods: Over a period of seven years 192 patients were subjected to CRT implantation (according to standard indication) at Critical care department, Faculty of medicine, Cairo University. Patients were assessed before implantation by history taking, clinical examination, ECG and echocardiographic parameters and then the patients were reevaluated after six months at follow visits to detect CRT effect on clinical outcome.

Results: Only 180 patients completed their follow-up visits and we found significant improvement in Ejection Fraction(EF)%, left ventricular dimensions, width of QRS complex and NYHA class (P-value<0.001) six months after CRT implantation. According to improvement in EF $\geq 10\%$ and improvement in NYHA class ≥ 1 class about 58% of our patients were considered responders to CRT and 42% were considered non responders. The percentage of decrease of QRS complex width after CRT implantation correlated significantly with the improvement in EF% (P-value<0.01). The rate of complications was low (13.8%) and all complications were managed successfully.

Conclusion: Cardiac resynchronization therapy had great positive impact on clinical outcome in patients with congestive heart failure and according to our experience in this field CRT implantation is safe with low rate of complications.

Keywords: Cardiac resynchronization therapy; Ejection fraction; Electrocardiogram; QRS complex.

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Introduction

Cardiac Resynchronization Therapy (CRT) has emerged as an effective option in treating patients with symptomatic heart failure resulting from systolic dysfunction. CRT is only one aspect of the treatment of patients with heart failure [1].

Progression of left ventricular dysfunction to heart failure with low ejection fraction (EF) is frequently accompanied by impaired

electro mechanical coupling, which may further diminish effective ventricular systolic function [1,2].

Cardiac resynchronization therapy is the term applied to re-establishing synchrony between left ventricular free wall and ventricular septal contraction in an attempt to improve left ventricular efficiency and subsequently improve functional class in patients with heart failure [3].

Cardiac resynchronization therapy has been proposed as a

treatment of patients with idiopathic as well as ischemic left ventricular dysfunction with drug refractory heart failure and intra or inter ventricular conduction delay [1,4,5].

The proven benefit of CRT includes improvement in heart failure symptoms, exercise capacity (6 minutes' walk distance), quality of life, reduces heart failure re-hospitalization, induce LV reverse remodeling and improves systolic function [1,2].

The mechanical and hemodynamic effect of CRT occurs rapidly essentially within a beat after implantation as a consequence of improvement of excitation contraction coupling which is usually impaired in heart failure patients [6,7].

The chronic effect of CRT occurs through reduction in end-systolic and end-diastolic volumes, improvement in LVEF % and improvement in heart failure symptoms and quality of life within six months of implantation as observed by most studies of CRT patients [6,8].

Cardiac resynchronization therapy (CRT) has been shown to reduce the risk of death due to heart failure (HF), improves functional status of left ventricle (LV) in patients with advanced HF and improves LV dysfunction in patients with a wide QRS complex [9].

Several studies have been conducted to study the effect of CRT on clinical outcome and to determine the unique inclusion criteria for selection of patients [6-8].

Materials and Methods

Aim of the work

The aim of the present work is to detect the long term effect of CRT on clinical outcome in patients with HF.

Patients and methods

A total of 192 patients were successfully implanted with CRT in Critical Care Medicine Department, Cairo University. Only 180 patients (146 males and 34 females) completed their follow-up visits (at least 6 months after implantation), 11 patients died and one patient was lost during follow-up.

The indication of CRT implantation was New York Heart Association (NYHA) class II, III and ambulatory IV heart failure, Left Bundle Branch Block (LBBB) and QRS duration ≥ 120 ms or non LBBB with QRS duration ≥ 150 with ejection fraction (EF) $\leq 35\%$. Patients with recent myocardial infarction, severe valvular heart lesions and severe pulmonary hypertension are not subjected to this procedure.

In our study the Candidates were considered responders to CRT if there was an increase in LVEF $\geq 10\%$ and increase in NYHA class ≥ 1 after 6 months from CRT implantation.

The following data were obtained from the follow-up files of the patients at the pacemaker follow-up clinic, the main archiving system of the critical care department, Cairo University, electronic records of the critical care department, Cairo University and direct personal contact as well and include:

- Personal history (name, age, sex).

- History analysis and clinical examination.
- Assessment of the NYHA class.
- Indications for CRT implantation.
- CRT implantation data including (route of implantation, site of coronary sinus lead)
- 12 lead ECG to assess QRS morphology, width and axis and adequacy of capturing and sensing.
- Plain X-ray chest to detect leads positions and any complications e.g pneumothorax.
- Echocardiography to detect contractility of the heart, LV dimensions, degree of MR, and post implantation complications like hemopericardium in addition to vegetation or masses involving CRT leads.
- Pacemaker malfunction and complications and how they were managed.

Statistical methods

Data were statistically described in terms of mean \pm standard deviation (\pm SD), frequencies (number of cases) and percentages when appropriate.

Comparison of numerical variables between the study groups was done using Student t test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Accuracy was represented using the terms sensitivity and specificity.

p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

Our study included 180 patients (146 males and 34 females) with a mean age 56.7 ± 8.7 years who were successfully implanted with CRT in Critical Care Medicine Department, Cairo University.

Baseline data

Underlying heart disease and NYHA Class

There were 103 patients (57.2%) with Ischemic Cardiomyopathy (ICM) and 77 patients (42.8) with Dilated Cardiomyopathy (DCM). Most of the patients presented with NYHA class III as shown in **Figures 1 and 2**.

ECG Data before implantation

ECG rhythm was sinus in 162 (90%) patients and atrial fibrillation in 18 (10%) patients. The mean QRS complex duration was 135.6 ± 15.1 msec. and the QRS morphology was LBBB in most of the patients as shown in **Table 1**.

Echocardiographic data before CRT implantation

The mean LVEF % before implantation was $30.7 + 4.3\%$. Other echocardiographic data is shown in **Table 2** and **Figure 3**.

Underlying heart disease

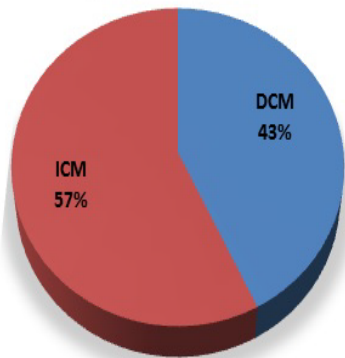


Figure 1 Underlying heart disease.

NYHA class before implantation

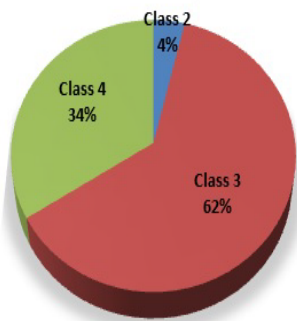


Figure 2 NYHA class before implantation.

Table 1 QRS morphology before implantation.

QRS	Frequency
LBBB	169 (93.8%)
RBBB	5 (2.7%)
IVCD	6 (3.3%)
Paced	2 (1.1%)

Table 2: LVEF and LV dimensions before CRT implantation.

Pre CRT	Mean
LVEF %	30.7+ 4.3%
LVEDd	71+7 mm
LVESd	60+ 7 mm

Cardiac resynchronization therapy implantation and complication

All the patients had the CRT device(143 CRT-Pacemaker and 49 CRT-Defibrillator) implanted, where 3 leads were implanted; one in the right ventricle (RV), one in the right atrium and the left ventricular (LV) lead was implanted via coronary sinus(CS) directed mainly to pace the lateral wall of the left ventricle as shown in **Figures 4, 5a and 5b**.

In our study complications occurred only in 25 patients (13.8%),

diaphragmatic pacing was the most common complication occurred as shown **Figure 6**.

Degree of MR before CRT implantation

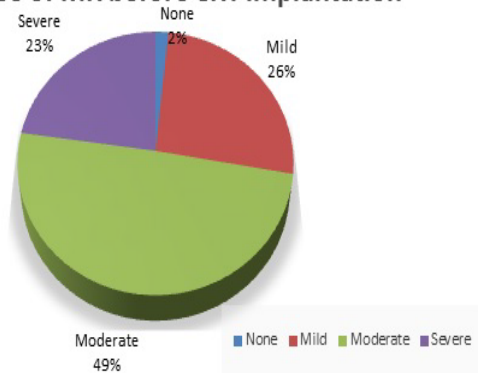


Figure 3 Degree of mitral regurgitation (MR) before CRT.

Place of LV lead

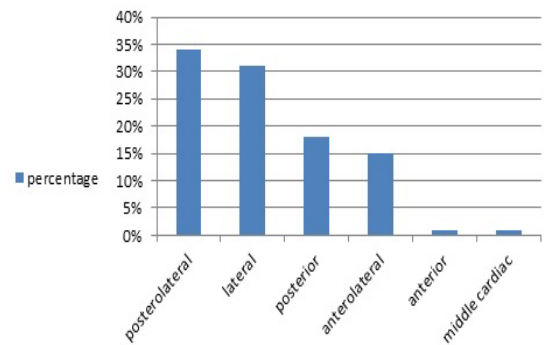


Figure 4 Position of LV lead.



Figure 5a Coronary venogram in the left anterior Oblique (LAO) view showing the coronary sinus anatomy.

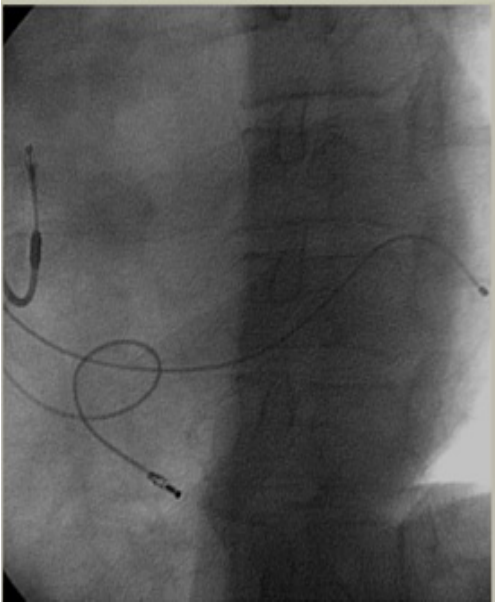


Figure 5b LAO view showing the CS lead in the posterolateral branch of CS, RV lead in the RV apex and atrial lead in the atrial appendage.

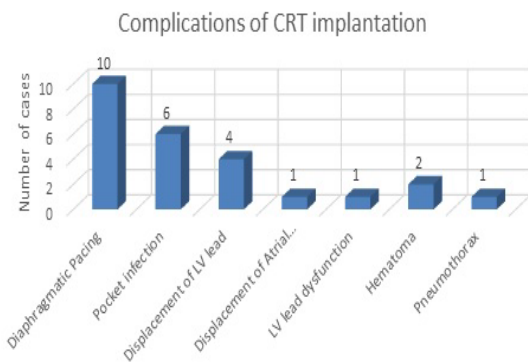


Figure 6 Complications of CRT implantation.

Post implantation data and comparing it with baseline data

NYHA class

There was a significant improvement of NYHA class after CRT implantation (P value<0.001), 72.2% of patients improved with at least 1 NYHA class, 61.6% improved in one NYHA class, 10.55% showed an improvement of two NYHA classes and 27.8% did not improve in NYHA class after CRT implantation (Table 3).

QRS width

There was a significant decrease in QRS width after CRT implantation (P value<0.001). As shown in Table 4 and Figures 7a and 7b.

Echocardiographic data

There was a significant improvement of LVEF%, LVEDd and

LVESd (P value<0.001) after CRT implantation. Also there was an improvement in the degree of MR after CRT implantation Table 5 and Figure 8.

Cardiac Resynchronization Therapy responders

The Candidates were considered responders to CRT if there was an increase in LVEF $\geq 10\%$ and improvement in NYHA class ≥ 1 class after CRT implantation, we found that 105 patients (58.33%) were considered responders and 75 patients (41.66%) were not responders. We did not found significant differences between responders and non-responders either in gender or the underlying heart disease (Figures 9-11).

Table 3 NYHA class before and after pacing.

NYHA	Pre CRT	Post CRT	P-Value
Class 2	7 (3.8%)	80 (44.4%)	
Class 3	112 (62.2%)	97 (53.8%)	
Class 4	61 (33.8%)	3 (1.6%)	
Mean NYHA	3.3 +/- 0.5	2.6 \pm 0.5	<0.001

Table 4 Duration of QRS complex before and after pacing.

	Pre-CRT		Post-CRT		P-value
	Mean	SD	Mean	SD	
QRS duration	135.6	15.1	105.9	13.7	<0.001

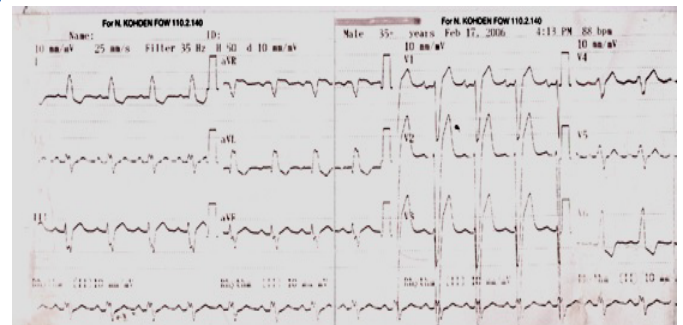


Figure 7a ECG before pacing (QRS width 150 ms).

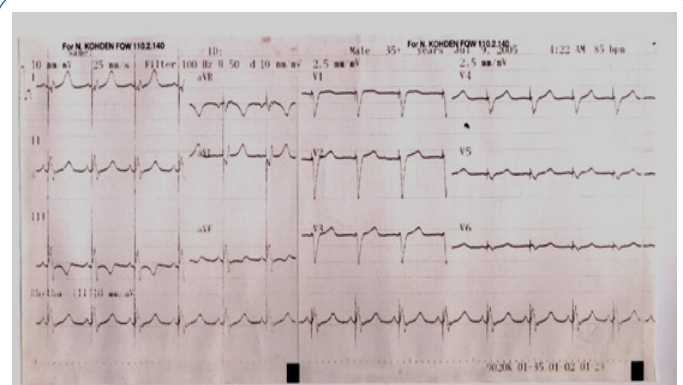


Figure 7b ECG after CRT (QRS width 130 ms).

Correlation between QRS width and improvement in LVEF% after CRT implantation

In our study, as the percentage of decrease in QRS width after CRT implantation increased, there was a significant improvement in LVEF % after CRT implantation, (P-value<0.01). This is shown in **Figure 12**.

Mortality after CRT implantation

Eleven patients died (5 with refractory heart failure, 4 with sudden cardiac death, 1 with cerebrovascular accident and 1 with lymphoma).

The underlying cardiac pathology of the 11 mortality patients was ischemic in 7 patients and idiopathic in 4 patients and the

Table 5 EF and LV dimensions pre and post pacing.

	Pre-CRT		Post-CRT		P-value
	Mean	SD	Mean	SD	
LVEF%	30.70%	4.3	36.60%	4.1	<0.001
LVEDd	71 mm	7	65 mm	7	
LVESd	60 mm	7	55 mm	7	

Degree of MR before and after pacing

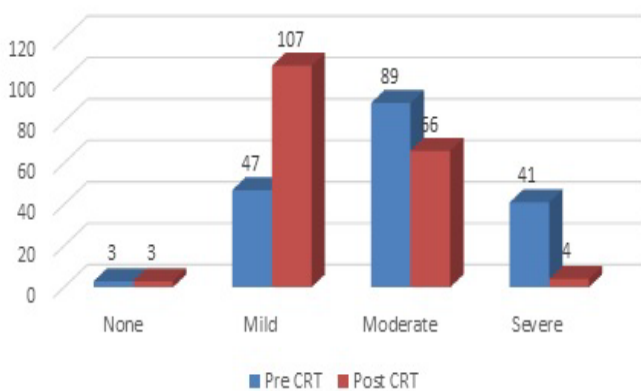


Figure 8 Degree of MR before and after CRT.

Percentage of responders to CRT according to increase in LVEF ≥ 10% and improvement of NYHA ≥ 1 class

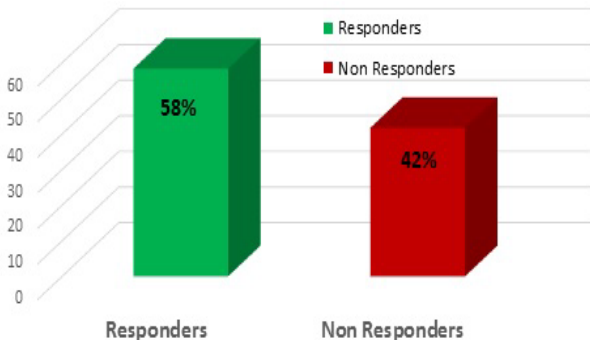


Figure 9 Percentage of responders to CRT.

Relationship between response to CRT and gender

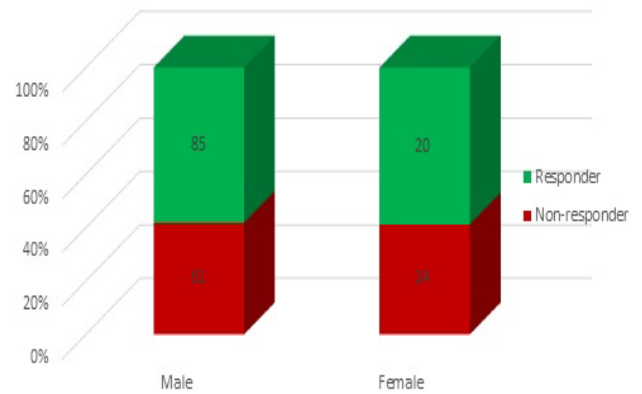


Figure 10 Relation between response to CRT and gender.

Relationship between Response to CRT and underlying cause of HF

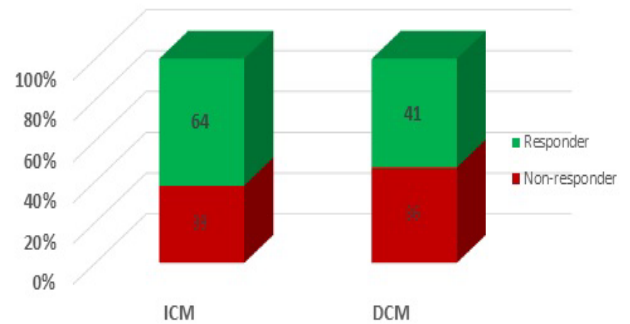


Figure 11 Relation between response to CRT and cause of HF.

Percentage of QRS narrowing

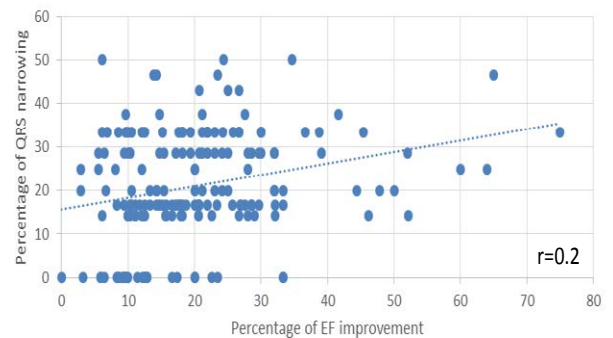


Figure 12 Percentage of QRS narrowing vs. percentage of EF improvement.

functional class was NYHA IV in 8 patients and NYHA III in 3 patients. The underlying rhythm was sinus in 10 patients and AF in one patient.

Discussion

Cardiac Resynchronization Therapy (CRT) has emerged as an effective option in treating patients with symptomatic heart failure resulting from systolic dysfunction. CRT is only one aspect of the treatment of patients with heart failure [1].

Cardiac Resynchronization Therapy has been shown to improve heart failure, reduce the risk of death and improve the status of LV dysfunction. However, a number of patients remain unresponsive to the therapy. The cause of unresponsiveness has been an issue of research in many trials and has a concern in follow-up of CRT patients [3,10-12].

In our study there were 103 patients (57.2%) had ischemic cardiomyopathy (ICM) and 77 patients (42.8%) had dilated cardiomyopathy (DCM), The large number of patients with ICM in our study was attributed to the large number of ischemic patients in our community and with advance in their management in our department including primary intervention, the mortality rate reduced and some of them became myopathic.

Contrary to our expectations there was no significant difference (P-Value 0.3) in response to CRT between patients with ICM and patients with DCM.

In our study, the position of LV pacing lead was in posterolateral branch of coronary sinus in 62 patients (34.3%), lateral branch in 55 patients (30.6%), posterior branch in 32 patients (17.8%), anterolateral branch in 28 patients (15.6%), and 3 patients in non-optimal position (anterior and middle cardiac branches), and we tried to follow the data obtained from the sub-analysis of MADIT-CRT which showed that an apical LV lead position resulted in a significant increased risk for heart failure and death [13] by inserting the leads in basal or mid ventricular position rather than an apical position.

In our study the rate of complications was low reflecting the experience of our center in this field. Complications occurred only in 25 patients (13.8%), most of them (10 cases) were diaphragmatic pacing which were corrected by reprogramming the device except in one patient who was managed by replacing the battery with another one with more LV pacing configuration. Six cases with pocket infection 2 of them were managed by removing the old system and re-implantation in the other side, after complete recovery of infection and the other 4 cases, the infection was mild and superficial and they were managed by IV antibiotics and local dressing. Four cases with LV lead displacement and repositioning was done, one case with LV lead dysfunction and the lead was changed and 1 case with atrial lead displacement and repositioning was done. Two cases with hematoma with conservative measures, one case with pneumothorax and intercostal chest tube was inserted then removed after expansion of the lung occurred.

Our study focused on the pre and post implantation echocardiographic changes that occur in patients after CRT implantation and the effect of CRT on clinical outcome of patients within months after implantation.

In our study and in concordance to other major and small studies there was a significant decrease in LV diameters, increase in EF% (P-value<0.001) and reduction in MR degree 6 months after CRT implantation [14-16].

Mitral regurgitation is one of the echocardiographic changes that predict CRT reverses remodeling and clinical improvement.

This improvement in MR could be explained by the effect of resynchronization on the papillary muscles and the better cooptation of the leaflets as a result of this synchronization. The decrease in the contraction time possibly leads to a decrease in the MR. The reverse remodeling and reduction of the LV dimensions can explain further improvement at follow-up.

Further investigations are warranted to combine CRT with specific MR therapeutic approaches such as surgical annuloplasty or percutaneous therapies to maximize the effect of CRT in MR patients [17].

In our study, The Candidates considered responders to CRT if there was an increase in LVEF $\geq 10\%$ after CRT and improvement in NYHA class ≥ 1 class 6 months after CRT implantation and according to this 105 patients (58.33%) were considered responders and 75 patients (41.66%) were not responders and this rate is in concordance with other studies [10-12,18,19].

In a trial to find any predictor to CRT response, gender and underlying heart disease failed to predict this response but ECG succeeded to predict CRT response where in our study when we correlated between the QRS width and improvement in LVEF% after CRT implantation, we found that there was a significant improvement in LVEF% as the percentage of decrease in QRS width increased (P-value <0.01).

Our results agreed with the study of Cazeau et al. [20], who studied 100 patients with successful CRT implantation, he found that 63 patients had a decrease in QRS complex post CRT implantation and as the percentage of decrease in QRS width after implantation increased; there was an improvement in LVEF % and clinical outcome post implantation [20].

The results of Zhang et al. were in concordance with our study as he studied 132 patients with different QRS durations in 3 groups, a group of Cardiac Contractility Modulation therapy, CRT group with narrow QRS complex and a third group with CRT and a wide QRS complex. Cardiac Contractility Modulation (CCM) is a new device therapy for advanced heart failure due to systolic dysfunction. It works by applying a relatively high voltage electrical signal to the myocardium during the absolute refractory period of the contractile cycle [21].

The study found that there was a significant improvement in CCM group in NYHA class and life style of the patients but better results were observed in CRT group patients who had a wide QRS complex ≥ 150 ms [21].

Approximately 200 CRT devices were implanted in Critical Care Medicine Department, Cairo University. We tried to help the poor patients with severe heart failure refractory to medical treatment. The patients showed variable degrees of improvement and we achieved acceptable experience in this field.

Conclusion

Cardiac resynchronization therapy had great positive impact on

clinical outcome in patients with congestive heart failure and according to our experience in this field CRT implantation is safe and with low rate of complications.

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