Cardiac Resynchronization Therapy for Heart Failure in National Hospital of Sri Lanka from Year 2005 to 2020 – A Retrospective Observational Study.

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Abstract

Background

Cardiac resynchronization therapy (CRT) has been a well-established treatment modality for moderate to severe left ventricular systolic dysfunction with dyssynchrony. This is the pioneering study which has been conducted in Sri Lankan context to analyze the cohort which has undergone CRT implantation in National Hospital of Sri Lanka (NHSL), Colombo from 2005–2020.

Objectives

This study was carried out to describe socio demographic factors, improvement in clinical outcome (symptoms, electrocardiographic and echocardiographic features) and post CRT complications in the study population and also to determine the efficacy of CRT in heart failure.

Method

A retrospective observational study was conducted on patients who have undergone CRT implantation from 2005 to 2020. The data was gathered from all the consented patients who visited device programming clinic using a physician-administered questionnaire and clinical records. Data was analyzed using software SPSS 25 and significant statistics were assessed with McNemer test, Student T test and Chi-Squared test.

Results

Study included 50 patients with a mean age of 52.82+/-11.66 years and female predominance (56%, n = 28). Idiopathic dilated cardiomyopathy (50%, n = 25) was the leading etiological factor followed by ischemic Cardiomyopathy (28%, n = 14). Clinical symptoms had been improved significantly with CRT implantation ($p < 0.001$). A significant improvement was found in NYHA functional class ($p < 0.001$, 95% CI = 0.072 to 0.284), QRS width ($p < 0.001$, 95% CI = 0.229 to 0.534), ejection fraction ($p < 0.001$, 95% CI = -16.437 to -8.504) and LV EDD ($p < 0.001$, 95% CI = 2.89 to 9.24). Post CRT complications included lead malfunction acute (6%, n = 3) and chronic (14%, n = 7), bleeding/ hematoma (2%, n = 1), pocket erosion/ infection (6%, n = 3), infective endocarditis (2%, n = 1).

Conclusion

The study has shown the efficacy of CRT in moderate to severe heart failure with significant clinical and functional improvement.

Introduction

Heart failure(HF) is defined as a complex clinical syndrome, which results from any structural or functional disorder that impairs the ability of the ventricle to fill or eject blood, characterized by specific symptoms such as orthopnea and dyspnea, and signs such as edema [1]. With the prolonged survival of the aging population and the prolongation of lives of cardiac patients by modern therapeutic modalities, heart failure prevalence is on the rise [2]. The etiology of heart failure can be due to a defect in pericardium, epicardium, myocardium, endocardium, heart valves or a metabolic cause. Despite the definitive management of the etiological factor, the management of heart failure always follows the same strategic principles as the pathophysiological mechanisms of heart failure are the same.

According to the international guidelines, the management of heart failure with reduced ejection fraction includes the management of the cause of HF and comorbid diseases, monitoring and prevention of further deterioration, lifestyle modifications, pharmacological therapy, cardiac rehabilitation, palliative care, device therapy and cardiac transplantation. The devices used in heart failure include CRTs, ICDs, left ventricular assist devices and cardiac contractility modulation therapy [4, 5, 6]. In cardiac resynchronization therapy (CRT), cardiac pacing is used in patients with left ventricular (LV) systolic dysfunction and dyssynchronous ventricular activation. The mechanism it helps to correct in failing heart is; providing simultaneous or nearly simultaneous electrical activation of the LV and right ventricle (RV) via stimulation of the LV and RV (biventricular pacing) or LV alone. This is achieved by a CRT-pacemaker (CRT-P) and the CRT-P combined with a Defibrillator(CRT-D) provides treatment for malignant ventricular arrhythmias. The bi-ventricular pacing is usually done by a routine intravenous RV pacing and specifically placed LV lead through coronary sinus branch to achieve LV pacing as intra-cavitary LV pacing is fraught with technical difficulties and high risk of systemic thrombo-embolism.

Randomized clinical trials have demonstrated that CRT reduces mortality, reduces hospitalizations, and improves functional status in patients with LVEF $\leq$ 35 percent and QRS duration $\geq$ 150 ms (largely with LBBB) with NYHA functional class II, III, or ambulatory IV HF [6–10]. Depending on these criteria, the response to CRT varies, with a non-respondent rate ranging from 25–30%. CRT devices are expensive, particularly for a resource poor country like Sri Lanka where most patients are dependent on government free health services. Therefore proper selection of suitable candidates is very important.

There are large number of trials which have investigated on CRT implantation outcome parameters in developed countries. Despite CRT implantations been in operation in Sri Lanka for more than a decade, there is no previously published data on this area. This study has been conducted to fill that deficit and it will eventually help in improving proper selection and deliver of CRT in the Sri Lankan contest.

Methodology

Patient selection and eligibility criteria

A retrospective observational study was done using the details of all the heart failure patients who have undergone CRT implantation during the period of 2005 to 2020 in National Hospital of Sri Lanka – Colombo. Ethical review committee approval was obtained from Postgraduate Institute of Medicine (Ethical approval number : ERC/PGIM/047). Physician-administered questionnaire was used as the study instrument which consisted of 4 subsections, namely socio demographic factors, clinical background, pre CRT implantation (clinical, ECG and echo) assessment, post CRT implantation assessment (clinical, ECG and echo) and complications associated with CRT implantation. The list of patients who fulfilled the eligibility criteria were identified from the patient registry and prepared according to the chronological order. The patients/relatives were contacted and requested to pay a visit to the hospital after giving brief introduction about the study verbally. At the hospital visit, prior to administration of the questionnaire, an information sheet and consent form was distributed among the subjects. The questionnaires were administered by the investigators for the consenting participants during their device programming clinic visit and clinic records were used to gather retrospective data. The data gathering was continued and finished over a 6 months period.

Statistical analysis

All the gathered data was analyzed using descriptive statistics. Correlational statistics were used to analyze the relationship between indication and clinical improvement parameters. Considering the sample size, the statistical significance of observed parameters were determined as follows. The paired dependent qualitative variables were analyzed using Mc Nemer test, while paired dependent quantitative variables were analyzed using Student T test. Chi-square test was used to analyze the significance of independent paired variables. Data was analyzed using the software SPSS version 25.

Results

The total number of participants who has been undergone Cardiac Resynchronization Therapy (CRT) for heart failure during the study period (2005–2020) at NHSL Colombo and presented to follow-up clinics was 50 with a mean age of 52.82 years (standard deviation +/- 11.66). There was a female predominance (56%, n = 28) and majority of patients (60%, n = 30) had received CRT implantation within 5 years of heart failure been diagnosed (Table 1). Diabetic Mellitus (50%, n = 25), hypertension (42%, n = 21), dyslipidemia (28%, n = 14) and coronary artery disease (24%, n = 12) were the leading comorbidities in descending prevalence with CRT implanted cohort.

Table 1
Baseline characteristics of the overall study population (n = 50)

	Frequency	Percentage (%)
Men/Women (n)	22/28	44/56
Duration of symptoms	30	60
• < 5 years	7	14
• 5–10 years	13	26
• > 10 years		
Associated comorbidities	25	50
• Diabetes Mellitus	21	42
• Hypertension	14	28
• Dyslipidemia	12	24
• Coronary artery disease	10	20
• BA/COPD	8	16
• Others (Hypothyroidism, Obesity, AF)		

BA- Bronchial Asthma, COPD- Chronic Obstructive Pulmonary Disease, AF- Atrial Fibrillation

The most frequent etiological factor for the heart failure was idiopathic dilated cardiomyopathy (52%, n = 26) followed by ischemic cardiomyopathy (28%, n = 14) with an equal contribution from hypertension and peripartum cardiomyopathy (6%, n = 3). (Table 2)

Table 2
Etiologies for CRT Implantation RV- Right ventricular, LV- Left Ventricular

Etiology	Frequency	Percentage
Idiopathic Dilated Cardiomyopathy	26	52%
Ischemic Cardiomyopathy	14	28%
Hypertension	3	6%
Peripartum Cardiomyopathy	3	6%
High RV pacing	1	2%
Pacemaker induced heart failure	1	2%
Intermittent heart block leading to LV dysfunction	1	2%
Valvular Heart Disease	1	2%
Total	50	100%

CRT showed a significant clinical improvement ($p < 0.001$) in heart failure associated symptoms following cardiac resynchronization. (Table 3)

Table 3
Symptomatic improvement following CRT implantation

Symptoms	Pre CRT-Percentage	Post CRT-Percentage	Mcnemer test value	95% CI
Dyspnea on exertion	96%	48%	< 0.01	0.254–4.276
Dyspnea at Rest	32%	2%	< 0.01	0.972–1.092
Orthopnea	54%	14%	< 0.01	0.593–0.926
Paroxysmal nocturnal dyspnea	42%	2%	< 0.01	0.866–1.048
Fatigue	58%	8%	< 0.01	0.745–0.997
Edema	36%	6%	< 0.01	0.678–1.025

NYHA class

The majority (66%) belongs to NYHA class III and IV before CRT implantation. In the assessment of NYHA class improvement, at least 1 class increment was considered as an ‘improvement’ (n = 42, 84%), whereas

reduction or unchanged NYHA class were considered as ‘not improved’ (n = 8, 16%). A significant improvement of NYHA functional class was identified with therapeutic CRT Implantation (Fig. 1) ($p < 0.001$, 95% CI = 0.072 to 0.284). EF improvement following CRT implantation in less symptomatic heart failure (NYHA class I, II) was 60% (n = 9) and more symptomatic heart failure (NYHA class III, IV) was 79.3% (n = 23).

QRS width Improvement

Majority of patients’ QRS width was > 150ms before CRT implantation (Fig. 2). Out of the total study population, narrowing of QRS width by cardiac resynchronization was 59.08% (n = 26) while further widening of QRS or unchanged was 40.92% (n = 18). Overall a statistically significant improvement in QRS width was highlighted ($p < 0.001$, 95% CI = 0.229 to 0.534).

Out of QRS width improved population (n = 26), EF improved in 73.07% (n = 19), EF not improved in 26.92% (n = 7).

Out of QRS width improved, (n = 26), 88.4% have improved their NYHA class while 11.53% have not improved the NYHA class

EF Improvement

Mean pre CRT left ventricular ejection fraction of study population was 30.91% with a standard deviation of +/-10.28%. Following CRT implantation the mean EF was improved to 43.38% with standard deviation of +/-13.27%. Paired sample T test highlights a significant improvement in ejection fraction ($p < 0.001$, 95% CI = -16.437 to -8.504), with a mean of 12.47% EF improvement with standard deviation of +/-13.047%. There is a significant difference in EF improvement in female subgroup (n = 22, 78.57%) compared to male subgroup (n = 10, 45.45%), which shows a higher beneficial effects of CRT in females compared to males. In addition LV EDD following CRT has improved significantly $p < 0.001$, 95% CI = 2.89 to 9.24)) to mean Post CRT LVEDD 53.8+/-12.49mm from mean Pre CRT LVEDD 59.8+/-10.59 mm. Average LV EDD improvement was 10.7mm and median LVEDD improvement was 10mm.

Level of recommendation of CRT implantation according to guidelines

Out of the total study population, 73.33% (n = 33) CRT implantations had been carried out according to guideline recommendation and 26.66% (n = 12) CRT implantations were not according to guideline recommendation.

EF improvement in guideline recommended implantations were 78.78% compared to EF improvement in cases in which CRT implantations done without guideline recommendation was 21.21%. But it is not statistically significant as chi-square test value was 0.170 (95% CI = 0.175 to 0.259).

Complications

The most frequent complication seen in this study was acute (6%, n = 3) and chronic (14%, n = 7) lead malfunctions. The rest of the complications seen were bleeding/ hematoma (2%, n = 1), pocket erosion/ infection (6%, n = 3), infective endocarditis (2%, n = 1) in descending frequencies. No other significant complications like pneumothorax, vascular /cardiac damage was noted peri or post operatively.

Discussion

The Institute of cardiology, National Hospital of Sri Lanka, Colombo has been the leading tertiary care center, which entertain the referrals from all around the country as well as direct admissions. The cardiac electrophysiology service has started in year 2005 and since then for more than a decade, this institute was the main service supplier. This study has bridged the gap of evidence deficiency in CRT implantation including follow up consequences by evaluating the demographics and clinical parameters and analyzing the efficacy of CRT as a heart failure treatment modality.

According to the international literature, the mean age of CRT implantation in USA was 65.4 (+/-10.8) years, UK 63.9 ± 10.7 years and a meta-analysis done in Korea has shown a range from 58 to 72 years [1, 2, 12]. These age ranges are higher compared to the mean age of the study population which was 52.82+/-11.66 years. This shows the impact of age in selecting patients for CRT implantation as well as life expectancy differences in Sri Lanka compared to other developed countries with higher health care facilities and higher life expectancy.

According to census data in National Statistics in Sri Lanka the gender distribution of the country is male 48.4% and female 51.6% [3]. This might have been a factor for this study population to have a female predominance (56%). In contrast, most of the studies done in developed countries has shown a male predominance such as in USA 72%, UK 68%, France 81.2% [1, 2, 13]. The beneficial effects of CRT implantation in the study population of females has shown better values than male (female = 78.57%, male = 45.45%). This trend has been seen in a study which was conducted in USA in 2015 [14].

The prevalence of associated comorbidities of heart failure in the CRT implanted population in Sri Lanka has shown that hypertension and diabetic mellitus as the predominant conditions. A study conducted in Canada in year 2010 has shown similar distribution of comorbidities in heart failure patients who had undergone resynchronization therapy, which highlights a prevalence of hypertension (52%) and diabetic (16%) [15].

A meta-analysis on cardiac resynchronization in patients with symptomatic heart failure and a study which was conducted by Mark A. Ileret et al have shown that ischemic cardiomyopathy as the leading etiological factor for heart failure (58% and 65% respectively) [16, 17]. But in this study, most of the patients had idiopathic dilated cardiomyopathy as the major contributing factor for heart failure. This might not have affected the outcome of data, as it was shown by meta-analysis done in USA in 2013, that CRT has similar benefits in both ischemic and non ischemic groups [18].

There was a significant improvement in NYHA functional class with CRT implantation in this study population and almost a similar functional class improvements have been observed in two separate studies done in USA in 2007, 2008 (59% improvement) and UK in 2022 (52% improvement) [2, 19]. In contrast to subgroup analysis of NYHA functional class in this study, Alan J. Banka et al. has conducted a study done in Minnesota during 2012 which shows that, improvement of clinical status, LV function and size of NYHA functional class I/II CRT patients were good or better than those in NYHA functional class III/ IV [20]. A similar trend has been observed in a meta-analysis which was done by Nawaf S. Al-Majed et al. in 2011[11].

QRS width has been considered as a surrogate marker to measure the efficacy of CRT implantation improvement. The functional class improvement of NYHA has been 88.4% for the subgroup of QRS width improved. Studies done in Canada and Korea have shown the similar beneficial effect of QRS improvement with regard to CRT efficacy [21, 12]. Sander G. Molhoek et. al. in Netherlands has observed that baseline QRS width is not a good predictor to determine the efficacy of CRT [22].

Several international studies have shown a pre CRT EF of 20% – 30%, whereas our study has a mean pre CRT EF of 30.91+/-10.28%. This might be resulted by less stringent adherence of guideline recommendation to CRT implantation [7, 13, 23]. Most of the meta-analysis done in western part of the world during early 21st century proves a significant improvement in EF following CRT [7, 9, 24].

A significant improvement of LV EDD has been noted in a study done by William T. Abraham et al. in UK which has shown a median LV EDD improvement with CRT implantation of -3.5mm in patients with mean of pre CRT LV EDD as 70 ± 10mm comparable to the similar findings in our study which has been noted as 10mm median LV EDD improvement in patients with 59.8+/-10.59 mm mean pre CRT LVEDD [9].

The rate of complications have been low in this study compared to other international systematic reviews and meta-analysis done during 2003 to 2007 [7, 11, 16], but this may be due to the low population number.

Limitations :

The cardiac electrophysiology was a new entity in cardiology field of Sri Lanka which was introduced in year 2005 with the limited resources. It was gradually expanded over past years gaining new experiences. With these circumstances, there was a limitation of data which had led to reduced total number of patients who were eligible for the study as well as less availability of medical records as some of them were discarded and missing. In addition, In addition the number of implants were low particularly in the early years as CRT was a relatively new procedure and as most patients were dependent on free devices through the National Health system, the availability of devices were also restricted. Mortality could not be assessed as planned due to difficulty of following up patients over past 15 years.

Conclusion

CRT implantation in Sri Lanka has provided significant improvement clinically, as well as in assessments of ECG, echo criteria in our patients, comparable to international results.. The availability of CRT as a treatment modality for heart failure patients should be improved in our country as it has proven benefits. Strict adherence to international criteria would further improve results, particularly in a resource poor country such as ours.

Declarations

Ethics approval and consent to participate - This study was approved by the Ethics Review Committee of the Post Graduate Institute of Medicine in Sri Lanka (ERC/PGIM/2018/55). Patient's informed consent was also obtained. All methods were performed in accordance with all relevant guidelines and regulations.

Consent for publication – Not applicable

Availability of data and materials - The datasets used during this study are available from the corresponding author on reasonable request.

Competing interest - All authors declare that they do not have any conflicts of interest.

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References

1. *Hypertension and heart failure | circulation* (no date). Available at: https://www.ahajournals.org/doi/full/10.1161/circulationaha.111.059303 (Accessed: May 2, 2023).
2. D; HK. B.L. (no date) *The epidemiology of heart failure: The framingham study*, *Journal of the American College of Cardiology*. U.S. National Library of Medicine. Available at: https://pubmed.ncbi.nlm.nih.gov/8376698/ (Accessed: May 2, 2023).
3. (No date) *Department of Census and Statistics*. Available at: http://www.statistics.gov.lk/GenderStatistics/StaticalInformation/Population (Accessed: 10 June 2023).
4. 2021 *ESC guidelines for the diagnosis and treatment of acute and chronic heart failure* (no date) *European Society of Cardiology*. Available at: https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Acute-and-Chronic-Heart-Failure (Accessed: May 2, 2023).
5. Overview. : *Chronic heart failure in adults: Diagnosis and management: Guidance* (no date) *NICE*. Available at: https://www.nice.org.uk/guidance/ng106 (Accessed: May 2, 2023).
6. *2022 AHA/ACC/HFSA guideline for the management of heart … pubmed* (no date). Available at: https://pubmed.ncbi.nlm.nih.gov/35363499/ (Accessed: May 2, 2023).
7. McAlister FA, Ezekowitz J, Hooton N, Vandermeer B, Spooner C. ;Dryden DM;Page RL;Hlatky MA;Rowe BH; (no date) *Cardiac resynchronization therapy for patients with left ventricular systolic dysfunction: A systematic review*, *JAMA*. U.S. National Library of Medicine. Available at: https://pubmed.ncbi.nlm.nih.gov/17565085/ (Accessed: May 2, 2023).
8. Cazeau S;Leclercq C;Lavergne T;Walker S;Varma C;Linde C;Garrigue S;Kappenberger L;Haywood GA;Santini M;Bailleul C;Daubert JC;; (no date) *Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay*, *The New England journal of medicine*. U.S. National Library of Medicine. Available at: https://pubmed.ncbi.nlm.nih.gov/11259720/(Accessed: May 2, 2023).
9. Abraham WT;Fisher WG;Smith AL;Delurgio DB;Leon AR;Loh E;Kocovic DZ;Packer M;Clavell AL;Hayes DL;Ellestad M;Trupp RJ;Underwood J;Pickering F;Truex C;McAtee P;Messenger J;; (no date) *Cardiac resynchronization in chronic heart failure*, *The New England journal of medicine*. U.S. National Library of Medicine. Available at: https://pubmed.ncbi.nlm.nih.gov/12063368/(Accessed: May 2, 2023).
10. St John Sutton MG;Plappert T;Abraham WT;Smith AL;DeLurgio DB;Leon AR;Loh E;Kocovic DZ;Fisher WG;Ellestad M;Messenger J;Kruger K;Hilpisch KE;Hill MR;; (no date) *Effect of cardiac resynchronization therapy on left ventricular size and function in chronic heart failure*, *Circulation*. U.S. National Library of Medicine. Available at: https://pubmed.ncbi.nlm.nih.gov/12668512/(Accessed: May 2, 2023).
11. *Meta-analysis: Cardiac resynchronization therapy for patients with less …* (no date). Available at: https://www.ncbi.nlm.nih.gov/books/NBK81822/ (Accessed:May 2, 2023).
12. Kang S-H et al. (no date) *Cardiac resynchronization therapy and QRS duration: Systematic Review, meta-analysis, and meta-regression*, *https://doi.org*i>/10.3346/jkms.2015.30.1.24. Available at:

<urlz>https://jkms.org/DOIx.php?id=10.3346%2Fjkms.2015.30.1.24</urlz> (Accessed: May 2, 2023).

13. Lecoq G et al. (2005) *Clinical and electrocardiographic predictors of a positive response to cardiac resynchronization therapy in advanced heart failure*, *OUP Academic*. Oxford University Press. Available at: https://academic.oup.com/eurheartj/article/26/11/1094/2888016 (Accessed: May 2, 2023).
14. Costanzo MR. (2015) "Cardiac resynchronization therapy in women," *Cardiac Electrophysiology Clinics*, 7(4), pp. 721–734. Available at: https://doi.org/10.1016/j.ccep.2015.08.018.
15. Thibault B et al. (2011) "Evaluation of resynchronization therapy for heart failure in patients with a QRS duration greater than 120 ms (greater-earth) trial: Rationale, design, and Baseline Characteristics," *Canadian Journal of Cardiology*, 27(6), pp. 779–786. Available at: https://doi.org/10.1016/j.cjca.2011.03.010.
16. McAlister FA et al. (2004) "Systematic review: Cardiac resynchronization in patients with symptomatic heart failure," *Annals of Internal Medicine*, 141(5), p. 381. Available at: https://doi.org/10.7326/0003-4819-141-5-200409070-00101.
17. Iler MA et al. (2008) "Prognostic value of electrocardiographic measurements before and after cardiac resynchronization device implantation in patients with heart failure due to ischemic or nonischemic cardiomyopathy," *The American Journal of Cardiology*, 101(3), pp. 359–363. Available at: https://doi.org/10.1016/j.amjcard.2007.08.043.
18. Makki N, Swaminathan PD, Olshansky B. (2013) "Does cardiac resynchronization therapy benefit patients with ischemic and non-ischemic cardiomyopathy similarly?," *International Journal of Cardiology*, 168(4), pp. 4378–4380. Available at: https://doi.org/10.1016/j.ijcard.2013.05.052.
19. De Marco T et al. (2008) "Impact of cardiac resynchronization therapy on exercise performance, functional capacity, and quality of life in systolic heart failure with QRS prolongation: Companion trial sub-study," *Journal of Cardiac Failure*, 14(1), pp. 9–18. Available at: https://doi.org/10.1016/j.cardfail.2007.08.003.
20. Bank AJ et al. (2012) "Comparison of cardiac resynchronization therapy outcomes in patients with New York Heart Association Functional Class I/II versus III/IV Heart Failure," *Journal of Cardiac Failure*, 18(5), pp. 373–378. Available at: https://doi.org/10.1016/j.cardfail.2012.01.015.
21. Bryant AR et al. (2013) "Association between QRS duration and outcome with cardiac resynchronization therapy: A systematic review and meta-analysis," *Journal of Electrocardiology*, 46(2), pp. 147–155. Available at: https://doi.org/10.1016/j.jelectrocard.2012.12.003.
22. MOLHOEK SG, et al. QRS duration and shortening to predict clinical response to cardiac resynchronization therapy in patients with end-stage heart failure. Pacing Clin Electrophysiol. 2004;27(3):308–13. 10.1111/j.1540-8159.2004.00433.x.
23. Trucco E et al. (2018) "Improvement of reverse remodeling using electrocardiogram fusion-optimized intervals in cardiac resynchronization therapy," *JACC: Clinical Electrophysiology*, 4(2), pp. 181–189. Available at: https://doi.org/10.1016/j.jacep.2017.11.020.

24. Sutton SJ, M.G., et al. Effect of cardiac resynchronization therapy on left ventricular size and function in chronic heart failure. Circulation. 2003;107(15):1985–90. 10.1161/01.cir.0000065226.24159.e9.

Figures

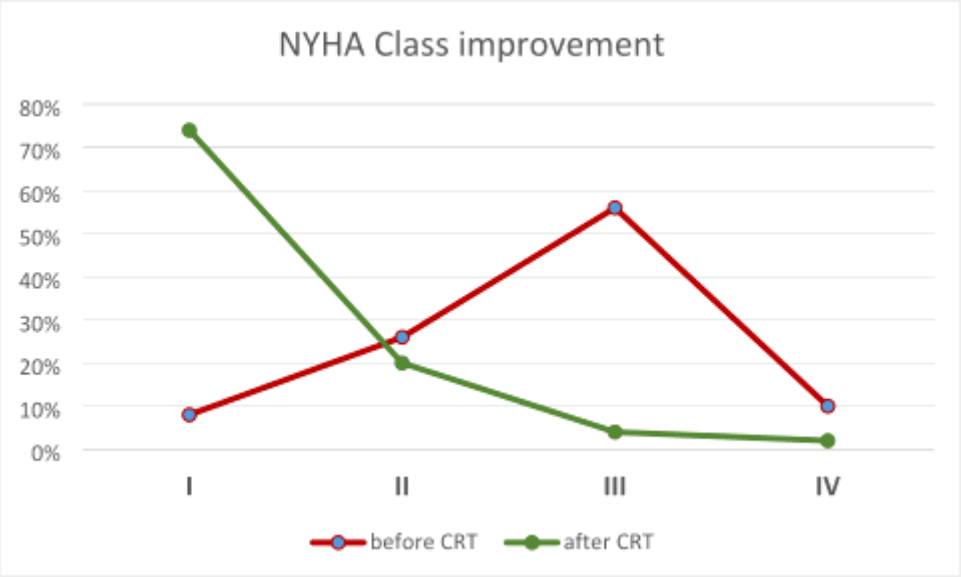

Figure 1

Distribution of NYHA functional class before and after CRT implantation

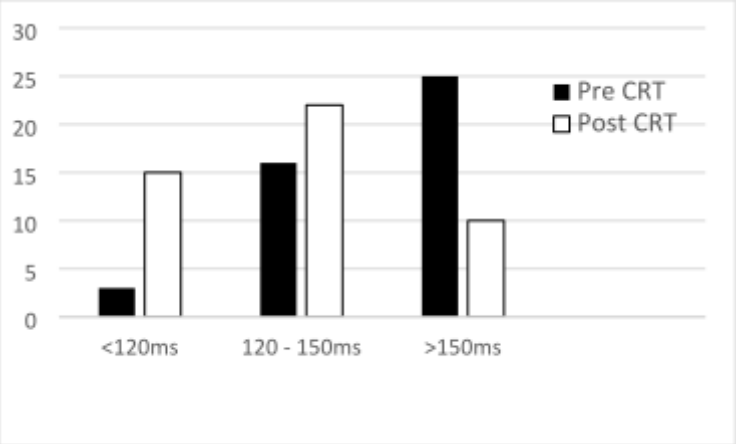

Figure 2

Change of QRS width by CRT implantation