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ORIGINAL RESEARCH ARTICLE

Response predictors to cardiac resynchronization therapy in chronic heart failure: a 10-year-cardiovascular center experience

Predictores de respuesta a la terapia de resincronización cardíaca en insuficiencia cardíaca crónica: 10 años de experiencia en un centro cardiovascular

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Abstract

Background: *Cardiac resynchronization therapy (CRT) has been established as an effective therapy for heart failure with reduced ejection fraction. Randomized clinical trials have shown its impact on mortality and HF hospitalizations, as well as improvement of symptoms and quality of life.* **Objectives:** *Finding clinical, electrocardiographic, and echocardiographic variables that may predict the response to cardiac resynchronization therapy (CRT).* **Methods:** *We performed a single-center, observational, analytic, and retrospective study that included 102 patients with heart failure (HF) diagnosis who underwent CRT according to guideline-directed therapy from January 2010 to April 2020 in a third-level center. CRT response was defined as an improvement of New York Heart Association functional class in at least 1 category associated with a recovery of ≥ 5% in the left ventricular ejection fraction (LVEF).* **Results:** *Our study population was 102 patients of which 61 (59.8%) were men. The mean age at HF diagnosis was 54 ± 18.7 years. Ischemic heart disease was the etiology in 37 (36.3%) cases. Fifty-one (50%) patients were classified as responders. Responders had wider QRS, and lower LVEF and right ventricular fractional area change at baseline. After CRT, responders had a greater reduction of QRS duration, and improvement in LVEF, global longitudinal strain, and echocardiographic dyssynchrony parameters. Multivariate regression analysis showed that left bundle branch block (LBBB), left ventricular end-diastolic volume (LVEDV), tricuspid annular plane systolic excursion (TAPSE), and baseline difference of pre-ejection periods were predictors of a positive response to CRT in this population.* **Conclusions:** *LBBB, TAPSE, LVEDV, and pre-ejection time difference are independent variables that can predict adequate response to CRT.*

Keywords: *Heart failure. Cardiac resynchronization therapy. Predictors. Ventricular synchrony.*

Resumen

Antecedentes: *La terapia de resincronización cardíaca (TRC) se ha establecido como una terapia efectiva para la insuficiencia cardíaca con fracción de eyección reducida. Ensayos clínicos aleatorizados han demostrado su impacto en la mortalidad y hospitalizaciones por insuficiencia cardíaca, así como la mejora de los síntomas y la calidad de vida.* **Objetivos:** *Determinar las variables clínicas, electrocardiográficas y ecocardiográficas que puedan predecir la respuesta a la terapia de resincronización cardíaca (TRC).* **Método:** *Estudio unicéntrico, observacional, analítico, retrospectivo, que incluyó 102 pacientes con diagnóstico de IC sometidos a TRC y terapia dirigida por guías, de enero de 2010 a abril de 2020, en un centro de tercer nivel. La respuesta a TRC fue definida como mejoría de la clase funcional de la New York Heart Association en al menos 1 categoría, asociado*

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con una recuperación ≥ 5% en la fracción de expulsión del ventrículo izquierdo (FEVI). **Resultados:** *Incluimos a 102 pacientes, 61 (59.8%) fueron hombres. El promedio de edad al diagnóstico de IC fue 54 ± 18.7 años. La cardiopatía isquémica fue la etiología en 37 (36.3%) pacientes. 51 (50%) pacientes, fueron clasificados como respondedores. Los respondedores presentaron QRS amplio, menor FEVI y menor fracción de acortamiento del ventrículo derecho al inicio del estudio. Después de la TRC, los respondedores tuvieron una mayor reducción en la duración del QRS, mejoría en la FEVI, strain longitudinal global y parámetros de disincronía ecocardiográfica. El análisis de regresión multivariado mostró que el bloqueo de rama izquierdo (BRI), el volumen telediastólico del ventrículo izquierdo (VTDVI) la excursión sistólica del plano anular tricuspídeo (TAPSE) y la diferencia basal del período expulsivo fueron predictores de respuesta positiva a TRC.* **Conclusiones:** *BRI, TAPSE, VTDVI y la diferencia basal de períodos preexpulsivos son variables independientes que predicen respuesta adecuada a TRC.*

Palabras clave: *Insuficiencia cardíaca. Terapia de resincronización cardíaca. Predictores. Sincronía ventricular.*

Introduction

Cardiac resynchronization therapy (CRT) has been established as an effective therapy for heart failure (HF) with reduced ejection fraction. Randomized clinical trials have shown its impact on mortality and HF hospitalizations, as well as improvement of symptoms and quality of life (QoL)[1-8]. However, a substantial proportion of patients receiving CRT, ranging from 20% to 40%, is classified as non-responders, presenting a lack of improvement or even worsening of outcomes after the intervention[1,7,9-14]. Considering this, as well as the increasing list of guideline-approved indications for CRT and, with the understanding that CRT is a high-cost therapy that is not exempt from complications, interest has migrated toward the identification of variables that predict response to CRT before its application.

The present research aims at analyzing clinical, electrocardiographic, and echocardiographic variables that can act as predictors of CRT response.

Materials and methods

We conducted an observational, retrospective, retrolective, and single-center study in patients with HF diagnosis who underwent CRT in a period from January 2010 to April 2020 in the National Institute of Cardiology in Mexico City. The study was designed to analyze clinical, electrocardiographic, and echocardiographic data before and after CRT to identify variables capable of predicting a successful response to therapy.

A successful response to CRT was defined as an improvement in New York Heart Association (NYHA) functional class in conjunction to an increase of at least 5% in the left ventricle ejection fraction (LVEF).

Inclusion criteria for the study were adults over 18 years old, with HF diagnosis and who had undergone CRT, based on recommendations approved for this treatment, from January 2010 to April 2020. All those with recommendation IA, IIa, and IIb for CRT were considered candidates[15]. Patients were excluded if they had a previous diagnosis of atrial flutter/fibrillation, previous pacemaker implantation, and loss of follow-up or incomplete data up to 6 months after CRT. We defined the left bundle branch block (LBBB) according to AHA/ACC/HRS recommended criteria[16].

Statistical analysis

Qualitative variables were described as frequencies and proportions and were analyzed with Pearson's independence test (χ^2) or Fisher's exact test. Quantitative variables were analyzed with Shapiro-Wilk's normality test and described as parametric (mean, standard deviation, and minimum-maximum) or non-parametric (median, interquartile range, and minimum-maximum). We constructed a block-entry logistic regression model, adjusted by age and sex, for determining the risk factors that predicted response to CRT. $P < 0.05$ was considered statistically significant for all analyses. Data were analyzed with Statistical Package for the Social Sciences ver. 25.

Results

The overall population of our study included initially 127 patients, after applying the exclusion criteria only 102 patients were considered (Fig. 1). Within these exclusion criteria, we considered those who had previously had a pacemaker placed and those with previously diagnosed atrial fibrillation or flutter, as they are not based on the same selection criteria for CRT.

Of these 102 patients, 41 were women (40.2%), and 61 were men (59.8%). The mean age at HF diagnosis was 54 ± 18.7 years, and the mean age at CRT device implantation was 56 ± 14.5 years. The average time from diagnosis to CRT was 3.16 ± 2.7 years. HF etiology was ischemic heart disease in 37 (36.7%) patients, while non-ischemic etiology (chagasic, peripartum, chronic myocarditis, etc.)

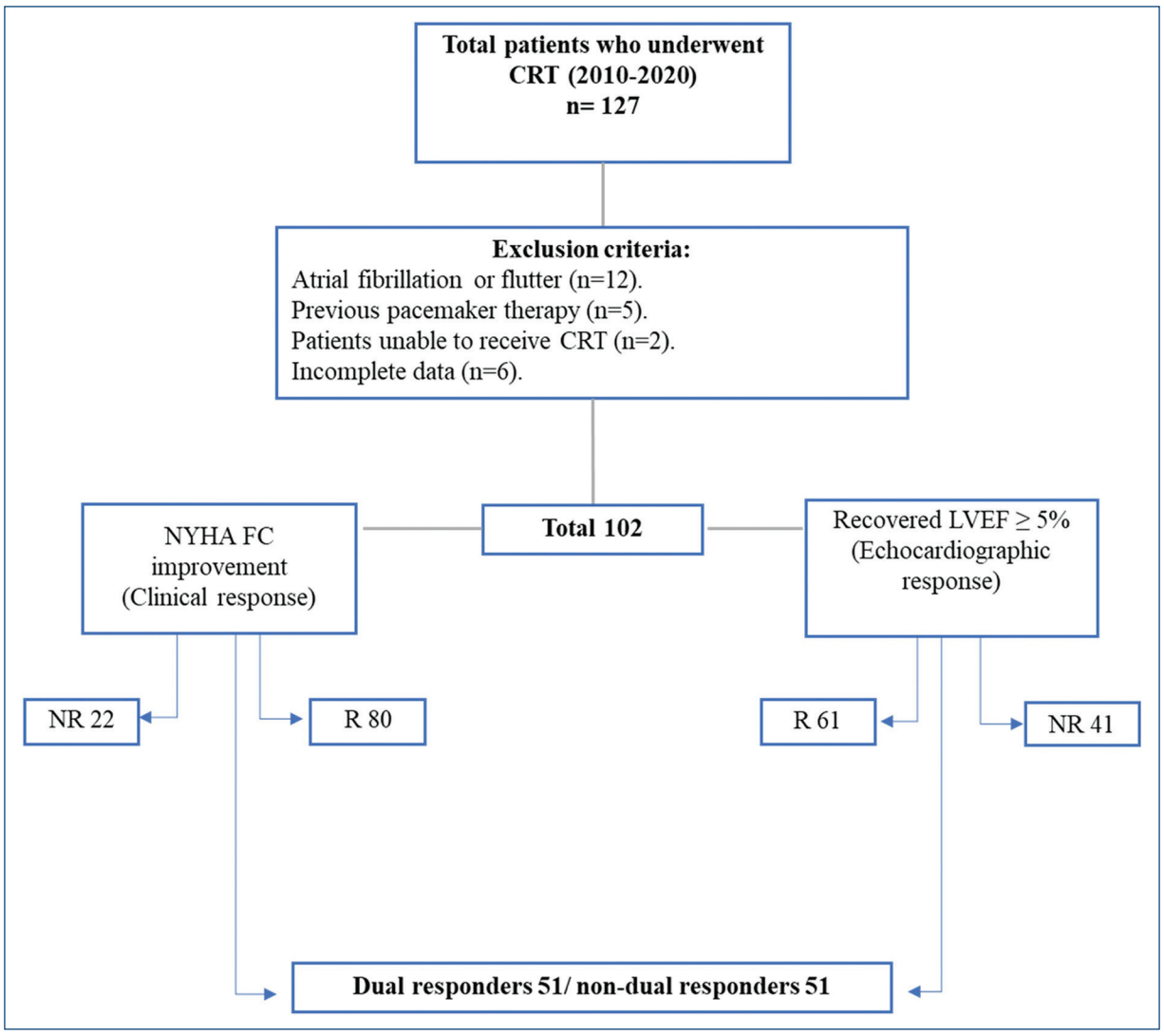

Figure 1. Patient selection and classification.
CRT: cardiac resynchronization therapy; FC: functional class; LVEF: left ventricular ejection fraction; NR: non-responder; NYHA: New York Heart Association; R: responder.

was diagnosed in the remaining population. Systemic hypertension was present in 50 (49%) patients and diabetes mellitus in 27 (26.5%). Most patients were classified as NYHA II-III (92.2%). Regarding the type of device implanted, 80 (78.4%) were undergone to CRT-defibrillator (CRT-D).

A successful response to CRT according to functional class and LVEF was achieved in 51 (50%), while the rest were classified as non-responders. Only 87 patients (85.3%) had an electrocardiogram (ECG) with LBBB registered before device implantation. PR interval was 188.7 ± 47.5 ms and 148.9 ± 35.8 ms before and after therapy, while QRS mean duration went from 160 ± 29.4 ms to 124.7 ± 28 ms.

The baseline echocardiographic data showed mean LVEF of 23.7 ± 7.7%, left ventricular end-diastolic volume (LVEDV) of 139.1 ± 66.4 mL, left ventricular end-systolic volume (LVESV) of 108.5 ± 60.5 mL and global longitudinal strain (GLS) –8.1 ± 4.4% before CRT, all of which improved afterward (LVEF 35.5 ± 11.2%, LVEDV 121.3 ± 51.1 mL, LVESV 87 ± 47.5 mL, and GLS –11 ± 3.3%). General population characteristics are summarized in table 1.

Analysis of the population divided into responders and non-responders showed similar clinical and biochemical characteristics (Table 2). ECG findings showed a wider baseline QRS in responders (155 ± 31 ms vs. 167 ± 26 ms; p = 0.04). Furthermore, QRS reduction

Table 1. General population: clinical, biochemical, electrocardiographic, and echocardiographic characteristics before and after CRT

Variables	Total (n = 102)
Age at HF diagnosis (years)	54 ± 18.7
Women, n (%)	41 (40.2)
Age at CRT (years)	56 ± 14.5
Time from HF diagnosis to CRT (years)	3.16 ± 2.7
Device CRT-D/CRT-P, n (%)	80 (78.4) / 22 (21.6)
Hypothyroidism (%)	18 (17.3)
Arterial hypertension, n (%)	50 (49)
Diabetes mellitus, n (%)	27 (26.5)
BMI Kg/m^2	26 ± 3.9
Ischemic etiology of HF, n (%)	37 (36.3)
Complete OMT before CRT, n (%)	67 (65.7)
NYHA class, n (%) I II III I	 6 (5.82) 53 (51.9) 41 (40.3) 2 (1.98)
LVEF improvement > 5% after CRT, n (%)	61 (58.7)
NYHA class improvement after CRT, n (%)	80 (78.4)
Dual responder, n (%)	51 (50)
Sodium before CRT mEq/L	138 ± 3.9
Creatinine before CRT mg/dL	1.14 ± 0.6
Uric acid pre-CRT mg/dL	7.05 ± 2.4
NT pro-BNP pre-CRT pg/mL	9020 ± 17913
Sodium post-CRT mEq/L	139 ± 3.2
Creatinine post-CRT mg/dL	1.16 ± 0.47
Uric acid post-CRT mg/dL	6.5 ± 2.2
NT proBNP post-CRT pg/mL	7926 ± 15608
Electrocardiogram LBBB pre-CRT, n (%) PR segment pre-CRT (ms) QRS duration pre-CRT (ms) PR segment post-CRT (ms) QRS duration post-CRT (ms)	 87 (85.3) 188.7 ± 47.5 160 ± 29.4 148.9 ± 35.8 124.7 ± 28
Echocardiogram before CRT LVEF (%) LVEDV mL/m^2 LVESV mL/m^2 LA volume mL/m^2 GLS RVFAC (%) TAPSE PSAP mmHg VA coupling	 23.7 ± 7.7 139.1 ± 66.4 108.5 ± 60.5 51.2 ± 18.5 –8.1 ± 4.4 37.8 ± 12.7 18.6 ± 4.9 40.6 ± 14.6 0.53 ± 0.22

(Continues)

Table 1. General population: clinical, biochemical, electrocardiographic, and echocardiographic characteristics before and after CRT *(continued)*

Variables	Total (n = 102)
Echocardiogram after CRT LVEF (%) LVEDV mL/m^2 LVESV mL/m^2 LA volume mL/m^2 GLS RVFAC (%) TAPSE PSAP mmHg VA coupling	 35.5 ± 11.2 121.3 ± 51.1 87 ± 47.5 49.9 ± 23.9 –11 ± 3.3 38.9 ± 15.2 18.4 ± 4.8 40.1 ± 16 0.62 ± 0.90

CRT: cardiac resynchronization therapy; BMI: body mass index; GLS: global longitudinal strain; HF: heart failure; LA: left atrium; LBBB: left bundle branch block; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricle ejection fraction; LVESV: left ventricle end-systolic volume; NYHA: New York Heart Association; PSAP: pulmonary arterial systolic pressure; RVFAC: right ventricle fractional area change; TAPSE: tricuspid annular plane systolic excursion; VA: ventriculoarterial; CRT-P: CRT-pacing.

after CRT was significantly higher in the responder subgroup (16 ± 23% vs. 24 ± 17%; p = 0.04). There was no significant difference in the prevalence of LBBB among groups, even though it was more commonly present in responders (Table 3).

In echocardiographic variables, we identified a lower LVEF (26 ± 8.5% vs. 21.6 ± 6.2%), and right ventricular fractional area change (RVFAC) (41 ± 13% vs. 35 ± 12%) in patients with an adequate response to treatment (p < 0.05). Among measurements of ventricular dyssynchrony, the delay between right and left ventricular pre-ejection times was higher in the responder group (38 ± 23 ms vs. 53 ± 27 ms; p = 0.04) (Table 4).

After CRT, responders had a greater improvement in LVEF (27.4 ± 10.2% vs. 37.6 ± 9.8%; p = 0.001), GLS (–7 ± 2.5% vs. –14 ± 2.8%; p = 0.02), LVESV (100 ± 50 mL vs. 67 ± 37 mL; p = 0.01), and LVEDV (132 ± 55 mL vs. 106 ± 42 mL; p = 0.04). There was also a reduction in the proportion of patients with severe mitral regurgitation, the difference between pre-ejection times, and the delay in peak-to-peak septal to posterior wall strain, all of which indicate a greater improvement of the left ventricular function and ventricular synchrony in patients responding to CRT (Table 5).

Age and sex-adjusted multivariate regression analysis demonstrated that LBBB (OR 3.81, 95% IC 1.110-35.5; p = 0.003), LVEDV (OR 0.926, 95% IC 0.7-0.97; p = 0.009), tricuspid annular plane systolic excursion (TAPSE) (OR 2.147, 95% IC 1.203-3.832; p = 0.01), and the basal difference between pre-ejection times (OR 4.5, 95% IC 1.170-27.12; p = 0.001) were associated to

Table 2. Clinical and biochemical variables according to CRT response

Variables	Non-responders (n = 51)	Responders (n = 51)	p
Women, n (%)	19 (18.6)	22 (21.6)	0.5
Age at HF diagnosis (years)	53 ± 12	55 ± 13	0.56
Age at CRT	56.3	55.6	0.81
Device, n (%) CRT-P CRT-D	 10 (19.6) 41 (80.4)	 12 (23.5) 39 (76.5)	0.81
Arterial hypertension, n (%)	25 (24.5)	25 (24.5)	1.0
Diabetes, n (%)	11 (10.8)	16 (15.7)	0.26
BMI kg/m^2	25.9 ± 4.5	26.1 ± 3.4	0.79
Ischemic etiology of HF, n (%)	19 (18.6)	18 (17.6)	0.83
OMT previous to CRT, n (%)	30 (29.4)	37 (36.3)	0.14
NYHA pre-CRT, n (%) I II III IV	 6 (5.9) 27 (26.5) 17 (16.7) 1 (1)	 0 (0) 26 (25.5) 24 (23.5) 1 (1)	0.65
Sodium pre-CRT mEq/L	138.2 ± 3.9	138.3 ± 4	0.91
Sodium post-CRT mEq/L	138.6 ± 3	139.4 ± 3.4	0.29
Creatinine pre-CRT mg/dL	1.23 ± 0.7	1.06 ± 0.4	0.21
Creatinine post-CRT mg/dL	1.2 ± 0.5	1 ± 0.3	0.09
Uric acid pre-CRT mg/dL	7.3 ± 2.7	6.8 ± 2.1	0.4
Uric acid post-CRT mg/dL	6.9 ± 2.6	6.1 ± 1.8	0.15
NT proBNP pre-CRT pg/ml	7935.8 ± 15090	10053 ± 20571	0.71
NT proBNP post-CRT pg/ml	7412 ± 14911	8591 ± 16909	0.82

HF: heart failure; BMI: body mass index; NYHA: New York Heart Association; CRT: cardiac resynchronization therapy; CRT-D: CRT-defibrillator; CRT-P: CRT-pacing.

Table 3. Electrocardiogram before and after CRT according to response to therapy

Variables	Non-responders (n = 51)	Responders (n = 51)	p
LBBB (%)	41 (80.3)	46 (90.2)	0.16
No LBBB (%)	10 (19.7)	5 (9.8%)	0.18
PR segment pre-CRT (ms) mean ± SD	186 ± 41	191 ± 54	0.65
QRS duration pre-CRT (ms) mean ± SD	155 ± 31	167 ± 26	0.04
QRS ≥ 150 ms, n (%)	26 (51)	36 (70.5)	0.03
QRS 120-149 ms (%)	25 (49)	15 (29.4)	0.52
PR segment post-CRT (ms) mean ± SD	152 ± 43	145 ± 27	0.41
QRS duration post-CRT (ms) mean ± SD	126 ± 31	123 ± 26	0.58
Delta QRS (%) mean ± SD	16 ± 13	24 ± 17	0.04

LBBB: left bundle branch block; SD: standard deviation; CRT: cardiac resynchronization therapy.

Table 4. Echocardiographic parameters before CRT according to response to therapy

Variables	Non-responders (n = 51)	Responders (n = 51)	p
LVEF (%)	26 ± 8.4	21.5 ± 6.2	0.003
LVEDV mL/m^2	139 ± 54	139 ± 80	0.98
LVESV mL/m^2	101 ± 50	118 ± 72	0.37
LA volume mL/m^2	52 ± 19	50 ± 18	0.65
GLS	–6 ± 2.5	–11 ± 2.9	0.054
E/e´ relation	19 ± 10	19 ± 9	0.47
RVFAC (%)	41 ± 13	35 ± 12	0.04
TAPSE	18 ± 5	20 ± 5	0.06
TRV m/s	3 ± 1	3 ± 1	0.68
Tricuspids' velocity	9 ± 2	9 ± 3	0.64
PSAP (mmHg)	41 ± 17	41 ± 13	0.92
VA coupling	1 ± 0	1 ± 0	0.69
LVOT pre-ejection period (ms)	127 ± 55	148 ± 38	0.19
RVOT pre-ejection period (ms)	105 ± 31	104 ± 30	0.64
Difference between LVOT and RVOT pre-ejection periods (ms)	38 ± 23	53 ± 27	0.04
Septal and posterior wall activation delay (ms)	200 ± 89	205 ± 71	0.90
Diastolic filling time (%)	48 ± 15	50 ± 13	0.60
Severe mitral regurgitation n (%)	12 (23)	8 (15.6)	0.07

CRT: cardiac resynchronization therapy; GLS: global longitudinal strain; LA: left atrium; LBBB: left bundle branch block; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricle ejection fraction; LVESV: left ventricle end-systolic volume; LVOT: left ventricular outflow tract; NYHA: New York Heart Association; PSAP: pulmonary arterial systolic pressure; RVFAC: right ventricle fractional area change; RVOT: right ventricular outflow tract; TAPSE: tricuspid annular plane systolic excursion; VA: ventriculoarterial.

successful response to CRT. Unlike previously reported in other cohorts, gender, HF, and basal QRS duration were not predictors of improvement (Table 6 and Fig. 2).

Discussion

There is robust evidence that shows a reduction in mortality and improvement of symptoms and QoL in HF patients that undergo CRT[1-8]; however, even with strict application of currently approved selection criteria, 20-40% of patients do not respond adequately to therapy[1,7,9-14]. This is a growing concern on account of the rise on prevalence of HF globally and broadening of selection criteria for CRT by international guidelines[17].

In our population, the mean age at diagnosis of HF was 54 years old, lower than other studies in which it is around 65 years old[18-20], and the proportion of women was higher than in most other studies on the matter (40.2 vs. 20-30%)[19,21]. Furthermore, ischemic heart disease was the etiology of HF in only 36.7%, while in other studies, such as that of van Bommel et al.[21], it represented the majority of the population. All of these differences from other studies in the literature could be explained by the selection bias conditioned by our center's patient population and explain the fact that age, sex, and etiology were not predictors of response to therapy.

There is no universally accepted definition of response to CRT, and the reported success of treatment varies from 32% to 91% according to the criteria used[22]. Our study used a definition of response to CRT that considered an improvement by clinical assessment (NYHA functional class) associated with LVEF improvement (≥ 5%) by echocardiography since it is the most widely used echocardiographic parameter due to its clinical prognostic value[23]. While it is true that there is no specific cutoff point for LVEF increase to consider a patient a responder, multiple studies have proposed a cutoff of at least 5%[18,24].

Table 5. Echocardiographic parameters after CRT according to response to therapy

Variables	Non-responders (n = 51)	Responders (n = 51)	p
LVEF (%)	27.4 ± 10.2	37.6 ± 9.8	0.001
LVEDV mL/m^2	132 ± 55	106 ± 42	0.04
LVESV mL/m^2	100 ± 50	67 ± 37	0.01
LA volume mL/m^2	53 ± 25	46 ± 23	0.34
GLS	–7 ± 2.5	–14 ± 2.8	0.02
E/e´ relation	15 ± 7	13 ± 7	0.5
RVFAC (%)	37 ± 16	42 ± 13	0.2
TAPSE	15 ± 5	20 ± 5	0.01
TRV m/s	3 ± 1	3 ± 0	0.8
Tricuspids' velocity	10 ± 4	11 ± 2	0.27
PSAP (mmHg)	41 ± 19	39 ± 12	0.52
VA coupling	1 ± 1	1 ± 0	0.1
LVOT pre-ejection period (ms)	136 ± 36	125 ± 33	0.30
RVOT pre-ejection period (ms)	107 ± 35	107 ± 30	0.99
Difference between LVOT and RVOT pre-ejection periods (ms)	39 ± 26	22 ± 20	0.03
Septal and posterior wall activation delay (ms)	137.5 ± 30	97.5 ± 37	0.04
Diastolic filling time (%)	48.5 ± 14	47.0 ± 15	0.76
Severe mitral regurgitation n (%)	8 (15.6)	3 (5.8)	0.02

CRT: cardiac resynchronization therapy; GLS: global longitudinal strain; LA: left atrium; LBBB: left bundle branch block; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricle ejection fraction; LVESV: left ventricle end-systolic volume; LVOT: left ventricular outflow tract; NYHA: New York Heart Association; PSAP: pulmonary arterial systolic pressure; RVFAC: right ventricle fractional area change; RVOT: right ventricular outflow tract; TAPSE: tricuspid annular plane systolic excursion; VA: ventriculoarterial.

When assessing both aspects of the definition the rate of response in the population of our study was 50%. If patients were classified as responders according to functional class only, the rate of success would be 78.4%, and it would be 58.7% if the classification was through LVEF exclusively. This confirms the findings in other studies that describe clinical improvement as predominant over echocardiographic parameters[18].

The heterogeneous approach to defining response to CRT is a potential barrier to progress in this field. If these different response criteria show poor agreement, then the ability to generalize results from multiple studies is severely impaired, and a standard criteria need to be developed[22].

Another important aspect of the population of this study is that only 65.7% fulfilled the requirement of optimal medical therapy for HF before device implantation which is considerably lower than compliance in other studies that reached up to 80%[25]. This could be a factor associated with a lower response to CRT in our study.

Analysis between responders and non-responders in this study showed no significant difference in clinical or biochemical variables. Both groups have CRT-D devices implanted in 80% of cases; this indicates a high risk of sudden cardiac death in the cohort and may correlate with greater severity of disease compared to other studies that had a greater proportion of patients implanted with CRT-Pacing[24,26].

Responders to CRT had a longer basal QRS duration and a greater shortening after device implantation. This finding is compatible with Lapidot et al., who described a reduction of QRS duration of 20 ms or more as an independent predictor of improvement as measured by major adverse cardiovascular events[27].

About echocardiographic measurements, LVEF and RVFAC before initiation of therapy were lower in

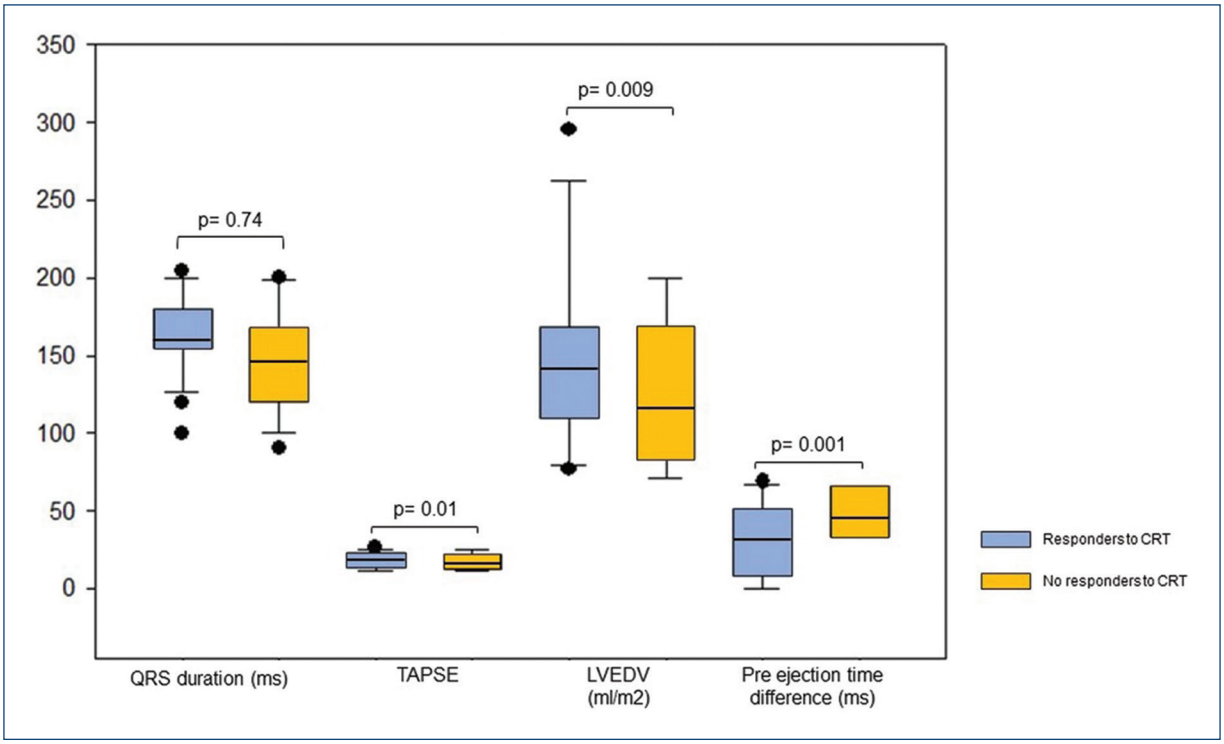

Figure 2. Predictors of good response to CRT.
CRT: cardiac resynchronization therapy; TAPSE: tricuspid annular plane systolic excursion; LVEDV: left ventricular end-diastolic volumen.

responders than non-responders. These parameters and electrocardiographic differences previously described are consistent with a population with worse ventricular function and more evidence of dyssynchrony responding favorably to therapy.

After CRT, responders had a significant reduction of the left ventricular volumes and mitral regurgitation which represents reverse ventricular remodeling and functional improvement in this group, as reported previously by Pitzalis et al.[28] and Jin et al.[25].

Before device implantation, there was no significant difference in GLS between groups; however, responders had a greater improvement in this parameter. This coincides with a meta-analysis by Bazoukis et al.[29] who propose GLS as a defining factor of a successful response to CRT.

Comparison between groups also showed a significant difference in TAPSE, which was reduced in non-responders after CRT while staying the same in those with a proper response. This is probably a sign of adverse remodeling and a continuation of the natural progression of HF in the non-responder population. TAPSE has also been previously assessed as a predictor of CRT response by Cappelli et al., who found a significant correlation between this parameter and reverse remodeling of the left ventricle, unlike with other right ventricle parameters[30].

After multivariate regression analysis, LBBB, LVEDV, TAPSE, and the delay in pre-ejection periods were response predictors. LBBB as a predictor of CRT response has been extensively validated, nevertheless, the latino population are underrepresented in all cohort studies designed to discern predictors of good response to CRT[20,31-33]. The role of basal ventricular volumes is confirmed, as lower quantities are associated with a higher rate of clinical response[19,25,31,34].

Dyssynchrony measurement by echocardiography has not been a predictor of response in previous studies[35]; however, it showed a significant correlation in this population, which might be related to demographic and etiologic particularities outlined earlier.

We highlight that previously validated variables such as sex, etiology, and QRS duration[1-3,7,8,19] were not predictors of response to therapy in our study. This could be explained by various factors, including the more significant proportion of women and non-ischemic etiology of heart disease as compared with previous cohorts.

Table 6. CRT response prediction variables multivariate regression analysis

Variables	OR (95% IC)	p
Female sex	2.54 (0.172-37.57)	0.49
Ischemic etiology	1.2 (0.76-18.9)	0.89
LBBB	3.81 (1.110-35.5)	0.003
QRS duration pre-CRT	0.962 (0.759-1.219)	0.74
LVEF pre-CRT	0.886 (0.732-1.076)	0.226
LA volume pre-CRT	0.943 (0.861-1.03)	0.205
LVESV pre-CRT	0.814 (0.7-1.94)	0.78
LVEDV pre-TCR	0.926 (0.7-0.97)	0.009
Severe mitral regurgitation pre-CRT	2.82 (0.26-30.78)	0.39
TAPSE pre-CRT	2.147 (1.203-3.832)	0.01
Difference between LVOT and RVOT pre-ejection periods	4.5 (1.170-27.12)	0.001
Age at CRT	0.95 (0.861-1.05)	0.37
Time between HF diagnosis and CRT	1.25 (0.786-2.1)	0.34
BMI	0.94 (0.805-1.26)	0.94

CRT: cardiac resynchronization therapy; BMI: body mass index; GLS: global longitudinal strain; HF: heart failure; LA: left atrium; LBBB: left bundle branch block; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricle ejection fraction; LVESV: left ventricle end-systolic volume; LVOT: left ventricular outflow tract; NYHA: New York Heart Association; PSAP: pulmonary arterial systolic pressure; RVFAC: right ventricle fractional area change; RVOT: right ventricular outflow tract; TAPSE: tricuspid annular plane systolic excursion.

Conclusions

The present study is the first to assess the characteristics and response of HF patients undergoing CRT in Mexico, showing a population with demographic and clinical variables different from those reported in the international literature and confirming that there are electrocardiographic and echocardiographic variables such as LBBB, LVEDV, TAPSE, and the basal difference between pre-ejection times capable of predicting successful response to treatment, in addition to showing that other previously validated variables were not predictors of response in our study.

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None.

Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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