Comparison of echocardiographic parameters of biventricular versus left ventricular pacing in cardiac resynchronization therapy

Comparaison des paramètres échographique de la resynchronisation par stimulation biventriculaire versus la stimulation VG unique

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Summary

Introduction: Cardiac resynchronization therapy (CRT) improves systolic function in heart failure patients with ventricular conduction delay by stimulating the left ventricle (LV) or both ventricles (biventricular, BIV). Optimal LV site selection is of major clinical interest for CRT device implantation. However, little is known about LV versus BIV pacing. Thus, the objective of this study was to compare electrical and echographic parameters before and after CRT and to compare BiV and LV pacing via echocardiographic parameters.

Methods: LV and BIV pacing were tested sequentially in 20 patients (mean age 54 ± 13 years, 80% males) with preexisting biventricular devices. Initial BIV configuration was switched to LV configuration or vice versa, and echocardiographic images were acquired for analysis. Regional and global LV longitudinal mechanics were assessed with 2D speckle-tracking echocardiography.

Results: A total of 20 patients (mean QRS interval before resynchronization: 161,17 ±7 ,mean LV ejection fraction (LVEF) before resynchronization: 27.9 ± 8.9) enrolled in this study. CRT was administered with LV and BV stimulation in DDD mode. LV stimulation was at the lateral free wall, whereas right ventricular stimulation was fixed near the apex. Different echographic parameters were compared for LV to BIV pacing: LVEF, diastolic function, and LV global longitudinal strain.

There was no significant difference in the echographic study of the left ventricle between LV pacing and BIV pacing (BIV LVEF: 43,33 ± 12,48 % VS LV LVEF: 42,57 ± 14,32 %, p=0,64; BIV LGS: -11,00 ± 4,51% vs LV LGS: -11,05±4,02 p=,925); time to peak between opposite walls (septal and lateral) (53,23 ±68,89 VS 153,3 ±158,7 , p=0,118).

Conclusion: There is no difference in the echocardiographic parameters of the LV between BIV and LV pacing stimulation.

Keywords

Heart failure, resynchronization, Asynchronisme, Echocardiography, longitudinal global strain

Résumé

Introduction : La resynchronisation cardiaque améliore la fonction systolique du ventricule gauche chez les patients atteints d'insuffisance cardiaque avec un bloc de branche gauche en stimulant le ventricule gauche (VG) ou les deux ventricules (biventriculaire, BIV). Le choix optimal du site de stimulation du VG est d'un grand intérêt clinique pour l'implantation des dispositifs de resynchronisation. Cependant, Il n'y a pas beaucoup de données dans la littérature sur la stimulation du VG par rapport à la stimulation BIV. Ainsi, l'objectif de cette étude était de comparer les paramètres électriques et échographiquesdes patients avec une stimulation BIV versus la stimulation VG unique.

Méthodes: La stimulation du VG et la stimulation BIV ont été testées de manière séquentielle chez 20 patients (âge moyen 54 ± 13 ans, 80 % d'hommes) ayant des dispositifs de resynchronisation préexistants. La configuration initiale BIV a été changée en configuration VG ou vice versa, et des images échographiques ont été acquises pour analyse. L'étude du Strain longitudinal régional et global du VG a été évaluée par échocardiographie 2D.

Résultats : Au total, 20 patients (intervalle QRS moyen avant resynchronisation : 161,17 ± 7ms, moyenne de la fraction d'éjection du ventricule gauche (FEVG) avant resynchronisation : 27,9 ± 8,9%) ont été inclus dans cette étude. Différents paramètres échographiques ont été comparés pour la stimulation VG par rapport à la stimulation BIV : FEVG, fonction diastolique et déformation longitudinale globale du VG.

Aucune différence significative n'a été observée dans l'étude échographique du ventricule gauche entre la stimulation VG et la stimulation BIV (FEVG BIV : 43,33 ± 12,48 % contre FEVG VG : 42,57 ± 14,32 %, p = 0,64 ; déformation longitudinale globale BIV : -11,00 ± 4,51 % contre déformation longitudinale globale VG : -11,05 ± 4,02 %, p = 0,925) ; temps jusqu'au pic entre les parois opposées (septale et latérale) (53,23 ± 68,89 contre 153,3 ± 158,7, p = 0,118).

Conclusion : Il n'y a pas de différence significative entre les paramètres échocardiographiques du VG entre la stimulation BIV et la stimulation VG unique.

Mots-clés

Insuffisance cardiaque, resynchronisation, asynchronisme, échocardiographie, Strain longitudinal global

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INTRODUCTION

Chronic heart failure is still a major challenge for healthcare. Currently, cardiac resynchronisation therapy (CRT) is an established treatment for patients with heart failure and left ventricular ejection fraction ≤35 % and prolonged QRS duration (1). By targeting ventricular dyssynchrony, a condition that plagues as many as one-third of patients with highly symptomatic systolic HF, CRT attempts to give the failing heart a mechanical advantage that can substantially improve symptoms and mortality.

Patients are usually assessed by echocardiography, which is an integral part of the entire process of cardiac resynchronization therapy providing several anatomical and functional information used for cardiac dyssynchrony assessment, prognostic stratification, identification of the optimal site of pacing in the left ventricle, optimization of the CRT device, and patient follow-up.

Ideally, the LV lead of a CRT device would be placed at the precise location of latest electromechanical activation. However, in practice, positioning the LV lead transvenously is limited by the accessibility of suitable epicardial coronary veins and the usual target for CRT lead placement is the lateral or posterolateral left ventricle(2).

Left univentricular pacing is an option that may be considered to maximize response to CRT and at least as an alternative in nonresponders to biventricular pacing (3). Synchronized left univentricular pacing is based on the concept that ventricular activation may be best obtained by recruiting the intrinsic AV conduction, especially over the right bundle branch which may be intact in many candidates to CRT(4).

The purpose of this study is to Evaluate the response to cardiac resynchronization therapy in patients with ischemic or non-ischemic cardiomyopathy based on echocardiographic features and to compare electrical and mechanical parameters using two methods of resynchronization left ventricular versus simultaneous biventricular pacing.

PATIENTS AND METHODS

Study design

This was a retrospective single center study including heart failure patients with cardiac resynchronization therapy (CRT) recruited from the outpatient of Cardiology Department of Hedi Chaker hospital between April 2020 and Juin 2023. Every patient received device control, followed by an ECG and echocardiogram during programming in biventricular pacing, and a second ECG and echography when stimulating left ventricle only.

we didn't include patients who didn't consent, patients and those who couldn't join us and patients who could not be reached according to the data obtained from the records.

We didn't include also patients who had a lack of recorded data. We excluded patients with LV lead dysfunction.

We collected for each patient:

• The clinical and demographic characteristics, comorbidities, medications, preoperative and post-operative indicators of the patients and the data collected during the follow-up visits were recorded and stored for later analysis.

All patients underwent a 12 lead ECG recording using biventricular pacing program and a second ECG when using left ventricular pacing only. QRS duration was measured from the beginning of the Q wave to the end of the S wave in every ECG(5).

All participants underwent transthoracic echocardiography by tow experienced cardiologists, using Philips Epic 7 machine. Ultrasound machine and a 1 to 5MHZ transducer. Qsza&@ During echocardiography, a single lead electrocardiogram was recorded simultaneously, an average of 2 beats was required.

All patients had a complete standard echocardiographic study using time motion TM, two dimensional 2D, and doppler modes. Left ventricular size consisting in end diastolic EDD and end systolic diameters ESD were assessed by TM mode. Left ventricular ejection fraction was assessed by Simpson-s biplane method as recommended.

The peak value of the mitral valve early diastolic flow velocity (E) was measured with pulsed-wave Doppler. Tissue Doppler was used to obtain the septal and lateral mitral annular systolic (S') and early diastolic velocities (E'). Systolic pulmonary artery pressure was estimated using continuous wave doppler CW mode.

Speckle tracking echocardiography (STE) is a novel echocardiographic modality, which tracks the movement of echogenic speckles in the LV wall to estimate deformation in any axis, thus providing calculation of longitudinal strain. The longitudinal strain was evaluated by using the speckle tracking technique, in 4, 2, and 3 chamber views. The region of interest (ROI) was manually rendered, with subsequent manual adjustments to obtain the best delineation of the myocardium to be analyzed. The LV was divided into 6 segments to be analyzed-basal, mid-ventricular, and apical, in each view. Two cardiac cycles were recorded for offline analysis in each view. The global longitudinal strain was calculated on the resultant bull's eye mode)(6).

In a healthy subject, uniformly red pattern of the bull's eye plot represents a normal range in strain values varying from -16 to -22 %(7,8). The peak strain dispersion (PSD), a synchronization marker of the myocardial contraction was calculated. It represents the standard deviation of the time-to-peak longitudinal strain for each left ventricular (LV) segment over the entire cardiac cycle .and evaluates how myocardial segment contractility is or is not coordinated and synchronized throughout LV systole(9).

To assess opposing wall mechanics after CRT, we calculated difference in time to peak between opposite walls (septal and lateral), cut off value > 65 ms to define dyssynchrony(9–14).

All echocardiographic parameters were assessed twice, once when pacing in biventricular and then when LV only.

We tested the devices using a novel device-based algorithm SmartDelay™. SmartDelay recommends the pacing chamber based on the patient's intrinsic atrioventricular conduction, offering potential to avoid unnecessary RV pacing in patients with intact RBB conduction(15). We programmed each device for either biventricular or left ventricular pacing, as the algorithm SMART CRT suggests .

A positive response to CRT was defined as ≥ 15% reduction in LVEDD or ≥ 10% increase in LVEF on any follow-up echocardiogram after CRT implantation. The patients who did not meet those criteria were classified as non-responders(16).

Statistical analysis

Continuous variables were presented as means ± standard deviation, and categorical variables as numbers and proportions. Continuous variables were compared between baseline and 3-/6-month follow-up using paired Student's t-test or Wilcoxon signed-rank test. For comparisons of continuous variables between the LVP and BVP groups, independent Student's t-test or Mann–Whitney U test was applied. Categorical variables were compared using the chi-square test or Fisher's exact test. Statistical significance was defined as a p < 0,05. All analyses were performed with SPSS software (version 23; SPSS).

RESULTS

Patient characteristics before CRT

Thirty-eight (38) patients had a CRT from January 2020 to April 2023 and was eligible to our study.

We didn't reach 13 of them, data were incomplete for 3 of them and Two patient died. So, 20 consecutive patients were retrospectively enrolled. Baseline characteristics of the population are presented in Table I.

Table 1. Baseline characteristics of our patients

Age (years)	N: 20	%
Sex (male)	54 ± 13	80
Cardiomyopathy		
IHD	7	35
NIHD	13	65
QRS duration (ms)	161,17 ± 7	
LVEF (%)	27,9 ± 8,9	
LVEDD (mn)	5,76	

IHD: ischemic heart disease , NIHD : non ischemic heart disease, EDD ; end diastolic diameter, LVEF; left ventricular ejection fraction

They were predominantly late middle-aged men (aged 54 ± 13 years, 80% male), with most having non-ischemic heart disease (65%) and an underlying left bundle branch block (figure 6).

The mean baseline LVEF was (27,9% ± 8,9%). All patients had a prolonged QRS duration of 161 ± 7 ms Electrical and echograhic parameters before and after CRT are shown in table II.

Table 2. Electrical and echographic parameters of our patients before and after CRT

Before CRT		After CRT		P Value
QRS (ms)	161,17 ± 6,74	QRS (ms)	132,92 ± 33,06	0,016
EDD (ms)	61,50 ± 5,76	EDD (ms)	58,89 ± 9,36	0,267
LVEF (%)	27,90 ± 8,93	LVEF (%)	42,6 ± 12,48	0,000

EDD; end diastolic diameter, LVEF; left ventricular ejection fraction, CRT; cardiac resynchronization therapy.

The decrease of QRS duration and the increase of LVEF were significative statistically.

Correlations with response to CRT

There were 85% responders and 15% nonresponders. By univariate analyses, sex, underling cardiomyopathy, baseline QRS duration does not predict CRT response. However, baseline LVEF was inversely correlated to response P = 0,03.

Comparison of electrical and echocardiographic outcomes in Biv pacing Versus LV pacing

The comparison of BiV pacing and LV-only pacing on electrical and echographic responses is shown in tables IV and V, respectively.

The QRS duration, as measured on the surface echocardiogram (ECG), decreased more with LV pacing than with BiV pacing but difference was not statistically significant (P = 0.087). (table III)

Table 3. Difference in QRS duration in BIV versus LV pacing

QRS/ Pacing mode	Moyenne (ms)	P
QRS BIVP	139,75 ± 38,13	0,087
QRS LVP	137,50 ± 40,89	

BIVP: biventricular pacing, LVP: left ventricular pacing

The echocardiographic parameters LVEF, longitudinal strain (2C, 3C, 4C, global), and mitral profile (E, A) were similar with the 2 pacing modes with P > 0.05.

We calculated difference in time to peak between opposite walls (septal and lateral), with Biv pacing than with LV pacing but difference was not statistically significant (P =0,113) (Table IV).

Table 4. Comparison of echographic parameters in BIV versus LV pacing

Echographic parameters		Moyenne	P
Paire 1	LVEF BIVP	43,33 ± 12,48	0,647
	LVEF LVP	42,57 ± 14,32	
Paire 2	SLG 2C BIVP	-11,35 ± 4,80	0,956
	SLG 2C LVP	-11,38 ± 4,76	
Paire 3	SLG 3C BIVP	-10,82 ± 6,03	0,814
	SLG 3C LVP	-11,58 ±	
Paire 4	SLG 4C BIVP	-11,48 ± 4,43	0,803
	SLG 4C LVP	-11,26 ± 4,11	
Paire 5	SLG GL BIV	-11,00 ± 4,51	0,925
	SLG GL LVP	-11,05 ± 3,84	
Paire 6	E BIV	81,65 ± 27,05	0,862
	E LVP	80,53 ± 13,86	
Paire 7	A BIVP	90,35 ± 54,06	0,259
	A LVP	72,71 ± 29,89	
Paire 8	Vit E BIVP	129,88 ± 53,19	0,370
	Vit E LVP	147,44 ± 57,01	
Paire 9	Time to SLD BIVP	53,23 ± 68,89	0,113
	Time to SLD LVP	153,38 ± 158,7	

LVEF: left ventricular ejection fraction, SLG: global longitudinal strain, C; cavity; SLD: septal lateral delay

According to these results, no statistically significant differences in hemodynamic responses were seen in the two groups. Moreover, no statistically significant differences in the electrical responses were seen between the two pacing programs.

DISCUSSION

Cardiac resynchronization therapy (CRT) has been a cornerstone in the treatment of advanced, medically refractory heart failure. Studies evaluating CRT have shown reduction in mortality, reduction in HF hospitalizations, and improvement in functional outcomes, and therefore, carry a class I indication per the 2021 ESC guidelines on management of heart failure (1).

Delayed left ventricular (LV) free wall activation has long been thought to be the hallmark of LBBB. Resynchronization therapy, therefore, is directed to recruiting the LV free wall, which is the premise of LV lead placement in a lateral branch vein of the coronary sinus. Despite showing promising improvements in LV function and reverse remodeling in selected patients, up to 30-35% of patients do not derive a positive CRT response(17).

Response to CRT: Echocardiographic features

The primary end point was a change in LV end-diastolic diameter (LVEDD) and changes in LVEF and rate of response to CRT .

There are a significant number of current issues that exist when assessing CRT response. Firstly, the CRT response definition is highly dependent on the criteria used to define the response. Studies have suggested that the response rate will vary from 32% to 91%, depending on the criteria that were used.

Echocardiography is the preferred technique to evaluate improvement in LV ejection fraction after CRT and cardiac reverse remodeling.

In 20 patients with heart failure, a significant improvement in LV ejection fraction from 27,9% to 42,5% was demonstrated after 6 months or more of CRT.

In our study ischemic cardiomyopathy was not associated with lower rates of response compared to non-ischemic cardiomyopathy. Also, there was no correlation of age or sex with CRT response.

However, LVEF was inversely correlated to CRT response: the more LVEF was low the more response to CRT was higher.

John Sutton ET AL recently evaluated a cohort of 228 patients included in the MIRACLE trial and demonstrated that the gradual improvement in LV ejection fraction was related to the etiology of heart failure. Patients with non-ischemic cardiomyopathy exhibit an immediate improvement in LV ejection fraction, whereas the improvement occurs more gradually in patients with ischemic cardiomyopathy(18).

In REVERSE trial Of 353 subjects with acceptable echocardiography remodeling data to define Levi response, 52% were Improved, 23% were Stabilized, and 25% were Worsened(19,20)

The Worsened patients were more likely to be male, have ischemic etiology, a non-LBBB morphology, diabetes, and a shorter QRS duration.

Reduction of EDD wasn't statically significant in our trial (from mean to mean,)

Response to CRT was positive in 85%of our patients and was not correlated to sex or underlying cardiomyopathy.

Comparison of Biv versus LV pacing

The main objective of this study was to compare the hemodynamic responses of BiV pacing with those of LV pacing.

According to the European Society of Cardiology (ESC) guidelines on cardiac pacing and CRT, LV pacing alone may be considered as an alternative mode for resynchronization. Furthermore, a respective 21% of patients who did not respond clinically or echocardiographically to BiV pacing responded to LV pacing mode (21,22).

Moreover, a recently conducted meta-analysis has demonstrated that in patients with moderate-to-severe heart failure, these two pacing modalities did not differ with regard to death/heart transplantation or need for hospitalizations (23).

Non-responders to BiV pacing may respond favorably to LV pacing (24).

The present study addressed this important question by comparing the echocardiographic responses of BiV versus LV only pacing in patients with a standard indication for ventricular pacing.

In the GREATER-EARTH trial LV-CRT has no advantage over conventional BiV-CRT with regard to LV and RV remodeling parameters (25).

The Biventricular Versus Left Univentricular Pacing With ICD Back-Up in Heart Failure Patients (B-LEFT HF) trial found that LV pacing was noninferior to BiV pacing in terms of a composite outcome consisting of NYHA functional class and 5-mm reduction in LV end-systolic diameter at 6 months(26).

Our study showed no difference between two pacing programs; BiV and LV pacing.

So, in practice, left univentricular pacing could be an alternative in nonresponders to biventricular pacing.

Limits

The main limitation of our study is represented by the small number of patients treated with CRT, was not randomized. Because of the small patient population and the short period of enrollment, we could not further analyze the impact of some factors on our results. In addition to that, more dyssnchrony parameters could be assessed by echocardiography. Finally, comparing Biv versus LV pacing programs over a longer period of time could be interesting and could impact the results.

CONCLUSION

Cardiac resynchronization therapy (CRT) is currently recommended in drug-refractory heart failure with reduced left ventricular (LV) ejection fraction (LVEF) and prolonged QRS duration. CRT improves heart failure symptoms as well as LV function and size and is associated with a reduction in morbidity and mortality.

The role of echocardiography in patients with CRT can be defined in the selection of CRT candidates by demonstration of LV dyssynchrony to assess immediate response to CRT, including detection of acute LV resynchronization. Also, echocardiography is useful to evaluate the long-term benefit of CRT (LV reverse remodeling).

Our study aimed to compare two pacing programs, BIV pacing and LV only pacing, using echocardiographic parameters such as LVEF, diameters, mitral profile, longitudinal strain, and time to peak values and to evaluate rates of response to CRT via echocardiographic parameters.

A positive response was found in 85% of our patients. Our research found No statistically significant difference between

BiV and LV pacing. But the sample size was reduced, and further randomized studies should be performed.

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