

# Relationship Between Left Ventricular Remodeling Assessed by Strain Echocardiography and Conventional Echocardiography Before and After Cardiac Resynchronization Therapy in Severe Heart Failure Patients

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## Key Words

Left ventricular remodeling • Strain echocardiography • Conventional echocardiography • Before and after CRT • Severe heart failure

## Abstract

**Background/Aims:** To assess the relationship between left ventricular remodeling as evaluated by strain echocardiography and conventional echocardiography before and after cardiac resynchronization therapy (CRT) in patients with severe heart failure patients. **Methods:** A cross-sectional descriptive study with follow-up comparison before and after. The study was conducted on 33 heart failure patients indicated for CRT at the Vietnam National Heart Institute, Bach Mai Hospital from late 2015 to December 2021. **Results:** The study showed some correlations and changes in left ventricular remodeling assessed by strain echocardiography and conventional echocardiography before and after CRT. Left ventricular end-systolic volume and end-diastolic volume significantly decreased after 3 months of follow-up ( $p < 0.001$ ) and had a strong inverse correlation with QRS recovery in study patients ( $r = 0.65$ ). A positive correlation was observed between changes in left atrial volume index (LAVI) and 4B strain ( $r = 0.96$ ,  $p < 0.05$ ). After 3 months of CRT implantation, there was a positive correlation between the isovolumic relaxation time (IVRT) and left atrial volume (LAVI) ( $p < 0.05$ ) and between the left atrial volume and E/e' obtained from tissue Doppler ( $r = 0.53$ ,  $p < 0.05$ ). However, there was no correlation observed between E/e' and total EF ( $r = -0.36$ ,  $p > 0.05$ ), between 2B strain and total EF ( $r = -0.36$ ,  $p > 0.05$ ) and between 2B strain and left atrial volume LAVI ( $r = 0.36$ ,  $p > 0.05$ ). **Conclusion:** Strain echocardiography is an important tool that cannot be overlooked in diagnosing, assessing risk factors, and monitoring heart failure. After 3 months

of CRT implantation, there was significant improvement in left ventricular volume and ejection fraction (EF). This indicates better treatment effectiveness.

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## Introduction

Globally, the prevalence of heart failure is 1-2% [1], and it is most common in the elderly. In Vietnam, the incidence of heart failure is also high [2], and following global trends, Vietnam is also performing Cardiac Resynchronization Therapy (CRT) for patients with severe heart failure who meet the indications [3].

The emergence and development of CRT since the 1990s have opened a new direction in heart failure treatment and have raised many new issues related to the pathogenesis of heart failure, especially in the context of cardiac remodeling and myocardial dyssynchrony (MDB) [3].

Echocardiography helps assess ejection fraction (EF), and is an important tool for evaluating cardiac function, identifying structural abnormalities, helping to determine the cause of heart failure or other risk factors, helping to monitor early treatment, assessing heart function improvement and related factors. As people age, natural aging processes can cause changes in heart structure such as thickening heart walls, enlarged chambers, and reduced contractility. Simultaneously, an aging population also faces an increased risk of cardiovascular diseases like coronary artery disease, hypertension, and valvular heart disease. However, studies on the relationship and changes in left ventricular function have been conducted worldwide, but an in-depth assessment of heart failure patients indicated for CRT has not been extensively investigated. Therefore, we conducted this study to understand the relationship between left ventricular remodeling assessed by strain echocardiography before and after cardiac resynchronization therapy compared to conventional echocardiography in heart failure patients indicated for CRT.

## Materials and Methods

### *Research Design*

The study was conducted as a cross-sectional descriptive study with follow-up comparison before and after.

**Study Subjects:** The study subjects included patients with severe heart failure, with an EF < 35%, who were undergoing optimal medical treatment for heart failure in NYHA III - IV, and who were indicated for cardiac resynchronization therapy based on echocardiographic results, electrocardiogram, biochemical results, and clinical symptoms when implanted with cardiac resynchronization devices at Bach Mai Hospital Heart Institute. Patients receiving cardiac resynchronization devices were selected based on ACC/AHA 2008 guidelines [4].

### *Time and location research*

The study was conducted at the Vietnam National Heart Institute, Bach Mai Hospital, from late 2015 to December 2021.

### *Sampling Method*

Convenience sampling. A total of 33 patients who met the inclusion criteria and agreed to participate in the study were selected. These were all patients who met the criteria and followed all steps in the research process.

### Research Progress

**Clinical Examination:** All patients underwent a general examination to assess heart failure status NYHA III – IV (NYHA Class I: Cardiac disease, but no symptoms and no limitation in ordinary physical activity; NYHA Class II: Mild symptoms and slight limitations during ordinary activity; NYHA Class III: Significant limitations in activity due to symptoms, comfortable only at rest.; NYHA Class IV: Severe limitations, symptoms even while at rest).

The follow-up period after implantation was 6 months. Patients were treated according to ACC/AHA 2008 guidelines for at least 6 months. [4]. Patients received priority treatment for various types of medications such as ACE inhibitors, ARBs, Beta-blockers, and Digoxin.

### Biochemical Tests

Some main biochemical parameters were collected, including: Pro BNP, Urea, Creatinine, SGOT, SGPT.

**Imaging:** Doppler ultrasound, tissue Doppler ultrasound. The classify heart failure (HF) based on Left ventricular Ejection Fraction (LVEF): HF with Reduced Ejection Fraction (HrEF) is  $EF \leq 40\%$ ; HF with Midly Reduced Ejection Fraction (HmrEF) 41-49%; FF with Preserved Ejection Fraction (HpfEF)  $\leq 50\%$ .

### Research procedure (Research diagram)

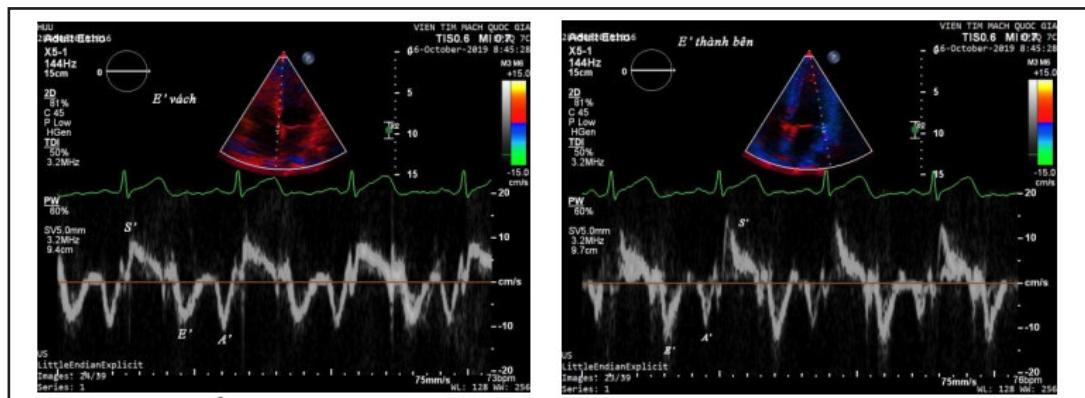
Select patients with severe heart failure (NYHA III – IV),  $EF < 35\%$ , after optimal medical treatment, sinus rhythm was restored. Perform Doppler echocardiography beforehand. Patients with indications for pacemaker implantation will have a CRT implanted. Each patient will undergo echocardiography 4 times: Before pacemaker implantation, immediately after pacemaker implantation, after 1 month, and after 3 months.

### Cardiac Doppler Ultrasound Method

The Cardiac Doppler ultrasound was performed on all selected patients participating in the study using a JIS6 ultrasound machine at the cardiac ultrasound room of the Vietnam National Heart Institute. The measured results were assessed by a group including cardiac ultrasound specialists at the cardiac ultrasound department of the Vietnam National Heart Institute. Ultrasound parameters were measured and calculated according to the guidelines of the American Society of Echocardiography (2008) on an ultrasound machine with Tissue Doppler and myocardial tissue tagging functions, using the JIS6 ultrasound machine.<sup>4</sup> The ultrasound parameters were examined in the following sequence (Fig. 1).

### M-Mode Echocardiography

Measured from the parasternal long axis view, the following parameters were measured: Dd: left ventricular end-diastolic diameter; Ds: left ventricular end-systolic diameter; %D: fractional shortening; Vd: left ventricular end-diastolic volume; Vs: left ventricular end-systolic volume; Aortic diameter, left atrial diameter, and right ventricular long-axis diameter; EF (Teichholz): left ventricular ejection fraction.



**Fig. 1.** Doppler ultrasound image of myocardial tissue

## 2D Echocardiography

Measured from the apical four-chamber and two-chamber views. Left ventricular volume and ejection fraction were calculated using the Biplane Simpson's method (four-chamber and two-chamber views). Left ventricular end-systolic volume and end-diastolic volume were measured. The parameters for left ventricular end-diastolic volume (Vd) and end-systolic volume (Vs) were averaged from the two views (Biplane). The average left atrial volume index (LAVi) was calculated from both the apical four-chamber and two-chamber views.

## Pulsed Wave Doppler Echocardiography

Measured from the apical four-chamber and five-chamber views. In the apical four-chamber view, the Pulsed Wave Doppler sample volume was placed at the free edge of the anterior mitral leaflet, measuring the maximum velocity of E wave, A wave, and E wave deceleration time (DT). In the apical five-chamber view, the Pulsed Wave Doppler sample volume was placed between the left ventricular outflow tract and the free edge of the anterior mitral leaflet, measuring the isovolumic relaxation time (IVRT).

## Continuous Wave and Color Doppler Echocardiography

Measured from the apical four-chamber and two-chamber views.

## Tissue Doppler Echocardiography

Measured from the apical four-chamber view with the Tissue software available on the ultrasound machine. The Doppler sample volume was placed at the basal interventricular septum using the TDI software, measuring the velocity of e', a', and s' waves. The Doppler sample volume was placed at the basal lateral wall of the left ventricle using the TDI software, measuring the velocity of e', a', and s' waves.

## Speckle Tracking Echocardiography (Myocardial Tissue Tagging)

Measured from the apical long-axis, two-chamber, and four-chamber views, using the Speckle tracking software to measure online and calculate the myocardial strain parameter; This includes Longitudinal Strain, Four-Chamber Strain, Two-Chamber Strain, and Global Longitudinal Strain (GLS) for all cardiac chambers. Whether strain analysis was performed by a team of echocardiography experts at the Vietnam National Heart Institute, and the final analysis result and agreed upon by the team and the expert leader.

## Doppler Ultrasound to Evaluate Cardiac Resynchronization Therapy (CRT) Response

Patients underwent Doppler echocardiography with all the same parameters as measured before CRT device implantation. Each patient had echocardiography performed immediately after CRT implantation at 1 month, and at 3 months post-implantation, and these parameters were monitored. The EF value presentation was clarified (Change in EF value relative to baseline).

## Data Collection Method

All data was collected according to a pre-designed patient follow-up form. Collected data included demographic characteristics, clinical symptoms, and echocardiographic parameters of patients (echocardiography collected according to hospital results) upon admission and until the 3rd month after cardiac resynchronization device implantation.

## Data processing and statistical analysis method

Data was processed using SPSS 17.0 (SPSS Inc South Wacker Drive, Chicago, IL) and Stata 12.0 to identify significant values and find statistically significant parameters. The results were presented using tables or appropriate graphs; for continuous variables, results were presented as mean  $\pm$  standard deviation, for categorical variables, results were presented as percentages. T-test (for 2 variables), ANOVA test (for more than 2 variables) were used to compare continuous variables; Pearson correlation test was used to examine the relationship between categorical variables, Fisher's exact test was used for small sample size categorical variables. Odds ratios (OR) were used to analyze factors influencing the results of pacemaker implantation in a 2x2 table. Statistically significant differences were defined as  $p < 0.05$  [5].

## Research Ethics

The study was only conducted with the consent of participating patients. Patients participating in the study were treated according to the professional regulations of the Vietnam Ministry of Health, as well as those of the Vietnam National Heart Institute, Bach Mai Hospital. All patient information was kept absolutely confidential, and the results were used solely for research purposes.

## Results

### *General Characteristics of the Study Population*

The study included 33 patients with severe heart failure indicated for CRT. The mean age of the patients was 57.8 years; patients aged  $\geq 60$  years accounted for 57.6% (n = 19), while patients  $< 60$  years accounted for 42.4% (n = 14). The male-to-female ratio was 81.8% (n = 27) to 18.2% (n = 6).

### *Changes in Conventional Echocardiographic Parameters After CRT*

After 3 months of CRT implantation, left ventricular end-systolic volume (LVESV) and end-diastolic volume (LVEDV) significantly decreased compared with baseline (both  $p < 0.001$ ). Left ventricular ejection fraction (EF) also showed a significant improvement after CRT implantation (Table 1).

### *Relationship Between QRS Duration and Left Ventricular Remodeling*

After 3 months of CRT implantation, QRS duration significantly decreased compared with baseline ( $p < 0.001$ ). QRS recovery showed a strong inverse correlation with left ventricular volumes, with a correlation coefficient of  $r = 0.65$  (Table 1).

Changes in EF differed according to QRS duration. In patients with QRS between 120 and 140 ms, the mean change in EF was  $6.88 \pm 3.40\%$ , whereas in patients with QRS  $\geq 140$  ms, EF increased by  $10.29 \pm 8.04\%$  (Table 1).

Significant changes in myocardial strain parameters were also observed according to QRS recovery after CRT implantation (Table 1).

### *Relationship Between Left Atrial Volume and Myocardial Strain*

A significant positive correlation was observed between changes in left atrial volume index (LAVI) and four-chamber (4B) myocardial strain in patients with QRS  $\geq 140$  ms ( $r = 0.96$ ,  $p < 0.05$ ) (Table 2).

### *Diastolic Function Parameters After CRT*

At 3 months after CRT implantation, a significant inverse correlation was observed between E/e' ratio and total EF ( $r = -0.36$ ,  $p < 0.05$ ) (Table 3). A significant inverse correlation was also found between two-chamber (2B) strain and EF ( $r = -0.36$ ,  $p < 0.05$ ), as well as a positive correlation between 2B strain and left atrial volume ( $r = 0.36$ ,  $p < 0.05$ ) (Table 5).

In addition, a significant positive correlation was observed between isovolumic relaxation time (IVRT) and LAVI at 3 months after CRT implantation ( $r = 0.66$ ,  $p = 0.001$ ) (Table 4). A positive correlation was also found between LAVI and E/e' measured by tissue Doppler ( $r = 0.53$ ,  $p < 0.05$ ) (Table 3).

**Table 1.** Relationship of Positive change in echocardiographic parameters according to QRS duration at baseline and after 3 months of CRT implantation. Comments: Left ventricular volume and EF significantly improved after CRT implantation after 3 months, with  $p < 0.001$ . There was a strong inverse correlation with QRS recovery on the electrocardiogram of patients in the study group, with a correlation coefficient of 0.65

Parameter	QRS < 120 ms (Mean $\pm$ SD)	QRS $\geq 140$ ms (Mean $\pm$ SD)	p
LAVI	$4.73 \pm 2.94$	$5.29 \pm 2.50$	$0.001 < 0.01$
Changes from baseline of EF (%)	$6.88 \pm 3.40$	$10.29 \pm 8.04$	$<0.0001$
Longitudinal Strain	$3.14 \pm 1.68$	$3.46 \pm 1.59$	$<0.0001$
2B Strain	$3.71 \pm 1.89$	$1.91 \pm 1.36$	$<0.0001$
4B Strain	$3.02 \pm 3.76$	$3.41 \pm 0.95$	$0.0004 < 0.001$

**Table 2.** Relationship between positive changes in left atrial volume (LAVI) and myocardial strain according to QRS duration before and after CRT implantation. Comments: There was a significant positive correlation between the positive change in left atrial volume (LAVI) and myocardial 4B strain in the QRS (ms)  $\geq 140$  group ( $r = 0.96$ ,  $p < 0.05$ )

Index	EF (%)	Longitudinal Strain	2B Strain	4B Strain
120 < QRS < 140 ms	r	0.03	-0.02	-0.09
	p	0.88	0.91	0.66
QRS (ms) $\geq 140$	r	-0.01	0.003	0.55
	p	0.98	0.99	0.20

**Table 3.** Relationship between tissue Doppler echocardiographic parameters and total EF (%), LAVI, Vd, Vs at 3 months after CRT implantation. Comments: At 3 months after implantation: There was a significant inverse correlation between E/e' ratio and total EF ( $r = -0.36$ ,  $p < 0.05$ )

Parameter	EF (%)	LAVI (ml/m <sup>2</sup> )	Vd (ml)	Vs (ml)
E/e' (r)	-0.36	0.33	0.24	0.28
	p	0.04	0.18	0.12
e' (r)	0.09	-0.02	0.13	-0.03
	p	0.59	0.47	0.86
a' (r)	0.17	-0.25	0.01	-0.17
	p	0.34	0.15	0.33

**Table 4.** Relationship between echocardiographic parameters and isovolumic relaxation time (IVRT) at 3 months after implantation. Comments: At 3 months after implantation: There was a significant positive correlation between IVRT and left atrial volume index (LAVI) ( $p < 0.05$ )

Parameter	EF (%)	LAVI (ml/m <sup>2</sup> )	Vd (ml)	Vs (ml)
IVRT (r)	-0.22	0.56	0.29	0.28
	p	0.22	0.001	0.12

**Table 5.** Relationship between 2D echocardiographic parameters and myocardial strain at 3 months after implantation. Comments: At 3 months after implantation, there was a significant inverse correlation between 2B strain and total EF ( $r = -0.36$ ,  $p < 0.05$ ) and a significant positive correlation with left atrial volume LAVI ( $r = 0.36$ ,  $p < 0.05$ )

Parameter	EF( %)	LAVI (ml/m <sup>2</sup> )	Vd (ml)	Vs (ml)
Longitudinal Strain (r)	-0.33	0.22	-0.07	-0.02
	P	0.06	0.22	0.68
2B Strain (r)	-0.36	0.36	0.01	0.06
	P	0.04	0.04	0.94
4B Strain (r)	-0.17	0.02	0.16	0.09
	P	0.34	0.93	0.60

## Discussion

### *Demographic Characteristics*

The mean age of patients in this study was 57.8 years, with a higher proportion of patients aged  $\geq 60$  years. This age distribution is consistent with the epidemiology of severe heart failure and reflects the typical population indicated for CRT [1,2].

### *QRS Duration and Left Ventricular Remodeling*

The present study demonstrated a significant association between QRS duration and left ventricular remodeling. QRS narrowing after CRT implantation was associated with reductions in left ventricular volumes and improvement in EF, supporting the concept that electrical resynchronization contributes to reverse remodeling. These findings are consistent with previous studies reporting improved ventricular function in patients with QRS narrowing after CRT implantation [6-10].

### *Role of Strain Echocardiography in CRT Assessment*

Strain echocardiography provides a sensitive assessment of myocardial deformation and allows detection of subtle functional changes that may not be apparent with conventional echocardiography. The observed associations between myocardial strain parameters and QRS recovery highlight the value of strain imaging in evaluating CRT response, particularly in patients with wider QRS complexes [13].

### *Left Atrial Volume and CRT Response*

Left atrial volume index reflects chronic diastolic burden and elevated filling pressures. The observed relationship between changes in LAVI and myocardial strain suggests that atrial remodeling parallels ventricular functional improvement following CRT implantation. This finding is in line with previous studies indicating that LAVI may serve as a predictor of CRT response [14,19].

### *Diastolic Function Parameters*

The observed relationships between E/e' ratio, EF, IVRT, and LAVI indicate that diastolic function improves alongside systolic function after CRT implantation. Increased E/e' ratio and prolonged IVRT were associated with impaired ventricular performance, supporting the role of tissue Doppler echocardiography in monitoring diastolic function in heart failure patients undergoing CRT [15-20].

### *Clinical Implications*

Overall, these findings emphasize the complementary role of strain echocardiography and conventional echocardiography in assessing left ventricular remodeling and treatment response after CRT. Echocardiography remains an indispensable tool for diagnosis, risk stratification, and follow-up in patients with severe heart failure.

## Conclusion

This study revealed several relationships between left ventricular remodeling assessed by strain echocardiography and conventional echocardiography before and after CRT in severe heart failure patients: Left ventricular volume before and after CRT implantation showed significant changes from 1 to 3 months ( $p < 0.001$ ) and had a strong positive correlation with the QRS complex on the electrocardiogram of patients in the study group ( $r = 0.65$ ). There was a significant positive correlation between the change in left atrial volume (LAVI) and myocardial 4B strain in the QRS (ms)  $\geq 140$  group ( $r = 0.96$ ;  $p < 0.05$ ). At 3 months after CRT implantation, there was a significant positive correlation between isovolumic relaxation

time (IVRT) and left atrial volume (LAVI) ( $p < 0.05$ ), and between left atrial volume and E/e' parameter measured by tissue Doppler ( $r = 0.53$ ;  $p < 0.05$ ). However, there was an inverse correlation between E/e' ratio and total EF ( $r = -0.36$ ;  $p < 0.05$ ), between 2B strain and total EF ( $r = -0.36$ ;  $p < 0.05$ ), and between 2B strain and left atrial volume LAV ( $r = 0.36$ ;  $p < 0.05$ ).

Thus, echocardiography, especially tissue Doppler echocardiography, is an indispensable tool in diagnosing, assessing risk factors, and monitoring heart failure. At 3 months after CRT implantation, there was a significant improvement in left atrial volume and ejection fraction (EF), with statistically significant results indicating better treatment effectiveness after 3 months of CRT implantation.

### Limitations And Recommendations

This study still has some limitations that need to be addressed in subsequent, larger-scale studies on this issue: The small sample size and sample size was not large enough (we recruited 33 patients), but each patient directly underwent echocardiography at 4 time points (before implantation, immediately after implantation, 1 month after implantation, and 3 months after implantation); The study was conducted at a single center (Single-center study); A comparative study with a control group was not performed (Lack of a control group); And the follow-up time was not long enough (Short follow-up period). Therefore, we recommend that new studies are needed on the role of echocardiography in evaluating the effectiveness of heart failure treatment after CRT implantation, with a larger sample size, and potentially conducted as a multi-center study on this issue.

### Abbreviations

**CRT ((Cardiac Resynchronization Therapy)** - Cardiac resynchronization therapy; **Dd (End diastolic diameter)** - End-diastolic diameter; **Ds (End systolic diameter)** - End-systolic diameter; **Ao (Aorta)** - Aorta; **EF (Ejection fraction)** - Ejection fraction; **NYHA (New York Heart Association)** - New York Heart Association classification; **Vd (End diastolic volume)** - End-diastolic volume; **Vs (End systolic volume)** - End-systolic volume; **VLT (Left Ventricle)** - Left Ventricle; **LA (Left Atrium)** - Left Atrium; **LAVi (Left atrium Interventricular)** - Left atrial volume index; **E/A (Early diastolic filling/Atrial contraction)** - Ratio of early diastolic flow velocity and atrial contraction velocity in mitral inflow (E wave and A wave); **E/e'** - Ratio of early diastolic mitral inflow velocity to early diastolic myocardial velocity at the mitral annulus; **e' (tissue Doppler velocity)** - Early diastolic myocardial velocity; **IVRT (Isovolumic Relaxation Time)** - Isovolumic relaxation time; **s' (s-prime)** - Peak systolic myocardial velocity; **a' (a-prime)** - Peak late diastolic myocardial velocity; **VTI (Velocity Time Integral)** - Velocity Time Integral; **TAPSE (Tricuspid Annular Plane Systolic Excursion)** - Tricuspid Annular Plane Systolic Excursion (TAPSE); **IVS** - Interventricular septum; **GLS (Global Longitudinal Strain)** - Global Longitudinal Strain.);

### Disclosure Statement

The authors have nothing to disclose.

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