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Left atrial strain is a predictor of left ventricular systolic and diastolic reverse remodelling in CRT candidates

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Aims The left atrium (LA) has a pivotal role in cardiac performance and LA deformation is a well-known prognostic predictor in several clinical conditions including heart failure with reduced ejection fraction. The aim of this study is to investigate the effect of cardiac resynchronization therapy (CRT) on both LA morphology and function and to assess the impact of LA reservoir strain (LARS) on left ventricular (LV) systolic and diastolic remodelling after CRT.

Methods and results Two hundred and twenty-one CRT-candidates were prospectively included in the study in four tertiary centres and underwent echocardiography before CRT-implantation and at 6-month follow-up (FU). CRT-response was defined by a 15% reduction in LV end-systolic volume. LV systolic and diastolic remodelling were defined as the percent reduction in LV end-systolic and end-diastolic volume at FU. Indexed LA volume (LAVI) and LV-global longitudinal (GLS) strain were the main parameters correlated with LARS, with LV-GLS being the strongest determinant of LARS ($r = -0.59$, $P < 0.0001$). CRT induced a significant improvement in LAVI and LARS in responders (both $P < 0.0001$). LARS was an independent predictor of both LV systolic and diastolic remodelling at follow-up ($r = -0.14$, $P = 0.049$ and $r = -0.17$, $P = 0.002$, respectively).

Conclusion CRT induces a significant improvement in LAVI and LARS in responders. In CRT candidates, the evaluation of LARS before CRT delivery is an independent predictor of LV systolic and diastolic remodelling at FU.

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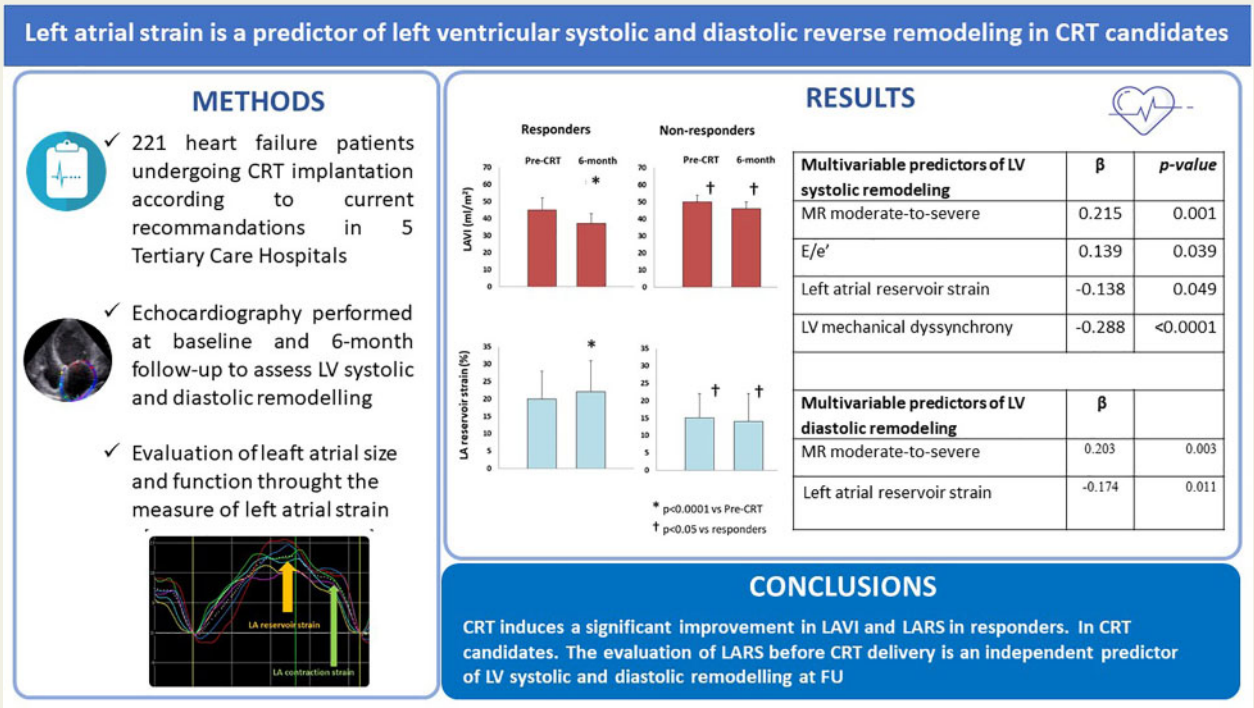
Graphical Abstract



Keywords cardiac resynchronization therapy • heart failure • left atrial strain

Introduction

Cardiac resynchronization therapy (CRT) is an established treatment in patients with systolic heart failure (HF), wide QRS (>120 ms), left ventricular ejection fraction (LVEF) <35%, who remains symptomatic despite optimized medical therapy.[1] Nearly 30% of patients undergoing CRT according to current recommendations are non-responders to treatment and can even be harmed by biventricular stimulation.[2] Several imaging-derived parameters have been proposed to improve the selection of CRT-candidates, predominately measures of left ventricular (LV) dyssynchrony.[3–5] Despite promising results, none of these parameters has shown enough predictive power to be included in recommendations. In recent years, left atrial (LA) function measured by speckle tracking echocardiography (STE)[6] has shown to be a significant predictor of prognosis in the general population[7] and patients with HF with reduced LVEF.[8] In the field of CRT, the MADIT investigators have shown that LA size is a predictor of CRT response.[5] However, only two small retrospective studies have demonstrated the role of LA deformation in LV remodelling after CRT.[9,10] The aims of this study are (i) to assess the correlation between LA reservoir strain and CRT-response in a large prospective population of CRT candidate and (ii) to evaluate the effect of CRT on LA size and function.

Methods

Patients

Two hundred and twenty-one patients undergoing CRT according to current recommendations[1] were prospectively recruited in five tertiary care hospitals (Rennes, Oslo, Leuven, Aalst, and Stockholm) from August 2015 to April 2019. All patients received optimized medical therapy before CRT implantation and underwent transthoracic echocardiography before CRT delivery and at 6-month follow-up. Clinical data including age, sex, and treatments were collected for each patient. The functional status was assessed by the estimation of the New York Heart Association (NYHA) functional class.[11] All patients gave their written informed consent for study participation. The study was conducted following the 'Good Clinical Practice' guidelines of the Declaration of Helsinki and was approved by the Regional Ethical Committees of every participating centre. The study was registered at clinicaltrials.gov (identifier NCT02525185).

Echocardiography

All patients underwent standard transthoracic echocardiography using a Vivid E9 and E95 ultrasound system (GE Healthcare, Horten, Norway) equipped with an M5S 3.5 MHz transducer at baseline and 6-month follow-up. Two-dimensional, colour Doppler, pulsed-wave, and continuous-wave Doppler data were stored on a dedicated workstation for offline analysis (EchoPAC, GE EchoPAC, GE Healthcare, Horten,

Norway). Indexed left atrial volume (LAVI), LV volumes, and LVEF were measured by the biplane method, as recommended.[12]

Mitral regurgitation (MR) was first visually assessed from 1 to 4 (1 = traces, 2 = mild, 3 = moderate, and 4 = severe). In patients with more than mild MR ($n = 40$), the application of a semiquantitative approach to estimate MR severity was possible in 31 patients and an effective regurgitant area (ERO)> 0.20 identified severe secondary MR as recommended.[12] The semiquantitative assessment of MR was not applicable in nine patients. In these patients, visual method was retained for the evaluation of MR severity. Peak velocity of early (*E*) and late (*A*) diastolic filling were derived from transmitral Doppler recordings, and the *E/A* ratio was calculated. Pulsed-wave tissue Doppler Imaging (TDI)-derived early diastolic velocity was obtained at the septal and lateral mitral annulus and the mean value (*e′*) was used to estimate the *E/e′* ratio. In the presence of tricuspid regurgitation, continuous Doppler was used to estimating maximal tricuspid velocity (TRV_{max}). Inferior vena cava diameter and respiratory changes, and TRV_{max} were then used to estimate systolic pulmonary artery pressure (PAPs).

Left atrial reservoir strain (LARS), left atrial contraction strain (LACS), and LV global longitudinal strain (GLS) were measured by STE using frame rates >60 s. LARS and LACS were calculated from apical four-chamber view, putting the zero strain reference at end-diastole as recommended, and reported as positive values.[6] GLS was assessed from LV apical four-, two-, and three-chamber views and reported as negative values. For patients in atrial fibrillation, R–R intervals with a similar duration were chosen for the calculation of GLS. An example of the LARS and LACS measurement is depicted in *Figure 1*.

Assessment of LV dyssynchrony

Septal flash (SF) and apical rocking (ApR) were assessed visually in Leuven by two experienced readers. In case of disagreement, a third reading was performed in Leuven by an independent expert to reach a consensus. SF was defined as pre-ejection septal shortening or rapid leftward septal motion immediately after onset QRS and was assessed visually in apical 2D images or, when in doubt, with longitudinal strain or M-mode in parasternal views.[13] ApR was defined as a transverse rightward motion of the apex immediately after onset QRS, followed by a leftward motion of the apex during ejection.[14] LV mechanical dyssynchrony was defined by the presence of SF and/or ApR.

Cardiac resynchronization therapy

CRT delivery followed a standardized protocol. The right atrial and ventricular leads were positioned conventionally. The LV lead was inserted in a lateral or postero-lateral vein if possible and coronary venography was used to optimize lead placement. The device was programmed in conventional biventricular pacing and CRT was optimized before discharge if needed, according to the local protocol. LV remodelling after CRT was defined by the reduction of LV end-systolic and end-diastolic volume at 6-month follow-up.

CRT-response was defined by a reduction in LV end-systolic volume of at least 15% at 6-month follow-up.

Study endpoint

The primary endpoint was to identify the predictors of LV reverse systolic and diastolic remodelling 6 months after CRT delivery.

Statistical analysis

Continuous variables are expressed as the mean and standard deviation and were compared using Student's *t*-test. Categorical data are expressed as frequencies and percentages and were compared with the χ^2 test. Univariable and multivariable linear regression analyses were performed to identify the independent predictors of LA strain parameters. Multivariate linear regression analysis was used to identify predictors of LV reverse systolic and diastolic remodelling. remodelling. The $P < 0.05$ was considered significant. Statistical analysis used procedures available with SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Two hundred and twenty-one patients were included in the study. Clinical and echocardiographic data from the overall population and according to CRT-response are provided in *Tables 1 and 2*. Atrial fibrillation was observed in 38 (17%) patients, 194 (88%) patients had typical left bundle branch block (LBBB). Pharmacological treatment did not differ between responders and non-responders.

At 6-month follow-up, 153 (69%) patients were CRT-responders. Responders were more often female, with a lower prevalence of ischaemic cardiomyopathy. They had less dilated LV and better GLS at baseline. CRT caused a significant improvement in LVEF and GLS in responders (*Table 1*, *Figure 2A*). Before CRT, diastolic function parameters (LAVi, *E/e′* ratio, TRV_{max}) were significantly more impaired in non-responders compared with responders.

LA morphology and function

LA dilatation was more pronounced in non-responders than in responders at baseline. CRT led to a significant reduction in LAVI in responders ($P < 0.0001$) and a lower reduction in non-responders ($P = 0.04$). LARS could be measured in almost all patients ($n = 217$, 98%), with only four excluded because of technically suboptimal strain traces. Before CRT delivery, LAS LARS was more impaired in non-responders ($P < 0.0001$). There was a significant improvement in LARS in CRT-responders, whereas CRT had no effect on LARS in non-responders (*Table 2*, *Figure 2*). Normalization of LARS for LA size did not impact the effect of CRT on LA function.

LAVI, *E/e′* ratio, GLS, and TRV_{max} were all correlated to LARS. At multivariable analysis, GLS, and LAVI were the only independent correlates of LARS (*Table 3*). LACS was significantly more impaired in non-responders. CRT did not modify LACS at 6-month follow-up in both responders and non-responders (*Table 2*).

Predictors of LV remodelling

Responders had significantly lower LV end-diastolic and end-systolic volume at both baseline and follow-up compared with non-responders.

The main predictors of reduction in LV-end systolic volume at univariable analysis included gender, ischaemic aetiology, LAVI, *E/e′* ratio, TRV_{max}, GLS, mechanical dyssynchrony, moderate-to-severe MR, and LARS. At multivariable analysis, LARS ($\beta = -0.13$, $P = 0.05$), moderate-to-severe MR ($\beta = 0.21$, $P = 0.001$), *E/e′* ratio ($\beta = 0.14$, $P = 0.04$), and LV dyssynchrony ($\beta = -0.29$, $P < 0.0001$) were the main parameters associated with reduction in LV-ESV (*Tables 4 and 5*).

The main predictors of reduction in LV end-diastolic volume at univariable analysis were ischaemic aetiology, *E/e′* ratio, TRV_{max}, moderate-to-severe MR, LV dyssynchrony, and LARS. At multivariable analysis, only LARS ($\beta = -0.17$, $P = 0.01$) and moderate-to-severe MR ($\beta = 0.20$, $P = 0.003$) remained significant predictors of LV diastolic remodelling (*Figure 3A and B*).

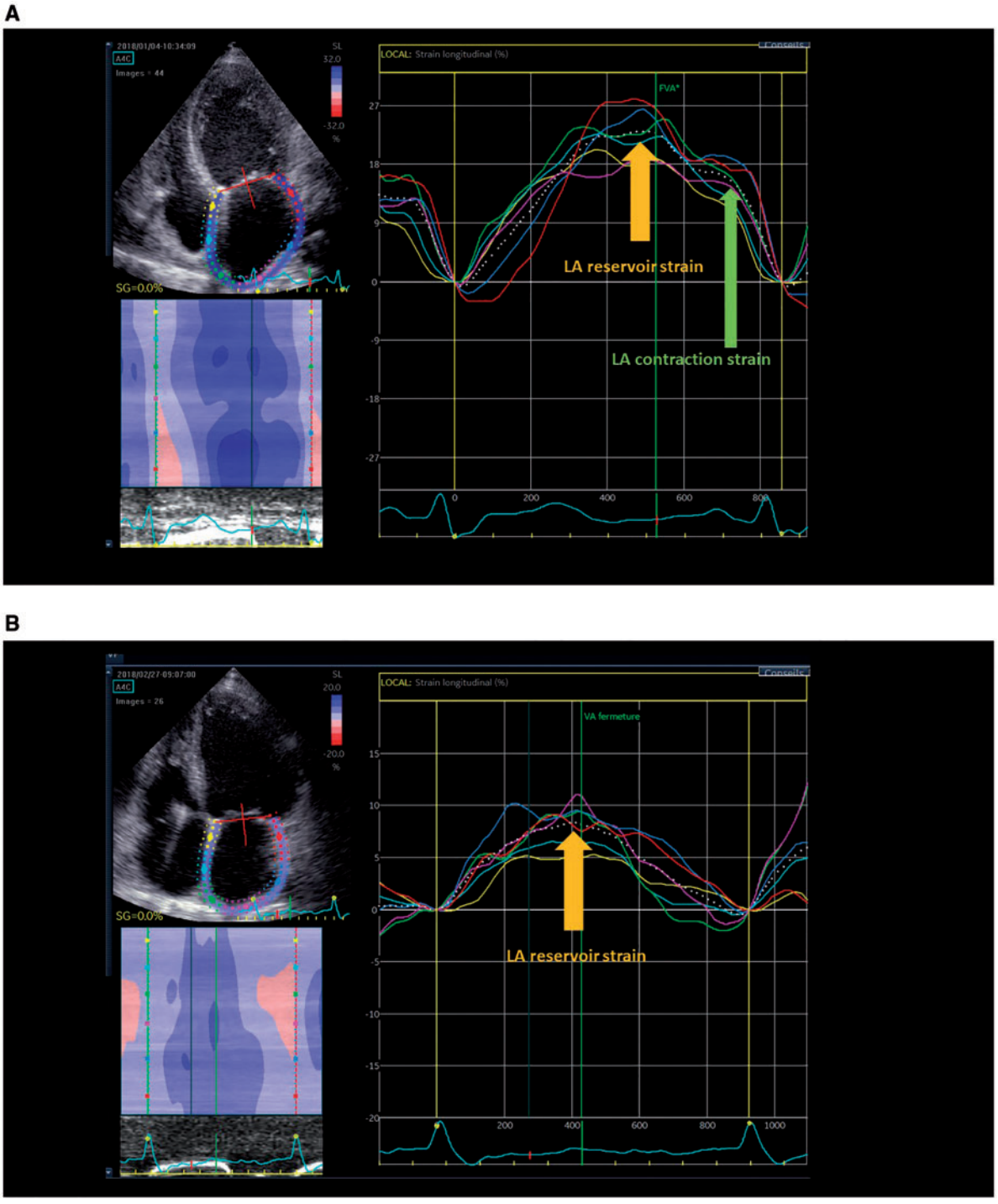


Figure 1 Example of the estimation of left atrial strain in a patient in sinus rhythm (*A*) and a patient in atrial fibrillation (*B*).
LA, left atrium.

Discussion

Until now, few small studies have addressed the effect of CRT on LA remodelling and function. The result of our large, prospective multicentre study confirms and extends previous findings by showing the positive effect of CRT-response on LA morphology and reservoir function. The additional contribution of our study is to provide evidence that LARS is an independent predictor of LV volumetric remodelling in CRT candidates.

Table 1 Characteristics of the overall population and according to CRT response

	All *n* = 221	Responders *n* = 153 (69%)	Non-responders *n* = 68 (31%)	*P*-value
Clinical data				
Age (years)	67 ± 11	67 ± 11	66 ± 11	0.39
Males, *n* (%)	67 (30)	96 (63)	58 (85)	<0.0001
NYHA class	2.3 ± 0.6	2.25±	2.41 ± 0.67	0.08
NYHA III–IV, *n* (%)	80 (36)	49 (31)	31 (46)	0.04
Ischaemic aetiology, *n* (%)	73 (33)	33 (22)	40 (59)	<0.0001
Arterial hypertension, *n* (%)	93 (42)	69 (45)	24 (35)	0.15
Diabetes, *n* (%)	48 (22)	29 (19)	19 (28)	0.09
Dyslipidaemia, *n* (%)	76 (34)	52 (34)	24 (35)	0.50
COPD	28 (13)	18 (12)	10 (15)	0.34
Medications				
ACEI/Sartans, *n* (%)	181 (82)	142 (93)	60 (88)	0.19
Betabloquers, *n* (%)	199 (90)	136 (89)	63 (93)	0.27
Anti-aldosteron, *n* (%)	78/198 (39)	51/136 (38)	27/62 (44)	0.26
Diuretics, *n* (%)	152 (69)	102 (66)	50 (73)	0.15
ECG				
Atrial fibrillation, *n* (%)	38 (17)	27 (18)	11 (16)	0.48
LBBB morphology, *n* (%)	194 (88)	138 (90)	56 (82)	0.08
QRS duration (ms)	165 ± 26	166 ± 23	162 ± 31	0.27
QRS width ≥ 150 ms	144 (65)	119 (78)	45 (66)	0.05
Echocardiographic data				
Moderate-to-severe MR, *n* (%)	40 (18)	22 (14)	18 (26)	0.03
LV dyssynchrony	158 (71)	127 (83)	31 (46)	<0.0001

ACEI, angiotensin-converting-enzyme inhibitors; COPD, chronic obstructive pulmonary disease; LBBB, left bundle branch clock; LV, left ventricle; MR, mitral regurgitation; NYHA, New York Heart Association functional class.

Table 2 Left ventricular and left atrial morphologic and functional variables at baseline and 6-month follow-up in CRT-responders and non-responders

	Responders			Non-responders		
	Baseline	Follow-up	*P*-value	Baseline	Follow-up	*P*-value
LV end-diastolic volume index (mL/m^2)	104 ± 42	68 ± 33	<0.0001	116 ± 34*	105 ± 43**	0.02
LV end-systolic volume index (mL/m^2)	75 ± 34	40 ± 424	<0.0001	84 ± 31*	76 ± 36**	0.02
LVEF (%)	29 ± 7	46 ± 12	<0.0001	28 ± 9	29 ± 10**	0.58
LV-GLS (%)	-9.7 ± 3.2	-13.2 ± 3.4	<0.0001	-7.6 ± 2.9*	-8.2 ± 2.9**	0.58
LAVI (mL/m^2)	45 ± 16	37 ± 17	<0.0001	50 ± 15*	46 ± 15**	0.04
E/*e*′	14 ± 7	12 ± 6	0.02	19 ± 12*	18 ± 12**	0.63
TRV$_{max}$ (m/s)	2.5 ± 0.5	2.5 ± 0.4	0.52	2.8 ± 0.6*	2.7 ± 0.4**	0.26
Left atrial reservoir strain (%)	20 ± 8	22 ± 9	<0.0001	15 ± 7*	14 ± 8**	0.06
Left atrial reservoir strain/LAVI (mL %/m^2)	0.50 ± 0.36	0.77 ± 0.56	<0.0001	0.33 ± 0.24*	0.36 ± 0.32**	0.22
LA contraction strain	14 ± 7	14 ± 6	0.68	9.7 ± 4.5*	8.8 ± 4.9**	0.27

GLS, global longitudinal strain; LAVI, left atrial volume index; LV, left ventricle; LVEF, left ventricular ejection fraction; TRV$_{max}$, maximal tricuspid regurgitation velocity.
$^*P < 0.05$ vs. CRT-responders at baseline.
$^{**}P<0.05$ vs. CRT-responders at follow-up.

Assessment of LA function in CRT candidates

The assessment of LA function can be performed by several methods which include phasic evaluation of LA volumes, TDI, or STE. Compared with LA volumes and TDI, which are, respectively, plagued by atrial foreshortening and angle dependency, STE is a more straightforward method and allows the assessment of LA deformation in all phases of the cardiac cycle.[6] In this study, we focused on

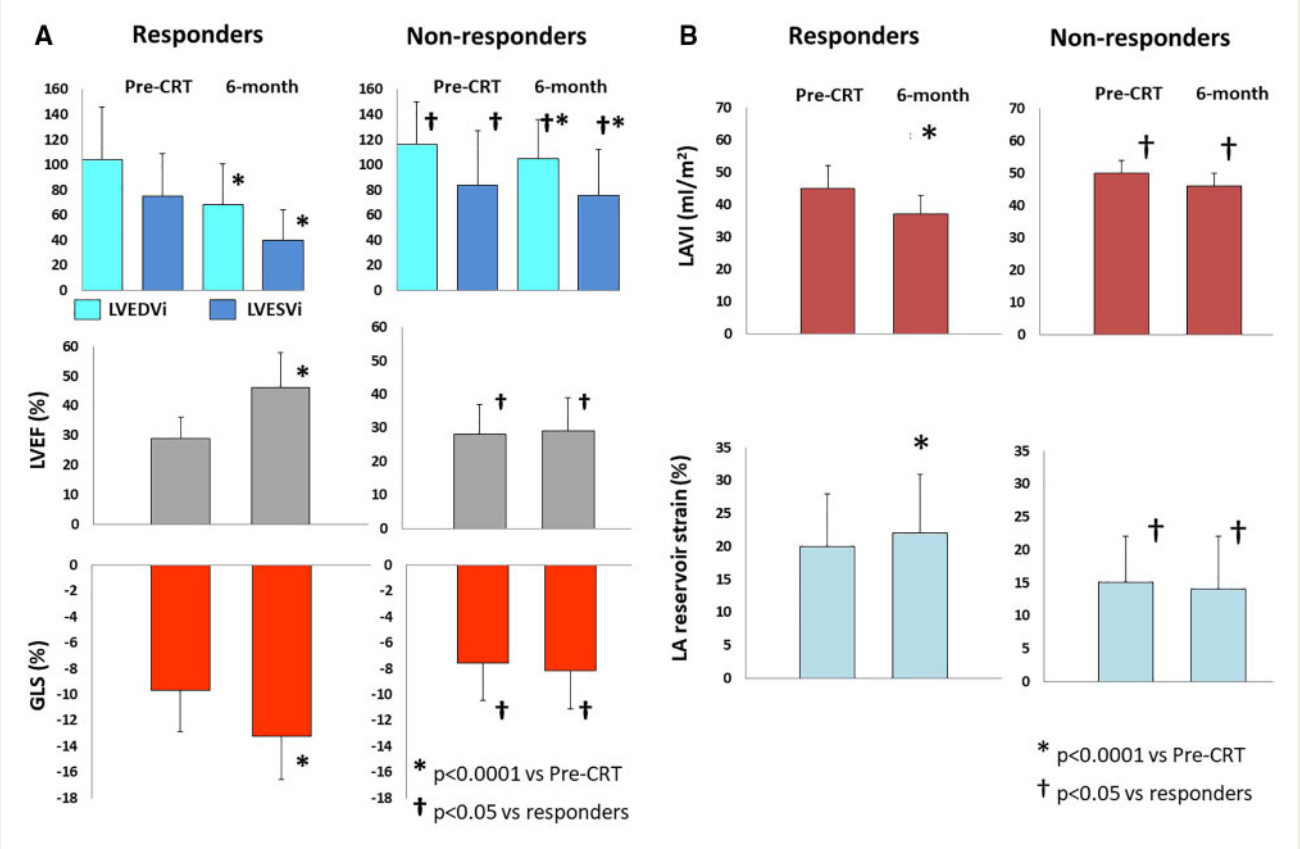


Figure 2 Comparison of left ventricular size and function (*A*) and left atrial size and function (*B*) between responders and non-responders before CRT and 6 months after CRT delivery. GLS, global longitudinal strain; LA, left atrium; LAVI, indexed left atrial volume; LVEF, left ventricular ejection fraction; LV-EDVi, indexed LV end-diastolic volume; LVESVi, indexed left ventricular end-systolic volume.

the estimation of LARS, which corresponds to the LA filling which occurs during LV systole and is measurable also in patients with atrial fibrillation.

In our study, LAVI and LV-GLS were the main independent determinants of LARS.

LA volume is a well-known marker of chronically elevated LV filling pressure.[15] In the initial phase of diastolic dysfunction, LA dilatation acts as a compensatory mechanism that allows preserving LA filling and cardiac output.[16] With more advanced disease, LA dilatation is associated with LA fibrosis, increased stiffness, and decline in LA function[17] and explain the negative relationship existing between LAVI and LARS observed in our population. The other important determinant of LARS is the descent of the cardiac base during systole, which drives LA expansion and draws blood from the pulmonary veins into the LA.[18] This process justifies the significant relationship between LV-GLS and LARS also observed in previous studies.[19,20]

Reduction in LARS is known to be associated with LV diastolic dysfunction.[21] Nevertheless, the relationship between LARS and the echocardiographic markers of reduced LV diastolic function (*E*/*e*′ ratio and TRV_{max}) we observed at univariable analysis was lost at multivariable analysis.

This is in line with previous studies in CRT patients,[9] and might be attributed to the intrinsic limitations of *E*/*e*′-based estimation of LV filling pressures in patients with conduction abnormalities and pacing,[15,22] and portend the hypothesis that LA deformation might be a better method to estimate LV diastolic function in CRT candidates.

Table 3 Main correlates of left atrial reservoir strain

	Univariable		Multivariable	
	Standardized coefficient (β)	*P*-value	Standardized coefficient (β)	*P*-value
LV-GLS (%)	-0.59	<0.0001	-0.53	<0.0001
LAVI (mL/m^2)	-0.40	<0.0001	-0.21	0.002
E/*e*′	-0.34	<0.0001	-0.07	0.29
TRV_{max} (m/s)	-0.37	<0.0001	-0.09	0.16

In this study, there was a significant reduction in LA size and improvement in LARS in CRT-responders at FU compared with baseline. In non-responders, we observed only a slight reduction in LAVI, whereas LARS was unaffected. This might be explained by the fact that the modest reduction of LA volume and absence of improvement in LV function observed in non-responders were not enough

Table 4 Univariate (A) and multivariable (B) linear regression analyses with LV systolic volume reduction at follow-up as the independent variable

Variables	Missing values	Parameter estimate	Standard error	Standardized estimate (β)	*P*-value
(A)					
Age	0	-0.0001	0.002	-0.005	0.949
Male gender	0	0.101	0.041	0.166	0.016
NYHA Classes III–IV	1	0.035	0.041	0.059	0.389
Ischaemic aetiology	0	0.162	0.040	0.268	<0.0001
LBBB morphology	0	-0.061	0.060	-0.070	0.308
QRS width ≥150 ms	0	-0.036	0.044	-0.056	0.416
Moderate-to-severe MR	0	0.127	0.039	0.220	0.001
LVEF (%)	0	0.003	0.003	0.076	0.274
LV-GLS (%)	13	0.013	0.006	0.152	0.032
LAVI (mL/m^2)	0	0.004	0.001	0.219	0.001
E/*e*′	13	0.007	0.002	0.231	0.001
Max TR velocity (m/s)	45	0.139	0.039	0.269	0.0004
Left atrial reservoir strain	3	-0.009	0.002	-0.276	<0.0001
LV mechanical dyssynchrony	0	-0.209	0.040	-0.034	<0.0001
(B)					
MR moderate-to-severe		0.123	0.037	0.215	0.001
E/*e*′		0.004	0.003	0.139	0.039
Left atrial reservoir strain		-0.004	0.002	-0.138	0.049
LV mechanical dyssynchrony		-0.175	0.039	-0.288	<0.0001

Table 5 Univariate (A) and multivariable (B) linear regression analyses with LV diastolic reduction at follow-up as the independent variable

Label	Missing values	Parameter estimate	Standard error	Standardized estimate (β)	*P*-value
(A)					
Age	0	0.001	0.002	0.006	0.933
Male gender	0	0.063	0.037	0.115	0.094
NYHA Classes III–IV	1	0.049	0.036	0.094	0.172
LBBB morphology	0	-0.069	0.054	-0.088	0.201
QRS ≥150 ms	0	0.011	0.039	0.018	0.789
MR moderate-to-severe	0	0.127	0.035	0.243	0.0003
LVEF (%)	0	-0.001	0.002	-0.023	0.740
LV-GLS (%)	13	0.005	0.006	0.069	0.329
LAVI (mL/m^2)	0	0.001	0.001	0.049	0.477
E/*e*′	13	0.006	0.002	0.198	0.005
Max TR velocity (m/s)	46	0.089	0.035	0.195	0.012
Left atrial reservoir strain	3	-0.006	0.002	-0.217	0.002
LV mechanical dyssynchrony	0	-0.13	0.038	-0.240	0.001
(B)					
MR moderate-to-severe		0.107	0.036	0.203	0.003
Left atrial reservoir strain		-0.005	0.002	-0.174	0.011

to portend a significant reverse functional remodelling of the left atrium.[23] On the other hand, the significant improvement in LARS observed in responders can be explained by the combined improvement in LAVI and systolic function.

LA reservoir strain is a predictor of LV remodelling after CRT

In a previous small single centre study, we demonstrated that LA deformation assessed by strain rate is an independent predictor of

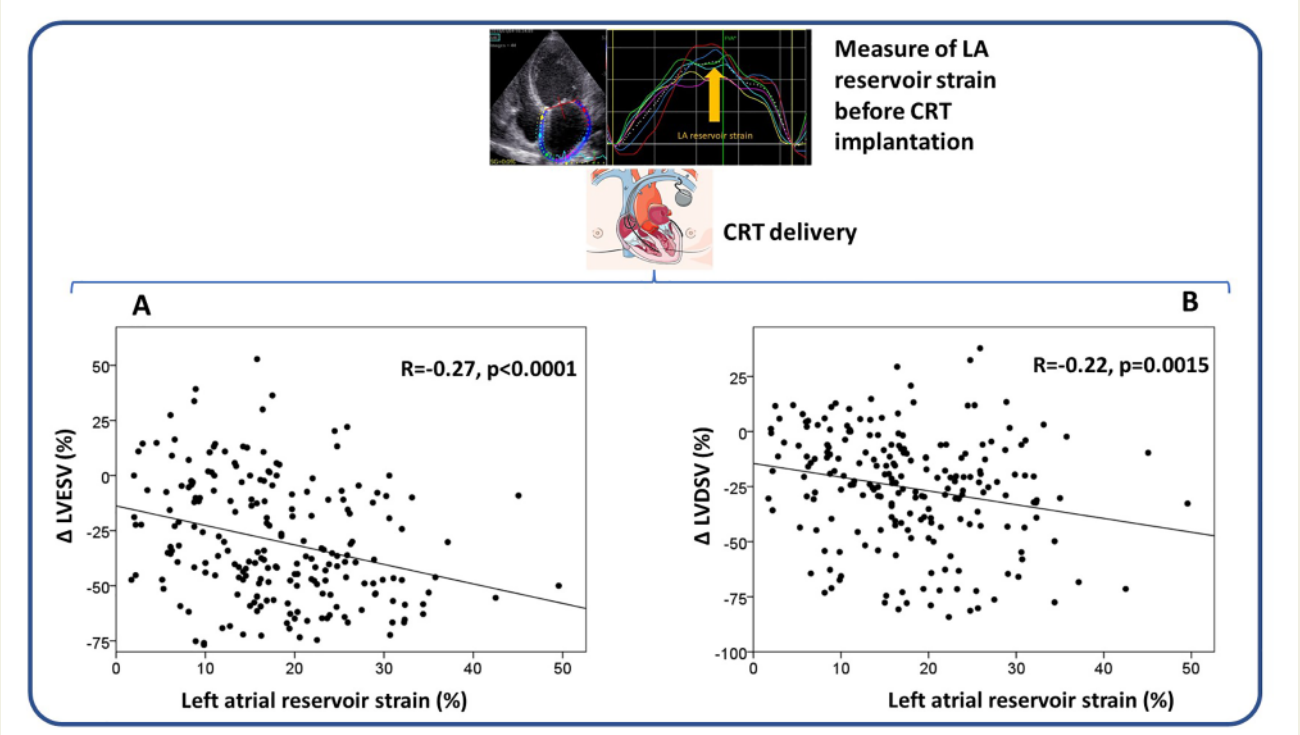


Figure 3 Left atrial reservoir strain measured before CRT-delivery is an independent predictor of both LV systolic and diastolic reverse remodelling. This picture shows the correlation between left atrial reservoir strain and reverse systolic (*A*) and diastolic (*B*) remodelling after CRT. CRT, cardiac resynchronization therapy; LV-EDV, left ventricular end-diastolic volume; LV-ESV, left ventricular end-systolic volume.

CRT-response.[10] Nevertheless, the assessment of atrial strain rate is plagued by poor reproducibility and difficult interpretation, which prevent its application in clinical practice. In this study, the measure of LARS was possible in the majority of patients, including those with atrial fibrillation.

Interestingly, we found that the quantification of LA function/deformation by LARS was able to predict the LV (systolic and diastolic) remodelling induced by CRT.

The predictive value of LARS was maintained after adjustment for other known clinical, electrocardiographic, and echocardiographic predictors of CRT response, such as QRS morphology and duration, LAVI, HF aetiology, and LV dyssynchrony.

As underscored in the previous paragraph, LARS is significantly correlated to LV-GLS, which means that LARS is more impaired in patients with more advanced LV longitudinal dysfunction.

LV-GLS correlates with the entity of LV fibrosis and remodelling in CRT candidates and it is a well-known predictor of CRT-response.[24] Nevertheless, LA reservoir function might also be impaired because of significant LA remodelling and more advanced diastolic dysfunction.[25] This means that LARS might allow a comprehensive assessment of both the systolic and diastolic LV impairment. The more impaired LARS, the more advanced is the ongoing left ventricular disease, and the less likely is CRT-induced reverse remodelling.

Interestingly, LARS was also a significant independent predictor of LV diastolic remodelling after CRT.

The definition of LV ventricular reverse remodelling is an object of debate. Many studies in the field of CRT have focused on the reduction of LV-ESV at follow-up, which has the undeniable advantage of combining LV volume and systolic function assessment.

Several studies in patients with HFrEF have shown that the percent reduction of LVEDV is a marker of positive LV remodelling and prognosis.[26]

In this study, we found that LARS and MR were both independently associated with LV volumetric remodelling in diastole. The effect of MR on LV diastolic size might be explained by the increased preload associated with moderate-to-severe MR, which promotes progressive LV dilatation.

The relationship between LA reservoir function and LV diastolic reverse remodelling is more subtle. Several studies have shown that the degree of LV fibrosis assessed by late gadolinium enhancement is directly associated with the entity of LV dilatation and reduction in LV diastolic volume.[27] Nevertheless, the degree of LV fibrosis is also a marker of advanced diastolic dysfunction and increased LV filling pressure, which significantly limits LA preload reserve and causes a progressive decline in all LA function parameters, including LARS.[25]

This observation might contribute to explain why patients with lower LARS at baseline also have a lesser extent of LV diastolic remodelling after CRT.

Limitations

This study has several limitations: (i) this is an observational prospective study performed on a relatively limited number of patients. (ii) The assessment of LARS was feasible also in patients with atrial

fibrillation, which might represent a strength allowing the assessment of LARS also in CRT candidates with atrial arrhythmia. Nevertheless, the percentage of patients with atrial fibrillation in our population was relatively low, and the potential application of our results to this specific group of HF patients deserves further investigation. (iii) The correlation between LARS and LV systolic remodelling is poor. Nevertheless, we found a similar degree of correlation for other well-known predictors of CRT response, such as LV mechanical dyssynchrony or MR entity. This might be since CRT-response is influenced by several concomitant factors including clinical parameters, ECG, biomarkers, and imaging-derived parameters. Therefore, the results of our study suggest that LA deformation can be one of the parameters to be looked for in CRT candidates and underscore the value of the assessment of LA function in HF patients, including those undergoing CRT. (iv) The relationship between LARS and LV reverse remodelling after CRT underscores the value of LA reservoir function as a measure of both LV systolic and diastolic dysfunction. This might be of particular interest because the correct modality to assess diastolic function in CRT candidate is still an object of debate.[15] Nevertheless, the pathophysiologic role of LARS for the evaluation of diastolic function in patients undergoing CRT is only inferred in our study. There is the need for a specific trial aimed at assessing the correlation between LA strain, diastolic function parameters, and filling pressures in this specific subset of patients. (v) Despite 3D-echocardiography has shown to be a promising approach to evaluate LA phasic function,[28] we did not apply this method in our population. The potential usefulness of 3D-echocardiography to predict CRT response deserve attention and should be evaluated in future studies.

Conclusions

CRT causes significant improvement in LA size and reservoir function in responders. LARS assessed before CRT implantation is an independent predictor of both LV systolic and diastolic reverse volumetric remodelling.

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Data availability

The data that support the findings of this study are available from the corresponding author, EG, upon reasonable request.

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