Cardiac resynchronization therapy : determinants of patient outcome and emerging indications

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Chapter 3

Assessment of left ventricular dyssynchrony by speckle-tracking strain imaging, comparison between longitudinal, circumferential, and radial strain in CRT

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ABSTRACT

Background: Different echocardiographic techniques have been proposed for assessment of left ventricular (LV) dyssynchrony. The novel 2D speckle-tracking strain analysis technique can provide information on radial (RS), circumferential (CS) and longitudinal strain (LS). The objective of this study was to assess the usefulness of each type of strain for LV dyssynchrony assessment and their predictive value for a positive response after cardiac resynchronization therapy (CRT). Furthermore, changes in extent of LV dyssynchrony for each type of strain were evaluated during follow-up.

Methods: In 161 patients, 2D echocardiography was performed at baseline and after 6 months of CRT. Extent of LV dyssynchrony was calculated for each type of strain. Response to CRT was defined as a decrease in LV end-systolic volume ≥15% at follow-up.

Results: At follow-up, 88 patients (55%) were classified as responders. Differences in baseline LV dyssynchrony between responders and non-responders were only noted for RS (251±138 ms vs. 94±65 ms; p<0.001), whereas no differences were noted for CS and LS. A cut-off value of ≥130 ms for RS was able to predict response to CRT with a sensitivity of 83% and a specificity of 80%. In addition, a significant decrease in extent of LV dyssynchrony measured with RS (from 251±138 ms to 98±92 ms; p<0.001) was demonstrated only in responders.

Conclusions: Speckle-tracking radial strain analysis constitutes the best method to identify potential responders to CRT. Reduction in LV dyssynchrony after CRT was only noted in responders.

INTRODUCTION

By stimulating the right ventricle and the postero-lateral wall of the left ventricle (LV), cardiac resynchronization therapy (CRT) has been shown to decrease LV volumes, increase LV systolic function and improve clinical status in patients with end-stage heart failure.[1] However, in previous studies, the percentage of non-responders is more than 30% when response to CRT is defined by echocardiographic criteria (e.g. LV reverse remodeling).[2] The lack of mechanical LV dyssynchrony has been suggested as one of the reasons for non-response to CRT.[3]

In recent years various imaging techniques have been tested for their ability to quantify LV dyssynchrony and for their predictive value for response to CRT, including magnetic resonance imaging, nuclear imaging and echocardiography.[3-7] Most experience has been obtained with echocardiography using color-coded tissue Doppler imaging (TDI) by measuring peak systolic velocities in different segments of the LV. Several studies in CRT patients proved that TDI was highly predictive for response to CRT and event-free survival at 1-year follow-up.[3, 5, 8, 9]

Speckle-tracking strain analysis is a novel method based on gray-scale 2-dimensional (2D) images, which permits the assessment of myocardial deformation in two dimensions. Using apical and parasternal short-axis views, three different patterns of myocardial deformation can be assessed; radial strain (RS) represents the myocardial thickening in a short-axis plane; circumferential strain (CS) represents myocardial shortening in a short-axis plane; and longitudinal strain (LS) represents the myocardial shortening in the long-axis plane.[10] To date, few studies used either RS, CS or LS to asses LV dyssynchrony, and it is currently unclear which type of strain used for LV dyssynchrony assessment best predicts response to CRT.[11-14] Furthermore, data on changes in LV dyssynchrony after CRT according to the different strain types are scarce.

Therefore, using 2D speckle-tracking echocardiography, the aims of the present study were: 1) to determine which type of strain for assessment of LV dyssynchrony best predicts echocardiographic response after 6 months of CRT and, 2) to evaluate changes in LV dyssynchrony as derived from RS, CS and LS, after 6 months of CRT. In addition, the predictive value of the strain parameters was compared to the established value of TDI.[3]

METHODS

Population and study protocol

One-hundred sixty-one consecutive patients who were scheduled for CRT were included in the present study. The current selection criteria used for CRT included: drug-refractory

symptomatic heart failure, with patients in New York Heart Association functional class III or IV, and depressed LV ejection fraction (≤35%) with wide QRS complex (>120 ms).[15] The study protocol included evaluation of clinical status and transthoracic echocardiography before CRT implantation with follow-up evaluation after 6 months of CRT.

Device implantation

The coronary sinus was cannulated with the use of a guiding balloon catheter and a venogram was obtained. Thereafter, the LV pacing lead (Easytrak 4512-80, Guidant Corporation, St. Paul, Minnesota; or Attain-SD 4189, Medtronic Inc., Minneapolis, Minnesota) was inserted into the coronary sinus, and positioned in a lateral or posterolateral vein. The right atrial and ventricular leads were traditionally positioned and all leads were connected to a dual-chamber biventricular implantable cardioverter-defibrillator (Contak CD or TR, Guidant Corporation; or Insync III or CD, Medtronic Inc.).

Clinical follow-up

Clinical status was evaluated at baseline and after 6 months of follow-up. Assessed parameters included New York Heart Association functional class, quality-of-life score according to the Minnesota Living with Heart Failure questionnaire,[16] and 6-minute walking distance.[17]

Echocardiography

Baseline and follow-up echocardiographic studies were performed with the patient in the left lateral decubitus position using commercially available equipment (Vingmed Vivid-7, General Electric Vingmed, Milwaukee, Wisconsin, USA). Data acquisition was performed with a 3.5-MHz transducer at a depth of 16 cm in the parasternal and apical views (standard 2- and 4-chamber images). Standard M-mode and 2D images were obtained during breath hold and stored in cineloop format from 3 consecutive beats. LV end-diastolic diameter was obtained from the M-mode images of the parasternal long-axis view. LV end-diastolic and end-systolic volumes were measured from the apical 2- and 4-chamber views and the LV ejection fraction was calculated using the Simpson's rule.[18] The LV volumes were also indexed to the body surface area.

LV diastolic function was evaluated by the mitral inflow pattern obtained by pulsed-wave Doppler echocardiography, and classified as normal filling, abnormal relaxation, pseudonormal filling or restrictive filling pattern.[19]

In addition, conventional color-coded TDI was performed to determine LV dyssynchrony (EchoPac 6.1, GE Medical Systems, Horten, Norway).[3] The sector width and the depth were adjusted to obtain the highest frame rate (100-120 frames/s) and pulse repetition frequencies between 500 Hz to 1KHz were used resulting in aliasing velocities between 16 and 32 cm/s. The extent of LV dyssynchrony was calculated as the maximum time delay between peak systolic velocities of basal septal, lateral, anterior and inferior LV segments.[3]

Speckle-tracking strain analysis

For speckle-tracking analysis, standard gray-scale 2D images were acquired in the 2- and 4-chamber apical views as well as the parasternal short-axis views at the level of the papillary muscles. Special care was taken to avoid oblique views from the mid-level short-axis images and to obtain images with the most circular geometry possible. All the images were recorded with a frame rate of at least 30 fps to allow for reliable operation of the software (EchoPac 6.1, GE Medical Systems, Horten, Norway).[14]

From an end-systolic single frame, a region of interest was traced on the endocardial cavity interface by a point-and-click approach. Then, an automated tracking algorithm followed the endocardium from this single frame throughout the cardiac cycle. Further adjustment of the region of interest was performed to ensure that all the myocardial regions were included. Next, acoustic markers, the so-called speckles, were distributed equally in the region of interest and can be followed throughout the entire cardiac cycle. The distance between the speckles was measured as a function of time and parameters of myocardial deformation could be calculated. Finally, the myocardium was divided into 6 segments that were color-coded as previously described[20] and displayed into 6 segmental time-strain curves for respectively RS, CS and LS (Figure 1).

For each type of strain analyzed, 2 different parameters for dyssynchrony were obtained; maximal time delay between peak systolic strain of 2 segments (most frequently observed between the (antero)septum and (postero)lateral wall) as well as an asynchrony index of the LV by calculating the standard deviation of time to peak systolic strain.

For RS and CS, difference between time to peak systolic strain of the (antero)septal and posterior segments (AS-P delay) and the standard deviation of time to peak systolic strain for all 6 segments (SDt_{6S}) were measured. For LS, the 2-and 4-chamber views were used to calculate the difference between time to peak systolic strain of the basal-septal and basal-lateral LV segment (BS-BL delay) as well as the standard deviation of time to peak systolic strain for 12 LV segments (SDt_{12S}).
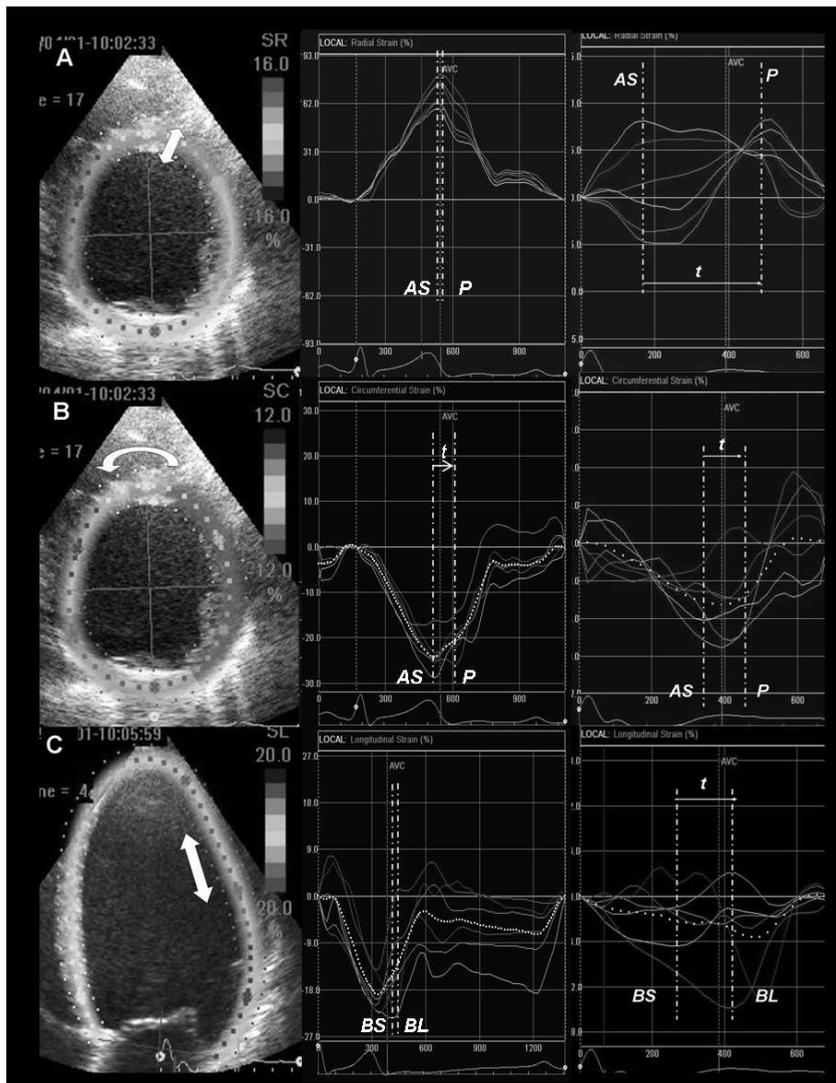
Figure 1. Two dimensional strain imaging: radial strain (A), circumferential strain (B) and longitudinal strain (C).
In the left corner the 2D strain images are represented. The light arrows depict the type of deformation assessed in each view: radial thickening (A), circumferential shortening (B) and longitudinal shortening (C). The middle and right panels demonstrate the segmental time-strain curves for a synchronous (middle) and dyssynchronous (right) LV for each view. Time differences in peak systolic strain (t) between anteroseptal (AS) and posterior (P) segments, in short-axis view, and between basal-septal (BS) and basal-lateral (BL) segments, in 4-chamber view, can be obtained from these curves.

Definition of response to CRT

Responders to CRT were defined as displaying a reduction of ≥15% in LV end-systolic volume at 6-month follow-up (2). Patients who died within the 6-month follow-up period or underwent heart transplantation were classified as non-responders.

Statistical analysis

Continuous variables are presented as mean±SD and compared with 2-tailed Student t test for paired and unpaired data. Categorical data are presented as number and percentage and compared with χ^2-test. Linear regression analysis was performed to assess the relation between the changes in LV end-systolic volume and baseline LV dyssynchrony. In addition, the extent of baseline LV dyssynchrony, as assessed with the different echocardiographic methods, needed to predict response to CRT was determined by receiver operator characteristic curve analysis. The optimal cut-off value was calculated as (sensitivity + specificity)/2. Finally, 20 patients were randomly selected to test the intra- and interobserver variability for the LV dyssynchrony measurements. Subsequently, linear regression analysis and Bland-Altman analysis were performed. A p-value <0.05 was considered statistically significant.

RESULTS

Patient baseline characteristics

The baseline characteristics of the 161 patients (125 men, age 66±11 years) included in the present study are summarized in Table 1. According to the inclusion criteria, all patients had severe heart failure (mean functional class 3.0±0.5), with severe LV dysfunction (mean LV ejection fraction 23±7%) and wide QRS complex (mean 164±32 ms). Mean LV dyssynchrony as assessed with TDI was 84±55 ms. All patients had optimized medical therapy, including angiotensin-converting enzyme inhibitors or angiotensin-receptor antagonists, beta-blockers and diuretics/spironolactone, at maximum tolerated dosages. Device implantation was successful in all patients and no complications were observed.

Table 1. Baseline characteristics of the study population

	All patients (n = 161)	Responders (n = 88)	Non-responders (n = 73)	p-value
Age (years)	66 ± 11	67 ± 10	66 ± 12	0.4
Male gender	125 (78%)	64 (73%)	61 (84%)	0.1
Body surface area (m²)	1.9 ± 0.2	1.9 ± 0.2	2.0 ± 0.2	0.2
Ischemic etiology	92 (57%)	48 (55%)	44 (60%)	0.3
QRS duration (ms)	164 ± 32	171 ± 31	155 ± 32	**0.002**
Sinus rhythm	123 (76%)	64 (73%)	59 (81%)	0.4
NYHA functional class	3.0 ± 0.5	3.0 ± 0.5	3.0 ± 0.5	0.2
Quality-of-life score	41 ± 16	39 ± 16	44 ± 16	0.1
6-minute walking distance (m)	279 ± 132	294 ± 122	263 ± 142	0.2
LV end-diastolic diameter (mm)	70 ± 11	71 ± 11	69 ± 11	0.2
LV end-diastolic volume (ml)	245 ± 89	260 ± 90	226 ± 86	**0.01**
LV end-diastolic volume index (ml/m²)	126 ± 48	136 ± 50	114 ± 42	**0.005**
LV end-systolic volume (ml)	191 ± 82	208 ± 85	171 ± 75	**0.004**
LV end-systolic volume index (ml/m²)	99 ± 44	108 ± 47	86 ± 37	**0.001**
LV ejection fraction (%)	23 ± 7	21 ± 6	25 ± 8	**0.001**
Diastolic function				0.1
Normal filling pattern	11 (7%)	3 (11%)	8 (3%)	
Abnormal relaxation pattern	59 (37%)	37 (30%)	22 (42%)	
Pseudonormal filling pattern	36 (22%)	20 (22%)	16 (23%)	
Restrictive filling pattern	55 (34%)	28 (37%)	27 (32%)	
LV dyssynchrony by TDI (ms)	84 ± 55	106 ± 54	58 ± 44	**<0.001**
AS-P delay by RS (ms)	180 ± 135	251 ± 138	94 ± 65	**<0.001**
SDt$_{6S}$ by RS (ms)	107 ± 71	130 ± 67	79 ± 65	**<0.001**
AS-P delay by CS (ms)	162 ± 128	204 ± 143	162 ± 128	0.1
SDt$_{6S}$ by CS (ms)	128 ± 69	145 ± 59	128 ± 69	0.1
BS-BL delay by LS (ms)	136 ± 101	170 ± 134	136 ± 101	0.1
SDt$_{12S}$ by LS (ms)	115 ± 42	121 ± 42	109 ± 41	0.1

AS-P delay = difference between time to peak systolic strain of the anteroseptal and posterior segments; BS-BL delay = difference between time to peak systolic strain of the basal-septal and basal-lateral segments; CS = circumferential strain; LV = left ventricular; LS = longitudinal strain; NYHA = New York Heart Association; RS = radial strain; SDt$_{6S}$ = Standard deviation of the time to peak systolic strain of 6 segments; SDt$_{12S}$ = Standard deviation of the time to peak systolic strain of 12 segments; TDI = tissue Doppler imaging

Speckle-tracking strain analysis and LV dyssynchrony

All patients were analyzed at baseline and at 6-month follow-up. In the mid-ventricular short-axis images, RS by speckle-tracking was possible in 90% of 1896 attempted segments. Reliable CS-time curves were obtained in 85% of the same 1896 attempted segments. The feasibility for LS in 2- and 4-chambers views was 79%, and only 2990 segments from 3792 attempted segments could be reliably evaluated. The lesser feasibility for assessment of LS was due to non-valid tracking at the apical segments, where 30% of the segments had to be discarded. Furthermore, reproducibility for the different time delays was better when 2D RS was used (Table 2).

In the overall population, substantial baseline dyssynchrony was present as indicated by long time-delays in peak systolic strain between the anteroseptal and posterior wall, as well

as high standard deviations either by RS and CS (Table 1). Also, an important BS-BL delay was observed with longitudinal strain, as well as an important SDt_{12S}.

Table 2. Intra- and Interobserver variability for the different LV dyssynchrony parameters

	Intraobserver		Interobserver	
	Difference	*r*	*Difference*	*r*
AS-P delay by RS (ms)	-3 ± 23	0.98*	0.3 ± 24	0.97*
SDt_{6s} by RS (ms)	-5 ± 29	0.88*	3 ± 28	0.88*
AS-P delay by CS (ms)	11 ± 53	0.91*	-10 ± 55	0.80*
SDt_{6s} by CS (ms)	6 ± 36	0.66[†]	-6 ± 27	0.70[†]
BS-BL delay by LS (ms)	-17 ± 36	0.93*	4 ± 22	0.92*
SDt_{12s} by LS (ms)	7 ± 22	0.72*	-7 ± 13	0.88*

Abbreviations as in Table 1
*p<0.001; [†]p <0.05

Response to CRT

Before the 6-month follow-up evaluation, 2 patients underwent heart transplantation and 4 died from worsening heart failure. In the entire patient group, a significant improvement in clinical status was noted, with a reduction in functional class (from 3.0±0.5 to 2.1±0.7, p<0.001), a reduction in quality-of-life score (from 41±16 to 27±19, p<0.001) and an increase in 6-minute walking distance (from 279±132 m to 377±139 m, p<0.001).

On echocardiography, LV ejection fraction improved significantly from 23±7% to 30±9% (p<0.001) and significant reductions in LV end-diastolic volume (245±89 ml to 215±81 ml, p<0.001) and LV end-systolic volume (191±82 ml to 155±71 ml, p<0.001) were observed.

In Table 3, the different parameters for LV dyssynchrony are reported at baseline and at 6-month follow-up. Both the AS-P delay and SDt_{6s} as assessed with RS showed a significant reduction in time delay at 6-month follow-up. In contrast, for the same parameters assessed with CS, only the SDt_{6s} demonstrates a significant reduction after CRT. In addition, BS-BL delay as assessed by LS also showed a significant reduction at 6-month follow-up, whereas the SDt_{12s} remained unchanged.

Table 3. LV dyssynchrony measurements at baseline and after 6 months of CRT in overall population

|	Baseline	6 months follow-up	p-value
AS-P delay by RS (ms)	180 ± 135	112 ± 101	**<0.001**
SDt$_{6S}$ by RS (ms)	107 ± 71	63 ± 52	**<0.001**
AS-P delay by CS (ms)	162 ± 128	165 ± 117	0.2
SDt$_{6S}$ by CS (ms)	128 ± 69	109 ± 63	**0.04**
BS-BL delay by LS (ms)	136 ± 101	112 ± 86	**0.01**
SDt$_{12S}$ by LS (ms)	115 ± 42	111 ± 86	0.7

Abbreviations as in Table 1

Responders vs. non-responders to CRT

At 6-month follow-up, 88 patients (55%) were classified as responders to CRT, according to the pre-defined criterion of a reduction in LV end-systolic volume by more than 15%. Conversely, 73 patients (45%) were non-responders including the 6 patients who died or underwent heart transplantation before the 6-month follow-up.

Responders showed (by definition) a reduction in LV end-systolic volume (from 208±85 ml to 140±72 ml, p<0.001) and in LV end-diastolic volume (from 260±90 ml to 203±82 ml, p<0.001, see Figure 2). Furthermore, an improvement in LV ejection fraction was noted (from 21±6% to 33±9%, p<0.001). In contrast, non-responders showed no improvement in LV ejection fraction (from 25±8% to 25±7%, p = NS) and showed a trend towards an increase in both LV end-systolic volume (from 171±75 ml to 175±66 ml, p = NS) and LV end-diastolic volume at 6-month follow-up (from 226±86 ml to 230±77 ml, p = NS).

Baseline clinical and echocardiographic parameters between responders and non-responders were comparable; except for smaller LV volumes, higher LV ejection fraction and shorter QRS duration in non-responders. Furthermore, responders exhibited more baseline LV dyssynchrony as assessed with TDI as compared to non-responders (see Table 1).

Concerning the LV dyssynchrony parameters assessed with speckle-tracking analysis at baseline, AS-P delay and SDt$_{6S}$ as assessed by RS were significantly larger in responders as
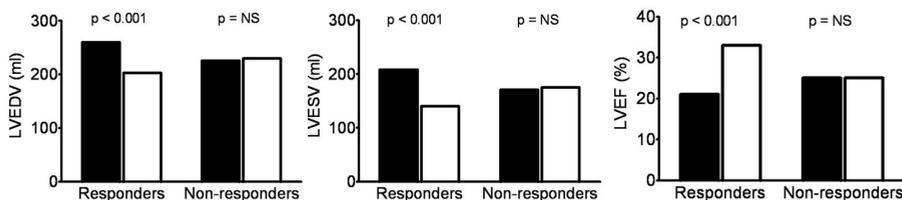

Figure 2. Changes in LV end-diastolic volume (LVEDV, A) LV end-systolic volume (LVESV, B) and LV ejection fraction (LVEF, C) during follow-up according to CRT response. Dark bars represent baseline values whereas light bars represent 6 month follow-up values.
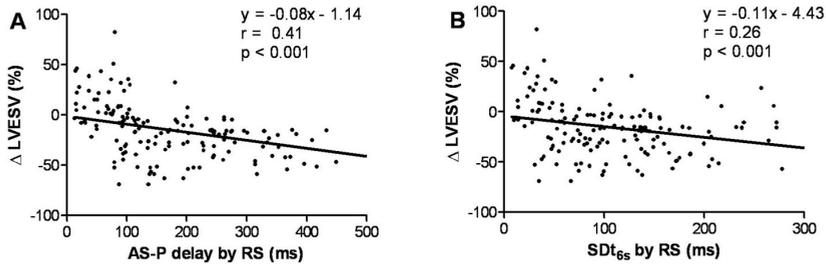
Figure 3. Relationship between respectively baseline AS-P delay (A) and SDt$_{6S}$ (B) and the LV reverse remodeling (expressed as reduction in LV end-systolic volume) after 6 months of CRT.

compared to non-responders (251±138 ms vs. 94±65 ms, p<0.001 and 130±67 ms vs. 79±65 ms, p<0.001, respectively). However, there were no differences between both groups in either AS-P delay and SDt$_{6S}$ by CS or BS-BL delay and SDt$_{12S}$ evaluated by LS (see Table 1). Linear regression analysis demonstrated a modest but significant relation between respectively baseline AS-P delay by RS and extent of LV reverse remodeling and baseline SDt$_{6S}$ by RS and LV reverse remodeling (Figure 3); a higher value of baseline radial dyssynchrony corresponded with a larger reduction in LV end-systolic volume.

Furthermore, after 6 months of CRT, responders showed a significant reduction in AS-P delay and SDt$_{6S}$ as assessed by RS and in the BS-BL delay assessed by LS (see Figure 4). In non-responders, none of the dyssynchrony parameters showed a significant reduction.

Radial Strain



Circumferential Strain

Longitudinal Strain
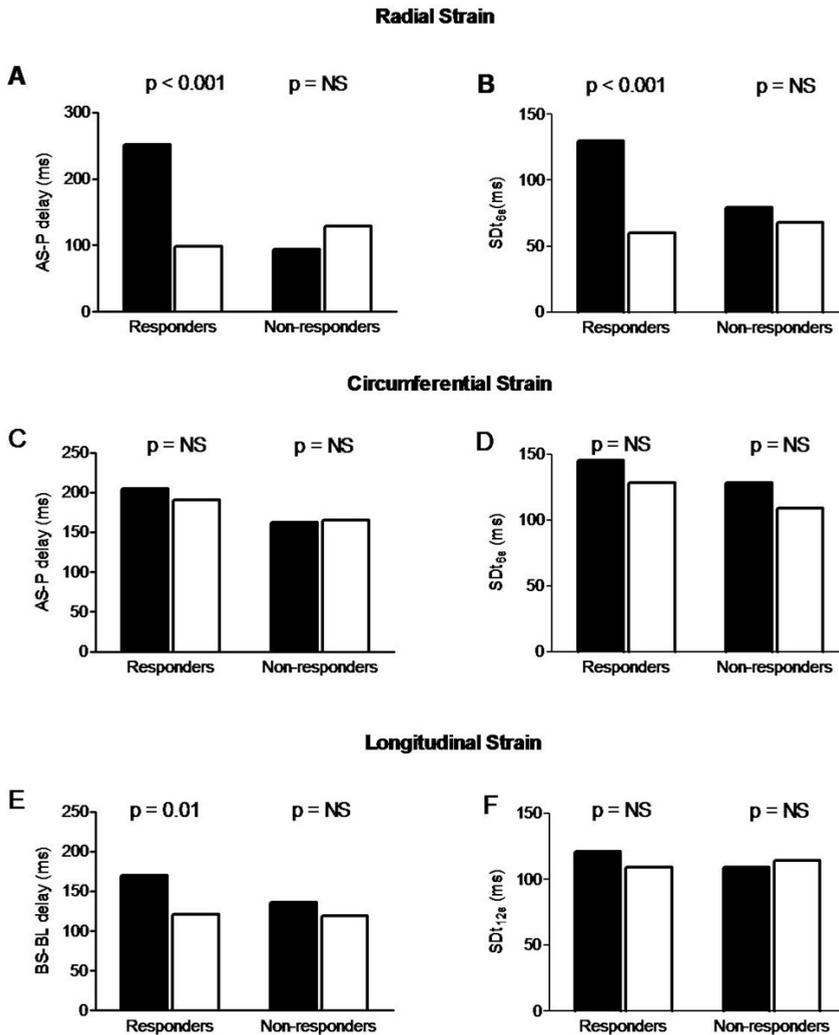
Figure 4. Changes in LV dyssynchrony as assessed with radial strain (A, B), circumferential strain (C, D) and longitudinal strain (E, F) after CRT in responders and non-responders. Dark bars represent baseline values whereas light bars represent values at 6 month follow-up.

Prediction of response to CRT

Receiver operating characteristic curve analysis was performed to define the optimal cut-off value for both AS-P delay and SDt$_{6s}$ as assessed with RS to predict response to CRT. In addition, the optimal cut-off value for LV dyssynchrony as assessed by TDI was calculated.

The area under the curve for AS-P delay was 0.88 and the optimal cut-off value to predict response to CRT was 130 ms, yielding a sensitivity and specificity of respectively 83% and 80% (Figure 5A). In addition, the area under the curve for SDt$_{6s}$ was 0.74 and the optimal cut-off value to predict response was 76 ms, yielding a sensitivity and specificity of respectively 77% and 60% (Figure 5B). The area under the curve for TDI-derived LV dyssynchrony was 0.76 and the accepted cut-off value of 65 ms to predict response to CRT yielded a sensitivity and specificity of 81% and 63% respectively (Figure 5C).
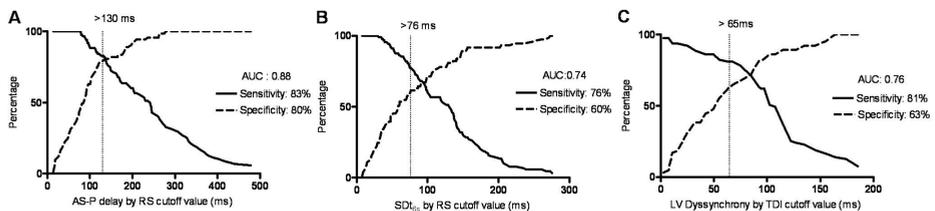
Figure 5. Receiver operating characteristics curves for AS-P delay (A) and SDt$_{6s}$ (B) as assessed by radial strain (RS) and LV dyssynchrony (C) as assessed by tissue Doppler imaging (TDI). AS-P delay = difference between time to peak systolic strain of the anteroseptal and posterior segments; AUC = area under the curve; SDt$_{6s}$ = Standard deviation of the time to peak systolic strain of 6 segments.

DISCUSSION

The present study demonstrates that evaluation of LV dyssynchrony using speckle-tracking strain analysis is feasible and that substantial LV dyssynchrony is present in all three deformation types, radial, circumferential and longitudinal, in CRT candidates with depressed LV function and dilated cardiomyopathy. Furthermore, only baseline LV dyssynchrony parameters assessed with RS (both AS-P delay and SDt$_{6s}$ delay) were able to identify potential responders to CRT, defined as a decrease of ≥15% in LV end-systolic volume after 6 months of CRT. In addition, a decrease in extent of LV dyssynchrony during follow-up was only noted in responders to CRT for parameters assessed with RS (both AS-P delay and SDt$_{6s}$ delay) and LS (BS-BL delay); no changes in LV dyssynchrony with CS were observed in responders to CRT. Non-responders to CRT did not show any significant change in extent of LV dyssynchrony using RS, LS or CS.

Changes in LV dyssynchrony after CRT

Three forms of strain were assessed before and 6 months after CRT to assess the effect bi-ventricular pacing: radial, circumferential and longitudinal strain. Only few data are available on the changes in strain (assessed by 2D speckle-tracking analysis) after CRT. Knebel et al.[13] evaluated 38 heart failure patients and demonstrated that responders to CRT revealed a significant decrease in time delays assessed with RS (from 168±104 ms at baseline to 98±44 ms at follow-up, p = 0.04) and LS (from 168±104 ms at baseline to 112±81 ms at follow-up, p = 0.02), whereas non-responders did not show reductions in dyssynchrony according to RS and LS analyses during follow-up. The results of the current study are in agreement with these previous findings. In the present study, responders to CRT demonstrated a significant decrease in LV dyssynchrony as assessed with RS (using both the AS-P delay and the SDt_{6S}) and LS (only using the BS-BL delay). However, evaluation of dyssynchrony changes for CS did no reveal significant changes after CRT.

Initially, tagged magnetic resonance imaging was used for assessment of myocardial strain in radial, circumferential and longitudinal orientation. Feasibility of this magnetic resonance imaging technique for assessment of LV mechanical dyssynchrony has been demonstrated in previous studies.[21, 22] Currently, no magnetic resonance imaging studies evaluated assessment of dyssynchrony with RS. However, Leclercq et al used tagged magnetic resonance imaging with CS in an animal model on heart failure and demonstrated that biventricular pacing resulted in acute reduction LV dyssynchrony after biventricular pacing.[23] In a subsequent animal study from the same group, both CS and LS analyses were used to evaluate LV dyssynchrony.[12] Biventricular pacing improved synchronicity for both parameters, however this improvement was more pronounced using CS maps. In line with these results, although different parameters of LV dyssynchrony were used, CRT resulted in improvement of most dyssynchrony parameters. However, reductions in dyssynchrony parameters were largest using RS as compared to LS and CS.

Speckle-tracking strain analysis and response to CRT

In the current study, 2D speckle-tracking strain analysis was applied to 161 heart failure patients and 3 forms of strain were derived to assess LV dyssynchrony and predict response to CRT: radial, circumferential and longitudinal strain. Currently, data on 2D speckle-tracking strain analysis in CRT candidates and prediction of response are scarce. Radial strain was first applied in 64 heart failure patients by Suffoletto and colleagues.[14] Baseline AS-P delay was significantly higher in the patients that showed acute response, defined as an increase in stroke volume of ≥15%, as compared to patients who did not show an acute response (261±86 ms vs. 90±69 ms, p<0.001), and a pre-defined cut-off value of ≥130 ms predicted acute response

after CRT with 91% sensitivity and 75% specificity. This same cut-off value predicted long-term response (≥15% in LVEF after 8±5 months) with 89% sensitivity and 83% specificity.[14] In contrast, the aforementioned study by Knebel et al.[13] evaluated 38 heart failure patients undergoing CRT implantation, and reported that RS derived from 2D speckle-tracking analysis could not predict response to CRT.[13] The current findings are in line with the results presented by Suffoletto and coworkers;[14] a cut-off value of ≥130 ms for AS-P delay assessed with RS was able to predict response with good sensitivity and specificity (Figure 4A). In addition, the results from the current study revealed that SDt_{6S} measured with RS is also a useful parameter to predict long-term response to CRT (Figure 4B), although the area under the curve was less than the area under the curve for the AS-P delay.

2D CS has been applied in only one previous study to assess LV dyssynchrony in patients undergoing CRT.[11] Although that study was more focused on the effect of LV lead position in relation to outcome after CRT, the results also indicated that CS was not different between patients with and without response to CRT (161±32 ms vs. 159±35 ms, p = 0.84).[11] Similarly, the current results also showed no differences in dyssynchrony assessed by CS between responders and non-responders; neither the baseline AS-P delay nor the SDt_{6S} delay could identify patients who responded to CRT.

Data on LS assessed by 2D speckle-tracking analysis are also limited. Knebel et al.[13] reported more extensive LV dyssynchrony according to LS strain (217±125 ms vs. 168±91 ms), although prediction of response to CRT was not possible with LS strain.[13] The present findings are in agreement with these results; regardless the parameters used (BS-BL delay or SDt_{12S}), LS was not able to predict response to CRT. Finally, the value of the LV dyssynchrony parameters assessed by novel 2D RS in CRT candidates was comparable to the conventional TDI parameter of LV dyssynchrony.[3, 24]

Value of speckle-tracking strain analysis in CRT

The myofiber orientation in the human heart is complex with a characteristic helical distribution of the muscular fibers.[25] In summary, the typical arrangement of the myocardial layers and its changes during the cardiac cycle has been related to the LV deformation in 3 directions: radial thickening, circumferential shortening and longitudinal shortening.[10, 25] 2D speckle-tracking imaging is a new echocardiographic technique which allows the study of all 3 types of deformation. Measurement of RS, CS and LS has recently been validated by cardiac magnetic resonance imaging.[26] More importantly, 2D speckle-tracking imaging is angle-independent and, as strain imaging technique, enables to differentiate those myocardial segments with active movement from those with passive movement (i.e. scarred tissue tethered by the non-scarred segments).[27, 28]

In the present study, both parameters measured with RS were able to predict response to CRT, whereas neither LS nor CS were able to predict response. However, focusing on the SDt_{6s} or SDt_{12s}, a decrease in their values at follow-up was observed in the overall population. A possible explanation may be that radial thickening mirrors the circumferential and longitudinal shortening;[28, 29] the decrease in SDt_{6s}, assessed with RS could be accounted for a decrease in both SDt_{6s}, assessed with CS, and $SD-t_{12s}$, assessed with LS. As a consequence, the evaluation of LV dyssynchrony with RS with speckle-tracking may provide more information in one single assessment than CS and LS could provide separately.

Of note, superior feasibility and reproducibility were noted for assessment of the RS parameters which may have influenced the current results. Larger studies are needed to further elucidate the relationship between electrical and mechanical activation of the LV and its impact on benefit from CRT.

Conclusions

2D speckle-tracking RS enables the assessment of LV dyssynchrony and constitutes the best deformation study to identify potential responders to CRT. In addition, the predictive value of 2D RS was comparable to color-coded TDI. Furthermore, the long-term effect of CRT on LV dyssynchrony is better characterized with RS as compared to CS or LS. Reduction in LV dyssynchrony after CRT was only noted in responder patients, whereas in non-responders no changes were demonstrated.

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