Apical transverse motion is associated with speckle-tracking radial dyssynchrony in patients with non-ischemic dilated cardiomyopathy

Emre Gürel, Kürşat Tigen[1], Tansu Karaahmet[2], Cihan Dündar[3], Ahmet Güler[4], Yelda Başaran[1]

Department of Cardiology, Ordu State Hospital; Ordu-*Turkey*
[1]Department of Cardiology, Faculty of Medicine, Marmara University Hospital; İstanbul-*Turkey*
[2]Department of Cardiology, Faculty of Medicine, Acıbadem University Hospital; İstanbul-*Turkey*
[3]Department of Cardiology, Samsun Atasam Hospital; Samsun-*Turkey*
[4]Department of Cardiology, Kartal Koşuyolu Heart and Research Hospital; İstanbul-*Turkey*

Abstract

Objective: Apical transverse motion (ATM) is a new parameter for assessing left ventricular (LV) dyssynchrony. Speckle-tracking radial strain analysis seems to be the best method to identify potential responders to cardiac resynchronization therapy. The aim of our study was to investigate the association between ATM and radial dyssynchrony assessed by speckle-tracking echocardiography in patients with non-ischemic dilated cardiomyopathy (NDC).
Methods: We examined 35 NDC patients (mean age 49.2±28.1 years; 21 males). Cardiac dimension and ejection fraction (EF) were measured. Speckle-tracking analysis was performed on two-dimensional greyscale images in the mid-LV short axis view and apical views to calculate global radial, circumferential, and longitudinal strain (GRS, GCS, GLS), as well as rotational indexes (LV twist and torsion). Radial dyssynchrony was defined as a difference in time to peak systolic radial strain between the anteroseptal and posterior segments with a cut-off value of 130 ms. ATM was estimated using motion traces of 2 opposite apical segments.
Results: Radial dyssynchrony was significantly correlated with ATMloop (r=0.78, p<0.001), ATM4CV (r=0.71, p=0.001), ATM3CV (r=0.67, p=0.003), GRS (r=-0.51, p=0.04), GCS (r=-0.55, p=0.03), LV twist (r=-0.58, p=0.02), and LV torsion (r=-0.56, p=0.03). The receiver operating characteristics analysis for ATMloop to distinguish between patients with and without radial dyssynchrony revealed an area under the curve value of 0.88 (CI: 0.73-1.04, p=0.005). The best cut-off value was 2.5 mm for ATMloop (85% sensitivity and 86% specificity).
Conclusion: Apical transverse motion is closely associated with radial dyssynchrony assessed by speckle-tracking echocardiography. Quantitative measure of apical rocking has the potential for clinical applications. *(Anatol J Cardiol 2015; 15: 620-5)*
Keywords: speckle tracking, tissue Doppler, dyssynchrony

Introduction

Cardiac resynchronization therapy (CRT) is an established therapeutic option for patients with advanced heart failure and wide QRS duration. Heart failure symptoms (New York Heart Association functional class III or IV) refractory to optimal medical therapy, reduced left ventricular (LV) ejection fraction (≤35%), and the presence of a prolonged QRS complex (≥120 ms) are the currently accepted criteria for patient selection (1). Because up to 30% of patients undergoing CRT do not respond favorably, several echocardiographic techniques have been of interest to quantify LV mechanical dyssynchrony as a means to predict patient response (2). Speckle-tracking strain analysis is a novel method based on grayscale 2-dimensional (2-D) images that permits the assessment of radial strain (myocardial thickening) and circumferential strain (myocardial shortening) in the short-axis views and of longitudinal strain (myocardial shortening) in the apical views (3, 4). Suffoleto et al. (5) demonstrated that baseline speckle-tracking radial dyssynchrony (defined as the time difference in peak anteroseptal to posterior wall radial strain ≥130 ms) predicted a significant increase in ejection fraction after CRT, while dyssynchrony by longitudinal tissue Doppler velocities was not sufficient to do this. Further, these preliminary findings were also confirmed by several larger studies showing that a radial strain was the best among speckle-tracking strain parameters to identify responders (3, 6, 7).

Recently, apical transverse motion (ATM), to quantify 'apical rocking,' has also been introduced as a new parameter for assessing LV dyssynchrony and as a promising predictor of response to CRT. Studies related to this issue revealed that both quantitative measures and visual assessment of apical rocking

Address for Correspondence: Dr. Emre Gürel, Bahçelievler Mh. 293.Sk.
Gürsoy-Varol Sitesi, B-Blok, No: 4/13, Ordu-*Türkiye*
Phone: +90 533 423 21 51 Fax: +90 452 234 32 32 E-mail: emregurelctf@yahoo.com
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Table 1. Clinical and echocardiographic characteristics of the patients with and without radial dyssynchrony

	DYS-radial (+) (n=21)		DYS-radial (-) (n=14)		
	Median	**Max/Min**	**Median**	**Max/Min**	***P***
Age, years	51	68/21	48	77/34	0.572
Male gender, n (%)	13 (61)		8 (57)		0.512
NYHA class, n	2.66	4/1	2.78	4/1	0.825
QRS duration, ms	140	178/95	142	189/95	0.812
BMI, kg/m^2	25.2	22.1/28.2	24.1	22.4/26.2	0.923
Current smoking, n (%)	7 (33)		5 (35)		0.752
Hypertension, n (%)	6 (28)		6 (42)		0.828
Diabetes mellitus, n (%)	5 (23)		9 (64)		0.145
Acetylsalicylic acid, n (%)	19 (90)		13 (92)		0.794
Beta-blocker, n (%)	18 (85)		12 (85)		0.856
ACEI-AR blocker, n (%)	19 (90)		13 (92)		0.768
Diuretics, n (%)	20 (95)		13 (92)		0.642
LA diameter, cm	4.09	4.82/3.14	4.20	4.95/3.04	0.649
End-systolic diameter, cm	5.77	7.21/4.69	4.88	6.06/4.09	0.025
End-diastolic diameter, cm	6.89	8.45/5.31	5.90	7.26/5.12	0.019
EF, % (Simpsons)	28	40/18	31	40/20	0.132
LV twist, degree	2.89	18.3/-8.1	8.12	16.8/2.9	0.023
LV torsion, degree/cm	0.33	2.1/-0.8	1.01	2.0/0.3	0.038
GLS, %	-7.19	-12.6/-3.5	-9.79	-12.7/-3.1	0.223
GRS, %	-12.5	-23.8/-6.6	-17.9	-29.8/-11.1	0.201
GCS, %	-5.41	-13.4/-1.8	-7.69	-17.1/-3.4	0.145
Radial dyssynchrony, ms	225	283/152	87	122/27	0.000
ATM_{loop}, mm	4.08	8.90/2.41	1.95	3.93/1.20	0.004
ATM_{4CV}, mm	3.32	7.63/1.85	1.69	3.14/0.50	0.015
ATM_{3CV}, mm	2.71	7.34/1.82	0.91	2.46/0.74	0.001
ATM_{2CV}, mm	1.92	4.93/1.00	1.71	2.82/0.65	0.156

ACEI - angiotensin-converting enzyme inhibitor; AR - angiotensin receptor; ATM - apical transverse motion; BMI - body mass index; DYS - radial dyssynchrony; EF - ejection fraction; GCS - global circumferential strain; GLS - global longitudinal strain; GRS - global radial strain; LA - left atrium; LV - left ventricular; NYHA - New York Heart Association; 4CV - four-chamber view; 3CV - three-chamber view; 2CV - two-chamber view

were clinically feasible and reproducible and that ATM was correlated to the difference between tissue Doppler-derived averaged longitudinal strains of the septal and lateral wall of the LV (8, 9). However, the modern speckle-tracking technique measures myocardial strain without angle dependency and allows a more accurate analysis of regional myocardial function. The aim of our study was to investigate the association between ATM and radial dyssynchrony assessed by speckle-tracking echocardiography in patients with non-ischemic dilated cardiomyopathy (NDC).

Methods

Study population

The study population consisted of 35 NDC patients (mean age 49.2±28.1 years; 21 males) with an ejection fraction of less than 40%. The ischemic origin of cardiomyopathy was proven by coronary angiography and not included. A 12-lead electrocardiography (ECG) was recorded. All patients were in sinus rhythm and on optimized pharmacological therapy. Patients with more than mild valvular disease, a permanent pacemaker, and cardiac arrhythmias exceeding occasional premature beats were also not included. Functional capacities were evaluated according to the New York Heart Association (NYHA) classification. The study population was divided into two groups based on the presence or absence of radial dyssynchrony. The clinical, ECG, and echocardiographic characteristics of the groups are summarized in Table 1.

All patients gave informed consent prior to inclusion. The study was approved by the local ethics committee.

Echocardiography

All echocardiographic measurements were performed with a commercially available echocardiography system (Vivid 7,

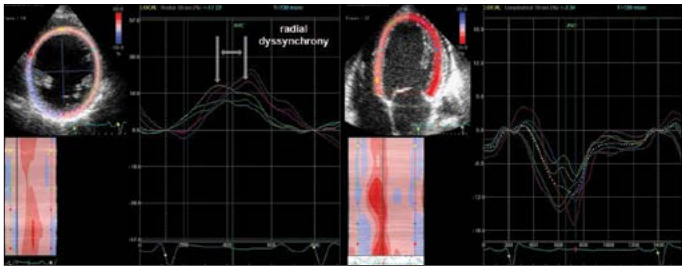

Figure 1. Radial dyssynchrony was defined as a difference in time to peak systolic radial strain between the anteroseptal and posterior segments

GE-Vingmed, Horten, Norway). Data acquisition was performed with a 3.5-Mhz transducer from the parasternal and apical views. Standard 2D greyscale, M-mode, and color-coded tissue Doppler imaging (TDI) data were obtained and stored as three consecutive heart cycles for later post-processing (EchoPAC 6.1; GE Vingmed Ultrasound AS). Care was taken to achieve the highest possible frame rate (60-70 fps for speckle tracking, 190-220 fps for TDI analysis) with optimized sector and depth settings. Cardiac dimensions were measured, and ejection fraction (EF) was assessed by biplane Simpson rule using manual tracing of digital images (10).

Speckle-tracking analysis

Standard 2D greyscale images were analyzed for frame-by-frame movement of stable patterns of natural acoustic markers or speckles (11). Radial and circumferential strain was assessed from mid-LV short-axis views, and the longitudinal strain was assessed from the apical views. An each region of interest was traced on the end-systolic endocardial cavity interface (minimum LV cavity) using a point-and-click approach. A second larger concentric circle was then automatically generated and manually adjusted near the epicardium. An automated tracking algorithm followed the endocardium and speckles from one single frame throughout the cardiac cycle. The parameters of myocardial deformation could be calculated from the distance between these speckles. Images from the mid-LV short-axis views were divided into six standard segments, and the corresponding strain curves were obtained. Global radial strain (GRS) and global circumferential strain (GCS) were derived from the average of the six regional peak systolic strain values. Images from the apical two- (2CV), three- (3CV), and four-chamber (4CV) views were also divided into six standard segments, and the corresponding strain curves were obtained. The average longitudinal strain was obtained by averaging the six regional peak systolic strain values for each apical plane. Global longitudinal strain (GLS) was then derived from the average of the average longitudinal strains in the 2CV, 3CV, and 4CV. Radial dyssynchrony was defined as a difference in time to peak systolic radial strain between the anteroseptal and posterior segments, with a cut-off value of 130 ms (Fig. 1) (3, 5).

Additionally, myocardial rotation, twist, and torsion were calculated from 2D grayscale images of short-axis views at the basal and the apical levels. The basal short-axis views contained the mitral valve, while the apical short-axis views were acquired distally to the papillary muscles. Apical rotation (rot-A) and basal rotation (rot-B) were obtained by speckle-tracking analysis. Values were expressed in 'degrees.' Left ventricular twist was calculated as the net difference between LV peak rotation angles obtained from the basal (clockwise) and apical (counterclockwise) short-axis views. LV torsion was calculated as the net LV twist normalized with respect to ventricular diastolic longitudinal length between the LV apex and the mitral plane [i.e., LV torsion (degree/cm) = (apical LV rotation - basal LV rotation)/LV diastolic longitudinal length] (12).

Apical transverse motion analysis

Myocardial velocity curves of each apical segment (septal, lateral, anteroseptal, posterior, anterior, inferior) were extracted from color-coded TDI data. All regions of interest were manually tracked during the cardiac cycle. We used a dedicated MATLAB (The Math Works Inc., Natick, Massachusetts, USA)-based analysis software (TVA version 14.7, JU Voigt, Leuven, Belgium, with permission) for further post-processing. Our method of calculating ATM has been described earlier (8). In short, we assumed that the apex is a homogeneous 'cap,' where the opposite walls are pulling on and calculated the ATM for the 2CV, 3CV, and 4CV by averaging the integrated longitudinal velocity curves (in other words, longitudinal motion curves) of 2 opposite apical regions after inverting the curves from the anterior, lateral, and anteroseptal side, respectively. ATMloop was then reconstructed by combining the curves of the three apical views (ATM4CV, ATM3CV, ATM2CV), with the assumption that they intersected at 60° angles. The main direction and amplitude of the ATM curves were noted (Fig. 2).

Statistical analysis

Statistical analysis was performed using statistical software (SPSS for Windows, version 15.0; SPSS Inc, Chicago, Illinois, USA). Continuous variables were presented as median (maximum, minimum), and categorical variables were presented as number and percentages, because of the non-normal distribution for all parameters by Kolmogorov-Smirnov test. Mann-Whitney U test was used to compare continuous variables. Categorical variables were compared by the Pearson χ^2 test. Correlation analysis was performed to determine the relationship between continuous variables using Spearman's correlation coefficient. A receiver operating characteristics (ROC) curve was generated to establish the discriminative power of ATM between the patients with and without radial dyssynchrony and to define the best cut-off value for ATM. A value of $p<0.05$ was considered significant.

Ten randomly selected datasets were re-acquired and then re-analyzed to determine the intraobserver variability of strain and ATM measurements by means of Bland-Altman analysis. Peak systolic strain and time to peak systolic strain correlated well between the two analyses (r=0.78 and r=0.82, resp.). Bland-Altman analysis revealed a small difference (mean±SD): 0.5±2.9% and 0.0±60 ms. ATM correlated well (r=0.98) and

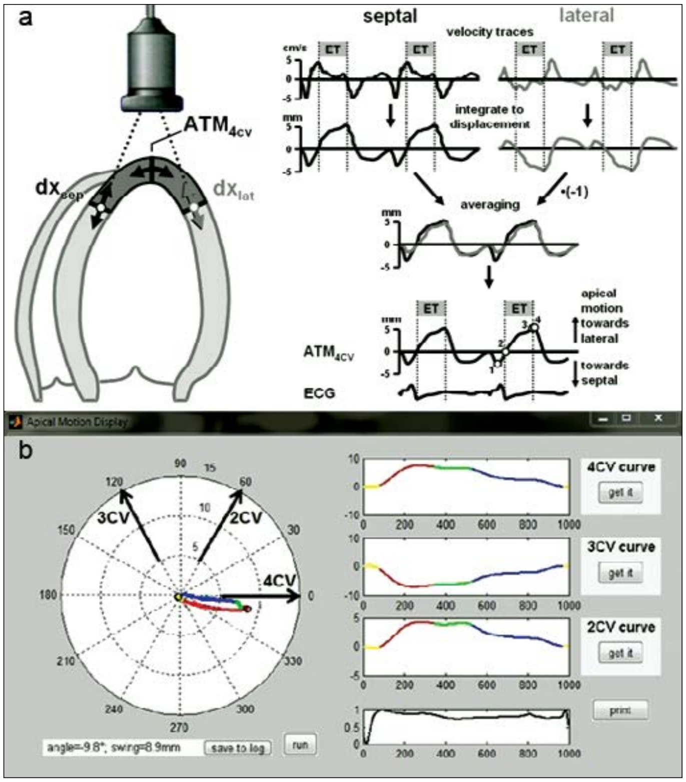

Figure 2. a, b. (a) ATM was calculated by dedicated software for each of the 3 apical scan planes by averaging longitudinal myocardial motion (displacement) traces of 2 opposite apical regions of interest after inverting the data from the anterior, lateral, and anteroseptal sides, respectively. (ET-ejection time) (this part of the figure is from 'reference 8,' with permission of the authors). (b) We used dedicated MATLAB (The Math Works Inc., Natick, Massachusetts, USA)-based analysis software (TVA version 14.7, JU Voigt, Leuven, Belgium, with permission) for further post-processing. ATM_{loop} was reconstructed by combining the curves of the three apical views (ATM_{4CV}, ATM_{3CV}, ATM_{2CV}), with the assumption that they intersected at 60° angles. An ATM_{loop} of 8.9 mm was calculated in a patient with radial dyssynchrony

showed only minor variability between readings (mean±SD): 0.1±0.5 mm.

Results

One thousand and fifty regional strain curves were assessed. Of those, 95 curves could not be analyzed (90% feasibility). Due to strict patient selection for image quality, apical transverse motion could be calculated in all patients (100% feasibility).

Table 1 demonstrates the clinical and echocardiographic characteristics of the patients with and without radial dyssynchrony [DYS-radial (+) and DYS-radial (-), respectively]. The groups were similar with respect to age, gender, NYHA class, QRS duration, body mass index, smoking, diabetes, hypertension, and previous medication. However, ATMloop, ATM4CV, ATM3CV, and end-systolic and end-diastolic diameter were significantly higher (p=0.004, 0.015, 0.001, 0.025, and 0.019, respectively) and LV twist and LV torsion were significantly lower (p=0.023, 0.038, respectively) in DYS-radial (+) compared to DYS-radial (-), while other echocardiographic parameters did not differ.

Table 2. Correlation of radial dyssynchrony to the other echocardiographic and clinical parameters

	R	*P*
ATM_{loop}	0.78	0.000
ATM_{4CV}	0.71	0.001
ATM_{3CV}	0.67	0.003
ATM_{2CV}	0.41	0.098
GLS	-0.29	0.524
GRS	-0.51	0.04
GCS	-0.55	0.03
LV twist	-0.58	0.02
LV torsion	-0.56	0.03
EF (Simpson's)	-0.16	0.587
LA diameter	0.32	0.265
End-systolic diameter	0.39	0.114
End-diastolic diameter	0.41	0.092
QRS duration	0.35	0.198
Age	-0.03	0.925
NYHA class	0.18	0.826

ATM - apical transverse motion; EF - ejection fraction; GCS - global circumferential strain; GLS - global longitudinal strain; GRS - global radial strain; LA - left atrium; LV - left ventricular; NYHA - New York Heart Association

Radial dyssynchrony correlated significantly with ATMloop (r=0.78, p<0.001), ATM4CV (r=0.71, p=0.001), ATM3CV (r=0.67, p=0.003), GRS (r=-0.51, p=0.04), GCS (r=-0.55, p=0.03), LV twist (r=-0.58, p=0.02), and LV torsion (r=-0.56, p=0.03), while no significant correlation was observed with the others (p>0.05, all) (Table 2) (Fig. 3). The ROC curve analysis for ATMloop to distinguish between DYS-radial (+) and DYS-radial (-) revealed an area under the curve value of 0.88 (CI: 0.73-1.04, p=0.005). The best cut-off value for ATMloop for the distinction between these groups was 2.5 mm, with 85% sensitivity and 86% specificity (Fig. 4).

Discussion

We could demonstrate in our study a close correlation of ATM to radial dyssynchrony assessed by speckle-tracking echocardiography. ATM could distinguish well between patients with and without radial dyssynchrony. The quantitative measure of ATM was feasible and reproducible.

Speckle-tracking echocardiography is an advanced echocardiographic technique that allows angle-independent measurement of regional strain and time to peak radial strain of different myocardial segments (13). Several types of speckle tracking applications have been described, such as radial strain (myocardial thickening in short-axis views), circumferential strain (myocardial shortening in short-axis views), and longitudinal strain (myocardial shortening in apical views). Knebel et al. (14) reported that longitudinal dyssynchrony, measured from apical views, significantly decreased after CRT in the respond-

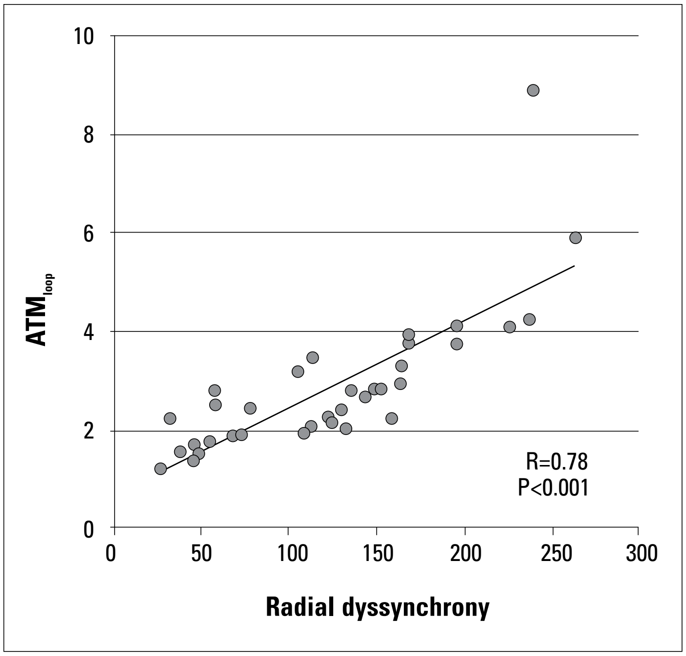

Figure 3. Correlation between radial dyssynchrony and ATM_{loop} (r=0.78, p<0.001)

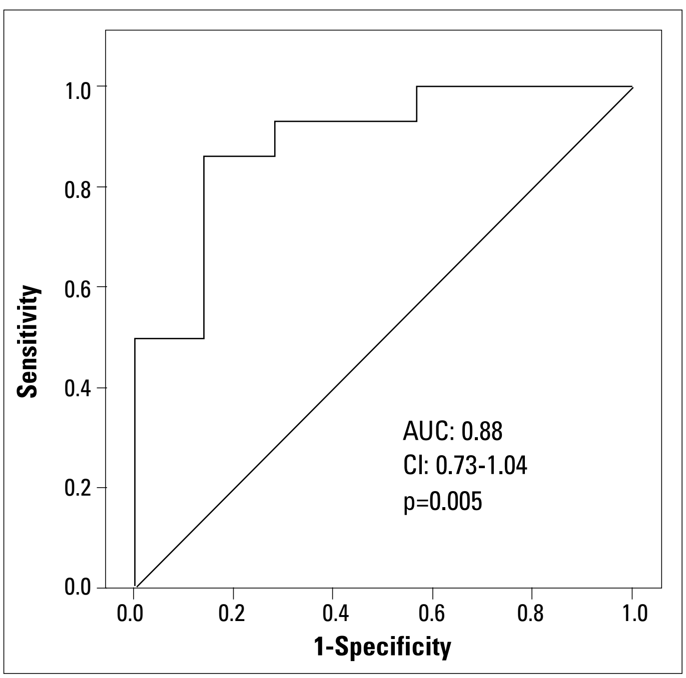

Figure 4. Receiver operating characteristics (ROC) curve analysis for ATM_{loop} to differentiate between patients with and without radial dyssynchrony revealed an area under the curve value of 0.88 (CI 0.73-1.04; p=0.005). The best cut-off value was 2.5 mm (85% sensitivity and 86% specificity)

ers, but baseline longitudinal dyssynchrony failed to predict the response to CRT. However, Suffoletto et al. (5) demonstrated that a time difference between peak speckle-tracking radial strain of the anteroseptal and posterior segments ≥130 ms (or radial dyssynchrony) predicted both immediate and long-term response to CRT, and later, Delgado et al. (3) documented that radial dyssynchrony was superior to circumferential and longitudinal speckle-tracking strain in predicting responders in a larger patient series. Finally, the recently published STAR (The Speckle-Tracking and Resynchronization) trial by Tanaka et al. (15) showed that dyssynchrony by speckle-tracking echocardiography using the radial strain and transverse strain (markers of myocardial thickening) was associated with better EF response and long-term outcome after CRT, while circumferential and longitudinal strain failed to identify dyssynchrony in the responders. These findings suggest that speckle-tracking radial dyssynchrony seems to be the most ideal echocardiographic tool for the selection of CRT candidates, complementary to the conventional parameters (QRS duration, NYHA class, and EF).

Apical transverse motion was recently proposed by Voigt et al. (8) as a new and integrative parameter for the evaluation of LV dyssynchrony and is promising in the prediction of response to CRT (9). They suggested that ATM integrated information on both regional and temporal function inhomogeneities of the LV and exhibited a significant correlation with the difference between tissue Doppler-derived average strains of the septal and lateral wall. In our study, ATM was found to be well correlated with speckle-tracking radial dyssynchrony, which is the most reliable echocardiographic predictor of CRT response. Further, a cut-off value of 2.5 mm for ATMloop could clearly differentiate between patients with and without radial dyssynchrony. ATM4CV and ATM3CV were also greater in patients with radial dyssynchrony than in those without it. Because the direction of ATMloop is very close to the septal-lateral plane (or to the direction of ATM4CV) but not to the antero-inferior plane, the contribution of ATM2CV to the ATMloop curve is too small. Thus, ATM2CV did not differ in the radial dyssynchrony group.

Previous studies showed that LV rotational mechanics are altered in advanced heart failure patients with prolonged QRS duration (16). In those with significant dyssynchrony, not only torsion is reduced but the basal and apical rotation sometimes follows the same direction of rotation (17). Further, Sade et al. (18) evaluated the changes in LV twist and torsion in 33 heart failure patients treated with CRT. They showed that CRT significantly restored the altered rotational mechanics and suggested these rotational indexes (LV twist and torsion) for predicting responders to CRT. Our study demonstrated that LV twist and torsion were also correlated with radial dyssynchrony but that this correlation was weaker than the correlation between ATM and radial dyssynchrony.

Study limitations

The major limitation of this study was the lack of follow-up data for the patient population. Although the majority of the patients had poor functional capacity (NYHA III or IV) and a wide QRS complex, CRT implantation could only be performed in 4 patients, due to financial causes. The small size of the study was also another limitation. Additionally, speckle-tracking radial strain analysis represented some technical disadvantages in our

NDC patients. Due to enlarged ventricles, sector width and depth could not be easily optimized, and it was sometimes difficult to obtain a sufficient frame rate. Thinned LV walls made it difficult to trace endocardial borders, causing noise that affected peak strain measures and ambiguous strain curves. Lastly, strain measurements were highly dependent on the image quality, and the parasternal mid-short axis could not be scanned optimally in all cases. Our study population comprised only patients with non-ischemic cardiomyopathy. Therefore, the relationship between ATM and infarcted myocardial segments could not be analyzed, which requires further investigations.

Conclusion

Apical transverse motion is a new and promising parameter for the evaluation of LV mechanical dyssynchrony. It is closely associated with radial dyssynchrony assessed by speckle-tracking echocardiography. A cut-off value of 2.5 mm could clearly differentiate between patients with and without radial dyssynchrony. A quantitative measure of apical rocking has the potential for clinical applications.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - E.G., K.T.; Design - E.G.; Supervision - Y.B.; Resource - Y.B.; Materials - Y.B.; Data collection and/or processing - A.G., E.G., K.T., T.K., C.D.; Analysis and/or interpretation - A.G., E.G., K.T., T.K.; Literature search - A.G., E.G., T.K.; Writing - E.G.; Critical review -K.T., Y.B.

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