Patterns of Decrease in Multidirectional Myocardial Deformations in Patients With Fluctuating Left Ventricular Ejection Fraction

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Summary

Few studies have examined the variations in longitudinal/circumferential/radial strain (LS/CS/RS) and strain rate (LSr/CSr/RSr) in individual hearts when the left ventricular ejection fraction (LVEF) has changed. We hypothesized the relationships of strain/strain rate and LVEF are not linear, but vary with multiple inflection points (IPs) in individual hearts.

Twenty-five patients with fluctuating LVEF (ΔLVEF > 10%) who had 2-D speckle tracking echocardiography available for analysis were enrolled. After models of best fit were obtained from the 'collective' plots to determine inflection points, the decrements of slopes above inflection points (IP) were compared with those below IPs in the 'individual hearts' plots.

In the 'collective' plots, both LS and LSr linearly decreased in proportion to LVEF when LVEF ≥ 40% but remained constant regardless of LVEF when LVEF < 40% (IPs when LVEF = 40%, $P < 0.0001$). The RS-LVEF relationship was sigmoid with two IPs when LVEF = 30% and 50% ($P < 0.0001$). However, in the 'individual hearts' plots, the decrements of slopes above and below IPs were not different for LS-LVEF and LSr-LVEF, and marginally different for RS-LVEF ($P = 0.049$, across IP when LVEF = 50%).

Collectively, the relationship of LS/LSr/RS and LVEF seemed to be not linear, but inflective, however, we could not prove the inflective relationship in individual hearts with fluctuating LVEF. Further study with more patients is needed to prove our hypothesis. (Int Heart J 2014; 55: 319-325)

Key words: Heart failure, Myocardial strain, Strain rate imaging

Left ventricular (LV) systolic work is produced by a combination of the following 3-dimensional myocardial deformations: longitudinal, circumferential and radial strain.

Longitudinal strain and strain rate can be measured by Doppler tissue velocity imaging (TVI), which seems superior to conventional echocardiographic parameters at predicting LV systolic dysfunction in various cardiac diseases.[1-3]

Since the introduction of 2-dimensional speckle tracking echocardiography (2DSTE) to the field of cardiac imaging, radial and circumferential strain can be analyzed in addition to longitudinal strain. Furthermore, early detection of ischemic heart disease and various cardiomyopathies is now feasible with 2DSTE.[4-7]

Despite these advances, the variations in multidirectional myocardial deformations in individual hearts with fluctuating LV systolic function have not yet been fully elucidated.

We previously described a different pattern of multidirectional impairment in doxorubicin-induced cardiomyopathy models in rats,[8] and tried to prove a similar pattern of impairment in human subjects in the current study, by investigating functional changes in each LV axis by analyzing longitudinal/circumferential/radial strain (LS/CS/RS) and strain rate (LSr/CSr/RSr) of LV with fluctuating LVEF.

We also hypothesized the decrements in strain and strain rate are not constant but inflective as LVEF decreases, and the patterns of decrease in longitudinal strain/strain rate are different from those in circumferential and radial strain.

Methods

Patients and echocardiography: We collected echocardiograms of the patients who had significant fluctuation of LVEF during follow-up. For inclusion in the study, the maximal LVEF had to be more than 10% higher than the minimal LVEF (ΔLVEF > 10%) from serial examinations of each patient. Patients whose tests were not available for strain analysis were

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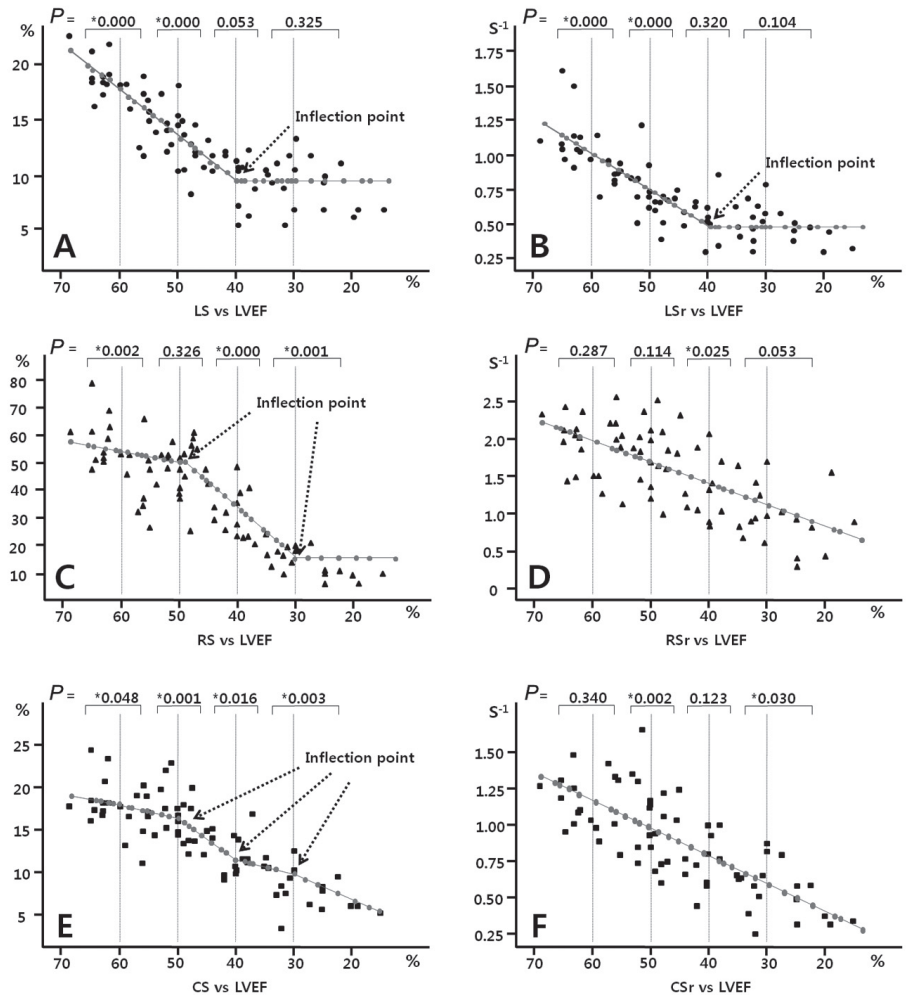

Figure 1. Relationship between strain or strain rate and left ventricular ejection fraction in 72 echocardiograms (Collective plots). The tests were stratified into quintiles by the value of left ventricular ejection fraction. LS indicates longitudinal strain; LSr, longitudinal strain rate; RS, radial strain; RSr, radial strain rate; CS, circumferential strain; CSr, circumferential strain rate; and LVEF, left ventricular ejection fraction.

excluded. Patients who had regional wall motion abnormalities, more than a moderate degree of valvular dysfunction, prosthetic cardiac valves, atrial fibrillation, history of pericardial injury, frequent premature ventricular complexes (PVCs), or other complex cardiac dysrhythmias were excluded.

LVEF was calculated using the biplane Simpson's method. For 2DSTE, the Vivid 7® (GE Vingmed, Horten, Norway) and a 3.5-MHz sector-array transducer were used. Standard 2D cine-loop images from three consecutive beats were stored in a workstation for offline analysis (EchoPAC 6.1; GE Vingmed Ultrasound AS). The minimally required frame rate was 50 frames per second for LS/LSr and 70 frames per second for RS/RSr and CS/CSr. LS/LSr was obtained and averaged from the apical 4- and 2-chamber views. RS/RSr and CS/CSr were obtained from parasternal short axis images at the level of mid-LV. The strain and strain rate values were averaged from three consecutive cardiac cycles. There were manual readjustments when speckle tracking was not appropriate. Examinations with inappropriate segments for strain analysis in spite of manual readjustment were also excluded from the analysis.

In order to evaluate the influence of systolic stress on strain/strain rate, end-systolic and peak wall stress were noninvasively obtained by the following formula:

LV end-systolic meridional wall stress (ESWS) = $0.334 \times (SBP \times PWT_{es}) / [LVID_{es} \times (1 + PWT_{es} / LVID_{es})]$,

LV peak wall stress (PWS) = $0.86 \times 0.334 \times (SBP \times PWT_{ed}) / [LVID_{ed} \times (1 + PWT_{ed} / LVID_{ed})]$,

where SBP = systolic blood pressure, PWT_{es} = posterior wall thickness at end-systole, PWT_{ed} = posterior wall thickness at end-diastole, $LVID_{es}$ = left ventricular diameter at end-systole, and $LVID_{ed}$ = left ventricular diameter at end-diastole.[9,10]

Each strain/strain rate was corrected by ESWS and PWS, and the corrected values at maximal LVEF were compared with those at minimal LVEF.

Statistical analysis: Echocardiograms from each patient were arranged in order of LVEF. The values of strain and strain rate were matched to corresponding values of LVEF and depicted in scatter-plots ('Collective' plots). On the 'collective' plots, the intra-patient variation of the echocardiographic parameters was not considered (Figure 1).

From the collective plots, the relation between longitudi-

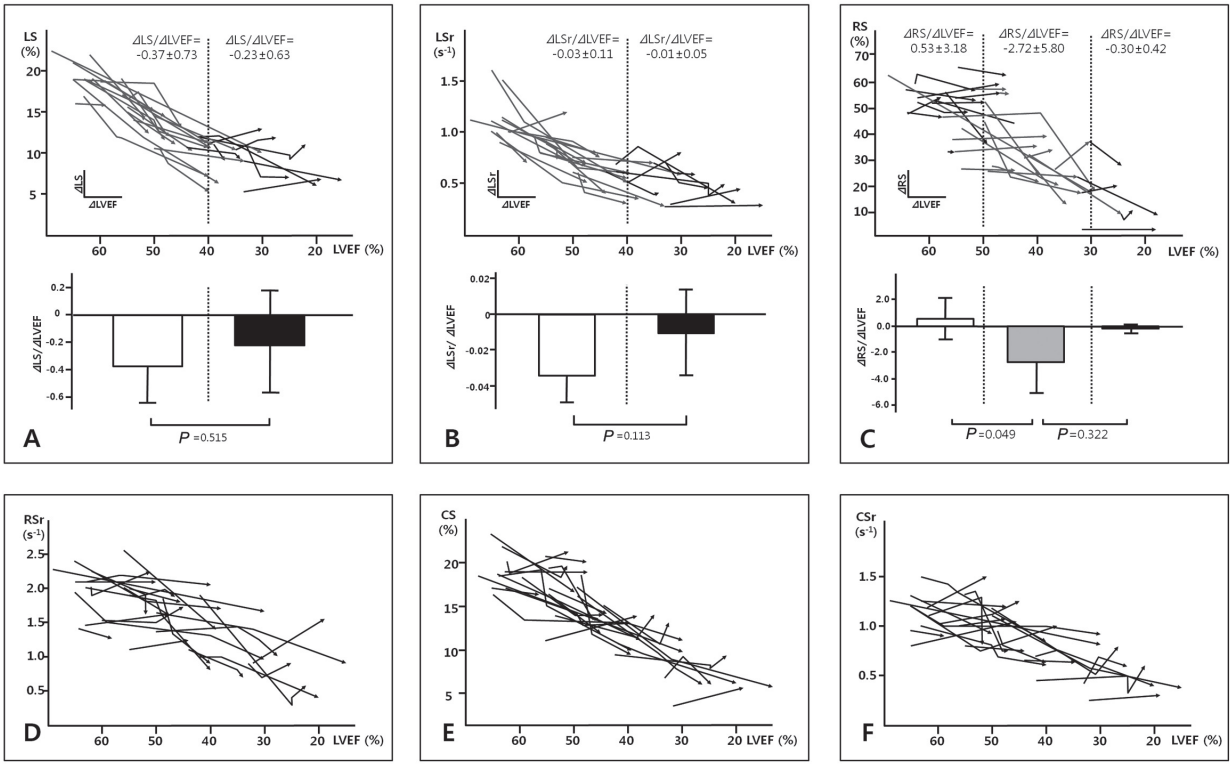

Figure 2. Curves of longitudinal, radial, and circumferential strain and strain rate from 44 pairs of echocardiograms as left ventricular ejection fraction decreases (Individual hearts plots). ΔLS/ΔLVEF indicates the decrement of longitudinal strain in proportion to decreasing left ventricular ejection fraction. The slopes of strain and strain rate were compared between above and below the inflection points. LS indicates longitudinal strain, LSr, longitudinal strain rate; RS, radial strain; RSr, radial strain rate; CS, circumferential strain; CSr, circumferential strain rate; and LVEF, left ventricular ejection fraction.

nal/circumferential/radial strain (LS/CS/RS), strain rate (LSr/CSr/RSr), and LVEF could vary dependent on LVEF. Thus, we fitted a segmented linear regression with dummy variables which were created from LVEF to consider different slopes by the intervals within the linear regression. In the study, we assumed that the linear slopes in the ranges, LVEF < 30, 30 ≤ LVEF < 40, 40 ≤ LVEF < 50, 50 ≤ LVEF < 60, and 60 ≤ LVEF, could be different and the same within each range. The considered segmented linear regression model was given by $S = \alpha + \gamma X + \Sigma_{k=1}^{4} \beta_k (X - c_k) I (X \geq c_k)$, where I(·) is an indicator function, S is strain or strain rate, X is LVEF value, $c_1 = 30$, $c_2 = 40$, $c_3 = 50$, $c_4 = 60$, and α, γ and β_k ($k = 1,2,3,4$) are regression coefficients. A stepwise variable selection method was used to identify significant terms. Models of best fit were obtained for longitudinal/circumferential/radial strain (LS/CS/RS) and strain rate (LSr/CSr/RSr) by the method described above.

The adjacent strain values in the 'collective' strain-LVEF plots were connected in each patient to represent the intra-patient variation of echocardiographic parameters ('individual hearts' plots) (Figure 2). From collections of the slopes of each patient, the calculated slope, Δ(strain)/Δ(LVEF) or Δ(strain rate)/Δ(LVEF), represented the decrement in strain values as LVEF decreased (Figure 1). When the inflection point (IP) was determined from the 'collective' plots, Δ(strain)/Δ(LVEF) above the IP was compared with Δ(strain)/Δ(LVEF) below the IP in the 'individual hearts' plots. The same calculations were applied for strain rates.

Continuous variables are presented as the mean ± standard deviation and were compared using the Mann-Whitney *U* test for two independent samples or the Kruskal-Wallis test for several independent samples because the variables did not satisfy the normality assumption.

A value of $P < 0.05$ was considered statistically significant. SPSS software was used for statistical analysis (version 13.0; SPSS Inc., Chicago, IL, USA).

Results

Seventy-two echocardiograms from 25 patients were acquired and processed for analysis. The median interval between the first and last echocardiogram was 172 days (range, 10 to 310 days), and the averaged ΔLVEF between the highest and lowest LVEF was 17 ± 9.0%.

Among 25 patients, 11 were men. Ten patients had chronic kidney disease, 13 had dilated cardiomyopathy, and two had fulminant myocarditis as the cause of LV systolic dysfunction. For the cause of LVEF fluctuation, fluid retention due to underdialysis was considered in two patients with chronic kidney disease (CKD). For 8 other patients with CKD, no particular aggravating factor was revealed and natural progression of cardiac disease (eg type 4 cardiorenal syndrome) was thought to be the cause of the continuous decrease in LVEF. Among 13 patients with dilated cardiomyopathy, 6 had the reversible type of DCM (two peripartum DCM and 6 alcoholic DCM) and their LVEF was improved since the first event of

Table I. Hemodynamic and Echocardiographic Parameters of Enrolled Patients at Highest and Lowest Left Ventricular Ejection fraction (LVEF)

Hemodynamic and conventional echocardiographic parameters (n = 25)	Mean ± SD Maximal LVEF	Mean ± SD Minimal LVEF	P
Systolic blood pressure (mmHg)	122 ± 18	123 ± 19	0.702
Diastolic blood pressure (mmHg)	73 ± 10	74 ± 12	0.586
Heart rate (/minute)	81 ± 11	82 ± 13	0.702
LV ejection fraction (%)	54.8 ± 10.0	38 ± 11.4	0.000
LV end-diastolic dimension (mm)	51.8 ± 6.8	54.9 ± 9.0	0.053
LV end-systolic dimension (mm)	38.0 ± 8.9	43.7±10.9	0.006
Septum thickness (mm)	10.9 ± 1.9	11.1 ± 2.0	0.488
Posterior wall thickness (mm)	10.3 ± 2.6	10.7 ± 1.9	0.425
Left atrial dimension (mm)	39.4 ± 7.3	42.2 ± 8.9	0.062
E velocity (cm/sec)	71.7 ± 25.3	76.5 ± 32.7	0.454
Deceleration time (msec)	193.5 ± 58.8	175.9 ± 69.2	0.239
Em velocity (cm/sec)	6.9 ± 2.9	6.7 ± 11.3	0.911
E/Em	12.2 ± 6.93	19.6 ± 11.3	0.010
ESWS (10^3·dyne/cm^2)	80.6 ± 29.2	114.3 ± 49.7	0.168
PWS (10^3·dyne/cm^2)	140.4 ± 31.4	153.9 ± 43.0	0.130
Strain or strain rate values			
LS (%)	-15.7 ± 4.1	-10.4 ± 3.1	0.000
LSr (s^{-1})	-0.90 ± 0.3	-0.58 ± 0.2	0.000
RS (%)	46.4 ± 16.4	31.9 ± 18.0	0.000
RSr (s^{-1})	1.77 ± 0.5	1.38 ± 0.5	0.005
CS (%)	-16.1 ± 4.8	-12.4 ± 4.7	0.000
CSr (s^{-1})	-0.97 ± 0.3	-0.75 ± 0.5	0.016
ESWS corrected LS (%·dyne^{-1}·cm^2)	-238.9 ± 151.9	-111.9 ± 73.3	0.001
ESWS corrected LSr (s^{-1}·dyne^{-1}·cm^2)	-14.3 ± 8.5	-6.7 ± 5.5	0.001
ESWS corrected RS (%·dyne^{-1}·cm^2)	720.2 ± 499.2	318.8 ± 260.1	0.000
ESWS corrected RSr (s^{-1}·dyne^{-1}·cm^2)	28.1 ± 16.5	15.4 ± 11.5	0.001
ESWS corrected CS (%·dyne^{-1}·cm^2)	-233.6 ± 172.1	-132.1 ± 96.8	0.002
ESWS corrected CSr (s^{-1}·dyne^{-1}·cm^2)	-13.9 ± 11.5	-6.3 ± 9.2	0.031
PWS corrected LS (%·dyne^{-1}·cm^2)	-117.0 ± 41.6	-74.0 ± 33.4	0.000
PWS corrected LSr (s^{-1}·dyne^{-1}·cm^2)	-6.7 ± 2.5	-4.2 ± 2.2	0.000
PWS corrected RS (%·dyne^{-1}·cm^2)	351.7 ± 158.3	231.3 ± 152.2	0.000
PWS corrected RSr (s^{-1}·dyne^{-1}·cm^2)	13.4 ± 5.1	9.9 ± 5.3	0.003
PWS corrected CS (%·dyne^{-1}·cm^2)	-122.5 ± 50.7	-89.2 ± 44.7	0.002
PWS corrected CSr (s^{-1}·dyne^{-1}·cm^2)	-6.9 ± 4.0	-5.1 ± 4.5	0.121

ESWS indicates LV meridional end-systolic wall stress, PWS LV peak wall stress, LS longitudinal strain, LSr longitudinal strain rate, RS radial strain, RSr radial strain rate, CS circumferential strain, and CSr circumferential strain rate.

heart failure. Among 7 patients with idiopathic DCM, 5 had severe infection (eg pneumonia, pyelonephritis), which seemed to cause fluid retention and LV systolic dysfunction. Six patients underwent 4 series of echocardiography, 10 patients underwent 3 series, and 9 patients underwent two series. At maximal LVEF (54.8 ± 10.0%), the LV end-diastolic internal dimension (LVEDD) was 51.8 ± 6.8 mm, LV end-systolic internal dimension (LVESD) was 38.0 ± 8.9 mm, and left atrial diameter (LAD) was 39.4 ± 7.3 mm. LS was -15.7 ± 4.1%, LSr was -0.90 ± 0.3 s^{-1}, RS was 46.4 ± 16.4%, RSr was 1.77 ± 0.5 s^{-1}, CS was -16.1 ± 4.8, and CSr was -0.97 ± 0.3 s^{-1}. When the LVEF of the patients was lowest, no significant elevation in blood pressure occurred. However, the LV end-diastolic dimension was significantly larger and the E/E_m was higher than when the LVEF was maximal. Signs of increased preload such as pulmonary or systemic congestion were common as well when LVEF was minimal. Although ESWS and PWS seemed higher at minimal LVEF than those at maximal LVEF, there was no statistical significance. On the other hand, the values of strain/strain rate were still significantly lower at minimal LVEF after being corrected by either of ESWS or PWS (Table I).

Seventy-two echocardiograms were categorized into quintiles according to the values of LVEF (Table II). Models of best fit for strain/strain rate-LVEF in 'collective' plots are shown in Table III. For LS and LSr, IPs occurred where LVEF was 40%. When LVEF was ≥ 40%, LS was proportionate to LVEF, while the slope became stationary when LVEF was < 40% (Figures 1A and 1B). RS had a different pattern of decrement. The slope decreased gently when LVEF ≥ 50%, became steep when 50% > LVEF ≥ 30%, and remained stationary when LVEF ≤ 30% (Figure 1C). Although there were statistically significant IPs in CS-LVEF plots, they did not seem clinically relevant (Figure 1D). There were no significant IPs in RSr-LVEF or CSr-LVEF plots (Figure 1E and 1F).

In the 'individual hearts' plots, we obtained 44 slopes for each of the strains and strain rates. The decrements of LS and LSr in individual hearts above and below the IPs (LVEF = 40%) were not different. This finding was different from the results of 'collective' plots. Both ΔLS and ΔLSr continuously decreased regardless of LVEF (ΔLS/ΔLVEF = -0.37 ± 0.73 above IP versus ΔLS/ΔLVEF = -0.23 ± 0.63 below IP, P = 0.515; ΔLSr/ΔLVEF = -0.03 ± 0.11 above IP versus ΔLSr/ΔLVEF = -0.01 ± 0.05 below IP, P = 0.113) (Figures 2A-B and 3A-B). On the other hand, ΔRS/ΔLVEF showed a marginal

Table II. Longitudinal, Radial, and Circumferential Strain and Strain rate Stratified by Left Ventricular Ejection Fraction

Quintiles	Q1	Q2	Q3	Q4	Q5
LVEF	≥ 60%	50-60%	40-50%	30-40%	< 30%
n	12	20	17	15	8
Longitudinal strain (LS, %)	-19.0 ± 1.9	-14.9 ± 2.4	-10.8 ± 2.3	-9.6 ± 2.2	-8.4 ± 2.2
Longitudinal strain rate (LSr, s^{-1})	-1.13 ± 0.2	-0.83 ± 0.2	-0.58 ± 0.1	-0.55 ± 0.2	-0.43 ± 0.1
Radial strain (RS, %)	55.7 ± 5.2	45.8 ± 9.6	40.3 ± 12.8	21.0 ± 8.8	10.3 ± 4.7
Radial strain rate (RSr, s^{-1})	1.96 ± 0.3	1.81 ± 0.4	1.57 ± 0.5	1.15 ± 0.4	0.78 ± 0.4
Circumferential strain (CS, %)	-18.9 ± 2.6	-16.9 ± 2.9	-13.5 ± 3.1	-10.5 ± 3.1	-6.9 ± 1.5
Circumferential strain rate (CSr, s^{-1})	-1.17 ± 0.2	-1.09 ± 0.3	-0.81 ± 0.2	-0.53 ± 0.5	-0.43 ± 0.1

Table III. Best-Fit Regression Model Strain-LVEF and Strain Rate-LVEF Plots

Strain or Strain rate	Fit regression model	Statistics, *P*
Longitudinal strain (LS)	y = 9.2, if LVEF < 40 y = -7.2 + 0.41LVEF, if LVEF ≥ 40	F (1, 70) = 211.84, *P* < 0.0001
Longitudinal strain rate (LSr)	y = 0.49, if LVEF < 40 y = -0.51 + 0.025LVEF, if LVEF ≥ 40	F (1, 70) = 147.31, *P* < 0.0001
Radial strain (RS)	y = 12.57, if LVEF < 30 y = -40.53 + 1.77LVEF, if 30 ≤ LVEF < 50 y = 27.97 + 0.4LVEF, if LVEF ≥ 50	F (1, 70) = 110.53, *P* < 0.0001
Radial strain rate (RSr)	y = 0.40 + 0.03LVEF	F (1, 70) = 63.46, *P* < 0.0001
Circumferential strain (CS)	y = 1.07 + 0.26LVEF, if LVEF < 40 y = -8.53 + 0.5LVEF, if 40 ≤ LVEF < 50 y = 9.97 + 0.13LVEF, if LVEF ≥ 50	F (1, 70) = 54.12, *P* < 0.0001
Circumferential strain rate (CSr)	y = 0.07 + 0.02LVEF	F (1, 70) = 89.67, *P* < 0.0001

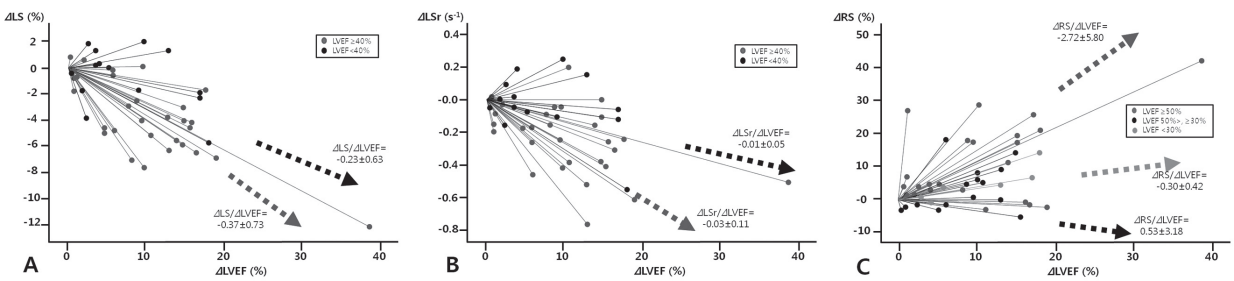

Figure 3. Lines indicative of decrements in longitudinal strain, longitudinal strain rate, and radial strain. ΔLS/ΔLVEF indicates the decrement of longitudinal strain in proportion to decreasing left ventricular ejection fraction. Averaged decrements are represented by dotted arrow and numbers (Mean ± standard deviation) LS indicates longitudinal strain; LSr, longitudinal strain rate; RS, radial strain; RSr, radial strain rate; CS, circumferential strain; CSr, circumferential strain rate; and LVEF, left ventricular ejection fraction.

difference across LVEF = 50% (ΔRS/ΔLVEF = 0.53 ± 3.18 above IP versus ΔRS/ΔLVEF = -2.72 ± 5.80 below IP, *P* = 0.049), but no difference across LVEF = 30% (*P* = 0.322) (Figure 2C and 3C).

Discussion

Among the layers of ventricular myocardial fibers, subendocardial ones responsible for longitudinal contraction, are more susceptible to cardiotoxic stimuli, while extended involvement of mid-myocardium may lead to the impairment of radial contraction.[11,12] Noninvasive prediction of future LV systolic dysfunction is feasible with tissue velocity imaging (TVI) by Doppler ultrasound, but Doppler TVI had limitations because circumferential and radial strain could not be evaluated with Doppler TVI. However, these limitations of Doppler TVI have been overcome with the development of 2DSTE, and 3-dimensional multidirectional strain or strain rate analysis is now feasible.[4-7]

Although early decrease in LS or LSr prior to the overt LV systolic dysfunction was previously reported, a majority of those studies was based on cross-sectional data. Therefore, we thought intra-patient changes of myocardial strain/strain rate along with the change of global LV systolic function, could have more important clinical implications.

We investigated the mechanism of LV functional deterioration in individuals with fluctuating LVEF by analyzing myocardial strain with 2DSTE. In the 'collective' plots, LS and LSr of LV seemed more readily impaired than radial or circumferential function in mild LV systolic dysfunction, while RS was preserved in mild LV systolic dysfunction and impaired in moderate LV systolic dysfunction. However, these findings were not observed in the 'individual hearts' plots. Strain and strain rate were impaired constantly as LV systolic function became worse.

There are several studies regarding the sequential change of multidirectional myocardial deformation in various heart disease populations, such as isolated diastolic LV dysfunction, hypertension and aortic stenosis with or without LV systolic dysfunction. However, most of the studies had a few limitations.[7)]

For example, many studies that reported the superior predictability of LS or LSr in future LV systolic dysfunction, measured the values by Doppler TVI, while radial and circumferential strain/strain rate were not considered because Doppler TVI is unable to measure radial or circumferential deformations.[13,14)]

Although there are studies that included circumferential or radial strain values, most were cross-sectional and did not examine intra-patient variation, which can be obtained only from serial echocardiography.[15-20)]

Among these cross-sectional studies, Kouzu, *et al* showed that LV radial strain was augmented to compensate for the decrease in longitudinal function and maintain stroke volume in early subclinical hypertensive heart disease.[21)] Ng, *et al* reported that radial strain and strain rate were preserved in mild and moderate aortic stenosis and significantly decreased in severe AS. Even with the cross-sectional nature of the studies, these findings suggest compensatory augmentation of radial contraction in the early phases of cardiac disease.[15)]

Several animal studies observed a sequential change in myocardial deformation as global LV function worsened.[8,22-24)] The strain and strain rate in some studies were validated with sonomicrometries implanted in the myocardium. In one of these studies, the dobutamine-induced ischemic stress in porcine hearts with ligated coronary arteries produced abnormalities in LS prior to abnormalities in RS.[24)] Despite limitations in the method of coronary artery ligation (eg uneven myocardial deformation and injured pericardium), the findings may suggest more susceptible longitudinal and more resilient radial function.

A few human studies with follow-up echocardiographic data reported that RSr as well as LSr could forecast future global LV systolic dysfunction.[21,25,26)] Interestingly, LSr decreased 6 months earlier than RSr, although LVEF was preserved during the one-year observation period.[21)] Vinereaunu, *et al*. suggested that a progressive decline in longitudinal systolic function is closely associated with global diastolic function, and the augmentation or preservation of radial contraction maintains normal ejection fraction.[27-29)]

In our study, we enrolled 25 patients whose LVEF values significantly fluctuated and who had more than two consecutive follow-up echocardiograms. We observed intra-patient variation of strain and strain rate along with LVEF from serial echocardiograms.

Although the connected lines in LS-LVEF, LSr-LVEF, and RS-LVEF in 'individual heart' plots made similar patterns of declining curves to those in 'collective' plots, the decrements across IPs were not different in either LS-LVEF or LSr-LVEF, and only a marginal difference was observed in RS-LVEF between mild and moderate LV systolic dysfunction in the 'individual heart' plots.

In 'individual hearts' plots, some patients seemed to have paradoxical increases in radial or circumferential strain/strain rate, while LVEF was decreased. Although this 'paradoxical increase' might be attributed to suboptimal tracking, we thought compensation by radial or circumferential deformations for a decrease in longitudinal deformation in a certain level of LVEF was a more reasonable explanation.

Further study with a larger patient population, more frequent tests, and longer follow-up data could have provided statistical significance to support our hypothesis.

If the exponential (LS and LSr-LVEF) or sigmoid (RS-LVEF) intra-patient variations are proven correct by further studies, this would be a reasonable explanation for how LV longitudinal function is useful as an early predictor of LV systolic dysfunction and radial function maintains global LV function in early cardiac disease.

Study limitations: The heterogeneity of the subject population and short length of the follow-up duration were crucial limitations. Our investigation enrolled only 72 echocardiograms from 25 patients. Further investigation with more patients should be carried out.

Because the tests were arranged in order of LVEF, our study did not represent true follow-up of progressive LV systolic dysfunction. However, the objective of our study was to evaluate the hypothesis that longitudinal function is more readily impaired than radial or circumferential function in individual subjects when LV systolic function varies.

Contrary to previous studies, the usefulness of LS in early prediction of LV systolic dysfunction was not demonstrated in this study. This may be because our patients did not undergo echocardiography in this narrow period with impaired LS, but normal LVEF.

LVEF does not accurately represent LV systolic function in certain cardiac diseases; however, this inaccuracy may not be significant in our study, because we excluded patients with diseases like valvular dysfunction, pericardial abnormality, regional wall motion abnormality, and others.

Because LVEF is influenced by load conditions and LV contractility, we could have obtained more convincing results if we had eliminated the influence of afterload and preload on the relationships. However, wall stress was not significantly increased when LVEF was minimal and strain/strain rate were still lower after being corrected by wall stress, which means the influence of wall stress on the strain/strain rate was not that great. In addition, we could not set "decrease in LVEF" apart from "increase in preload" in clinical practice because these 2 phenomena usually go together. Therefore, we deemed it unnecessary to adjust the influence of preload when we evaluated the relationships.

Of note, it is difficult to measure and compare the rate of impairment in longitudinal, radial and circumferential deformation when the progress of LV systolic dysfunction is indolent.

Conclusion: We investigated the function of each LV axis by analyzing longitudinal/circumferential/radial strain (LS/CS/

RS) and strain rate (LSr/CSr/RSr) of left ventricles (LV) with fluctuating LVEF.

In the 'collective' plots, it seemed that longitudinal function, as indicated by LS and LSr, was more susceptible than radial function to small changes in LVEF in mild LV systolic dysfunction. However, intra-patient variation in the 'individual hearts' plots did not show the varying decrements as LVEF declined.

Because this study was not a true follow-up of progressive LV systolic function and there was significant heterogeneity in the study population, further investigation with more patients is required to support our results.

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