



Classification of longitudinal strain curves measured by speckle-tracking echocardiography in normal and pathological myocardial segments

Oana Mirea^{1*}, Mihaela Berceanu¹, Sorina Soldea¹, Ionuț Donoiu¹, Victor Raicea²

Abstract

Background: Two-dimensional speckle-tracking echocardiography (2D-STE) provides a quantitative tool to evaluate LV function at the regional level. The purpose of this study was to classify the types of regional longitudinal strain curves (LSC). Moreover, we propose a novel longitudinal strain curve index (LSCI) which we compared to the wall motion score index (WMSI).

Methods: We enrolled 100 healthy volunteers and 50 patients with prior myocardial infarction (MI). Each LSC was classified considering the positive peak (peak P), peak maximum strain (PMS), and time to maximum peak strain (TPMS) as follows: Type 1 (Peak P<6%, PMS>6%, TPMS before aortic valve closure [AVC]); Type 2 (Peak P<6%, PMS≥6%, TPMS after AVC); Type 3 (Peak P≥6%, PMS≥6%, TPMS before AVC); Type 4 (Peak P≥6%, PMS≥6%, TPMS after AVC); Type 5 (Peak P<6%, PMS≥6%, TPMS first third of systole); Type 6 (Peak P<6%, PMS<6%); and Type 7 (Peak P≥6%, PMS<6%). The longitudinal curve score index (LCSI) was obtained (sum of LSC type/18 segments).

Results: A total of seven types of LSC were identified. In the healthy subjects, LSC Type 1 (T1) and Type 2 (T2) were the most frequent. Type 3 (T3) and Type 4 (T4) were found in insignificant percentages while Type 5 (T5), Type 6 (T6), and Type 7 (T7) were not identified. When analyzed for the entire population, LSCI correlated strongly with WMSI ($r=0.83$, $p<0.01$).

Conclusions: Analysis of LSC may provide a substantial support to visual assessment of regional LV function and the LSCI represents an index that is highly reproducible, independent of the examiner's experience.

Keywords

speckle tracking echocardiography, longitudinal strain, segmental strain

Introduction

For decades, grey scale echocardiography and Doppler measurements have been the only available imaging tools for the non-invasive evaluation of the left ventricle (LV) function. Although the methods for calculating LV global systolic function are well established, assessment of segmental function is still dependent on individual expertise to recognize motion abnormalities.

Visual wall motion score index (WMSI) was shown to be a valuable predictor for mortality in ischemic subjects and superior to LV ejection fraction.^[1,2] However, in clinical routine, the assessment of segmental function can often be challenging, even to expert examiners.

Two-dimensional speckle-tracking echocardiography (2D-STE) represents a promising advancement in the field of cardiac imaging. The method provides a non-invasive, objective tool for analysis of both global and regional deformation and is comparable to CMR data.^[3]

Of all the strain components, longitudinal strain proved to be the most robust. While global longitudinal strain (GLS) has been extensively studied and validated as a marker of LV function,

^[4] segmental longitudinal strain has received far less attention. Regional longitudinal strain can be quantified by measuring peak systolic strain (PSS), peak maximum strain (PMS), or by qualitative analysis of the strain curve, which reflects the segmental work during the entire cardiac cycle.^[5]

For this study we aimed to identify and classify the types of longitudinal strain curves (LSC) in normal and ischemic segments. Secondly, we investigated the relationship between different LSC types and the underlying wall motion score in an attempt to identify patterns of active or passive segments. Furthermore, we compared the LSC index (LSCI) obtained from 2D STE to echo derived WMSI and CMR-WMSI.

Methods

Study Population

For this study we included 100 young healthy subjects (males, $n=69$) with no history of cardiovascular disease and normal cardiac examination, including ECG and blood pressure measurements. A comprehensive resting 2D-TTE was performed to establish normal function of the LV.

Additionally, we enrolled 50 patients with a history of myocardial infarction (MI) in which LV function was assessed by both 2D-TTE and CMR.

*Corresponding author: Oana Mirea, Department of Cardiology, Craiova University, County Hospital, Tabaci, 1, Craiova, Romania; E-mail address: oana.mirea83@gmail.com

¹Department of Cardiology, University of Medicine and Pharmacy Craiova

²Department of Cardiovascular Surgery, University of Medicine and Pharmacy Craiova

For all subjects, anthropometric information was collected at the time of study, including age, weight, and body surface area. This study was approved by the local medical ethics committee.

Echocardiographic imaging and measurements

Echocardiographic images were obtained following our laboratory protocol using the commercial Vivid 9 (GE Vingmed, Norway) ultrasound machine.

All subjects were in sinus rhythm with stable cardiac frequency during the echocardiographic examination. Left chamber was quantified in accordance with the recommendations for chamber quantification of the American Society of Echocardiography.^[6] The LV volumes were obtained from 2- and 4 chamber view by tracing the endocardium border. Biplane ejection fraction (modified Simpson's rule) was used to evaluate global LV systolic function.

Wall motion score (1=normokinesis, 2=hypokinesis, 3=akinesis, 4=dyskinesis, 5=aneurysm) was carefully attributed to each of the myocardial segments by an expert examiner and the WMSI was calculated as the average of the scores.

Cardiac magnetic resonance protocol

All CMR studies were performed on a 1.5T Philips Integra-CV using dedicated cardiac software, phased-array surface receiver coil, and ECG triggering. In brief, cine images in horizontal, vertical, and short-axis views were acquired using breath-hold cine steady-state free-precession sequence. Postcontrast breath-hold T1-weighted inversion-recovery segmented gradient-echo sequence was used for detection and quantification of LGE. The interpretation of LGE and segmental wall motion was performed by an expert examiner.

Two-dimensional speckle-tracking echocardiography measurements

Myocardium tracking

Apical 4-, 2-, and 3-chambers were acquired for evaluation of longitudinal strain. Special attention was given to avoid the sliding of basal segments during diastole.

At least three cardiac cycles were recorded for each projection at a frame rate of minimum 60 fps. The digital cine loops were analyzed offline using EchoPac version BT13 dedicated software and the tracking was performed by a single observer.

Longitudinal strain was analyzed using a predefined 18 segments model (6 segments for each of the 3 projections). The analysis was carried out by manually tracking the LV endocardium border and the automatically computed range of interest was adjusted consistent to myocardial thickness. Segments were excluded from the analysis in case of incorrect tracking due to non-distinguishable speckles, reverberations or sliding of the segment.

For each subject, we calculated global longitudinal systolic strain (GLSS) and global longitudinal maximum strain (GLMS), and for each segment we measured peak systolic strain (PSS), peak maximum strain (PMS) (Figure 1-red quadrant), and time to peak maximum strain (TPMS).

We also assessed presence of initial systolic lengthening (prestretch) measured as the positive peak (Peak P) (Figure 1-red quadrant). All images were analyzed with drift compensation on and smoothening set by default.

Time setting

End-diastole was manually chosen as the peak of the R wave on the EKG. Aortic valve closure (AVC), mitral valve opening, and

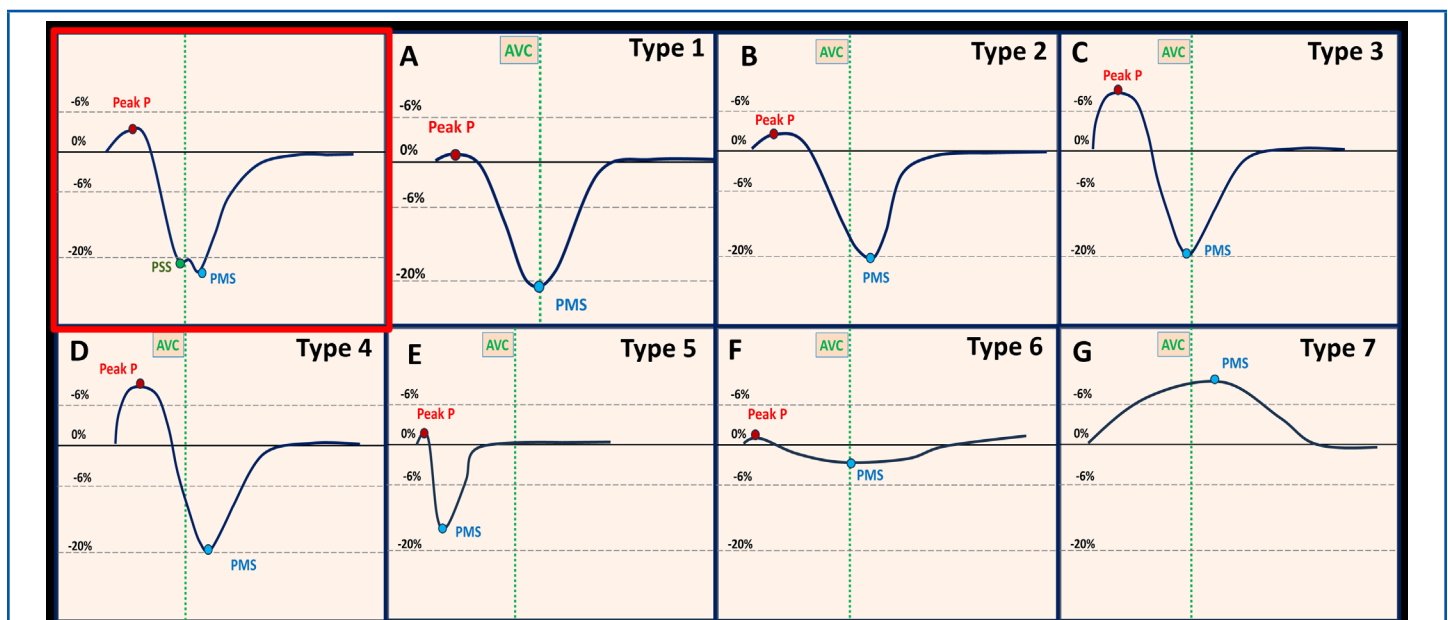


Figure 1 - Red quadrant: longitudinal strain curve showing all components: Peak P as initial lengthening; PSS: peak systolic strain as the maximum longitudinal deformation before aortic valve closure (AVC); PMS: peak maximum strain as the maximum longitudinal deformation during the cardiac cycle. A) Type 1 curve; B) Type 2 curve; C) Type 3 curve; D) Type 4 curve; E) Type 5 curve; F) Type 6 curve; G) Type 7 curve.

Table 1 - Characteristics of longitudinal strain curves

	Peak P (%)	PMS (%)	TPMS (ms)	Characteristics
Type 1 (T1)	<6	≥6	Before AVC	Normal segmental activation (Figure 1A)
Type 2 (T2)	<6	≥6	After AVC	Post systolic deformation (Figure 1B)
Type 3 (T3)	≥6	≥6	Before AVC	ISL followed by normal segmental activation (Figure 1 C)
Type 4 (T4)	≥6	≥6	After AVC	ISL followed by post systolic deformation (Figure 1 D)
Type 5 (T5)	<6	≥6	First third of systole	Early systolic shortening followed by no active event during systole (Figure 1E)
Type 6 (T6)	<6	<6	-	No active event during systole (figure 1F)
Type 7 (T7)	≥6	<6	-	Holo-systolic lengthening (Figure 1G)

AVC, aortic valve closure; PMS, peak maximum strain; TPMS, time to maximum peak strain.

mitral valve closure were manually measured using the pulsed wave Doppler obtained by sampling LV outflow tract, respectively, and mitral diastolic flow.

Longitudinal strain curve classification

The criteria mentioned were partially described by Carasso et al.^[7] Having as a starting point the descriptive analysis of strain patterns found in patients with dilated cardiomyopathy, we extended those criteria to consider the entire panel of the deformation profile that we found in our study population.

The criteria upon which the LSC classification was performed were the prevalent curve component (negative/shortening or positive/lengthening) and time to peak as follows:

- The maximum peak strain (positive or negative) was used to classify the LSC.
- If absolute value of maximum peak strain was (positive or negative) <6 % the deformation was considered a passive event (no active contraction).^[7]
- Segments with a maximum peak strain (positive or negative) that was >6% were classified considering the relation between TPMS and AVC and peak P (Table 1).

Longitudinal curve score index (LCSI) was calculated as the sum of the LCS curve types divided by the number of segments.

CMR analysis

We used an 18 segments LV model for the analysis. For each segment, the degree of LGE was assessed visually by an expert examiner and fibrosis was defined as 50–100% enhancement (transmural).

Statistical analysis

Statistical analyses were performed using SPSS version 20.0 (SPSS, Inc., Chicago, IL). All continuous data are expressed as mean±SD. Correlations between two parameters were performed using the Spearman rank correlation. The Cramer's V test for non-parametric variables was used to measure the strength of association between the LSC and WMS. P-values<0.05 were considered significant.

Results

Anthropometric and echocardiographic analysis

An overview of the echocardiographic characteristics of the two study groups are presented in Table 2.

Descriptive analysis of LSC

Overall, a number of 2680 (99%) segments could be analyzed. Following the previously described criteria, 7 types of LSC were identified (Figure 1 B to G). The average PSS and PMS for all LSC types are presented in Table 3.

Frequency and characteristics of LSC in the study groups

In the healthy subjects, T1 and T2 were the most prevalent strain curve types being identified in 78% (n=1396) and 22% (n=399) of the segments. T3 was found in 1 segment while T4 in 2 segments (0.2%). T5, T6 and T7 could not be found in any segment.

In the ischemic group, all seven types of curves were identified.

Transmural fibrosis could be identified in 57 segments. Average value of PMS was $-4.4\pm 3.1\%$ in the segments with transmural fibrosis. Type 6 curve was prevalent (47%), followed by Type 2 (31%), Type 7 (16%), and Type 4 (6%).

T2 curves reflect post systolic shortening (PSS). In the healthy group, PSS was found in 28% of the basal segments, 11% of the mid-wall segments, and 22% of the apical segments. In order to establish the limits of physiologic PSS we measured in the healthy subjects the difference between TPMS and AVC. The average delay was 40 ± 26 ms and a significant difference ($p<0.01$) between the delay calculated for the basal segments (47 ± 27 ms), mid-wall segments (37 ± 26 ms), and apical segments (30 ± 21 ms) was found.

In contrast to normal hearts, in the ischemic group T2 LSC was found in a considerable percentage (43%).

Comparison between WMS and LSC

LSC type correlated positively with the echocardiographic WMS for the basal segments (Cramer V test, $r=0.305$, $p<0.01$), apical segments (Cramer V test, $r=0.335$, $p<0.01$), and the mid-ventricular segments (Cramer V test, $r=0.406$, $p<0.01$). Overall correlation between LSC and WMS was weak to moderate (Cramer V test, $r=0.301$, $p<0.01$).

Table 2 - Anthropometric and conventional two dimensional and Doppler echocardiography measurements

	Unit	Control group (n=100)	Ischemic group (n=50)
Age	(years)	45±14	54±16*
SBP	(mmHg)	118±14	118±18
DBP	(mmHg)	71±9	72±9
HR	(bpm)	66±13	67±14
IVSd	(mm)	8.6±1.7	10.2±3.2*
PWd	(mm)	8.7±1.4	9.2±2.2
LVIDd	(mm)	47.4±4.8	57.0±8.5*
LVIDs	(mm)	30.8 ±5.3	43.3 ±12.7*
LVMi	(g/m ²)	78.5±22.3	116.7±39.7*
LV EDVi	(ml/ m ²)	56±13	79±29*
LV ESVi	(ml/ m ²)	21±7	44±26*
LV EF	(%)	64±6	48±14*
LAESVi	(ml/ m ²)	33±8	43±16*
E wave	(m/s)	72±15	72±19
DTE	(ms)	185±38	203±54
A wave	(m/s)	46±13	60±28*
E/A		1.7±0.5	1.5±1.0
LV s'	(cm/s)	10±2	7±3*
LV e'	(cm/s)	13±3	8±4*
LV a'	(cm/s)	10±3	7±3*
E/e'		6±1	11±6*
TAPSE	(mm)	23±3	16±3*

* p<0.01 control group vs. ischemic group

DTE, deceleration time E wave; EDA, end diastolic area; EDV, end diastolic volume; EF, ejection fraction; ESV, end-systolic volume; LA, left atrium; LV, left ventricle; LVM, left ventricular mass; IVSd, interventricular septum thickness; PWd, posterior wall thickness; TAPSE, tricuspid annular systolic excursion.

Table 3 - Average PSS and PMS in the two study groups for each LSC type

LSC	Control group (n=100)		Ischemic group (n=50)	
	PSS	PMS	PSS	PMS
Type 1	-22.4±4.0*	-22.6±4.0*	-19.0±5.8	-19.2±5.8
Type 2	-20.2±4.2*	-21.8±4.4*	-12.2±6.0	-14.9±5.8
Type 3	-	-	-12.3±2.4	-12.4±2.3
Type 4	-21.7±1.7*	-23.8±1.3*	-9.4±4.8	-13.9±5.3
Type 5	-	-	-8.1±2.1	-9.1±1.9
Type 6	-	-	-2.9±1.5	-3.8±1.5
Type 7	-	-	-2.3±1.1	-3.0±1.2

* p<0.01 control group vs. ischemic group

LSC, longitudinal strain curve; PMS, peak maximum strain; PSS, peak systolic strain

Longitudinal strain curve score index (LCSI) analysis

In the healthy group, WMSI and LSCI were 1 and 1.23, respectively, while in the ischemic group the calculated WMSI was 1.65 and LSCI was 1.85. When analyzed for the entire study population, LSCI correlated significantly with WMSI ($r=0.83$, $p<0.01$) (Figure 2). In the ischemic group, LSCI could also be compared with CMR-WMSI ($r=0.67$, $p<0.01$).

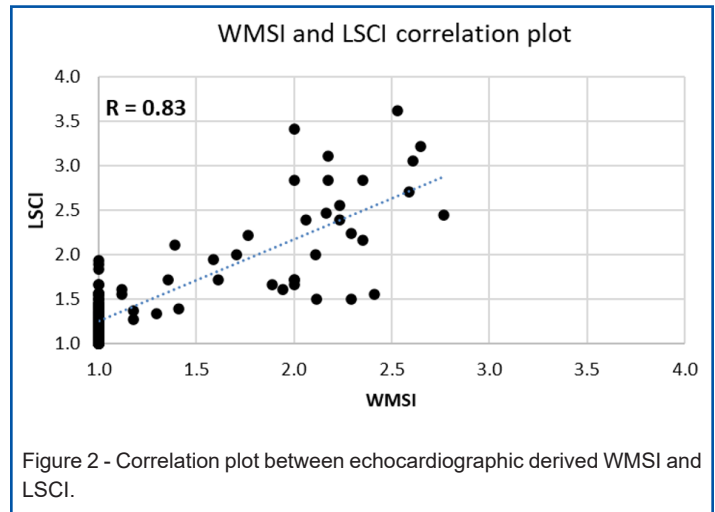


Figure 2 - Correlation plot between echocardiographic derived WMSI and LSCI.

Correlation between LSCI and conventional echocardiographic measures for systolic and diastolic function

LSCI correlated positively with GLSS ($r=0.70$, $p<0.01$), GLMS ($r=0.65$, $p<0.01$) and LV MPI ($r=0.46$, $p<0.01$). Similarly, LSCI also showed positive correlation with LV mass index ($r=0.55$, $p<0.01$), E/e' ($r=0.59$, $p<0.01$) and LA EDV ($r=0.51$, $p<0.01$). LVEF ($r=-0.44$, $p<0.01$) and LVs ($r=-0.49$, $p<0.01$) correlated negatively with LSCI.

Discussion

Two-dimensional speckle-tracking echocardiography is a valuable tool for the evaluation of LV global deformation, but equally importantly, it offers insights on segmental function by providing the strain curve that reproduces the local myofiber work during the cardiac cycle.

It was previously established with pressure-segment length loops that myocardial segments with an active work will shorten in systole and lengthen in diastole while passive segments will present systolic lengthening followed by diastolic shortening.^[8] The present study attempted to describe longitudinal deformation patterns in normal and pathologic segments, measured with 2D-STE.

The most frequently found strain profile in the healthy subjects was T1. This finding reflects that in more than three quarters of the normal segments, longitudinal deformation will begin during isovolumic contraction and myofibers will reach maximum of shortening before end-systole. Conversely, almost a quarter of the segments demonstrated PSS, expressed by T2 LSC. Presence of PSS in the healthy subjects has been described previously by Voigt et al.^[9] Using TDI, the authors demonstrated that PSS may be found in up to one third of the segments and can be interpreted as a physiological variant of deformation and as long as the magnitude of strain is preserved. The occurrence of PSS in our healthy subjects is in accordance with that reported in the aforesaid study. However, it is difficult to compare the delay to peak MS between the two studies since the method of measuring AVC and the delay to peak were different.

In our control group, PSS occurred more frequently in the basal and apical segments. Studies based on sonomicrometry measurements presented as a potential mechanism for accentuated PSS in the basal and apical segments' heterogeneity of electromechanical coupling as well as the delayed repolarization of the apex.^[10] The delay to peak MS increased from apex to base, in consistency with the direction of depolarization.^[11,12]

Nonetheless, PSS was also the most frequently found pattern in the ischemic subjects. The relationship between the PSS mechanism and different degrees of myocardial ischemia is still insufficiently understood. It has been previously demonstrated that the presence of PSS in the ischemic segments represent a marker of latent contractile activity, and therefore, a sign of myocardial viability.^[13,14] However, studies based on sonomicrometry measurements^[10] demonstrated that while the occurrence of PSS in the hipo- and akinetic segments reflect the presence of an active deformation component, PSS of the diskinitic segments represents an entirely passive mechanism.

T3 and T4 curves reflect the existence of initial systolic lengthening followed by systolic and post systolic shortening and recent studies demonstrated that increased duration of early systolic shortening is a strong predictor for the presence of coronary disease.^[15,16] We identified T3 LSC in a small percentage and exclusively in normal subjects, while T4 LSC was present in normal, hipo- and akinetic segments. Interestingly, in the healthy subjects, both patterns could only be found exclusively in the posterior and lateral walls. A potential explanation for this finding is that depolarization occurs the latest in the postero-lateral region^[17] and therefore, the early lengthening may be the result of tethering from adjacent, already activated segments. In summary, in normal subjects T3 and T4 LSC can be present as a variant of physiological deformation as long as the magnitude of longitudinal strain is not impaired.

The last three patterns, T5, T6, and T7 LSC clearly indicated the existence of an ischemic myocardial state. T5 LSC were mostly associated with the presence of diskinesia. According to this finding, a potential deformation profile of diskinitic segments may be active work of low amplitude during early systole while the LV intracavitary pressure is rising followed by a non-active state for the rest of the ejection period when the LV pressure exceeds the subendocardial pressure.

T6 LSC, which reflects no active work, was representative in an almost equal manner for hipo and akinesia and T7, and the expression of holo-systolic lengthening was associated most frequently with akinesia. T7 LSC can be explained as the passive lengthening of a non-viable segment during the rise of LV.

Although the qualitative analysis LSC can discriminate between clearly normal and clearly pathologic segments when we compared the LSC type with WMS, the correlation was only moderate. This can be attributed on one side to the considerable percentage of T2 LSC found in both normal and ischemic segments that could lower the value of correlation. On the other hand, it has been proven that the accuracy of the visual assessment of wall motion decreases from apex to base.^[18] This is consistent with our results, as the lowest correlation between WMS and LCS was found in the basal segments.

Another interesting finding is the strong association between WMSI and LSCI. Currently, visual assessment of regional function is widely used and WMSI has proved to be a strong indicator of the myocardial ischemic burden, having both diagnostic and prognostic values.^[19-21] The limitations of this index are the rather arguable reproducibility as recent studies demonstrated that even with the current developments of second harmonic imaging, the variability between expert examiners is still significant.^[18]

Conclusions

The present study describes the longitudinal strain curves obtained in normal and pathologic myocardial segments and offers a novel index for evaluating ischemic burden that provides almost overlapping data about the ischemic substrate as WMSI but overcomes the pitfalls of visual assessment.

Limitations

The algorithm used is vendor-specific, resulting in different strain values. Also, the final strain curve is the product of software regularization (drifting compensation and smoothing).

We did not have available follow-up data; therefore, we did not have the possibility to test the prognostic accuracy of LSCI to predict outcome of the ischemic patients.

Clinical implications

Longitudinal score index is based on numeric measurements, thus, the criteria can be easily integrated in mathematical functions to automatically compute the LSCI and exclude additional intervention from the examiner. These particularities make LSCI a highly reproducible parameter for the evaluation of ischemic burden. Further studies are warranted to test the prognostic value of the LSCI.

List of Abbreviations

2D	=	Two dimensional
CMR	=	Cardiac magnetic resonance
LV	=	Left ventricle
LSC	=	Longitudinal strain curve
LSCI	=	Longitudinal strain curve index
SS	=	Systolic strain
MS	=	Maximum strain
TMPS	=	Time to maximum peak strain
WMSI	=	Wall motion score index
STE	=	Speckle-tracking imaging

Conflict of interest

none declared.

REFERENCES

1. Savage ML, Hay K, Anderson B, Scalia G, Burstow D, Murdoch D, et al. The prognostic value of echocardiographic wall motion score index in ST-segment elevation myocardial infarction. *Crit Care Res Pract*. 2022 Nov 10;2022:8343785. doi: 10.1155/2022/8343785.
2. Jurado-Román A, Agudo-Quilez P, Rubio-Alonso B, Molina J, Díaz B, García-Tejada J, et al. Superiority of wall motion score index over left ventricle ejection fraction in predicting cardiovascular events after an acute myocardial infarction. *Eur Heart J Acute Cardiovasc Care*. 2019 Feb;8(1):78–85.
3. Amzulescu MS, Langet H, Saloux E, Manrique A, Boileau L, Slimani A, et al. Head-to-head comparison of global and regional two-dimensional speckle tracking strain versus cardiac magnetic resonance tagging in a multicenter validation study. *Circ Cardiovasc Imaging*. 2017 Nov;10(11):e006530. doi: 10.1161/CIRCIMAGING.117.006530.
4. Potter E, Marwick T. Assessment of left ventricular function by echocardiography: the case for routinely adding global longitudinal strain to ejection fraction. *JACC Cardiovasc Imaging*. 2018 Feb;11(2 Pt 1):260–274.
5. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *European Heart Journal - Cardiovascular Imaging*. 2015;16(1):1–11.
6. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: a report from the American society of echocardiography's guidelines and standards committee and the chamber quantification writing group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr*. 2005;18(12):1440–1463.
7. Carasso S, Rakowski H, Witte KK, Smith P, Carasso D, Garceau P, et al. Left ventricular strain patterns in dilated cardiomyopathy predict response to cardiac resynchronization therapy: timing is not everything. *J Am Soc Echocardiogr*. 2009;22(3):242–50.
8. Mirsky I, Parmley WW. Assessment of passive elastic stiffness for isolated heart muscle and the intact heart. *Circ Res*. 1973;33:233–43.
9. Voigt JU, Lindenmeier G, Exner B, Regenfus M, Werner D, Reulbach U, et al. Incidence and characteristics of segmental postsystolic longitudinal shortening in normal, acutely ischemic, and scarred myocardium. *J Am Soc Echocardiogr*. 2003 May;16(5):415–23.
10. Skulstad H, Edvardsen T, Urheim S, Rabben SI, Stugaard M, Lyseggen E, et al. Postsystolic shortening in ischemic myocardium: active contraction or passive recoil? *Circulation*. 2002;106(6):718–24.
11. Janse MJ, Sosunov EA, Coronel R, Opthof T, Anyukhovsky EP, de Bakker JM, et al. Repolarization gradients in the canine left ventricle before and after induction of short-term cardiac memory. *Circulation*. 2005 Sep 20;112(12):1711–8.
12. Sengupta PP, Khandheria BK, Korinek J, Wang J, Jahangir A, Seward JB, et al. Apex-to-base dispersion in regional timing of left ventricular shortening and lengthening. *J Am Coll Cardiol*. 2006 Jan 3;47(1):163–72.
13. Brown MA, Norris RM, Takayama M, White HD. Post-systolic shortening a marker of potential for early recovery of acutely ischaemic myocardium in the dog. *Cardiovasc Res*. 1987;21(10):703–716.
14. Hosokawa H, Sheehan FH, Suzuki T. Measurement of postsystolic shortening to assess viability and predict recovery of left ventricular function after acute myocardial infarction. *J Am Coll Cardiol*. 2000;35:1842–1849.
15. Zahid W, Eek CH, Remme EW, Skulstad H, Fosse E, Edvardsen T. Early systolic lengthening may identify minimal myocardial damage in patients with non-ST-elevation acute coronary syndrome. *Eur Heart J Cardiovasc Imaging*. 2014 May 27;pii:jeu101.
16. Smedsrud MK, Sarvari S, Haugaa KH, Gjesdal O, Ørn S, Aaberge L, et al. Duration of myocardial early systolic lengthening predicts the presence of significant coronary artery disease. *J Am Coll Cardiol*. 2012;60(12):1086–93.
17. Ramanathan C, Jia P, Ghanem R, Ryu K, Rudy Y. Activation and repolarization of the normal human heart under complete physiological conditions. *Proc Natl Acad Sci*. 2006 Apr 18;103(16):6309–14.
18. Blondheim DS, Beerli R, Feinberg MS, Vaturi M, Shimoni S, Fehske W, et al. Reliability of visual assessment of global and segmental left ventricular function: a multicenter study by the Israeli echocardiography research group. *J Am Soc Echocardiogr*. 2010;23(3):258–64.
19. Møller JE, Hillis GS, Oh JK, Reeder GS, Gersh BJ, Pellikka PA. Wall motion score index and ejection fraction for risk stratification after acute myocardial infarction. *Am Heart J*. 2006;151(2):419–25.
20. Cacciapuoti F, Arciello A, Fiandra M, Manfredi E, Cacciapuoti F, Lama D. Index of myocardial performance after early phase of myocardial infarction in relation to its location. *J Am Soc Echocardiogr*. 2004;17(4):345–9.
21. Zhang Y, Takagawa J, Sievers RE, Khan MF, Viswanathan MN, Springer ML, et al. Validation of the wall motion score and myocardial performance indexes as novel techniques to assess cardiac function in mice after myocardial infarction. *Am J Physiol Heart Circ Physiol*. 2007;292(2):H1187–92.