Speckle tracking echocardiography derived systolic longitudinal strain is better than rest single photon emission tomography perfusion imaging for nonviable myocardium identification

Martin Hutyrá^a, Tomas Skala^a, Milan Kaminek^b, David Horak^c, Martin Kocher^c, Zbynek Tudos^c, Jiri Jarkovsky^d, Jan Precek^a, Milos Taborsky^a

Background. The aim was to compare the speckle tracking echocardiography (STE) derived systolic longitudinal strain (SL_{smax}) with rest single photon emission computed tomography (SPECT) perfusion imaging (Q_{REST}), and to define the optimal cut-offs for SL_{smax} to discriminate transmural scar on contrast-enhanced magnetic resonance imaging (ceCMR).

Methods and Results. In 100 patients with chronic ischemic left ventricular (LV) dysfunction, myocardial viability was assessed using STE and rest SPECT to predict LV segmental relative extent of delayed enhancement (DE) >75% on ceCMR. Correlation was found between regional SL_{smax} ($r=-0.59$, $P<0.0001$) and DE on ceCMR. The SL_{smax} optimal cut-off -5.3% identified segments with DE>75% on ceCMR (sensitivity 83.1%, specificity 84.6%). Optimal cut-offs SL_{smax} for segments corresponding to individual perfusion territories (-3.6%, -5.3% and -4.7% for LAD, LCx resp. RCA perfusion territories) were identified. There was a significant difference (AUC 0.866 vs. 0.822 for SL_{smax} resp. Q_{REST} , $p=0.036$) in the accuracy of predicting non-viable segment due to the greater accuracy of SL_{smax} than Q_{REST} in the RCA perfusion territory (AUC 0.893 vs. 0.75 for SL_{smax} resp. Q_{REST} , $P=0.001$).

Conclusions. STE enabled identification of LV non-viable segments. Cut-off values derived for perfusion territories of individual coronary arteries improve the accuracy of predicting a transmural scar presence. In comparison with rest myocardial SPECT perfusion imaging, STE is more accurate in predicting non-viable myocardium.

Key words: myocardial viability, speckle tracking echocardiography, two-dimensional strain, rest myocardial perfusion imaging, cardiac magnetic resonance imaging, delayed enhancement

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^aDepartment of Internal Medicine I - Cardiology, University Hospital Olomouc, Czech Republic

^bDepartment of Nuclear Medicine, University Hospital Olomouc

^cDepartment of Radiology, University Hospital Olomouc

^dInstitute of Biostatistics and Analyses, Faculty of Medicine and the Faculty of Science, Masaryk University Brno

Corresponding author: Tomas Skala, e-mail: tomasskala@gmail.com

INTRODUCTION

Ischemic cardiomyopathy is the most frequent cause of LV systolic dysfunction with the heart failure syndrome¹. Revascularization in patients with coronary artery disease and left ventricular (LV) dysfunction has been shown to improve LV function, heart failure symptoms and prognosis^{2,3}. Unfortunately, only a percentage of revascularized patients show LV reverse remodeling. For this reason, pre-procedural identification of the ratio between viable and non-viable myocardium is necessary.

Contrast enhanced cardiac magnetic resonance (ceCMR) is considered as a reference imaging method in the diagnostics of myocardial viability in chronic ischemic heart disease. It has shown close correlation between the extent of delayed enhancement and myocardial scar size. CeCMR has a high accuracy in the identification of reversible myocardial dysfunction before revascularization⁴. Single photon emission computed tomography (SPECT) is considered to be a powerful predictor of myocardial viability⁵. CeCMR based parameters of segmental scar transmural extent have greater accuracy in predicting reverse

LV remodeling than rest SPECT results in predicting long term LV reverse remodeling and LV ejection fraction improvement after surgical revascularization⁶. Speckle tracking echocardiography (STE) has become a simple, rapid, relatively accurate and angle-independent echocardiographic method to assess and quantify regional myocardial function based on tracking of specific speckle patterns created by interference of ultrasound beams in the myocardium. Myocardial STE derived strain measurement has been validated, using sonomicrometry and tagged CMR as reference methods⁷. In individuals with chronic ischemic heart disease, STE derived parameters correlate with the extent of affected coronary arteries, predict the recovery of the LV function after surgical revascularization, and are capable of differentiating potentially viable segments from those showing scar extent above 50% (ref.⁸⁻¹⁰). However, these segments can display even more than 30 percent of the functional recovery after revascularization¹¹.

The aim of this study was direct comparison between the myocardial deformation analysis and rest perfusion imaging (cardiac gated SPECT) in predicting LV seg-

mental scar transmural over 75% thickness of the LV segment wall, which is viewed as a correlative to an unequivocally non-viable tissue with no possibility of functional recovery after myocardium revascularization⁴. This study also sought to define, in patients with ischaemic left ventricular dysfunction, whether the STE and SPECT accuracy in detecting a transmural scar is comparable with the area of the coronary circulation in the LV frontal, lateral, and inferior myocardial wall.

METHODS

Patient group

We consecutively enrolled 100 patients admitted to our department in the period from March 2005 to June 2009 with ischemic cardiomyopathy and LV ejection fraction <40% on 2D echocardiography (biplane Simpson formula). The patients were candidates for myocardial revascularization based on the coronary angiography findings. All had stable LV dysfunction but those who experienced myocardial infarction during the last 6 months prior to admission were excluded. Patients with acute coronary syndromes or any signs of acute myocardial ischemia as well as patients with significant valvular disease, atrial fibrillation or contraindications for ceCMR (claustrophobia, implanted pacemaker or ICD) were also excluded. All patients signed informed consent and the study protocol was approved by the local ethics committee. Within one week after coronary angiography patients underwent echocardiography, ceCMR and SPECT.

Speckle tracking echocardiography

Echocardiographic examinations were performed on the ultrasound Vivid 7 (GE Healthcare Technologies, Waukesha, Wisconsin, USA) equipped with an M3 ultrasound probe (3.5 MHz) with the possibility of a complete full-fledged analysis on archived sequences. The patients were examined in the left lateral decubitus position in respiration at rest, and the registered sequences for the follow-up evaluation were obtained in a calm exhalation to minimize translational motions of the heart. In compliance with the stated recommendations, the standardized 17-segment LV model was used for a detailed evaluation of the LV segments by all the applied methods¹². The resting examination with an obligatory synchronous registration of 1 ECG lead was performed standardly from parasternal projections on LV long and short axis and from apical long axis, 2 and 4 chamber projections. In order to set an adequate timing for the beginning and end of a systolic ejection phase, the flow in the left ventricular outflow tract was registered, and subsequently the beginning (aortic valve opening - AVO) and end (aortic valve closure - AVC) of the LV ejection phase were indicated. From the above projections, we registered the B-mode second harmonic sequence with a frame rate setting optimized for the specific method (optimal frame rate 70s⁻¹, range between 40-100s⁻¹). The evaluation of echocardiographic findings was performed off-line in an environment of ar-

chival program EchoPac 7 Option (version BT 10.0.0) by two independent physicians blindly without knowledge of clinical status or results of other examinations. While making the off-line analysis, in individual projections the LV endocardial surface was tracked, together with search for the region of interest (ROI) and its follow-up adjustment for the displayed left ventricle of the specific projection. The software divided the LV into individual segments for the specific projection and made subsequent semiautomatic quantitative spectral analysis with the possibility of manual corrections. The STE derived peak systolic longitudinal strain (SL_{Smax}) was the observed parameter. Intraobserver and interobserver agreement in the analysis of myocardial deformation parameters were determined in 10 subjects (160 LV segments). For intraobserver agreement, the Lin coefficient for SL_{Smax} was 0.98 (95% CI 0.96 to 0.99), and Pearson correlation coefficient was 0.95. For interobserver agreement, the Lin coefficient for SLs was 0.95 (95% CI 0.93 to 0.96) and Pearson correlation coefficient was 0.92 for SL_{Smax} .

Magnetic resonance imaging

The magnetic resonance examinations were performed on 1.5T Magnetom Avanto (Siemens Medical Solutions, Erlangen, Germany), Q engine (33 mT/m), Tim 76x18, equipped with software Syngo, advanced cardiac package and post processing software Argus. The standard myocardial viability evaluation protocol comprised a functional cinematic examination focused on LV using TrueFisp2D-CINE sequence (assessment of LV end-diastolic thickness and EF) and delayed enhancement (DE) depiction using high space-resolution sequences CE-IR-MRI. Both types of ceCMR evaluation of LV were performed using a 5-element phased-array cardiac coil with the patient placed supine in identical projections (series of layers in short axis, 4-chamber, 2-chamber and LV outflow tract projections). Typical parameters for trueFisp2D-CINE sequences were: matrix 192x156, FOV 366x297 mm, voxel size 1.9x1.9x6 mm, slice thickness 6 mm, TR/TE/FA 41.72 ms/1.25 ms/74 deg., 14 segments, phase 41.52 ms, total acquisition time 1.16 min. (TA), 9 slices, 9 breath-hold (BH), PAT factor 2, ECG retrospective gating, calculated 25 phases, bandwidth (BW) 930 Hz/Px. To assess DE a paramagnetic extracellular contrast agent (CA) based on gadolinium (1 molar Gadovist, Bayer Schering Pharma, Berlin, Germany) was applied intravenously dosed 0.15 mL/kg. Images were acquired during breath-holds. The scan started 15 min after CA application. Phase Sensitive Inversion Recovery (PSIR) sequence without a need for manual adjustment of inversion time (TI) to null the viable myocardium signal was used. Typical parameters for PSIR sequences were: matrix 256x256, FOV 400x275 mm, voxel size 2.2x1.6x8 mm, slice thickness 5 mm, TR/TE/FA 700 ms/1.35 ms/45 deg., non-selective IR, TI 300 ms, 65 segments, TA 5, BH, PAT factor 1, ECG trigger, 2nd trigger pulse, BW 780 Hz/Px. Automatically reconstructed pictures of this sequence were used to assess myocardial viability. Every LV segment was scanned for the extent and transmural of scar after MI: maximal

and average scar width in each segment (mm), average LV wall width in each segment (mm) and average scar extent in each segment (%). The segmental extent of delayed enhancement (DE) was calculated, defined as the percentage contrast-enhanced area of the total myocardial area $[\text{Area}_{\text{DE}}/\text{Area}_{\text{myocardium}}] \times 100$. LV segmentation was performed according to the standardized 17 segment LV model¹². Each segment was graded for the presence DE on a 5 point scale proposed by Kim et al. (segmental scar score 0 - absence of DE; 1 - DE of 1-25%; 2 - DE 26-50%; 3 - DE 51-75%; and 4 - DE 76-100%) (ref.⁴). A segments with a scar score of 4 represented segments with totally transmural scar and non-viable myocardium. All examinations were performed and assessed by an experienced radiologist blinded to patient clinical data.

Gated rest $\text{Tc}^{99\text{m}}$ sestamibi SPECT

Gated SPECT imaging was performed using a 2-detector Siemens e.cam gamma camera (Siemens Medical Solutions, Erlangen, Germany) equipped with a low-energy, high-resolution parallel-hole collimators. Sixty-four projections were acquired in a 64x64 matrix over a 180° from the 45° right anterior oblique projection to the 45° left posterior oblique projection. Images were gated at 8 frames per cardiac cycle. Processing was performed using a Butterworth filter with a frequency cut-off 0.45 cycles/pixel and an order of 5.0. All patients underwent 1-day rest imaging with nitrate administration: 8 mCi (296 MBq) $\text{Tc}^{99\text{m}}$ sestamibi (MIBI) was injected at rest, with SPECT imaging performed 1 hour after injection. Three hours later, 24 mCi (888 MBq) $\text{Tc}^{99\text{m}}$ MIBI was injected after sublingual nitrate administration 1 h before SPECT imaging. The data were analyzed visually and quantitatively. The segmental rest perfusion score was obtained through the use of the automated, commercially available software 4D-MSPECT (University of Michigan, Ann Arbor, USA). The tracer uptake was analyzed on computer-generated polar maps. In the perfusion analysis, the polar maps of each patient were compared on a pixel-by-pixel basis with the MIBI normal database derived from 70 normal volunteers. Pixels with MIBI activity greater than 2.5 SDs below the corresponding normal mean values were considered abnormal. A perfusion defect was automatically expressed by the computer as the number of abnormal pixels divided by the total number of LV pixels $\times 100$. Nonviable myocardial area was defined as that having MIBI uptake below 50% of the maximum. Rest myocardial segmental perfusion was scored on a semi-quantitative five-point score scale of 0 to 4; where 0=normal, 1=equivocal, 2=moderate, 3=severe reduction of segment perfusion (radioisotope uptake) and 4=totally absent perfusion with absence of radioisotope uptake.

Statistical analysis

Descriptive statistics used for the analysis: SL_{Smax} and DE were summarized as means and 95% confidence interval and medians with 5th – 95th percentile range. SL_{Smax} , DE and Q_{REST} in categories were described by their count and percentage. Inferential statistical tests were two-tailed, and all *P* values of less than 0.05 were considered statisti-

cally significant. To compare the STE and SPECT predictive accuracy, perfusion territories of the left anterior descending coronary artery (LAD), right coronary artery (RCA), and left circumflex artery (LCx) were evaluated separately. Segments 1, 2, 7, 8, 13, 14 were assigned to the LAD distribution. Segments 3, 4, 9, 10, and 15 were assigned to the RCA. Segments 5, 6, 11, 12, and 16 were assigned to the LCx distribution¹².

Receiver operating curve (ROC) analysis was used to identify SL_{Smax} optimal cut offs for DE categories. The results of the ROC analysis were described by area under curve (AUC), 95% confidence interval and sensitivity and specificity at optimal cut off. These cut offs were used in further analyses. Individual endpoint of non-viable myocardium was defined according to DE >75% values and it was predicted with SL_{Smax} and Q_{REST} . Predictions were made with univariate models based on logistic regression first, and multivariate models were then used. Finally, the results from multivariate model were used in ROC analysis to prove the power of prediction. Predictions of DE using Q_{REST} and SL_{Smax} were compared by means of ROC analysis. Comparison of their predictive power to endpoint DE >75% was computed using the method of DeLong et al. for the comparison of the ROC area under curve¹³. Intraobserver and interobserver variabilities were reported using the Lin and Pearson correlation.

Analyses were computed using SPSS 18.0.3 (IBM Corporation, 2010) and MedCalc 11 (MedCalc Software 2010).

RESULTS

Baseline study group characteristics

Clinical baseline characteristics of the patients are given in Table 1. Baseline heart rate and blood pressure were $78 \pm 8/\text{min}$, $134 \pm 11/82 \pm 7$ mmHg. The mean LV ejection fraction in the total study population was $34.3 \pm 4.8\%$, the mean LV enddiastolic and endsystolic volume were 282 ± 94 resp. 184 ± 67 mL respectively. Description of all parameters in the whole dataset and according to segments of LAD, LCx and RCA perfusion territory are clearly depicted in Tables 2 and 3.

In 1471 LV segments (92%) echocardiographic image quality allowed assessment of segmental function with STE compared with rest SPECT perfusion imaging in predicting transmural scar tissue on ceCMR (DE >75%). The distributions of DE and SL_{Smax} in the whole study group according to segments assigned to the LAD, RCx a RCA perfusion territory are depicted in Fig. 1.

Among the 1471 segments with adequate image quality tracking of acoustic markers, segmental analysis of ceCMR indicated 0% DE in 725 segments, 1–25% DE in 310 segments, 26–50% DE in 198 segments, 51–75% DE in 49 segments, and 76–100% DE in 189 segments (non-viable myocardium). There were 1035 segments with 0–25% DE (viable segments), 508 segments with 1–50% DE (remote non-transmural myocardial infarcts) and 238 segments with DE 51–100% (remote transmural myocardial infarcts).

Fig. 1. Distribution of DE and SL_{Smax} in the whole study group according to segments of LCx and RCA perfusion territory.

Fig. 2. Relationship between longitudinal peak systolic strain (SL_{Smax}) and delayed enhancement (DE).

Segmental analysis of rest perfusion SPECT imaging indicated Q_{REST} 0 in 876 segments, Q_{REST} 1 in 123 segments, Q_{REST} 2 in 216 segments, Q_{REST} 3 in 164 segments, and Q_{REST} 4 in 92 segments.

Prediction of segmental non-viability using myocardial deformation and rest SPECT perfusion analysis in all segments and in individual coronary artery territories

A relationship existed between longitudinal left ventricular deformation and extent of scar tissue. SL_{Smax} had a significant correlation with the relative extent of DE ($r=0.59$, $P<0.0001$). Peak systolic strain increased with

Table 1. Baseline study group characteristics.

Men/women	86/14
Age (years)	66±11
Height (cm)	170±10
Weight (kg)	87±13
History of myocardial infarction, n (%)	85 (85%)
History of stroke, n (%)	19 (19%)
Angina pectoris CCS class, (mean ± SD)	1.9±0.5
Ejection fraction, %	34.3±4.8%
Heart failure NYHA class, n (%)	
I	19 (19%)
II	46 (46%)
III	35 (35%)
IV	0 (0%)
Diabetes mellitus type 2, n (%)	42 (42%)
Hypertension, n (%)	72 (72%)
Dyslipidemia, n (%)	74 (74%)
Smoking, n (%)	39 (39%)
Coronary artery disease, n (%)	
One-vessel disease	5 (5%)
Two-vessel disease	25 (25%)
Multi-vessel disease	70 (70%)
Left main coronary artery disease	37 (37%)
LAD disease	90 (90%)
Concomitant therapy, (%)	
ACE-inhibitors/angiotensin receptor blockers	84%
Betablockers	93%
Calcium blockers	23%

Table 2. Description of parameters in the whole dataset.

n = 1 471		Total¹
DE (%)	Mean (95% CI)	22.5 (20.9; 24.1)
	Median	10.0 (0.0; 100.0)
	(5 th ; 95 th perc.)	
	0%	725 (49.3%)
	≤ 25%	979 (66.6%)
	> 75%	189 (12.8%)
SL_{Smax}	Mean (95% CI)	-10.0 (-10.4; -9.7)
	Median	-10.1 (-20.8; 1.2)
	(5 th ; 95 th perc.)	
SL_{Smax} cut-off	> -5.3	189 (12.8%)
Q_{REST}	0	876 (59.6%)
	1	123 (8.4%)
	2	216 (14.7%)
	3	164 (11.1%)
	4	92 (6.3%)
	1-2	339 (23.0%)
	3-4	256 (17.4%)
	1-4	595 (40.4%)
Segments	LAD	547 (37.2%)
	LCx	453 (30.8%)
	RCA	471 (32.0%)

¹ Categories of parameters as number and percentage of total, cut offs and categories are chosen according to definitions of endpoints used in the analysis

increasing scar transmural. Scatter plot for correlation between SL_{Smax} and DE is depicted in Fig. 2. There was also significant correlation between extent of scar tissue (DE) and rest perfusion score (Q_{REST}) ($r=0.6$, $P<0.0001$). Correlation analysis showed that SL_{Smax} also had a statistically significant relationship with the Q_{REST} ($r=0.22$, $P<0.0001$).

The mean SL_{Smax} in segments with no scar (DE 0%) was $-13.3\pm5.9\%$, with LV myocardial scar and DE 1-25% $-10.3\pm5.2\%$, DE 26-50% $-7.9\pm5.2\%$, DE 51-75% $-6.4\pm4.1\%$ and DE 76-100% $-0.6\pm5.5\%$.

Based on delayed enhancement findings by ceCMR, longitudinal strain analysis allowed distinction of segments with a transmural scar and totally non-viable myocardium (DE >75%) from segments with a non-transmural, potentially ischemic or morphologically normal myocardium. Performing ROC analysis for the distinction of transmural scarred non-viable myocardium from all other segments in the whole left ventricle, the area under the curve (AUC) was 0.866. The ROC analysis yielded a cut-off value of -5.3% for SL_{Smax} with a sensitivity of 83.1%, specificity of 84.8% to identify segments with non-viable myocardium presence (DE >75%) on ceCMR. Odds ratios and ROC analysis results of given model with a SL_{Smax} cut-off value -5.3% for endpoint prediction (DE >75%) in all

segments and in individual coronary arteries territories are depicted in Table 4.

To improve the accuracy of the model to predict an occurrence of non-viable myocardium, the optimum cut-off values SL_{Smax} for segments corresponding to individual perfusion territories were subsequently identified (-3.6%, -5.3% and -4.7% for LAD, LCx and RCA perfusion territory). The results of ROC analysis corresponding to the optimum cut-off values derived for perfusion territories are given in Table 5.

A Q_{REST} perfusion score 3-4 discriminated between segments with potentially viable myocardium and segments with DE >75% with a sensitivity of 86.2% and specificity of 66.3%. The results of the segmental analyses in all left ventricular segments and in LAD, LCx and RCA perfusion territory segments using Q_{REST} in prediction DE ≥75% endpoint are presented in Tables 6 and 7.

Comparison of myocardial deformation and rest perfusion analysis in predicting transmural segmental non-viability

Odds ratios and ROC analysis results for prediction of non-viable myocardium (DE ≥ 75% endpoint) using Q_{REST} and SL_{Smax} are given in Table 6. Comparison of their predictive power to endpoint non-viable myocardium (DE >75%) in all left ventricular segments and in LAD, LCx

Table 3. Description of parameters according to segments of LAD, LCx and RCA perfusion territory.

n = 1 471 ¹		Segments			P value ²
		LAD (n = 547)	LCx (n = 453)	RCA (n = 471)	
DE (%)	Mean (95% CI)	22.7 (19.9; 25.5)	23.2 (20.4; 26.0)	21.5 (18.8; 24.3)	-
	Median (5 th ; 95 th perc.)	0.0 (0.0; 100.0)	12.5 (0.0; 100.0)	10.0 (0.0; 100.0)	0.090
	> 75%	79 (14.4%)	52 (11.5%)	58 (12.3%)	0.346
SL _{Smax}	Mean (95% CI)	-9.9 (-10.5; -9.3)	-9.5 (-10.2; -8.9)	-10.7 (-11.3; -10.0)	-
	Median (5 th ; 95 th perc.)	-9.9 (-20.6; 0.8)	-9.8 (-20.7; 2.0)	-10.8 (-21.5; 1.2)	0.042
SL _{Smax} cut-offs ³	> -5.3	-	111 (24.5%)	-	-
	> -4.7	-	-	89 (18.9%)	-
	> -3.6	100 (18.3%)	-	-	-
Q _{REST}	0	369 (67.5%)	254 (56.1%)	253 (53.7%)	<0.001
	1	38 (6.9%)	35 (7.7%)	50 (10.6%)	0.091
	2	57 (10.4%)	69 (15.2%)	90 (19.1%)	<0.001
	3	55 (10.1%)	53 (11.7%)	56 (11.9%)	0.588
	4	28 (5.1%)	42 (9.3%)	22 (4.7%)	0.006
	1-2	95 (17.4%)	104 (23.0%)	140 (29.7%)	<0.001
	3-4	83 (15.2%)	95 (21.0%)	78 (16.6%)	0.047
	1-4	178 (32.5%)	199 (43.9%)	218 (46.3%)	<0.001

¹ Categories of parameters as number and percentage of total in given segment, cut offs and categories are chosen according to definitions of endpoints used in the analysis

² Statistical comparisons of segments were made with Kruskal-Wallis test for continuous parameters and with χ^2 test for categorical parameters

³ Optimal cut offs according to segments for DE $\geq$ 75% prediction

Table 4. Prediction of non-viable myocardium presence (DE >75% endpoint) using a SL_{Smax} cut-off > -5.3% in all left ventricular segments and in LAD, LCx and RCA perfusion territory segments.

Endpoint DE>75%				
Cut-off ¹	All segments n=1471	LAD n=547	LCx n=453	RCA n=471
SL _{Smax} > -5.3%	27.00 (17.93; 40.65)	19.69 (10.8; 35.9)	27.42 (12.4; 60.9)	43.39 (19.5; 96.7)
	<0.001	<0.001	<0.001	<0.001
ROC AUC	0.866	0.837	0.891	0.894
95% CI ²	0.833; 0.900	0.781; 0.892	0.833; 0.949	0.839; 0.949
P ²	<0.001	<0.001	<0.001	<0.001
Sensitivity ³	83.1%	79.7%	84.6%	86.2%
Specificity ³	84.6%	83.3%	83.3%	87.4%

¹ Odds ratio for models based on logistic regression

² Area under curve based on ROC analysis supplemented by its 95% confidence interval and statistical significance

³ Sensitivity and specificity of given model for endpoint prediction

and RCA perfusion territory segments was then calculated and results are depicted in Table 7. A minimum, but statistically significant difference (AUC 0.866 vs. 0.822 for SL_{Smax} resp. Q_{REST}, $P=0.036$) in accuracy of predicting an occurrence of non-viable myocardium, as defined by DE >75% on ceCMR, was achieved as a result of higher accuracy of the deformation analysis in comparison with Q_{REST} in the RCA perfusion territory (AUC 0.75 vs. 0.893 for Q_{REST} resp. SL_{Smax}, $P 0.001$).

DISCUSSION

The key conclusions of this study can be formulated as follows: 1) a cut-off value of -5.3% for speckle tracking derived parameter SL_{Smax} identified segments with non-viable myocardium presence (DE >75%) on ceCMR with a 83.1% sensitivity and 84.8% specificity; 2) the cut-off values SL_{Smax}, which increase accuracy of the model predicting an occurrence of non-viable myocardium even more, can be derived for perfusion territories of individual coronary arteries corresponding approximately to the region of the LV frontal, lateral, and inferior myocardial wall; 3) as compared to the rest perfusion myocardial SPECT,

Table 5. Identification of SL_{Smax} optimal cut offs according to segments of LAD, LCx and RCA perfusion territory.

Endpoint; DE >75% ¹	LAD	LCx	RCA
Risk group (n; %) ²	79 (14.4%)	52 (11.5%)	58 (12.3%)
AUC ³	0.896	0.904	0.945
95% CI ³	0.860; 0.932	0.855; 0.953	0.920; 0.971
P ⁴	<0.001	<0.001	<0.001
Cut-off ⁵	-3.6	-5.3	-4.7
Sensitivity ⁶	74.7%	84.6%	84.5%
Specificity ⁶	91.2%	83.8%	90.3%

¹ Non-viable myocardium² Proportion of segments with given endpoint in analyzed group of segments³ Area under curve based on ROC analysis supplemented by its 95% confidence interval⁴ Statistical significance of AUC⁵ Optimal cut off of SL_{Smax} with the best combination of sensitivity and specificity⁶ Sensitivity and specificity at optimal cut off**Table 6.** Prediction of non-viable myocardium (DE ≥ 75% endpoint) using Q_{REST} and SL_{Smax} in all left ventricular segments and in LAD, LCx and RCA perfusion territory segments.

Endpoint; DE >75% ¹	Total	LAD	LCx	RCA
Univariate² - Q_{REST}				
Q_{REST} 0	0.08 (0.05; 0.12) <0.001	0.04 (0.02; 0.08) <0.001	0.06 (0.03; 0.17) <0.001	0.19 (0.10; 0.36) <0.001
Q_{REST} 1-2	1.05 (0.73; 1.50) 0.789	2.09 (1.20; 3.63) 0.009	1.01 (0.51; 2.00) 0.983	0.52 (0.26; 1.03) 0.059
Q_{REST} 3-4	13.78 (9.77; 19.42) <0.001	19.16 (10.86; 33.80) <0.001	11.70 (6.16; 22.22) <0.001	13.09 (7.09; 24.19) <0.001
Multivariate^{2,3}				
Q_{REST} 0	0.20 (0.12; 0.33) <0.001	0.08 (0.04; 0.19) <0.001	0.15 (0.05; 0.45) 0.001	
Q_{REST} 3-4	5.59 (3.75; 8.32) <0.001	4.55 (2.39; 8.68) <0.001	4.47 (2.15; 9.30) <0.001	13.09 (7.09; 24.19) <0.001
Univariate² - SL_{Smax}				
SL_{Smax} ⁴	27.00 (17.93; 40.65) <0.001	30.72 (16.86; 55.98) <0.001	27.34 (12.31; 60.70) <0.001	50.77 (23.23; 110.98) <0.001
Multivariate²				
SL_{Smax} ^{4, 5}	14.11 (9.06; 21.98) <0.001	37.68 (19.78; 71.78) <0.001	14.22 (5.51; 36.73) <0.001	24.18 (10.31; 56.70) <0.001

¹ Non-viable myocardium² Odds ratio for univariate and multivariate models based on logistic regression; multivariate regression based on forward stepwise selection algorithm³ Only two Q_{REST} categories, which were most significant in univariate model, are chosen into the multivariate model⁴ Cut-off for SL_{Smax} is used from previous table; patients above given cut-off are taken as "risk" group in the analysis (despite the value of OR for given endpoint)⁵ Multivariate regression model using different SL_{Smax} cut-offs

the myocardium deformation analysis is more accurate in predicting LV non-viable myocardium, which is evident on the result obtained in the area of the inferior wall corresponding to the RCA myocardium perfusion territory.

Determination of myocardial non-viability

The assessment of myocardial viability might in future become a very important tool for preoperative risk stratification, since patients with pronounced LV systolic dysfunction have much increased perioperative risks and it would be desirable to identify subgroups of patients with the greatest potential benefits of revascularization. A meta-analysis showed that in patients with viability, subsequent revascularization was associated with 79.6% reduction in annual mortality, whereas the mortality of patients without viability after revascularization was much higher and not significantly different from medi-

cally treated patients². But the assessment of myocardial viability according to STICH (The Surgical Treatment for Ischemic Heart Failure) study protocol in patients with ischemic systolic dysfunction did not identify patients with a differential survival benefit from CABG, as compared with medical therapy alone¹⁴. Recently published data on patients with ischemic heart disease who underwent stress SPECT myocardial perfusion scintigraphy (MPS) suggest possible harm with revascularization in patients with extensive left ventricular scar (> 10% total myocardium fixed perfusion defect) especially if ischemia is not present¹⁵. These findings are consistent with the observation that cardiac stress PET imaging did not identify any therapeutic benefit in patients with ischemic left ventricular dysfunction (median LVEF 25%) in the setting of observed extensive left ventricular scar (median LVEF 30%) and little myocardial ischemia¹⁶. The above

Table 7. Comparison of receiver operating curve analysis area under curves for predictions of non-viable myocardium (DE >75% endpoint) using Q_{REST} and SL_{Smax} .

Endpoint; DE $\geq 75\%$ ⁵	Total	LAD	LCx	RCA
Q_{REST} ROC¹				
AUC ²	0.822	0.865	0.822	0.750
95% CI ²	0.788; 0.855	0.818; 0.911	0.764; 0.881	0.671; 0.828
P^2	<0.001	<0.001	<0.001	<0.001
Sensitivity ³	86.2%	88.6%	90.4%	60.3%
Specificity ³	66.3%	76.9%	62.1%	89.6%
SL_{Smax} ROC¹				
AUC ²	0.866	0.840	0.891	0.893
95% CI ²	0.833; 0.900	0.780; 0.900	0.833; 0.949	0.836; 0.950
P^2	<0.001	<0.001	<0.001	<0.001
Sensitivity ³	83.1%	74.7%	84.6%	84.5%
Specificity ³	84.6%	91.2%	83.3%	90.3%
Comparison of ROC AUC for Q_{REST} vs. SL_{Smax}				
P^4	0.036	0.458	0.100	0.001

¹ ROC based on models based on logistic regression (from previous table)² Area under curve based on ROC analysis supplemented by its 95% confidence interval and statistical significance³ Sensitivity and specificity of given model for endpoint prediction⁴ Statistical significance of comparison between AUC for multivariate model of Q_{REST} and AUC for multivariate model of SL_{Smax} ⁵ Nonviable myocardium

data indicate that the reverse remodeling with a positive influence on the prognosis and therapeutic benefit of revascularization, which significantly exceeds the periprocedural risk of revascularization, is feasible only in that percentage of patients having a minimum extent of the LV myocardial scar. This hypothesis is supported by the results of the previous study, which showed, that patients with 2 or less segments with the DE >75% can be expected to show reverse LV remodeling with a sensitivity of 71% and specificity 67% (ref.⁶).

Distinction between non-transmural and transmural infarction

Available references provide no study results predicting extent of LV segment scar, as detected by the ceCMR with use of DE >75% phenomenon. In DE >50% segments, as stated by Kim et al.⁴, merely 12% show a probability of functional improvement after revascularization of segments with impaired contractility. Nevertheless, the data published later, Schwartzman et al.¹¹, proved up to 35% of recoveries of regional contractility in originally dysfunctional segments with DE >50%, which was the reason for our choosing the DE >75% cut-off values, as a reliable marker for the occurrence of non-viable cicatrically-altered myocardium.

The deformation analysis of myocardium by means of evaluating two-dimensional strain was validated, both in an experimental and clinical model, as a relatively accurate and reproducible method in the differentiation between potentially viable myocardium with no or non-transmural scar tissue and chronic transmural myocardial infarct without the potential for functional recovery after

revascularization^{7,17}. Speckle tracking deformation analysis has increased sensitivity and specificity in comparison with tissue Doppler imaging for determining the transmural extent of a myocardial scar¹⁷. Becker et al. observed that radial strain predicted functional recovery after revascularization with an accuracy similar to that of ceCMR in patients with ischemic LV dysfunction⁹. Longitudinal strain parameters correlated with the degree of coronary artery stenosis, left ventricular (LV) ejection fraction (EF) and independently predicted LV remodeling following myocardial revascularization¹⁷⁻¹⁹. Roes et al. evaluated 90 patients with chronic ischemic LV dysfunction and reported that a regional longitudinal strain cutoff value of -4.5% could distinguish a nontransmural scar from a transmural infarct (cut-off DE >50%) with sensitivity of 81.2% and specificity of 81.6% (ref.¹⁰).

Deformation analysis and rest perfusion SPECT imaging in non-viable myocardium prediction in the current study

Compared to the results of the study by Roes et al.¹⁰, the longitudinal peak systolic strain parameter achieved a higher diagnostic accuracy in predicting non-viable myocardium, defined by the extent of myocardial scar LV >75% DE with 83.1% sensitivity and 84.6% specificity. The number of segments analyzed by deformation analysis was comparable in both studies (92% our study, 93% Roes et al.). Discrepancies in cut-off values derived for different endpoints (DE > 50% resp. 75%) can be speculatively interpreted by the gravity of global systolic dysfunction of the examined individuals, and thus by a different extent of hibernating myocardium and ischemic LV dysfunction. All the patients in our study showed the

baseline EF LV $\leq 40\%$ (average EF LV $34 \pm 5\%$), whereas Roes et al. presented the EF LV $28 \pm 8\%$, which could indicate a different deformation capability of segments with a relatively comparable morphological impairment (scar extent), but a difference in the gravity of ischemia depending on the preexisting global function. Another possible explanation lies probably in a higher quantity of hibernating segments with ischemia at rest which determines not only the global function of myocardium (EF LV), but also a regional deformation of individual LV segments, independently of the scar extent, especially at hibernating viable LV segments. As the first paper published on this issue, our study has proven a higher accuracy in predicting a transmural myocardial scar, using cut-off specifically for segments of perfusion territories of individual coronary arteries.

Cardiac gated perfusion SPECT imaging is relatively widely available and very sensitive for detecting nonviable myocardium^{5,15}. Rest perfusion imaging score 3–4, evaluated in a semi-quantitative scale by means of the gated SPECT myocardium, can be considered a correlate of non-viable myocardial tissue, and confirming a high rest summation score represents a strongly negative prognostic predictor^{5,15,20–22}. While comparing the perfusion and deformation analysis, the myocardium SPECT statistically achieved, probably as a result of attenuation artifacts in the territory of the right coronary artery corresponding to the localization of the LV inferior wall, a significantly lower accuracy in predicting segments with transmural scar, in comparison with the deformation analysis (AUC 0.822 vs. 0.866, $P=0.036$). So far this finding on the direct comparison between rest deformation analysis and perfusion of myocardium has not been published.

Limitations

The limitations of the present study included the lack of segmental function data and outcome after revascularization. Only 92% of segments with an adequate ultrasound quality for speckle tracking analysis were available for direct comparison with MR and SPECT. In order to definitely designate a significance of specifying viability of myocardium by means of the longitudinal rest deformation analysis and optimum management (revascularization vs. conservative therapy) of a patient with ischemic left ventricular systolic dysfunction, it will be indispensable to carry out a randomized prospective comparative study with a more strictly defined cut-off value that discriminates between viable (implying a profit from revascularization) and non-viable myocardium (conservative therapy), in comparison with the STICH study.

CONCLUSIONS

1. Myocardial deformation imaging based on 2-dimensional longitudinal peak systolic strain analysis could differentiate between viable myocardial tissue and a LV segment with transmural scar, as defined by $DE > 75\%$ (which can be considered as a reliable marker of myocar-

dium non-viability) in patients with ischemic left ventricular systolic dysfunction.

2. The cut-off value of -5.3% longitudinal peak systolic longitudinal 2D strain observed in the present study enabled the identification of non-viable segments with transmural scar tissue with a high accuracy demonstrating the potential use of longitudinal strain imaging for the selection of patients who will benefit from revascularization. For the first time, a definition was provided for cut-off values derived for perfusion territories of individual coronary arteries corresponding to myocardial segments of the frontal (LAD), lateral (LCx) and inferior walls (RCA), which further improve the prediction of transmural scars occurring in these regions.

3. This is the first study proving that the rest deformation analysis of myocardium is more accurate than that with perfusion myocardial SPECT, in predicting non-viable LV myocardium, which is derived from the result obtained in the area of the inferior wall corresponding to the RCA perfusion territory.

CONFLICT OF INTEREST STATEMENT

Author's conflict of interest disclosure: *None declared.*

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