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Magnetic resonance imaging techniques for risk stratification in cardiovascular disease

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Chapter 10

Validation of echocardiographic 2-dimensional speckle tracking longitudinal strain imaging for viability assessment in patients with chronic ischemic left ventricular dysfunction and comparison with contrast-enhanced magnetic resonance imaging

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Abstract

The purpose of the present study was to compare longitudinal strain assessed by two-dimensional (2D) speckle tracking with scar tissue on contrast-enhanced magnetic resonance imaging (MRI) in patients with chronic ischemic left ventricular (LV) dysfunction. The aim was also to define a cut-off value for regional strain to discriminate between viable myocardium and transmural scar. Ninety patients with chronic ischemic LV dysfunction underwent transthoracic echocardiography to measure global and segmental (regional) longitudinal LV strain using 2D speckle tracking and cine MRI followed by contrast-enhanced MRI to assess segmental LV function and the segmental/global (transmural) extent of scar tissue. The optimal cut-off value for regional strain discriminating between segments with viable myocardium and segments with transmural scar was also determined. A good correlation was found between global LV strain and global extent of scar tissue on contrast-enhanced MRI ($r = 0.62$, $p < 0.001$). Mean segmental strain in segments without scar tissue was -10.4 ± 5.2%, as compared to 0.6 ± 4.9% in segments with transmural scar tissue ($p < 0.001$). A strain value of -4.5% discriminated between segments with viable myocardium and segments with transmural scar tissue on contrast-enhanced MRI with a sensitivity of 81.2% and a specificity of 81.6%. In conclusion, global and regional longitudinal strain measured with 2D speckle tracking is associated with global and regional (transmural) extent of scar tissue on contrast-enhanced MRI. A cut-off value of -4.5% for regional strain discriminated between segments with viable myocardium and those with transmural scar tissue on contrast-enhanced MRI with a sensitivity of 81.2% and a specificity of 81.6%.

Introduction

Recently, echocardiographic strain imaging has been proposed as a novel approach for assessment of viability and scar tissue (1). Strain imaging permits assessment of active deformation rather than passive motion, and therefore, may improve discrimination between viable and scarred myocardium, particularly in patients with previous myocardial infarction. Myocardial strain can be derived using tissue Doppler imaging or two-dimensional (2D) speckle tracking (2). With recent technological developments, it has become possible to assess both the global strain of the (entire) left ventricle (LV), and regional strain of individual LV segments (3,4). Previous studies demonstrated that echocardiographic strain imaging has the potential to discriminate between viable and non-viable tissue (1,5). It would be useful however, to establish precise cut-off criteria for regional strain that may discriminate between transmural scar tissue and viable myocardium, since revascularization is not beneficial in patients with transmural scar tissue. Accordingly, the present study compares myocardial strain assessed using 2D speckle tracking with the transmural extent of scar tissue on contrast-enhanced magnetic resonance imaging (MRI) in patients with chronic ischemic LV dysfunction and defines a cut-off value for regional strain to discriminate between viable myocardium and transmural scar tissue.

Methods

The study population consisted of 90 consecutive patients with chronic ischemic LV dysfunction (on 2D echocardiography) who were referred for 2D transthoracic echocardiography and contrast-enhanced MRI for clinical reasons. All patients had evidence of coronary artery disease on coronary angiography. Patients with recent myocardial infarction (< 3 months before study entrance) were excluded to avoid the influence of infarct resorption on the results. Other exclusion criteria included (supra-) ventricular arrhythmias, pacemakers, intracranial clips, and claustrophobia. Patient characteristics are listed in Table 1.

The study protocol consisted of 2D transthoracic echocardiography for assessment of global strain of the entire LV using automated function imaging (AFI) and segmental (regional) strain (3,4). Furthermore, cine MRI was performed to evaluate segmental LV function, and contrast-enhanced MRI was performed to assess the extent and transmurality of scar tissue. Subsequently, AFI global LV strain (reflecting the global viability status of the LV) was compared with the global extent of scar tissue on contrast-enhanced MRI. Next, in the dysfunctional segments (on cine MRI), segmental (regional) strain was compared to the segmental transmural extent of scar tissue on contrast-enhanced MRI, and the optimal cut-off value for regional strain to discriminate between transmural scar tissue and (partially) viable myocardium was determined.

Echocardiographic images were obtained with the patient in the left lateral decubitus position using a commercially available system (Vivid Seven, General Electric-Vingmed, Milwaukee, Wisconsin, USA). Images were acquired using a 3.5-MHz transducer at a depth of 16 cm in the parasternal and apical views (apical long-axis, 2- and 4-chamber images). All echocardiographic data were analyzed offline using Echopac, version 7.0.0 (General Electric-Vingmed) by 2 independent observers unaware of all other patient data. Global LV longitudinal strain was assessed using the AFI technique (4). With this commercially available technique (General Electrics), myocardial tissue deformation is calculated using speckle tracking from 2D gray-scale images (using the apical long-axis, 2- and 4-chamber views) (3). Aortic valve closure timing was marked in the selected views, and 3 points were anchored inside the myocardial tissue, 2 placed at the basal segments along the mitral valve annulus, and 1 at the apex. These points triggered the automatic process, which analyzed myocardial motion by tracking features (natural acoustic tags). The percent of wall lengthening and shortening was displayed for each plane and represented longitudinal strain. The results of all 3 planes are then combined in a single bull's-eye summary, which presents the analysis for each segment using a 17-segment model (17 segmental [regional] strain values per patient), along with a global strain value for the entire LV. Mean frame rate of the obtained images was 70 frames/s (range 40-100 frames/s). Previous work has shown that the intra-class correlation coefficients concerning intra- and interobserver reproducibility for assessment of AFI global LV strain were 0.95 and 0.92, respectively, with an average difference of

respectively -0.3 ± 0.6% and –0.2 ± 2.6% (mean ± 2 standard deviation, SD) according to Bland-Altman analysis (6).

Table 1. Clinical characteristics of the study population.

Clinical variables	No. (%) of patients (n = 90)
Age (years)	64 ± 11
Men	73 (81)
Diabetes	21 (23)
Hypertension*	27 (30)
Hypercholesterolemia†	44 (49)
Smoker	39 (43)
Previous revascularization	55 (61)
Number of coronary arteries narrowed	
1-vessel disease	20 (22)
2-vessel disease	28 (31)
3-vessel disease	42 (47)
Infarct location	
Anterior	66 (73)
Non-anterior	24 (27)
Left ventricular dysfunction	
Ejection fraction >35% and ≤45%	31 (34)
Ejection fraction >25% and ≤35%	34 (38)
Ejection fraction ≤25%	25 (28)

* Hypertension is defined as blood pressure ≥ 140 / 90 mmHg.
† Total cholesterol > 200 mg/dl.

A 1.5T Gyroscan ACS-NT/Intera MRI scanner (Philips Medical Systems, Best, The Netherlands) equipped with a 5-element cardiac synergy coil was used. Images were acquired during breath-holds of approximately 15 seconds using vector electrocardiographic gating. The heart was imaged from apex to base (7), with 10-12 imaging levels (dependent on the heart size) in the short-axis view using a balanced turbo field echo sequence with parallel imaging (SENSE, acceleration factor 2). Typical parameters were a field of view of 400 × 320 mm^2, matrix of 256 × 206 pixels, slice thickness of 10 mm, no slice gap, flip angle of 35°, time to echo of 1.67 ms, and time to repeat of 3.3 ms. The temporal resolution was 25 to 39 ms. Geometric settings of baseline scans were stored and repeated for contrast-enhanced images to ensure matching of the same slices (and hence, myocardial segments). Contrast-enhanced images were acquired approximately 15 minutes after a 0.15 mmol/kg bolus injection of gadolinium diethylenetriamine penta-acetic acid (Magnevist, Schering, Berlin, Germany) with an inversion-recovery three-dimensional turbo field echo sequence; the inversion

time was determined with real-time plan scan. Typical parameters were a field of view of 400 × 300 mm^2, matrix of 256 × 192 pixels, slice thickness of 5 mm, flip angle of 15°, time to echo of 1.1 ms, and time to repeat of 3.8 ms.

To determine global LV function, endocardial borders were outlined manually on short-axis cine images with previously validated software (MASS, Medis, Leiden, The Netherlands) (8). Papillary muscles were regarded as part of the LV cavity, and epicardial fat was excluded. LV end-systolic volume (ESV) and LV end-diastolic volume (EDV) were calculated. Subsequently, LV ESV was subtracted from LV EDV and LV ejection fraction (LVEF) was calculated.

To determine regional wall motion, cine MRI images were visually interpreted by 2 experienced observers using a 17-segment model (similar to segmental strain analysis with echocardiography) (9). Each segment was assigned a wall motion score using a 5-point scale: 0: normal wall motion, 1: mild hypokinesia, 2: severe hypokinesia, 3: akinesia, and 4: dyskinesia.

Contrast-enhanced images were scored visually by 2 experienced observers using the 17-segment model described above (9). Each segment was graded on a 5-point scale (segmental scar score), with 0: absence of hyperenhancement, 1: hyperenhancement of 1% to 25% of LV wall thickness, 2: hyperenhancement extending from 26% to 50%, 3: hyperenhancement extending from 51% to 75%, and 4: hyperenhancement extending from 76% to 100% (10). Accordingly, segments with a scar score of 3 and 4 represent segments with transmural scar tissue.

The total scar score, defined as the summed segmental scar scores per patient divided by 17 was calculated to determine the global extent of scar tissue per patient (for direct comparison with the global LV strain as determined using the AFI approach).

Continuous variables were tested for normal distribution using Kolmogorov-Smirnov and expressed as mean ± SD or median (interquartile range), as appropriate. The relation between AFI global LV strain and total scar score was calculated using Spearman's correlation coefficients (r) (AFI global LV strain is non-normally distributed). Segments were grouped according to segmental scar score on contrast-enhanced MRI (i.e., 5 groups; scar score ranging from 0 to 4) and the mean segmental (regional) strain in these groups was calculated and compared using Kruskal-Wallis analysis (segmental strain values are non-normally distributed). Furthermore, segmental strain values were used to divide the segments into quartiles and the proportion of segments with transmural scar in each quartile was evaluated. The optimal cut-off value for segmental strain to discriminate between segments with or without transmural scar tissue on contrast-enhanced MRI was determined by receiver operating characteristic curve analysis. For all tests, a p-value < 0.05 was considered statistically significant.

Results

Clinical data are presented in Table 1. The median AFI global LV strain of the study population was -7.6 (4.6)%. Strain values could not be measured in 103 segments (7%) of 1530 available segments because of poor echocardiographic image quality.

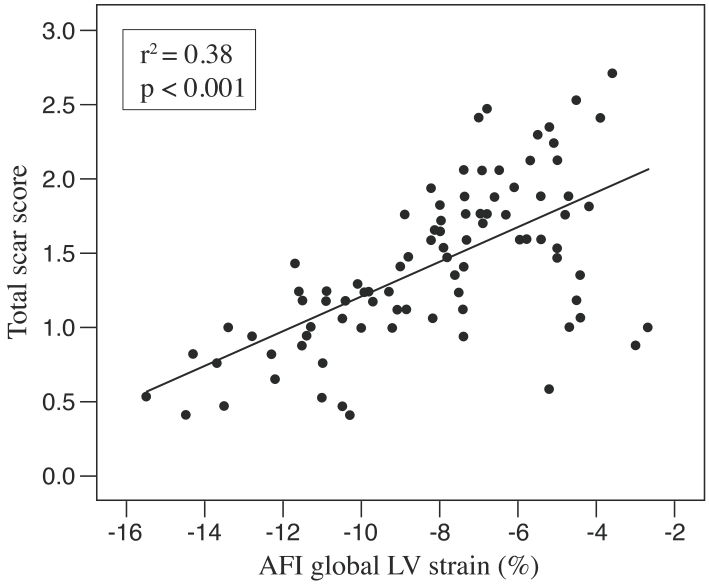
Mean LVEF in the total study population was 28 ± 8%. The median LV ESV and median LV EDV were 232 (123) ml and 315 (132) ml, respectively, and the mean total scar score was 1.4 ± 0.5.

Of the 1427 included segments (matching the echo segments), 1026 (72%) showed abnormal wall motion. These dysfunctional segments were used for further analysis. Of these segments, 194 (19%) showed mild hypokinesia, 377 (37%) showed severe hypokinesia, 391 (38%) segments were akinetic, and 64 (6%) were dyskinetic.

Of the 1026 dysfunctional segments, 685 (67%) segments showed scar tissue (hyperenhancement) on contrast-enhanced MRI; 127 (19%) segments showed minimal hyperenhancement (scar score 1), 185 (27%) segments had a scar score of 2, 176 (26%) had a scar score of 3, and 197 (29%) showed scar score 4 (transmural scar tissue).

A good relation ($r = 0.62$, $r^2 = 0.38$, $p < 0.001$) was observed between AFI global LV strain and total scar score on contrast-enhanced MRI (Figure 1), indicating good agreement between the two techniques for assessment of the global viability/scar status of the entire LV.

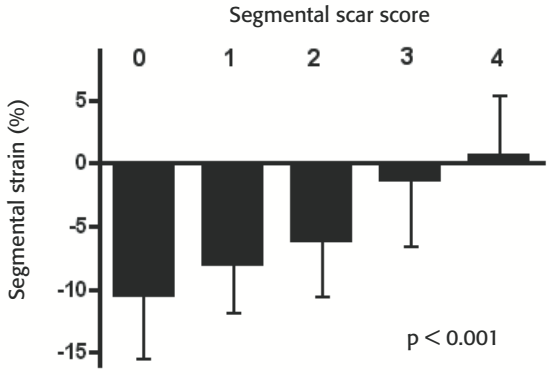
Figure 1.



Relation between AFI global LV strain and total scar score assessed with contrast-enhanced MRI. The standard error of the estimate is 2.26. AFI: automated functional imaging.

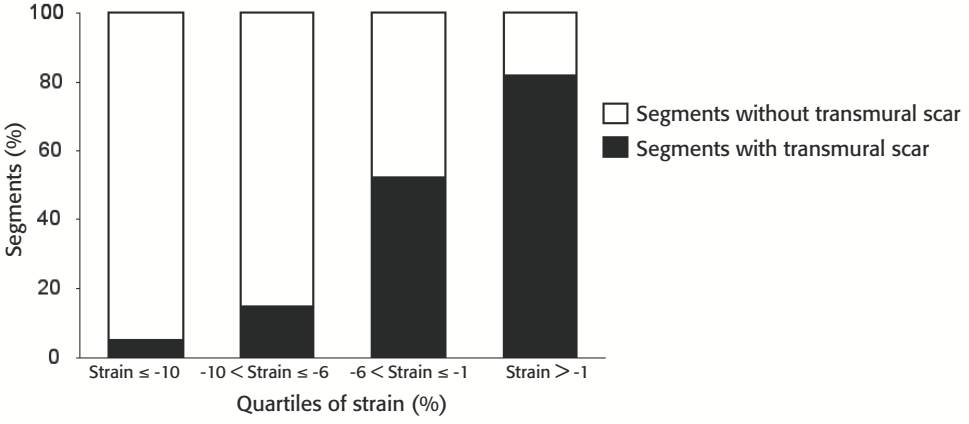
The results of segmental (regional) analyses are presented in Figures 2 and 3.

Figure 2.



Mean segmental (regional) strain in segments grouped according to scar score on contrast-enhanced MRI. Error bars represent standard deviation.

Figure 3.

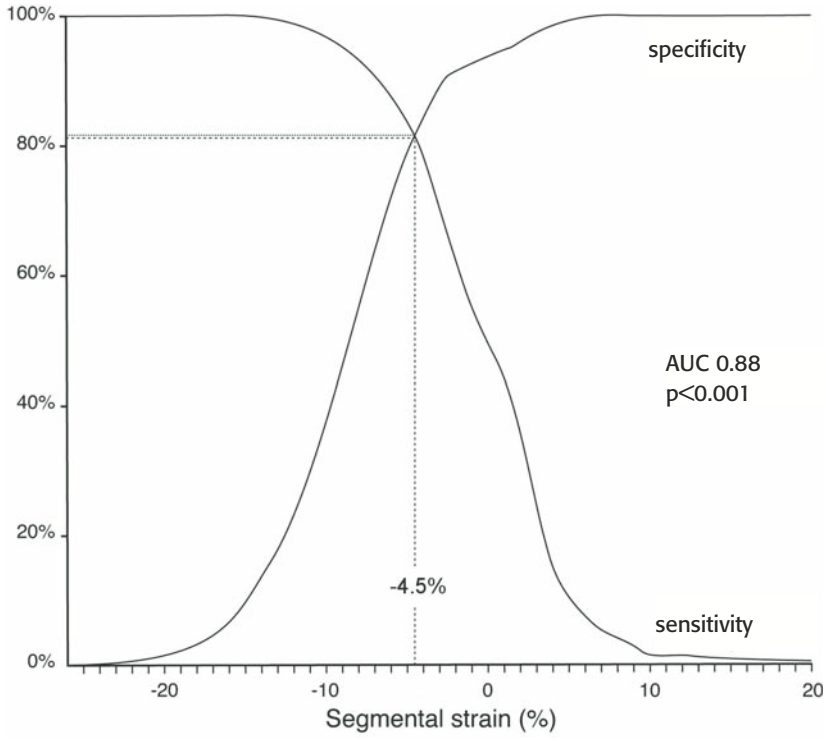


Transmurality of scar (according to contrast-enhanced MRI) in segments grouped according to quartiles of segmental strain on echocardiography.

First, the dysfunctional segments were grouped according to scar score on contrast-enhanced MRI, and the mean segmental (regional) strain for each group was calculated (Figure 2). The mean segmental strain in segments without scar (scar score 0) was -10.4 ± 5.2%, whereas the mean segmental strain in segments with a scar score of 3 and 4 (i.e. segments with transmural scar) was -1.3 ± 5.2% and 0.6 ± 4.9%, respectively ($p < 0.001$).

Next, segmental strain values were used to divide the dysfunctional segments into quartiles, and the proportion of segments with transmural scar in each quartile was evaluated (Figure 3). Only 12 segments (5%) in the lowest quartile of segmental strain (≤ -10%) had transmural scar tissue (scar score 3 or 4), whereas most segments (n = 219, 95%) had no transmural scar (scar score 0, 1 and 2) on contrast-enhanced MRI (Figure 3). Conversely, most segments (n = 196, 82%) in the highest quartile (segmental strain > -1%) showed transmural scar on contrast-enhanced MRI. The receiver operating curve analysis yielded a cut-off value of -4.5% for segmental strain, with a sensitivity of 81.2%, specificity of 81.6%, positive predictive value of 71.6%, negative predictive value of 88.4% and diagnostic accuracy of 81.5% to identify segments with or without transmural scar on contrast-enhanced MRI (Figure 4). Accordingly, segmental strain was ≥ -4% in 81.2% of the segments with transmural scar, and < -4% in 81.6% of the segments without transmural scar on contrast-enhanced MRI.

Figure 4.



Receiver operating curve analysis for identification of segments with or without transmural scar on contrast-enhanced MRI. A cut-off value of -4.5% for segmental strain corresponds with 81.2% sensitivity and 81.6% specificity to identify segments with or without transmural scar tissue. Accordingly, segmental strain was ≥ -4% in 81.2% of the segments with transmural scar, and < -4% in 81.6% of the segments without transmural scar tissue on contrast-enhanced MRI.
AUC: area under the curve.

Discussion

The main findings of the present study can be summarized as follows: 1) a good correlation between AFI global LV strain and the global extent of scar tissue on contrast-enhanced MRI was shown (both reflecting the global LV viability/scar status); 2) segmental (regional) analysis demonstrated that strain was associated with scar transmurality (e.g., decreasing myocardial deformation in segments with increasing scar transmurality); and 3) a cut-off value of -4.5% for segmental strain discriminated between segments with viable myocardium and transmural scar tissue, with 81.2% sensitivity and 81.6% specificity.

Assessment of viability is essential in patients with chronic ischemic LV dysfunction for optimization of treatment. Viability studies have used different techniques, including low-dose dobutamine stress echocardiography, nuclear imaging with positron emission tomography and single photon emission computed tomography and more recently, MRI (11-14). In particular, contrast-enhanced MRI has contributed significantly, since this technique has an extremely high spatial resolution, permitting precise detection of the amount of viable and scarred myocardium throughout the LV wall, making differentiation between small, subendocardial necrosis and transmural scar tissue possible (15). Previous studies evaluating patients with chronic ischemic LV dysfunction using contrast-enhanced MRI demonstrated that segments with transmural scar virtually never show improvement of function after revascularization (11,16,17). Accordingly, detection of transmural scar tissue is essential for therapeutic decision making in patients with ischemic LV dysfunction, since these patients will not benefit from revascularization.

Recently, echocardiographic strain and strain rate imaging has been introduced as a new method for assessment of myocardial function and enables measurement of active tissue deformation in three directions: longitudinal shortening, circumferential shortening, and radial thickening (2,18). Strain can be derived from tissue Doppler imaging and from 2D gray-scale B-mode imaging (speckle tracking) (18). With speckle tracking, acoustic markers (speckles) are tracked during the cardiac cycle, providing information of the lengthening or shortening of the myocardial segment (2). An important advantage of 2D speckle tracking compared with tissue Doppler-derived strain is that 2D speckle tracking is angle independent and less affected by artefacts (2). Moreover, strain is assessed at rest, and the infusion of dobutamine is not needed.

In a combined experimental and clinical study, Amundsen et al. (19) validated strain imaging with 2D speckle tracking against sonomicrometry in dogs and against tagged MRI in patients with previous myocardial infarction, demonstrating good agreement between these different techniques for assessing systolic strain.

Previous experimental and clinical studies showed that echocardiographic strain imaging enables discrimination between myocardium with non-transmural (viable)

and transmural scar tissue, highlighting the potential of strain imaging for viability assessment (5,20). Migrino et al. (20) used an animal model of ischemia-reperfusion and demonstrated that 2D speckle tracking-derived radial strain could distinguish between viable myocardium and transmural scar. Becker et al. (5) subsequently evaluated 47 patients with chronic ischemic LV dysfunction and reported that radial strain and strain rate decreased in parallel with an increasing extent of scar tissue as assessed with contrast-enhanced MRI. In addition, Chan et al. (21) studied 80 patients with chronic ischemic LV dysfunction and reported that discrimination between subendocardial and transmural scar tissue was possible with radial strain. Recently, Becker et al. (1) evaluated 53 patients with ischemic LV dysfunction who were scheduled for revascularization and observed that a cut-off value for systolic radial strain of 17.2% predicted functional recovery post-revascularization with accuracy similar to that of contrast-enhanced MRI.

The present study, however, is the first to report on the use of longitudinal strain assessed with 2D speckle tracking to discriminate between viable tissue and transmural scar in patients with chronic ischemic LV dysfunction. The cut-off value of -4.5% strain observed in this study enables identification of segments with transmural scar tissue with high accuracy, demonstrating the potential use of longitudinal strain imaging for selection of patients who will benefit from revascularization. Furthermore, quartile analysis (Figure 3) demonstrated that most segments with a segmental (regional) strain ≤ -10% showed no transmural scar, whereas most segments with a segmental (regional) strain of > -1% had transmural scar. However, an intermediate proportion of segments with strain > -10% but ≤ -1% showed transmural scar tissue. Accordingly, additional studies are needed to better characterize the segments with intermediate strain values. Limitations of the present study include the small sample size and the lack of outcome data after revascularization. Accordingly, future studies evaluating patients with longitudinal strain imaging are needed to determine the actual value of longitudinal strain to predict functional recovery after revascularization.

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