

Usefulness of Resting Strain Rate Imaging to Predict Viability following Acute Myocardial Infarction Strain Rate Imaging and Myocardial Viability

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Abstract

Background: We sought to explore the accuracy of resting strain (S) and strain rate (SR) to predict viability following myocardial infarction, taking ^{99m}Tc -sestamibi scintigraphy as the 'gold standard' for diagnosis.

Methods: We enrolled 60 consecutive patients presenting for myocardial viability assessment at least 4 weeks following ST segment elevation myocardial infarction. S and SR rate were individually measured for all myocardial segments at rest. Based on the results of scintigraphy, both strain and strain rate were compared between viable and non-viable segments in each individual segment position.

Results: S was significantly higher in viable as compared with non-viable segments in the basal inferior, basal anteroseptal, basal posterior, as well as apical inferior positions ($p < 0.05$ for all). Otherwise, no significant difference was found between the S of viable and non-viable segments in the rest of positions ($p > 0.05$ for all). Similarly, SR was significantly higher in viable as compared with non-viable segments in the mid-lateral, mid- and apical anterior, apical inferior, as well as basal anteroseptal positions ($p < 0.05$ for all). Otherwise, no significant difference was found between the SR of viable and non-viable segments in the rest of positions ($p > 0.05$ for all).

Conclusion: In patients undergoing viability assessment following ST segment elevation myocardial infarction, resting values of both S and SR have a poor diagnostic accuracy, taking ^{99m}Tc -sestamibi imaging as the gold standard.

Keywords: Strain rate imaging; ^{99m}Tc -sestamibi scintigraphy; Viability

Introduction

Identification of viable myocardium following acute myocardial infarction has gained a paramount importance with the recent progress in myocardial revascularization techniques [1]. Myocardial viability represents a state of impaired contractility with the potential for recovery when blood supply is adequately restored [2]. In turn, the amount of viable myocardial tissue is a potential 'surrogate' for future improvement of global left ventricular systolic function: the most powerful single predictor of long-term prognosis [3].

Traditionally, the evaluation of regional myocardial function was performed by visual assessment of the degree of thickening and inward displacement of individual myocardial segments. Obviously limited by inter- and intra-observer variability, and poor visualization of some myocardial segments, it was recently largely superseded by the novel quantitative techniques for estimation of tissue velocities, by means of tissue Doppler imaging (TDI). Although very promising initially, this technique proved to be influenced by whole heart translation and tethering movement from the adjacent myocardial segments [4].

A new milestone of development was the state-of-the-art technique of measuring myocardial deformation, again derived from TDI. Respectively, strain (S) and strain rate (SR) reflect the amplitude and rate of myocardial segment deformation; contraction is reflected as a negative value; relaxation as a positive one [5-7]. There is a growing body of literature that supports the superiority of S and SR measurement over tissue velocity assessment by TDI for the evaluation of regional myocardial function [5-9]. However, the value of myocardial deformation parameters (S and SR) in the detection of myocardial viability remains to be determined. Therefore, in a prospective study design, we sought to explore the accuracy of resting S and SR to predict myocardial viability following myocardial infarction, taking ^{99m}Tc -sestamibi scintigraphy as the 'gold standard' for diagnosis.

Materials and Methods

Patient selection and study design

Prospectively, we enrolled 60 consecutive patients who presented to our nuclear cardiology unit to undergo myocardial viability assessment at least 4 weeks following ST segment elevation myocardial infarction, during the period from May 2008 to May 2010. Patients were considered eligible for inclusion if they had regional wall motion abnormality in the anatomical distribution of the infarct zone as detected by resting 2-D echocardiography. We excluded patients with early post-infarction unstable angina or severe hemodynamic instability, clinically evident congestive heart failure, significant valvular or congenital heart disease, any myocardial disease apart from ischemia, severe mitral regurgitation, atrial fibrillation, bundle branch block, technically inadequate echocardiographic imaging defined as more than two non-analyzable segments in the infarct zone, and patients with limited life expectancy due to coexistent disease (for example: malignancy). Before inclusion, an informed written consent was obtained from each patient after full explanation of the study protocol. Finally, the study protocol was reviewed and approved by the Local Institutional Human Research committee of our center, as it conforms to the ethical guidelines of the 1964 Declaration of Helsinki, as revised in 2002.

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Baseline echocardiographic assessment

Assessment of regional and global left ventricular systolic function was performed in all patients by trans-thoracic echocardiography. Doppler echocardiography was performed using a General Electric Vivid 7 Pro cardiac ultrasound machine (GE Medical Systems, Horten, Norway) equipped with harmonic imaging capabilities. A 3.5 MHz phased-array transducer was used to obtain standard 2-D, M-mode, Doppler flow, and TDI. Patients were examined in the left lateral recumbent position using standard parasternal and apical views. Global left ventricular systolic function was assessed in apical 2- and 4-chamber views using the biplane Simpson's method. Regional wall motion was assessed according to the standard 16-segment model recommended by the American Society of Echocardiography [10].

Strain and strain rate imaging

SR color imaging was performed one wall at a time in order to achieve a frame rate above 140 frames/sec, and so that the angle between the Doppler beam and the longitudinal shortening direction of the wall was kept, as possible, below 30 degrees. Images were digitized in cine-loop format and saved for subsequent playback and analysis. Views were analyzed offline by a single echocardiographer (M.I.) employing the software program of the echocardiography machine (Echopac PC, GE Vingmed Ultrasound, GE Medical Systems). Systolic S and SR measurements were performed for all analyzable segments according to the standard 16-segment model. An offset to measure S and SR was set at 12 mm. The stationary region of interest was 10 mm in longitude, and 6 mm in latitude, centered in the middle of the targeted myocardial segment. Systolic time to measure systolic S and SR was determined from the electrocardiographic tracing as the time from the peak of the R wave to the end of the T wave. Peak systolic S was determined as the maximal negative S at the end of systole. Peak systolic SR was determined as the maximal negative SR within 350 msec after the onset of systole. Measurements were obtained from 3 cardiac cycles and an average was taken. Cardiac cycles associated with extra-systolic, post-extra-systolic beats, or any other rhythm disturbances were excluded from analysis.

^{99m}Tc-sestamibi SPECT imaging protocol

Patients underwent resting ^{99m}Tc-sestamibi imaging study with the administration of trimetazidine, using the standard imaging technique. Trimetazidine (Vastarel[®], Servier, France) was administered by the oral route the day before the study (60 mg in 3 divided equal doses 8 hours apart), and 1 hour before performing the study (60 mg single dose). Sublingual nitroglycerin 0.8 mg was administered in two divided doses with a 5-minute interval just before radioactive tracer administration. The second dose was not given if the heart rate increased by 10 beats/min or more, or the systolic blood pressure decreased by 10 mm Hg or more after the first dose. Injection of 20-25 mCi of radioactive tracer was performed 45-60 minutes before SPECT image acquisition. Images were acquired using a rotating single-head gamma camera (GE Medical Systems, Starcam 4000i, UK) equipped with low-energy all-purpose collimators. Energy windows of 20% were respectively centered on the 140-keV peaks of ^{99m}Tc-sestamibi. Thirty two images were obtained over 180° extending from the 45° right anterior oblique to the 45° left posterior oblique projections, using a 64 x 64 acquisition matrix. All studies were subjected to quality-control checks and corrections when necessary for camera non-uniformity, center-of-rotation offsets, patient motion, and "upward creep" [11].

^{99m}Tc-sestamibi SPECT image analysis

Two experienced nuclear cardiologists blinded to the clinical and

TDI data analyzed the SPECT images. Trans-axial reconstruction was performed using the standard back projection technique with a Ramp-Hanning filter. The reconstructed tomographic slices were 6 mm thick and reoriented along the short, horizontal long- and vertical long-axis for interpretation. The vascular assignment of myocardial segments to the conventional anatomic distribution of major coronary arteries was performed according to the 17 segments scoring system [12]. Images were interpreted by visual semi-quantitative analysis. Segmental ^{99m}Tc-sestamibi uptake was scored using the 5-point scoring system as follows:

- 0 = normal uptake,
- 1 = mildly reduced uptake,
- 2 = moderately reduced uptake,
- 3 = severely reduced uptake
- 4 = absent uptake.

Patterns of viability were based on the segmental radioactive tracer uptake [10] so that segments were then individually classified into viable or non-viable. Score of 0 was considered as normal; 1 and 2 as viable; 3 and 4 as non-viable.

Statistical analysis

All continuous variables were presented as mean \pm SD, if they were normally distributed. Data were tested for normal distribution using the Kolmogorov-Smirnov test. Categorical variables were described with absolute and relative (percentage) frequencies. According to the above assignment of myocardial segments (viable and non-viable), S and SR were compared among the 2 groups in each individual anatomical segment by means of the unpaired *t*-test. Eventually, we generated receiver-operating characteristics (ROCs) curve to identify the cutoff value of S and SR that best discriminates viable from non-viable myocardial segments based on ^{99m}Tc-sestamibi. The optimal cutoff value was defined as the value giving the largest area under the curve (AUC). Finally, twenty cases were randomly selected for analysis of intra-observer variability. Assessment of variability was performed using linear regression analysis. All analyses were 2-sided and a probability value of *p* < 0.05 was considered statistically significant. Analyses were performed with SPSS version 12.0 statistical package (SPSS Inc., Chicago, IL, USA).

Results

A total of 60 consecutive patients presenting at least 4 weeks following ST segment elevation myocardial infarction were enrolled in the current study. Baseline clinical and echocardiographic characteristics of the study cohort are presented in Table 1. The mean age was 54.8 \pm 10.9 years, 85% being males.

S was significantly higher in viable as compared with non-viable

	Total Cohort (N = 60)
Age (years)	54.8 \pm 10.9
Male gender	51 (85)
Diabetes mellitus	26 (43.3)
Hypertension	29 (48.3)
Smoking	43 (71.7)
Dislipidemia	13 (21.7)
Family history of IHD	18 (30)
2-D Ejection fraction (%)	35 \pm 8

Continuous variables are presented as mean \pm SD, while categorical variables are presented as numbers (percentage). IHD indicates ischemic heart disease

Table 1: Baseline clinical characteristics of the whole series.

Segment	Viable	Non-viable	p value
Basal lateral	-9.7 ± 5.5	NA	NA
Mid-lateral	-10.4 ± 6.2	-8.8 ± 4.9	0.44
Apical lateral	-5.5 ± 3.5	-5.3 ± 5.9	0.87
Basal posteroseptal	-17.0 ± 7.9	-16.1 ± 4.4	0.76
Mid-posteroseptal	-12.9 ± 9.6	-12.4 ± 9.3	0.82
Apical posteroseptal	-3.6 ± 9.8	-4.8 ± 7.4	0.57
Basal anterior	-15.6 ± 8.3	NA	NA
Mid-anterior	-7.7 ± 3.6	-5.7 ± 1.2	0.12
Apical anterior	-3.1 ± 4.1	-3.1 ± 5.7	1
Basal inferior	-13.5 ± 6.4	-8.3 ± 6.0	0.001
Mid-inferior	-10.5 ± 7.6	-7.5 ± 4.2	0.155
Apical inferior	-6.5 ± 4.7	-5.8 ± 6.7	0.0001
Basal anteroseptal	-15.1 ± 4.7	-7.9 ± 3.5	0.0001
Mid-antroseptal	-8.0 ± 3.8	-6.7 ± 4.9	0.27
Basal posterior	-11.3 ± 5.4	-7.7 ± 2.7	0.033
Mid-posterior	-7.7 ± 4.4	-4.5 ± 8.5	0.075

Table 2: Resting strain values in individual myocardial segments.

Segment	Viable	Non-viable	p value
Basal lateral	-0.9 ± 0.6	NA	NA
Mid-lateral	-0.8 ± 0.5	-0.4 ± 0.2	0.002
Apical lateral	-0.9 ± 0.5	-0.8 ± 0.3	0.91
Basal posteroseptal	-1.5 ± 0.9	-1.1 ± 0.8	0.31
Mid-posteroseptal	-1.3 ± 0.7	-0.9 ± 0.2	0.13
Apical posteroseptal	-0.7 ± 0.4	-0.4 ± 0.4	0.88
Basal anterior	-1.8 ± 0.9	NA	NA
Mid-anterior	-0.8 ± 0.6	-0.5 ± 0.1	0.0001
Apical anterior	-0.7 ± 0.3	-0.5 ± 0.3	0.04
Basal inferior	-1.3 ± 0.4	-1.2 ± 0.6	0.123
Mid-inferior	-0.8 ± 0.7	-0.9 ± 0.5	0.23
Apical inferior	-1.1 ± 0.3	-0.3 ± 0.5	0.0001
Basal anteroseptal	-1.4 ± 0.5	-1.0 ± 0.4	0.049
Mid-antroseptal	-0.7 ± 0.6	-0.6 ± 0.4	0.46
Basal posterior	-1.2 ± 0.7	-0.8 ± 0.5	0.17
Mid-posterior	-1.1 ± 0.4	-0.8 ± 0.4	0.076

Table 3: Resting strain rate values in individual myocardial segments.

	Segment	Cutoff value (%)	Sensitivity (%)	Specificity (%)
Resting strain (%)	Basal inferior	-11	42.9	61.1
	Basal anteroseptal	-13	100	66.7
Resting strain rate (%.s ⁻¹)	Mid-lateral	-0.35	83.3	93.1
	Apical anterior	-0.67	77.8	53.3
	Apical inferior	-0.69	87.8	100
	Basal anteroseptal	-1.1	77.8	64.1

Table 4: Cutoff values for resting strain and strain rate that best predict viability in individual myocardial segments.

segments in the basal inferior, basal anteroseptal, basal posterior, as well as apical inferior positions ($p < 0.05$ for all). S was higher in viable as compared with non-viable segments in the mid-posterior position with a trend to statistical significance ($p = 0.075$). Otherwise, no significant difference was found between the S of viable and non-viable segments in the rest of positions ($p > 0.05$ for all) (Table 2). Similarly, SR was significantly higher in viable as compared with non-viable segments in the mid-lateral, mid- and apical anterior, apical inferior, as well as basal anteroseptal positions ($p < 0.05$ for all) (Table 3). SR was higher in viable as compared with non-viable segments in the mid-posterior

position with a trend to statistical significance ($p = 0.076$). Otherwise, no significant difference was found between the SR of viable and non-viable segments in the rest of positions ($p > 0.05$ for all) (Table 3).

The results of the ROCs curve analysis to identify the cutoff value of individual S and SR that best discriminates viable from non-viable myocardial segments based on ^{99m}Tc-sestamibi are shown in Table 4. The best cutoff value for S was demonstrated for the basal anteroseptal position. A cutoff value of -13%, in that position, was able to discriminate viable from non-viable myocardial segments with 100% sensitivity and 66.7% specificity. Similarly, the best cutoff value for SR was demonstrated for the apical inferior position. A cutoff value of -0.69%.s⁻¹ was able to discriminate viable from non-viable myocardial segments with 87.8% sensitivity and 100% specificity.

Analysis of intra-observer variability revealed a close correlation between repeated measurements of the S and SR by the single operator, with a correlation coefficient $r = 0.91$.

Discussion

Main findings

The current study demonstrated that in patients undergoing viability assessment following ST segment elevation myocardial infarction, both S and SR values were somewhat higher in viable segments, as compared with non-viable ones, yet, with statistical significance in only a few segment anatomical positions. Moreover, a cutoff value of -13% for the S of the basal anteroseptal segments reliably identified viable from non-viable myocardial segments with an excellent sensitivity but a modest specificity, taking ^{99m}Tc-sestamibi scintigraphy as the gold standard for diagnosis. Moreover, a cutoff value of -0.69%.s⁻¹ for the SR of the apical inferior segments reliably identified viable from non-viable myocardial segments with a high sensitivity and an excellent specificity.

Deformation indices for detection of viability

Since the introduction of echocardiography for viability assessment, it has long been accused of being largely operator-dependent and greatly afflicted with high inter- and intra-observer variability. Nevertheless, being feasible, safe, inexpensive with a fairly high diagnostic and prognostic accuracy, stress echocardiography is widely acknowledged to explore myocardial viability following myocardial infarction. So far, in the quest to obviate the subjective visual assessment of regional contractility, a great deal of work has rigorously pursued to adopt quantitative measures of regional myocardial function. Although appealing at the outset, TDI-derived systolic tissue velocity was reportedly overwhelmed by 'tethering' effect from neighboring segments, as well as by whole heart translation movement [4,13]. Recently, in the pursuit to find a long-awaited solution to the problem of objective measurement of regional myocardial contractility, an emerging body of literature has tested the potential of the novel myocardial deformation indices for the evaluation of myocardial viability [14-17]. A recent report has demonstrated an incremental value of TDI-based S and SR during dobutamine stress echocardiography over wall motion analysis in the prediction of functional recovery following revascularization [18].

For the purpose of further simplicity, we tested the hypothesis whether measurement of resting S and SR for individual myocardial segments would serve as a useful screening tool for discrimination of viable segments from non-viable ones. Unfortunately the results were inconsistent, being favorable for a few segments, and disappointing for many. The lack of consistency of the results among individual myocardial segments in both S and SR may reasonably be attributed to

the fact that viability assessment by echocardiography frequently needs some form of 'stress'. Many viable segments would have been better discriminated if properly stimulated, for example, with dobutamine. Furthermore, angle dependency of strain imaging, a well-known shortcoming of the technique may have contributed to inconsistency of the results. Failure to keep the angle between the Doppler beam and the longitudinal shortening direction of the segment below 30 degrees may have precluded accurate measurement of S and SR in many segments. Additionally, the current technology of SR imaging is characterized by considerable noise in the SR signal. This noise increases further with higher heart rates and reduces image quality.

^{99m}Tc-sestamibi scintigraphy for detection of viability

Since ^{99m}Tc-sestamibi scintigraphy was taken as the gold standard for diagnosis of viability, we sought to improve the diagnostic accuracy of this 'gold standard'. In this regard, we adopted a test protocol that entails the administration of both trimetazidine and nitroglycerin before radiotracer injection. A recent study by Feola et al showed that the addition of trimetazidine to ^{99m}Tc-tetrofosmin scintigraphy improved the sensitivity of the perfusion scan for the detection of viable myocardial tissue, both at 2- and 6-months follow-up, as compared with placebo, maintaining a satisfactory specificity [19]. Furthermore, the predictive power of ^{99m}Tc-sestamibi scintigraphy was also enhanced with the addition of nitrates, obtaining an improvement in both sensitivity and specificity (up to 95% and 88% respectively) [20,21].

Conclusions

In patients undergoing viability assessment following ST segment elevation myocardial infarction, resting values of both S and SR have a poor diagnostic accuracy, taking ^{99m}Tc-sestamibi imaging as the gold standard.

Limitations of the Study

Our findings were based on a single center study with a relatively small sample size of the cohort, a fact that makes it difficult to generalize our results to all patients undergoing viability assessment for predicting contractile recovery after revascularization. Multicenter studies using the same protocol and examining a larger number of patients are needed. Additionally, we adopted ^{99m}Tc-sestamibi scintigraphy as the gold standard for diagnosis of viability. Actual improvement of myocardial segment contractility following revascularization would certainly offer a more 'real' gold standard for comparison.

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