Original Article

Evaluation of Regional Myocardial Systolic Function in the Early Stage of Acute Myocardial Infarction by Strain Rate Imaging

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Background: We sought to evaluate the impact of different therapeutic strategies on longitudinal regional myocardial systolic function in the early phase of acute myocardial infarction using strain rate imaging.
Methods: A total of 38 patients (34 males), with first acute myocardial infarction (AMI) were evaluated. Our patients were divided into 3 groups according to the kind of therapy. The mean age of the patients was 55 ± 9.4 years (range: 39- 75 years). Mean left ventricular ejection fraction (LVEF) in the patients was 41 ± 10.7%. Primary percutaneous coronary intervention (PCI) was performed in 10 patients. Sixteen patients were treated by thrombolytic therapy using streptokinase (SK) and 12 were followed-up conservatively. All patients underwent a comprehensive echocardiography study including SR imaging within 3- 5 days after AMI. The parameters measured included peak systolic strain (peakε) and strain rate (SRs), end-systolic strain (εes), post systolic shortening (PSS), time to peak systolic strain rate (tSRs), time to end of shortening (teSRs), post systolic strain (PSε), post-systolic strain index (PSI), PSS ratio (PSS/ ε_{Max}) and peak postsystolic strain rate (SRPSS).
Results: There was not any association either between WMSI and tå (P=0.4), or MI location and PSS ratio (P=0.13). But there was an inverse relationship between WMSI and mean SRS, especially when WMSI was more pronounced. A significant relationship was found between tε and teSRs with the kind of therapy (shorter in PCI group (P= 0.04). Using a simple linear regression model, no association was found between PSS ratio and SRs (â=0.056, P =0.70), PSI and teSRs (β= -0.772, P =0.12). Simple linear regression model showed a weak but significant relationship between PSI and Median tε (β = -0.851, P = 0.04; *r* =0.33).
Conclusion: Our study showed that PCI resulted in early recovery of regional systolic function of infarcted myocardium during the early stage of acute myocardial infarction.

Key words: Regional myocardial systolic function**,** Myocardial infarction, Primary PCI, Thrombolytic therapy.

Introduction

The evolution and widespread adoption of primary percutaneous coronary intervention (PCI) represents a major advance in the management of acute myocardial infarction (AMI), resulting in a significant reduction in early and late mortality compared with pharmacologic reperfusion therapy. The ability to quantify changes in regional myocardial function during both acute and chronic ischemia is important in clinical practice and has been shown to have both prognostic and therapeutic implications.[1] Ultrasonic strain rate (SR) imaging has been introduced as a new noninvasive method to quantify regional myocardial deformation.[2] But due to the high angle dependency, acquisition frame rate, and noise component in the acquired data, SR imaging has not been used as a clinical routine method. This

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study has concentrated on the assessment of regional myocardial longitudinal function as radial function is limited to a few segments of the parasternal long- and short-axis views.

The aim of this prospective clinical study was to evaluate the regional myocardial systolic function using SR imaging in patients with AMI early after the ischemic event that were treated by different therapeutic strategies including conservative medical management, thrombolytic therapy, and Primary percutaneous coronary intervention (PPCI).

Patients and Methods

Forty-one patients with first AMI, admitted to the coronary care unit in our institution, were enrolled into the study. The inclusion criteria was first AMI, with diagnosis based on standard criteria of typical chest pain, electrocardiographic (ECG) changes, and increases in blood concentrations of the biochemical markers, cardiac troponin I and CK– MB. Exclusion criteria were previous MI, hemodynamically unstable patients, intravenous inotropic support, intra-aortic balloon pump, previous coronary artery bypass surgery, and inability to assess ≥3 myocardial segments on echocardiogram. Three patients were excluded because of poor image quality, so the study was performed on the remaining 38 patients. Our patients were divided into 3 groups according to the kind of therapy. PCI was performed in 10 patients. Sixteen patients were treated by thrombolytic therapy using streptokinase (SK) and 12 subjects were followed-up conservatively. In respect of MI location, the majority of patients (26 patients) had anterior MI, followed by inferior MI (6 patients). Out of a total 38 patients, 28 underwent coronary angiography. The culprit artery was left anterior descending (LAD) artery in 18, right coronary artery (RCA) in 8, and circumflex artery (LCX) in 2 patients.

Study protocol

All patients underwent a comprehensive echocardiography study including SR imaging within 3- 5 days after AMI. Hospital charts were reviewed for troponin level, electrocardiogram at the initial presentation, and angiographic findings.

The patients' clinical data were evaluated by an independent investigator who was blinded to echocardiographic findings. The institutional review board at our center approved the study and informed consent was obtained from each patient.

Echocardiography

Two-dimensional/Doppler echocardiography

2D and Doppler echocardiography were performed at rest in the left lateral decubitus position with a Vivid 7 digital ultrasound scanner (GE, Milwaukee, Wisconsin, USA) equipped with an ergonomically-designed M3S transthoracic sector transducer (1.5-4 MHz).[3-6]

LV end systolic and end-diastolic dimensions were obtained in the parasternal long-axis view. Left ventricular (LV) ejection fraction (EF) was obtained in apical 4- and 2-chamber views by modified Simpson's method and averaged.[6] Wall motion score index (WMSI) was measured as the sum of segmental scores (1= normal, 2= hypokinetic, 3= akinetic, 4= dyskinetic) divided by the number of segments visualized.[3] A low-frequency (2.5-MHz) transducer was used for all Doppler examinations. The severity of mitral and tricuspid regurgitations was assessed visually by color flow Doppler as mild, moderate, moderate to severe, or

severe) and graded on a scale from +1 to +4, although, none of our patients had more than moderate MR or TR.

Color Doppler Myocardial Imaging (CDMI)

CDMI velocity data from the interventricular septum, lateral, anterior, inferior, anteroseptal, and posterior walls were recorded using apical 2,3 and 4-chamber views with the wall in the middle of the sector. All data sets were acquired over three consecutive heartbeats at high frame rate (180-200 frames/s), with an image depth of 11-14 cm. In all acquisitions, the 2D sector angle was minimized to obtain a high frame rate, and the pulse repetition frequency was adjusted in order to avoid aliasing. The digital cineloop raw data sets containing both gray scale and tissue velocity imaging information were stored for off-line analysis. The data were analyzed off-line to obtain regional myocardial velocity, strain, and strain rate imaging profiles using an 8x4 region of interest (ROI). Information on a total of 12 base and mid segments throughout the 3 end-expiratory beats was recorded and analyzed for each patient.

Event timing

As regional CDMI has been accurately reported for determination of cardiac time intervals,[7] we used the regional velocity curves as the event marker. The timing of aortic valve opening (AVO), aortic valve closure (AVC), mitral valve opening (MVO) and mitral valve closure (MVC) were obtained from the same cineloop by means of anatomic M-mode tracing taken at the level of mitral leaflet tips.

SRI parameters

Strain (ε) and strain rate (SR) curves in the basal and mid segments of each wall were displayed simultaneously with the corresponding electrocardiographic traces.

Both maximal and mean of median values of systolic ε and SR and their respective tim-

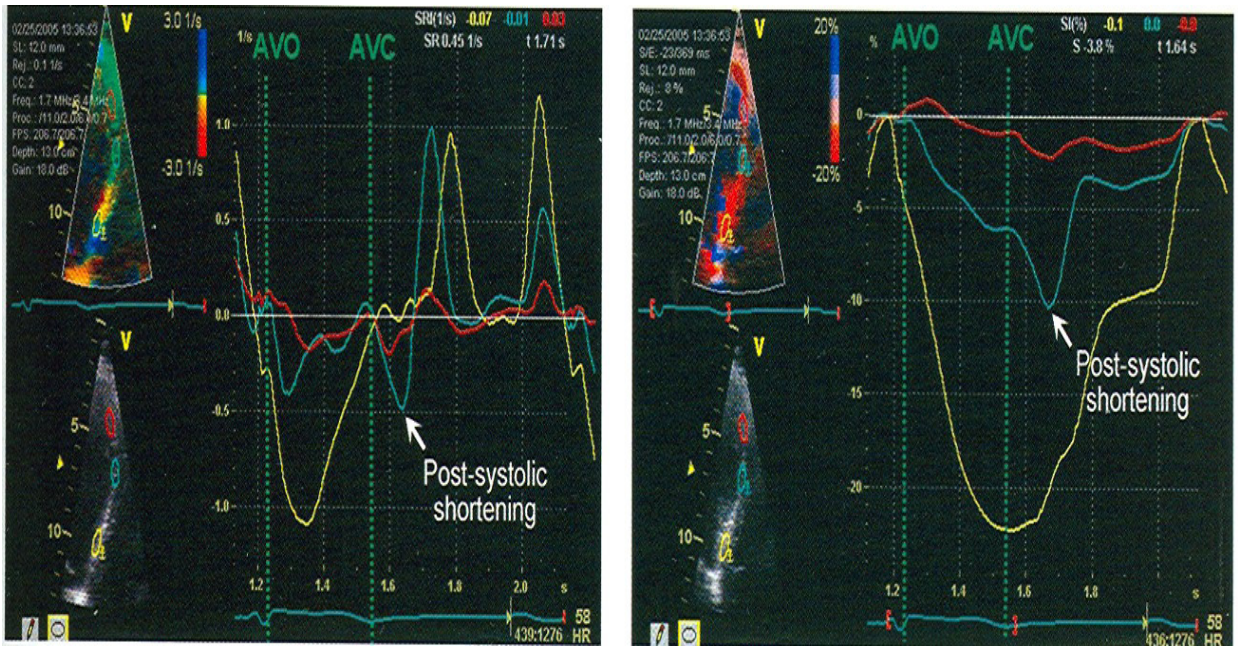

Figure 1. Left image shows strain rate trace and right image strain trace. The curve is from lateral wall and the green line of the curves illustrates PSS. AVC: aortic valve closure, AVO: aortic valve opening, PSS-post systolic shortening

ings were calculated.

Peak systolic strain (peakε) and strain rate (SRs) were determined as the maximal negative strain and SR value during ejection (between AVO and AVC), but end-systolic strain (εes) was measured at AVC. Post systolic shortening (PSS) was defined as myocardial segment shortening after AVC (Fig. 1). Peak postsystolic strain rate (SRPSS) was measured as the first negative wave after end-systole, and the cut-off between normal and pathological SRPSS was chosen as -0.2 s^{-1}.[8] Time to peak systolic strain rate (tSRs) and time to end of shortening (teSRs) were measured from peak R wave in ECG to maximal negative SR value during ejection time and AVC line, respectively. If maximal ε occurred after AVC, post systolic strain (PSε) was calculated as the ε value from AVC to peak PSε. Post-systolic strain index (PSI) [(peakε–εes)/ peakε][9] and PSS ratio as the percentage of total thickening occurring after AVC to maximal ε (PSS/ ε_{Max}) were also calculated.

Peak value versus timing

The peak value of the strain / strain rate curves can be affected by the insonation angle. A deviation of more than 15 degrees will reduce the peak value, provided that the velocity is perpendicular to the myocardium and the LV is normal. A deviation of more than 90 degrees, wall thickening/thinning will be measured instead of longitudinal shortening/ lengthening and the values shift from negative to positive.[10] Even if the angle deviation is small the calculation of the velocities is prone to small errors as the true motion of the myocardium will be unknown. Out of plan motion, either radial (lateral) motion or torsion affects the estimated velocities. Attempts to correct for the angle dependency have so far not been successful.[10] The timing of cardiac events is probably less affected by the angle dependency and might be more robust, especially regional phase changes from contraction to relaxation patterns.[1]

Coronary angiography and revascularization procedure

Patients in the invasive arm were transferred immediately to the catheterization unit and selective coronary angiography was performed in multiple views. The infarct-related lesion was identified based on the presence of a significant lesion defined as more than 50% diameter stenosis in culprit artery. Attention to treat was for revascularization of culprit lesion using percutaneous coronary intervention procedures. All patients received 600-mg loading dose of Clopidogrel, heparin and a GpIIb/IIIa inhibitor, mainly Eptifibatide as a routine basis.

Patients in medical treatment arm underwent coronary angiography as an ischemic-driven strategy during hospitalization.

Statistical analysis

Data were described by means of median±SD for intervals and count (%) for categorical data. Mean value of each variable between 12 cardiac segments were measured for total assessment of each echocardiographic parameter in all myocardium. One-Sample Kolmogorov-Smirnov test was applied to investigate the fitness of interval variables to normal distribution. Kruskal Wallis test was used for comparison of these values between the study groups. Pairwise comparisons were performed by Mann Whitney U and Bonferroni correction was applied to maintain the type one error at 0.05. Then for pairwise comparisons,

Table 1. Comparison of baseline data in the study participants

	PPCI (n = 10)	SK (n = 16)	Conservative (n = 12)	P value
Age(y)	50.0±6.0	56.0±8.0 *	59.0±10.0 †	0.02
Sex (F/M)	1/9	1/15	2/10	0.42
LVEDD(cm)	5.3±0.4	5.2 ± 0.5	5.3± 0.2	0.65
LVESD(cm)	3.61±0.62	3.78±0.84	3.7 ± 0.9	0.33
LVEDV(ml)	86.0±3.98	96.0±21.6	100.0 ± 18.1	0.24
LVESV(ml)	47.0±17.4	55.0±22.7	61 ± 22.1	0.27
LVEF(%)	42.0±6.6	42.0±11.9	41 ± 12.5	0.73
WMSI	1.9±0.3	1.94±0.56	1.71±0.52	0.47
PSS ratio	1.1±0.2	1.0±0.3	1.4±0.2	0.50

PPCI: primary percutaneous coronary intervention, SK: streptokinase treated group, C: conservative treated group, LVEDD: left ventricular end diastolic dimension; LVESD: left ventricular end systolic dimension; LVEDV: left ventricular end diastolic volume; LVESV: left ventricular end systolic volume; LVEF: left ventricular ejection fraction, WMSI: wall motion score index, PSS ratio: the ratio of PSS to maximal strain, * and †: statistically significant results in pairwise comparisons.

the significance level was set at 0.017 (0.05/3 ≈ 0.017). Other data were compared between the groups by one- way analysis of variance (ANOVA) models and Bonferroni post-hoc test for interval and chi square or Fisher's exact test for nominal variables. P value < 0.05 considered as statistically significant. Simple linear regression models were used to determine the associations between echocardiographic indices. Statistical analysis was performed using SPSS 15 for Windows (SPSS Corp., Chicago, Illinois).

Reproducibility

For inter and intraobserver variability 50 segments were analyzed. A total of 4 segments (1 normal and 3 infarcted) were randomly selected from each patient. Paired-t test was used for comparing the two equivalent measurements .

Table 2. Comparison of the mean TDI and SR imaging parameters between groups

	PPCI (n = 10)	SK (n = 16)	Conservative (n = 12)	P value
S	3.9 ± 0.+	3.9±1.5	3.8±1.364	0.78
peakε	-12.2±5.1	-13.1±5.7	-13.3±4.2	0.67
tåε	0.31±0.06 *	0.34±0.03	0.36±0.03 *	0.04
εes	-11.3±5.6	-12.5±5.3	-13.273±4.3	0.29
εPSS	-12.3 ± 5.6	-13.4±6.1	-14.0±5.677	0.46
SRs	-1.1 ± 0.35	-0.97±0.31	-0.98±0.28	0.59
SRPSS	-0.48±0.22	0.5±0.18	-0.51±0.15	0.22
tSRs	0.17±0.03	0.15±0.03	0.17±0.04	0.83
teSRs	0.29±0.04 *	0.33±0.03	0.36±0.03 *	0.02

PPCI: primary percutaneous coronary intervention, SK: streptokinase treated group, C: conservative treated group. S: peak systolic velocity, peakå: peak systolic strain, tå: time to peak strain, å es: end-systolic strain, å PSS: post systolic strain, SRs: peak systolic strain rate, SRPSS: post systolic shortening, tSRs: time to peak systolic strain rate, teSRs: time to end of shortening.

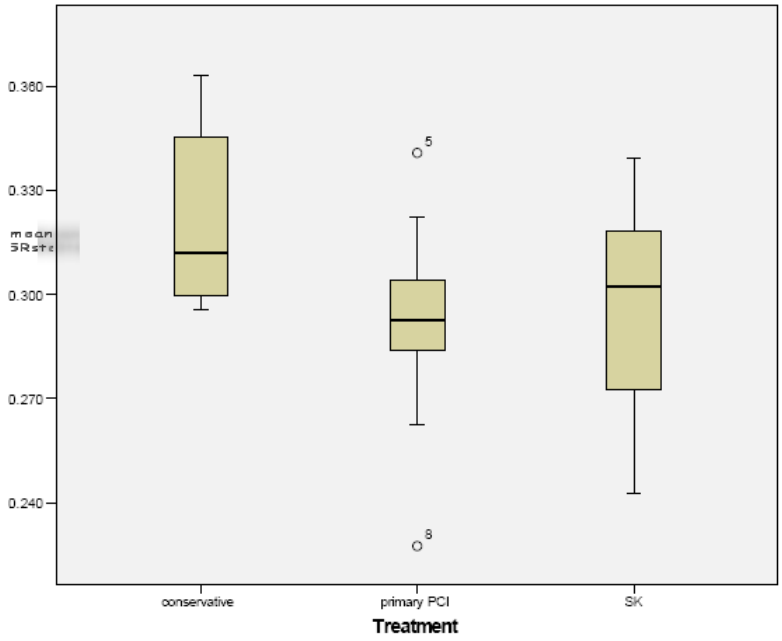

Figure 2. Box-Plot curves shows comparison of mean **teSRs** among 3 treatment groups.
teSRs: time to end of shortening.

Results

Thirty-eight patients, 34 males, mean age of 55±9.4 years (range:39-75 years), enrolled in the study. There was not any significant differences in mean LVEF, LV end- diastolic and end systolic diameters and volumes, WMSI, and PSS ratio between above mentioned groups. (Table1). There was not any relationship between either WMSI and tε (P=0.40) or MI location and PSS ratio (P=0.13).There was no

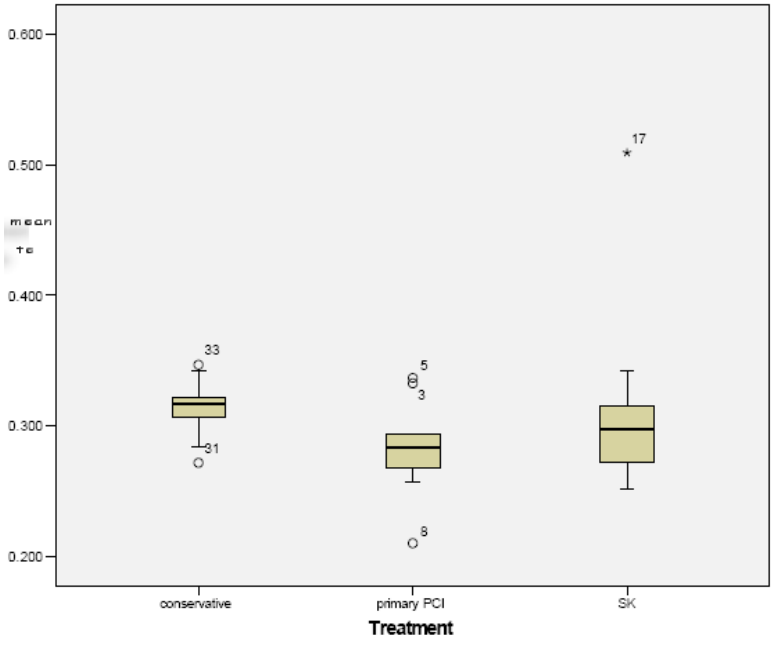

Figure 3: Box-Plot curves shows comparison of mean **tε** between groups.
tå: time to peak strain

difference in WMSI between PCI , SK and the groups receiving conservative medical treatment, but there was an inverse relationship between WMSI and mean SRS, especially when WMSI was more pronounced.

TDI, Strain and strain rate results

Table 2 showed the comparative measurements of the mean and standard deviation values of the peak systolic tissue velocity (S), peak systolic strain (peakε), end systolic strain (εes), time to peak systolic strain (tε), post systolic strain (εPS), peak systolic strain rate (SRs), post systolic shortening strain rate (SRPSS), time to peak systolic strain rate (tSRs), and time to end systolic strain rate (teSRs) of 12 LV segments .Using a simple linear regression model, no association was found between PSS ratio and SRs (β=0.056, P =0.70). Comparison of mean tε and teSRs among groups are presented in Figures 2 and 3.

Relation between PSI, tε and teSRs

A weak linear correlation (*r*=0.30), was found between PSI and mean tε (Fig. 4). Using simple linear regression model we found a weak but significant association between PSI and mean tε (β = -0.851, P=0.04), but no statistically significant association was found between PSI and teSRs (r^2 =0.08, β=-0.772, P=0.12) (Fig. 5).

Relationship between Regional Systolic Function and Kind of Therapy

A significant relation was observed between tε and teSRs with the kind of therapy (both P=0.02). Bonferroni post-hoc test revealed that significant difference existed only between primary PCI and conservative medically treated group (Table 2). This finding proposed that primary PCI resulted in early improvement in regional systolic function.

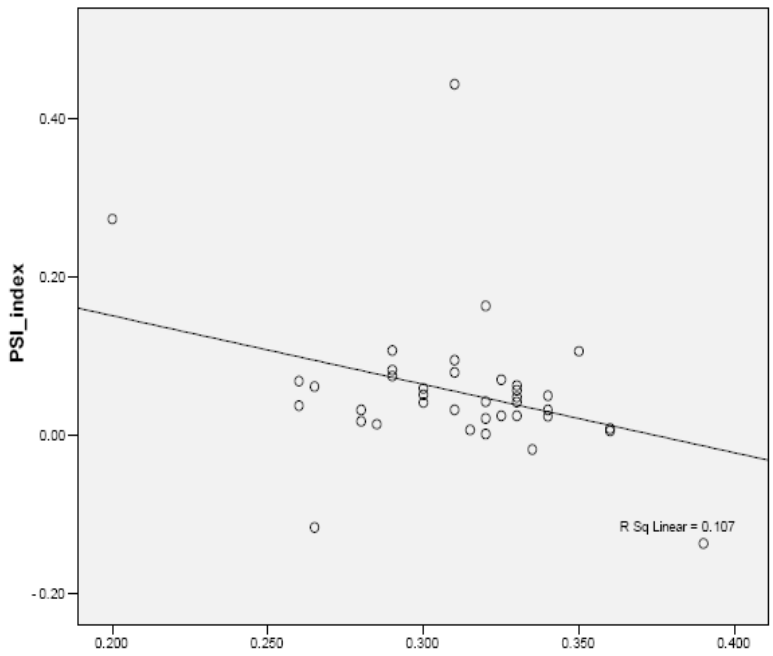

Figure 4: Scatter plot shows a weak linear correlation between PSI-index and tε.
PSI: Post systolic strain index ,tå: time to peak strain

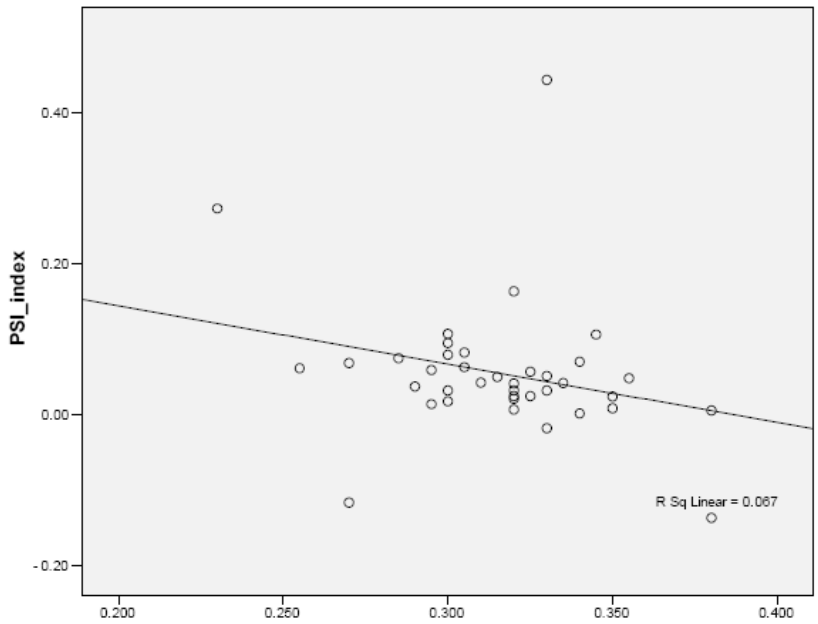

Figure 5: Scatter plot shows no correlation between PSI-index and teSRs. Post systolic strain index , teSRs: time to peak systolic strain rate.

Reproducibility

Paired-t test did not result in any significant inter and intraobserver variability difference between the first and second extracted data which was randomly selected from each patient.

Discussion

The first clinical study on SRI was a feasibility study by Heimdal et al, who demonstrated the use of SRI for regional dysfunction in six patients with MI.[2] Another initial study by Stoylen et al. found a good correspondence between semi-quantitative wall motion from color strain rate images (curved M-mode) and grey scale wall motion in patients with AMI within a week.[11] They have also demonstrated that SRI can be useful for both semi-quantitative and quantitative identification of the infarct-related artery in AMI.[12] On transmural infarcts, marked reduction in systolic and early diastolic strain and SR were shown in chronically infarcted segments compared to normal regions.[13] A clinical validation study of strain in patients with AMI found a good relationship between echocardiography and magnetic resonance imaging (MRI).[14] Tissue Doppler with a high temporal resolution has given a new insight into the mechanical events of the cardiac cycle. Acute ischemia induces sequential changes in the contraction pattern of which the longitudinal changes can be accurately quantified by SRI. In early systole, strain and strain rate traces will initially show positive values representing the early systolic lengthening, followed by a reduction in the peak value and a delayed peak strain rate, which was indicative of decreased contractility.[15]

Thereafter delayed contraction is represented by an extra peak after AVC, called PSS. Typical peak values of acute and chronic ischemia are SRs < -1 s^{-1} and εes <-15%.[8]

In the early phase of an AMI, it is impossible to differentiate between ischemic myocardium

with an inadequate flow and stunned myocardium with adequate reserve, as both show similar abnormal deformation pattern at rest.[8] Experimental studies found that strain/ strain rate patterns in stunned myocardium at rest resembled those during severe hypoperfusion. Derumeaux et al, have demonstrated that systolic myocardial velocity gradient partially recovered after the first minutes following reperfusion in stunned myocardium.[16] Although we could not follow the regional changes in the ischemic segments to observe an increase in peak systolic strain/strain rate after a recovery period. However, previous study showed an increase in peak systolic strain/strain rate after one week recovery period which indicated regression of stunning.[8] This is a promising for the follow-up of patients and the need for intervention. The main increases in ε and SR occurred during the first week. Other studies demonstrated late recovery because of stunning occurs during a period of weeks rather than months.[8] Several studies of WMS in patients receiving reperfusion treatment for AMI have shown delayed return of regional LV function.[17] PSS is a sensitive marker of ischemia.[18-22] However, as PSS is found in 30% of myocardial segments in control subjects,[23] its specificity is low. Differences in the definition of PSS may also cause discrepancies; hence, we used a strict definition, with a cut-off value between normal and pathologic PSS of -0.2 s^{-1}. (8) We chose this cutoff value since Voigt et al.[23] suggested that PSS is not pathologic unless it exceeds 20% of total myocardial shortening, which would correspond to our SR limit. The degree of PSS in infarcted segments did not seem to predict recovery of function.[8] We also did not find a significant difference in PSS between groups but found a significant relationship between PSI and median tε, which shows that time to peak systolic strain or shortening is delayed in the ischemic segments.

Our study was consistent with that of Bjork Ingul in that peak systolic SR seemed not to be a good parameter to predict the potential recovery after AMI in PCI groups, as there was only a partial and statistically insignificant increase in SR.[8] However, 3 days after PCI and using regional deformation parameters at rest, it was not possible to predict whether the tissue will recover completely. This might be due to the fact that those segments were still stunned. As expected for stunned myocardium there was no detectable improvement of wall motion scoring compared with the baseline.[24] This indicated that teSRs might be more sensitive than SR in detecting subtle increase in regional myocardial function, so that, at this very early time point after PCI both etSRs and tε of infarcted myocardium were still shortened compared to those values of thrombolysis and conservatively treated groups.

Our study suffered from a few limitations: Firstly, the total number of patients evaluated in the current study was small and the pretreatment study could not be attained in emergency ward and or CCU, which led to inability to obtain statistically significant differences in strain/ strain rate parameters between groups before and after different therapeutic strategies. Secondly, although the quantification of longitudinal deformation from apical views can potentially interrogate all myocardial segments, radial myocardial deformation was not measured in our study. Finally the angle dependency of all Doppler-based methods is another important drawback but continuous care was taken to align the ultrasound beam with the interrogated direction of myocardial motion. Current

developments in ultrasound machine allow the real-time ultrasonic measurement of ultrasound-derived 2D or 3D strains.

This study showed that SR imaging can accurately assess the efficacy of PCI versus different kinds of treatment regarding the recovery of systolic function of infarcted myocardium during the early stage after acute myocardial infarction.

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