Strain rate imaging pre- and post-percutaneous coronary intervention: a potential role in the objective detection of ischaemia in exercise stress echocardiography


Cardiothoracic Division, The James Cook University Hospital, Middlesbrough TS4 3BW, UK

Received 29 May 2007; accepted after revision 9 January 2008; online publish-ahead-of-print 12 February 2008

Aims To determine the feasibility of strain rate imaging (SRI) in the objective detection of exercise-induced ischaemia.

Methods and results Sixteen patients undergoing elective percutaneous coronary intervention (PCI) underwent treadmill exercise stress echocardiography (ESE) pre- and post-PCI. Measurement of systolic SRI parameters was attempted in all myocardial segments at baseline, peak stress, and in recovery. Segments were divided into those supplied by target (Group 1) and non-target vessels (Group 2).

Percutaneous coronary intervention was successful in all patients. In Group 1, there was no significant difference in post-systolic strain rate (SRps) at baseline or at peak stress but there was significantly greater SRps pre-PCI compared with post-PCI at 30 min into recovery ($2.0.37 \pm 0.53$ vs. $2.0.07 \pm 0.44 s^{-1}$, $P = 0.004$). There were similar findings with the SRps index [ratio of SRps:peak systolic strain rate (SRsys)]. Group 2 segments did not demonstrate any significant differences in SRI parameters pre- and post-PCI. At peak exercise pre-PCI, Group 1 segments had significantly delayed time to SRsys compared with Group 2 ($0.12 \pm 0.05$ vs. $0.09 \pm 0.05 s$, $P = 0.013$), a difference that was abolished post-PCI.

Conclusion This suggests a potential role for SRI in the objective detection of exercise-induced ischaemia by echocardiography at peak stress and during recovery at the time of improved image quality.

KEYWORDS
Strain rate imaging; Exercise stress echocardiography; Percutaneous coronary intervention

Introduction
Stress echocardiography is a well-established non-invasive method for the assessment of myocardial ischaemia and viability. This technique, based on two-dimensional visual evaluation of endocardial excursion and wall thickening, is subjective and dependent on operator experience. As such it is associated with considerable inter-observer variability and may not identify small but clinically significant changes in myocardial function that are below the threshold of visual resolution. Although exercise is a more physiological stimulus compared with pharmacological stress, dobutamine is conventionally used because the visual interpretation of images may be compromised by increased respiratory and body motion artefacts during exercise.

Tissue Doppler imaging has been introduced in an attempt to provide a more objective assessment of myocardial contractility but is subject to the confounding effects of cardiac translational motion and passive pathological tethering. These limitations may be overcome by the measurement of local myocardial deformation parameters with strain and strain rate echocardiography. Strain rate is defined as the rate of deformation in response to an applied force and is determined from the spatial gradient of local myocardial tissue velocities between two points. Strain is calculated from the time integral of strain rate and reflects the magnitude of deformation. As these ultrasound modalities are derived from the motion of segments relative to each other, any velocities contributed by tethering or translation are excluded because these would affect both sampled points equally. These parameters are potentially more accurate and specific measures of local myocardial function, and may offer an opportunity to improve the detection of dynamic regional abnormalities in response to stress.

The local deformation properties of normal, stunned, ischaemic, and infarcted myocardium in response to dobutamine challenge have been well established but there are limited data on the feasibility of strain and strain rate in exercise stress echocardiography (ESE). This study was designed to determine the role of strain and strain rate...
imaging (SRI) in the detection of exercise-induced ischaemia at peak stress as well as more subtle abnormalities of myocardial deformation that may persist into the recovery period at a time of improved image quality. In addition, this study assessed myocardial contractility following the relief of ischaemia by successful percutaneous coronary intervention (PCI).

**Methods**

**Subjects**

The study population was composed of 22 patients undergoing elective PCI with the physical capacity to perform a treadmill exercise test. Exclusion criteria were the presence of collateral arteries (to prevent the masking of myocardial ischaemia), greater than mild valvular heart disease, atrial fibrillation, and bundle branch block. The local research ethics committee approved the study and written informed consent was obtained from all participants.

**Study protocol**

Exercise stress echocardiography was performed on the day before elective PCI in all patients with a further study 6 weeks later, both by an expert investigator (J.T.) blinded to the patients’ clinical and angiographic data. Medication was not altered between the two echocardiography studies. Rate-limiting drugs were discontinued 48 h prior to testing. In each exercise stress study, tissue Doppler ultrasound loops were acquired at baseline before patients were exercised on a graded treadmill stress test to target heart rate using the standard Bruce protocol. Further, tissue Doppler loops were then obtained within 1 min, at 15 min as well as 30 min after the end of the exercise test. All patients received standard pre-, peri-, and post-procedural care and were discharged the day following the interventional procedure.

**Echocardiographic data acquisition**

A Vingmed Vivid 7 ultrasound scanner (GE Vingmed, Horten, Norway) was used to obtain conventional two-dimensional and colour tissue Doppler images from the standard apical four-chamber, three-chamber, and two-chamber views in the left lateral decubitus position in octave strain mode. Depth and image sector width were set to obtain the highest possible frame rates (120 ± 10 f/s). The pulse repetition frequency was adjusted carefully to avoid aliasing (16–32 cm/s). The velocity dataset was smoothed by spatial processing of five pixels radially and three pixels laterally. Care was taken to align the ultrasound beam with the interrogated direction of myocardial motion to reduce the confounding effects of angle dependency. Traces from the apical segments were extracted from the most proximal part of the segment and segments with an insonation angle >70° were excluded from analysis in order to avoid this potential source of error. For each view, data from three consecutive cardiac cycles during brief apnoea to minimize global cardiac movement were stored on magneto-optical discs for subsequent offline analysis using dedicated software (GE Vingmed).

Wall motion was manually tracked to maintain the sample area in the mid-wall position of the segment being interrogated throughout the cardiac cycle. For each myocardial segment, strain rate was calculated from the spatial derivative of myocardial velocity over a defined sample area of 6 mm within the mid-myocardial layer. Data from three consecutive cardiac cycles were averaged to improve the signal-to-noise ratio and used to determine the mean strain rate profile. This was then integrated over time to derive the mean natural longitudinal strain profile using end-diastole, defined by the onset of the peak R-wave of the ECG trace, as the reference point. Myocardial tissue velocity curves from the basal septum were used to define end-systole because aortic valve closure induces a clearly identifiable rapid directional change in the basal septal velocity curve coinciding with the peak negative left ventricular dP/dt. Mitral valve opening was determined at the tip of the mitral leaflets. By convention, strain rate and strain are expressed as a negative parameter for shortening and a positive parameter for lengthening. Longitudinal directional changes from the apical window in normal myocardium are characterized by systolic shortening and diastolic lengthening and thus, an increase in the magnitude of systolic shortening would be reflected by more negative strain or strain rate values and vice versa.

The following parameters were measured from the mean strain rate and strain profiles: (Figures 1 and 2).

**Strain rate (rate of deformation)**

- Peak systolic strain rate (SRsys)—greatest shortening during ejection period.
- Post-systolic strain rate (SRps)—defined as any shortening that occurs during isovolumetric relaxation.
- Post-systolic strain rate index (SRps/sys) = SRps/SRsys
Temporal parameter

- Time to peak systolic strain rate (t-SRsys) was measured as the time from the peak R-wave of the ECG trace to SRsys.

Strain (magnitude of deformation)

- End-systolic strain (Esys)—magnitude of the change in deformation measured from the end-diastolic reference point to end-systole.
- If the greatest magnitude in deformation over the entire RR interval (Emax) occurred after aortic valve closure, post-systolic strain (Eps) was calculated as the absolute change in strain occurring from aortic valve closure to Emax, i.e. Eps = Emax – Esys.
- Post-systolic strain index (Eps/sys) was calculated by expressing Eps as a ratio to Esys, i.e. Eps/sys = (Emax – Esys)/Esys.

The feasibility study was performed by determining if the waveform derived from the tissue Doppler loops conformed to the expected shape (Figures 1 and 2). Waveforms with apparently random structure were not analysed.\textsuperscript{15} Intra-observer variability was calculated based on repeated assessment of the same recordings from eight patients. Thus, repeatability was determined only in terms of measurement rather than separate recordings. The observer made these assessments in a blinded fashion with an interval of 3 months. The coefficient of variation was calculated as the absolute difference between the repeated measurements expressed as a percentage of the average of the two measurements. The mean (SD) relative difference in the measurements was 12 (9), 9 (3), and 8 (3)% at baseline and 17 (11), 13 (6), and 11 (5)% at peak stress for SRsys, Esys, and t-SRsys, respectively. In addition, visual assessment of wall motion score from grey-scale B-mode cineloops was performed by an expert investigator (J.T.). Myocardial wall segments were scored according to American Society of Echocardiography recommendations: normal = 1, hypokinetic = 2, akinetic = 3, and dyskinetic = 4.

Data and statistical analysis

The relationship between coronary anatomy and ventricular territory was analysed by assigning segments in the mid- and basal anterior septum and anterior wall, mid-septum and apex to the left anterior descending artery. The basal and mid-segments of the posterior and the lateral walls were considered to be in the territory of the circumflex artery and the basal and mid-segments of the inferior wall were allocated to the right coronary artery. No segments were designated to the right coronary artery if the system was left dominant. This approach is in accordance with that adopted by the American Society of Echocardiography.\textsuperscript{16} Myocardial segments were then divided into target and non-target groups. All allocated segments were considered to be in the culprit territory if the respective coronary artery was the target for intervention (target group). Coronary arteries that were not revascularized were free of flow-limiting stenoses and segments that were supplied by these arteries comprised the non-target group.

Data were analysed using SPSS for Windows 12.0. Means and standard deviations were used to describe continuous variables. Data were tested for normal distribution. Post-systolic strain rate index and Post-systolic strain index were positively skewed and were therefore log-transformed prior to analysis. Results are shown in natural units. Within the target and non-target groups, paired \( t \)-tests were used to compare segments pre-PCI with post-PCI. Unpaired \( t \)-tests were also used to compare segments in the target group with the non-target group, both pre-PCI as well as after revascularization. The test results are presented as two-tailed values and statistical significance was inferred at \( P < 0.05 \).

Results

Demographics

A total of 22 patients consented to participate in the study. However, four patients declined to attend for ESE following PCI. In addition, two patients had inadequate echo windows at baseline and were excluded. Therefore, the study population was composed of 5 women and 11 men with a mean (SD) age of 64.4 (8.0) years. Three patients had previous percutaneous revascularization and one had a previous cerebrovascular accident but none had a history of peripheral vascular disease or ST-elevation myocardial infarction. Cardiovascular risk factors included diabetes (\( n = 5 \)), hypertension (6), hypercholesterolaemia (16), family history (9), current smoker (1), and ex-smoker (11).
Exercise test
The exercise stress parameters pre- and post-PCI are depicted in Table 1. Although the haemodynamic responses to stress as measured by the change in blood pressure and heart rate, were similar, patients were able to exercise significantly longer and achieve a significantly higher workload following revascularization. Pre-PCI, five patients achieved their target heart rate (90% of age predicted for 1 min) and the exercise test was prematurely terminated in the remainder because of the development of ischaemic symptoms (chest pain or dyspnoea). Significant ST-segment depression (>1 mm) was noted in twelve patients. The target vessel(s) were left anterior descending artery (LAD) (n = 9), right coronary artery (RCA) (5), and LAD/RCA (2). PCI was performed using standard techniques and stents were implanted in all patients with good results and a residual stenosis <30%. At the follow-up visit, all but one patient reported a complete resolution of angina. Nine patients achieved their target heart rate in the exercise test and the reasons for premature termination in the remainder were fatigue (n = 6) and chest pain (n = 1). Two patients developed significant ST depression but this was at a higher workload compared with the pre-PCI exercise test.

Feasibility study
Excluding the two patients with inadequate echo windows, the feasibility of obtaining adequate SRI (strain and strain rate) imaging waveforms from each myocardial segment at each stress stage is depicted in Table 2. Interpretable waveforms were obtained from a total of 91 myocardial segments (58 in the territory of the target vessels). Poor signal-to-noise ratio precluded analyses of traces obtained from all apical segments other than the apical septal segment. Interpretation of all the posterior wall segments resulted in an insonation angle >20° and thus these segments were also excluded from analysis. The peak stage proved the most difficult to obtain adequate waveforms but there were similar percentages of satisfactory traces in the other stages. Of the segments that were included in this study, the lateral and septal segments yielded the highest percentage of analyzable data while the anterior territory proved to be least fruitful. The poor image quality at peak stress with inadequate endocardial border definition also impaired appropriate B-mode visual analysis in sufficient patients to be able to directly compare SRI with conventional analysis of wall motion. An ultrasound contrast agent was not used as this would have prevented strain rate analysis. Although the images were easier to interpret in recovery, there were no significant differences in visual assessment of wall motion score between the target and non-target segments pre- and post-PCI.

Paired t-tests comparing myocardial segments supplied by target vessels pre- and post-percutaneous coronary intervention
The echocardiography datasets of myocardial segments supplied by target vessels pre- and post-PCI are shown in Table 3. There was no significant difference in baseline heart rate pre- and post-PCI. The peak heart rate achieved on the treadmill (Table 1) was higher than that during acquisition of the peak tissue Doppler loops (Table 3) because it took up to a minute to reposition patients for echocardiography following the end of the exercise test allowing some recovery of the heart rate. Following intervention, patients achieved a significantly higher heart rate (107 ± 23 vs. 114 ± 28, P = 0.019). This remained significant at 15 min of the recovery phase (82 ± 11 vs. 86 ± 15, P = 0.016) but was similar by 30 min of the recovery phase (78 ± 9 vs. 79 ± 13).

There was no significant difference in SRps in myocardial segments supplied by target vessels at baseline pre- and post-PCI (−0.27 ± 0.54 vs. −0.21 ± 0.33 s⁻¹). At peak exercise there was a trend towards greater SRps pre-PCI compared with post-PCI (−0.42 ± 0.78 vs. −0.20 ± 0.47 s⁻¹, P = 0.11). This became significantly different at 15 min of recovery and remained so at 30 min [(−0.36 ± 0.50 vs. −0.17 ± 0.25 s⁻¹, P = 0.021) and (−0.37 ± 0.53 vs. −0.07 ± 0.44 s⁻¹, P = 0.004), respectively]. The SRps index was similar at baseline pre- and post-PCI (0.18 ± 0.48 vs. 0.29 ± 0.76) with a trend to a higher ratio pre-PCI at peak exercise (0.23 ± 0.39 vs. 0.12 ± 0.28, P = 0.12). However, this parameter was significantly higher pre-PCI compared with post-PCI at 15 and 30 min of recovery [(0.29 ± 0.41 vs. 0.15 ± 0.25, P = 0.041) and (0.30 ± 0.44 vs. 0.13 ± 0.46, P = 0.047), respectively]. The time to SRsys was similar at baseline pre-PCI compared with post-PCI (0.16 ± 0.05 vs. 0.18 ± 0.06 s) with a trend to a later time pre-PCI at peak exercise (0.12 ± 0.05 vs.

### Table 1 Exercise stress parameters pre- and post-percutaneous coronary intervention

<table>
<thead>
<tr>
<th></th>
<th>Pre-PCI</th>
<th>Post-PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (min)</td>
<td>7.2 (2.4)</td>
<td>7.9 (2.9)*</td>
</tr>
<tr>
<td>Workload (mets)</td>
<td>8.7 (2.5)</td>
<td>9.5 (2.9)*</td>
</tr>
<tr>
<td>Baseline HR (bpm)</td>
<td>79 (10)</td>
<td>79 (12)</td>
</tr>
<tr>
<td>Baseline SBP (mmHg)</td>
<td>143 (20)</td>
<td>143 (17)</td>
</tr>
<tr>
<td>Baseline DBP (mmHg)</td>
<td>74 (12)</td>
<td>75 (11)</td>
</tr>
<tr>
<td>Peak HR (bpm)</td>
<td>150 (20)</td>
<td>156 (23)</td>
</tr>
<tr>
<td>Maximum HR (%)</td>
<td>95 (12)</td>
<td>99 (12)</td>
</tr>
<tr>
<td>Peak SBP (mmHg)</td>
<td>200 (20)</td>
<td>194 (27)</td>
</tr>
<tr>
<td>Peak DBP (mmHg)</td>
<td>86 (11)</td>
<td>83 (16)</td>
</tr>
</tbody>
</table>

The values are expressed in the form of mean (SD). *P < 0.05.

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure.

### Table 2 The feasibility of obtaining adequate strain rate imaging waveforms from each myocardial segment at each stress stage (%)

<table>
<thead>
<tr>
<th>Segment</th>
<th>Baseline</th>
<th>Peak</th>
<th>15 min</th>
<th>30 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-septum</td>
<td>94</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Apical septum</td>
<td>94</td>
<td>88</td>
<td>94</td>
<td>94</td>
</tr>
<tr>
<td>Basal inferior</td>
<td>63</td>
<td>56</td>
<td>69</td>
<td>75</td>
</tr>
<tr>
<td>Mid-inferior</td>
<td>82</td>
<td>69</td>
<td>82</td>
<td>82</td>
</tr>
<tr>
<td>Basal anterior septum</td>
<td>63</td>
<td>50</td>
<td>57</td>
<td>63</td>
</tr>
<tr>
<td>Mid-anterior septum</td>
<td>75</td>
<td>50</td>
<td>57</td>
<td>63</td>
</tr>
<tr>
<td>Basal anterior</td>
<td>19</td>
<td>7</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Mid-anterior</td>
<td>25</td>
<td>25</td>
<td>19</td>
<td>25</td>
</tr>
<tr>
<td>Basal lateral</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Mid-lateral</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
However, there was no difference during the recovery phases. There were no significant differences in the other deformation parameters in myocardial segments supplied by target vessels pre- and post-PCI at any of the stages.

**Paired t-tests comparing myocardial segments supplied by non-target vessels pre- and post-percutaneous coronary intervention**

The echocardiography datasets of myocardial segments supplied by non-target vessels pre- and post-PCI are shown in Table 4. In contrast to the myocardial segments in the territory of the target vessels, segments that were supplied by non-target vessels did not demonstrate significant differences in SRps or SRps/sys pre- and post-PCI at any of the stages of the exercise test. There were no significant differences in the other deformation parameters.

**Unpaired t-tests comparing myocardial segments supplied by target and non-target vessels pre- as well as post-percutaneous coronary intervention**

The echocardiography datasets of myocardial segments supplied by target and non-target vessels pre-PCI are illustrated in Table 5 and post-PCI in Table 6, respectively. While there was no significant difference at baseline before intervention, segments within the territory of the target vessels took significantly longer to achieve SRsys at peak exercise compared with those segments supplied by non-target vessels (0.12 ± 0.05 vs. 0.09 ± 0.05 s, *P* = 0.013) (Table 5). This was no longer significantly different following revascularization (0.10 ± 0.05 vs. 0.11 ± 0.07) (Table 6). There were no statistical significant differences in the other measured strain or strain rate parameters at any of the stages either pre- or post-PCI.

**Discussion**

This study has demonstrated a potential role for local myocardial deformation indices in the objective assessment of ESE. Although there was no significant difference in SRps or SRps/sys between the myocardium supplied by target and non-target vessels pre-PCI, there was a significant reduction in these parameters only in segments in the territory of the target vessels following revascularization. In addition, myocardium supplied by the target vessels also had a significantly delayed t-SRsys at peak exercise pre-PCI, compared with myocardium subtended by non-target vessels, a difference that was abolished by revascularization.

Thus exercise SRI, but not conventional B-mode stress echocardiography, could document successful treatment of ischaemia by PCI.

Strain rate imaging has been established as an objective marker of ischaemia during dobutamine stress echocardiography in animal models and in patients with chest pain. Although exercise is a more physiological stressor than dobutamine and allows assessment of exercise capacity with reliable electrocardiograph data, it is constrained by suboptimal image quality at peak stress which impairs analysis of deformation parameters. Treadmill stress is also hampered by the delay in image acquisition after achieving peak exercise. This was confirmed by the present study,
### Table 4  Echocardiography datasets of myocardial segments supplied by non-target vessels pre- and post-percutaneous coronary intervention

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th></th>
<th>Peak</th>
<th></th>
<th>15 min</th>
<th></th>
<th>30 min</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-PCI</td>
<td>Post-PCI</td>
<td>Pre-PCI</td>
<td>Post-PCI</td>
<td>Pre-PCI</td>
<td>Post-PCI</td>
<td>Pre-PCI</td>
<td>Post-PCI</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>71 (11)</td>
<td>69 (11)</td>
<td>107* (23)</td>
<td>114 (28)</td>
<td>82* (11)</td>
<td>86 (15)</td>
<td>78 (9)</td>
<td>79 (13)</td>
</tr>
<tr>
<td>SRsys (s⁻¹)</td>
<td>–1.38 (0.46)</td>
<td>–1.23 (0.55)</td>
<td>–2.20 (0.70)</td>
<td>–1.85 (0.91)</td>
<td>–1.51 (1.04)</td>
<td>–1.38 (0.59)</td>
<td>–1.34 (0.69)</td>
<td>–1.45 (0.72)</td>
</tr>
<tr>
<td>SRps (s⁻¹)</td>
<td>–0.28 (0.78)</td>
<td>–0.30 (0.28)</td>
<td>–0.30 (0.70)</td>
<td>–0.37 (0.79)</td>
<td>–0.39 (0.67)</td>
<td>–0.21 (0.53)</td>
<td>–0.21 (0.48)</td>
<td>–0.25 (0.40)</td>
</tr>
<tr>
<td>SRps/sys</td>
<td>0.07 (0.57)</td>
<td>0.24 (0.25)</td>
<td>0.19 (0.33)</td>
<td>0.09 (0.94)</td>
<td>0.26 (0.37)</td>
<td>0.10 (0.48)</td>
<td>0.15 (0.61)</td>
<td>0.20 (0.33)</td>
</tr>
<tr>
<td>t-SRsys (s)</td>
<td>0.17 (0.06)</td>
<td>0.18 (0.07)</td>
<td>0.09 (0.05)</td>
<td>0.11 (0.07)</td>
<td>0.16 (0.04)</td>
<td>0.16 (0.05)</td>
<td>0.15 (0.04)</td>
<td>0.15 (0.05)</td>
</tr>
<tr>
<td>Esys</td>
<td>–17.0 (11.3)</td>
<td>–18.2 (9.7)</td>
<td>–19.3 (7.1)</td>
<td>–18.8 (8.9)</td>
<td>–18.6 (9.8)</td>
<td>–17.6 (8.4)</td>
<td>–18.2 (7.6)</td>
<td>–16.2 (11.0)</td>
</tr>
<tr>
<td>Eps</td>
<td>–4.49 (3.94)</td>
<td>–2.04 (1.39)</td>
<td>–2.30 (1.68)</td>
<td>–2.51 (1.61)</td>
<td>–2.28 (1.33)</td>
<td>–3.10 (2.62)</td>
<td>–3.91 (3.55)</td>
<td>–3.91 (4.05)</td>
</tr>
<tr>
<td>Eps/sys</td>
<td>0.25 (0.18)</td>
<td>0.13 (0.13)</td>
<td>0.33 (0.62)</td>
<td>0.18 (0.19)</td>
<td>0.16 (0.13)</td>
<td>0.31 (0.63)</td>
<td>0.57 (1.29)</td>
<td>0.78 (2.42)</td>
</tr>
</tbody>
</table>

The values are expressed in the form of mean (SD). *P < 0.05 pre-PCI compared with post-PCI.

### Table 5  Echocardiography datasets of myocardial segments supplied by target and non-target vessels pre-percutaneous coronary intervention

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th></th>
<th>Peak</th>
<th></th>
<th>15 min</th>
<th></th>
<th>30 min</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Target</td>
<td>Non- target</td>
<td>Target</td>
<td>Non- target</td>
<td>Target</td>
<td>Non- target</td>
<td>Target</td>
<td>Non- target</td>
</tr>
<tr>
<td>SRsys (s⁻¹)</td>
<td>–1.33 (0.58)</td>
<td>–1.38 (0.46)</td>
<td>–1.88 (1.43)</td>
<td>–2.20 (0.70)</td>
<td>–1.36 (0.55)</td>
<td>–1.51 (1.04)</td>
<td>–1.35 (0.58)</td>
<td>–1.34 (0.69)</td>
</tr>
<tr>
<td>SRps (s⁻¹)</td>
<td>–0.27 (0.54)</td>
<td>–0.28 (0.78)</td>
<td>–0.42 (0.78)</td>
<td>–0.30 (0.70)</td>
<td>–0.36 (0.50)</td>
<td>–0.39 (0.67)</td>
<td>–0.37 (0.53)</td>
<td>–0.21 (0.48)</td>
</tr>
<tr>
<td>SRps/sys</td>
<td>0.18 (0.48)</td>
<td>0.07 (0.57)</td>
<td>0.23 (0.39)</td>
<td>0.19 (0.33)</td>
<td>0.29 (0.41)</td>
<td>0.26 (0.37)</td>
<td>0.30 (0.44)</td>
<td>0.15 (0.61)</td>
</tr>
<tr>
<td>t-SRsys (s)</td>
<td>0.16 (0.05)</td>
<td>0.17 (0.06)</td>
<td>0.12* (0.05)</td>
<td>0.09 (0.05)</td>
<td>0.15 (0.05)</td>
<td>0.16 (0.04)</td>
<td>0.16 (0.05)</td>
<td>0.15 (0.04)</td>
</tr>
<tr>
<td>Esys</td>
<td>–17.2 (9.8)</td>
<td>–17.0 (11.3)</td>
<td>–18.8 (9.7)</td>
<td>–19.3 (7.1)</td>
<td>–16.6 (8.1)</td>
<td>–18.6 (8.9)</td>
<td>–17.1 (8.8)</td>
<td>–18.2 (7.6)</td>
</tr>
<tr>
<td>Eps</td>
<td>–2.41 (1.33)</td>
<td>–4.49 (3.94)</td>
<td>–2.99 (2.37)</td>
<td>–2.30 (1.68)</td>
<td>–2.61 (1.74)</td>
<td>–2.28 1.33</td>
<td>–1.93 (1.59)</td>
<td>–3.91 (3.55)</td>
</tr>
<tr>
<td>Eps/sys</td>
<td>0.20 (0.17)</td>
<td>0.25 (0.18)</td>
<td>0.20 (0.20)</td>
<td>0.33 (0.62)</td>
<td>0.31 (0.52)</td>
<td>0.16 (0.13)</td>
<td>0.24 (0.38)</td>
<td>0.57 (1.29)</td>
</tr>
</tbody>
</table>

The values are expressed in the form of mean (SD). *P < 0.05 target group compared with non-target group.
which demonstrated that poor endocardial border definition immediately after peak stress not only prevented meaningful B-mode visual assessment in many patients but also yielded the least number of analysable myocardial deformation waveforms. This was the consequence of increased acoustic noise because of greater cardiac translation and more laboured respiration. Coupled to the difficulty in maintaining breath-hold, these problems may explain the absence of significant differences in any deformation parameters at peak stress. In contrast, regional temporal events during the cardiac cycle, which can be accurately tracked by the high frame rate of SRI, are less sensitive to acoustic noise and not influenced by the insonation angle. These phase changes are easier to measure and may be the reason that t-SRs was the only measured parameter to reveal significant differences at peak stress in segments that were presumably more ischaemic prior to revascularization. There have been similar findings in a porcine model of acute ischaemia as well as in ischaemic segments of subjects undergoing dobutamine stress, lending support to the present work.

The reduction of acoustic noise in recovery was associated with improved image quality and increased numbers of adequate deformation waveforms. While this was not accompanied by detectable differences in B-mode visual assessment pre- and post-PCI, significant reductions in SRs and SRs/sys were demonstrated following revascularization. The development of ischaemia is associated with a progressive reduction in systolic contraction with a concomitant increase in post-systolic contraction.20,21 The short duration (40–110 ms) and small amplitude of post-systolic contraction may mean that subtle degrees of asynchrony between ischaemic and non-ischaemic regions cannot be detected by the temporal resolution of the human eye (90 ms).5 Furthermore, visual evaluation may erroneously interpret the development of post-systolic contraction as true systolic contractility and fail to recognize that a significant portion of deformation was occurring after aortic valve closure. SRI may overcome these limitations by offering a frame rate sufficient to resolve the timing and distinguish the true peak magnitude of brief local mechanical events.22 The present study suggests that SRI may improve the detection of exercise-induced ischaemia by the analysis of data acquired in recovery despite the absence of appreciable differences in conventional B-mode visual assessment. This is an important finding and raises the possibility of a greater applicability of this imaging modality. Post-systolic changes in myocardial deformation were shown to persist for at least 30 min following treadmill stress and this enables imaging to be delayed until patient is comfortable and in an optimal position and condition for echocardiographic imaging. The prolonged recovery also gives the potential for these studies to be performed using existing facilities with the patient being returned to the echocardiography department for ultrasound data acquisition following treadmill stress, without the need for specific purpose-built areas. However, additional studies with other stress modalities such as supine bicycle are needed to compare exercise and dobutamine stress echocardiography in this setting.

The time course demonstrated that post-systolic contraction developed at peak stress, persisted into recovery and was significantly reduced following revascularization in segments supplied by target vessels in conjunction with an
improvement in symptoms and exercise capacity. Although the pathophysiology remains to be fully established, this suggests that post-systolic contraction may represent myocardial stunning in response to ischaemia and is supported by previous work demonstrating similar findings during the recovery period following dobutamine stress in a canine model.\textsuperscript{23} These data suggest that SRps and SRps/sys may be able to predict an improvement in myocardial contractility and are potential markers of functional recovery following PCI.

Although significant differences in SRps and SRps/sys were demonstrated, the utility of these parameters as a clinical measure of ischaemia was limited by the overlap in values between segments in the territory of the target and non-target vessels, such that no cut-off values for the diagnosis of ischaemia could be derived. It is important to consider whether this precludes a role in the objective assessment of ischaemia or if the results may have arisen as a result of either inadequate sample size or methodological deficiencies. Although a relatively small number of patients was recruited, the study involved data analysis from 91 pairs of myocardial segments (pre- and post-PCI) and was thus adequately powered to detect within patient variation, but not inter-patient variation. Retrospective power calculation based on the present study with an 80% power ($\alpha = 0.05$) to detect a difference in SRps of 19% (the reduction in SRps during recovery following revascularization) between patients suggests that a sample size of 62 patients would be required to determine whether this technique could enable accurate diagnosis of ischaemia and to calculate the sensitivity and specificity.

Williams et al.\textsuperscript{24} measured tissue Doppler and deformation parameters at rest and following treadmill exercise stress only in the basal anterior segments in patients with significant proximal LAD disease and controls with normal coronary angiography. In contrast to the present study, patients had significantly lower systolic and diastolic tissue velocities, strain and strain rates at peak exercise compared with controls. Persistent changes in recovery were only identified in systolic and diastolic strain but post-systolic indices of deformation were not assessed. The present study did not measure diastolic parameters but the other conflicting findings may be explained by methodological differences. We adjudged all segments supplied by the target artery to be in the 'at risk' territory without considering the relationship between location of the culprit lesion and local myocardial function but these segments may not all be equally susceptible to the effects of ischaemia. Although the estimation of the segmental extent of coronary artery disease is difficult, it may be accomplished using the coronary artery jeopardy score.\textsuperscript{25}

Angiography was not performed at follow-up and thus, the presence of subclinical restenosis could not be excluded. However, all but one patient reported an improvement in symptoms and there was a significant increase in exercise capacity suggesting that ischaemia had been relieved in the territory of the target vessels. In addition, although the non-target vessels were not deemed to have flow-limiting stenosis, they may have had a degree of atherosclerotic disease. Although these factors may have masked some of the differences in the myocardial deformation indices between target and non-target segments, the present study was able to identify regional abnormalities and correction is likely to accentuate rather than reduce these differences.

Another limitation is background acoustic interference, which impairs the analysis of deformation parameters, particularly in segments with relatively low tissue velocities such as the apex. Angle dependency, common to all Doppler imaging techniques, precluded reliable data collection from the posterior segments in the apical three-chamber view. This could have been addressed by measuring radial strain from the parasternal short axis view but the short time-window at peak stress only enabled images from the apical views to be collected. Respiratory motion artefact reduced the number of satisfactory traces obtained from the anterior segments. Thus, adequate waveforms were only possible in eight segments but it is important that this is documented so that future studies can concentrate in certain key segments. Although this is a limitation, all three coronary vascular territories were still represented and the detection of significant changes in myocardial deformation indices was not prevented. Therefore, this study reveals a number of factors in terms of study power and design that are required to be addressed in order to refine future research to establish the sensitivity and specificity of myocardial deformation indices in the detection of ischaemia.

In conclusion, this study demonstrated a significant reduction in post-systolic deformation parameters following revascularization in segments subtended by arteries with flow-limiting stenoses, a difference that persisted into the recovery phase of the exercise test. In addition, the difference in t-SRsys at peak exercise between myocardium supplied by target and non-target vessels was no longer significant following intervention. This suggests that SRI offers an opportunity to improve the detection of dynamic regional abnormalities by echocardiography in response to exercise-induced stress at the peak stage as well as during the recovery phase of the treadmill test at a time of improved image quality. Larger studies are required to establish the sensitivity and specificity of this technique in order to determine the practical utility of ESE in the diagnosis of ischaemia.

Acknowledgements

The authors wish to thank the staff of the Cardiac Investigations Unit, The James Cook University Hospital Middlesbrough for their help with the treadmill exercise tests.

Conflict of interest: none declared.

References


