A comparison of wall motion analysis and systolic left ventricular long axis function during dobutamine stress echocardiography

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Aims To compare long-axis function and wall motion analysis for the detection of significant coronary artery stenoses in patients with single and multivessel disease.

Methods and Results We performed dobutamine stress echocardiography in 67 subjects, 14 with normal coronary anatomy, and 53 with significant coronary disease. A blunted increase in mean long-axis shortening of <0.25 cm was the best discriminator for coronary artery disease (sensitivity 85%, specificity 81%). Using this threshold, long axis function gave a sensitivity of 88% and specificity 89% for the detection of coronary artery disease in patients with normal resting wall motion while wall motion abnormality analysis had a sensitivity 73% and specificity 94%. Of 26 patients with a resting wall motion abnormality, 14 (54%) had multivessel disease. Long axis function detected multivessel disease in 12 of these (sensitivity 86%) compared with nine (sensitivity 64%) for wall motion analysis.

Conclusion Long axis function provides a promising, quantitative adjunct to wall motion analysis for the detection of coronary ischaemia using dobutamine stress echocardiography in patients with single and multivessel disease and with resting wall motion abnormalities.

Key Words: Long axis, dobutamine stress echocardiography.

Introduction

Left ventricular fibres are predominantly arranged longitudinally or obliquely in the subendocardium and subepicardium and circumferentially in the intermediate layers. During early systole, the longitudinal and oblique fibres begin to contract first causing the long-axis to shorten and the left ventricular cavity to become more spherical. After a mean delay of 25 (SD 40) ms the circumferential fibres also begin to contract and throughout the rest of systole both circumferential and longitudinal axes contract synchronously.

This normal pattern is disrupted early in coronary artery disease probably due to ischaemia of the subendocardial fibres. In animal models, acute ischaemia causes a reversible delay in the onset and a decrease in the amplitude of long axis shortening. Furthermore, in man, abnormal resting long axis function may revert to normal after successful revascularization. Therefore abnormalities of long axis function may be of practical use as indicators of ischaemia during stress testing. However, no study has yet compared long-axis function with wall motion analysis which remains the routine method of analysis despite being semi-subjective, and particularly difficult to interpret in the presence of a myocardial infarct on the baseline study.

The aims of this study were (1) to describe changes in long axis function during dobutamine stress echocardiography in patients with and without coronary artery disease, (2) to test whether a change in long axis function is more accurate than wall motion analysis for the detection of significant coronary artery disease in patients with normal resting wall motion and (3) to see if long axis function improves the detection of multivessel involvement in patients with a resting wall motion abnormality.
Methods

Patients
We studied 67 consecutive subjects, mean age 53 years (range 33 to 76 years), 55 of whom were male. All were referred for the investigation of suspected coronary artery disease. Patients with recent myocardial infarction (within 4 weeks) or with unstable angina (resting chest pain with or without ST segment changes on electrocardiography) were excluded as were those with stenosis severity between 50% and 70%. No patient had valve disease, uncontrolled hypertension (systolic blood pressure >200 mmHg, diastolic blood pressure >110 mmHg), left ventricular hypertrophy on echocardiography, left ventricular dilatation with normal coronary arteries, cardiac arrhythmia, or conduction disease. None was taking digoxin. Beta-blocking drugs were stopped for at least 3 days before stress testing and all other antianginal medication for one day.

Study
Approval for the study was granted by the local Committee on Ethical Practice and patients gave written informed consent. All patients had contrast coronary angiography within 3 months of stress testing. There were no cardiac events during this period.

Dobutamine stress echocardiography
Patients were studied in the left lateral position during continuous intravenous dobutamine infusion at 5, 10, 20, 30 and 40 µg . kg . min⁻¹, rising initially in 3 min stages. The last stage was continued for 6 min and atropine 300 to 600 µg was then given intravenously if the heart rate failed to rise to 85% of the age-predicted target (defined as 220 beats . min⁻¹ minus age in years for both men and women). Blood pressure and heart rate were recorded at 3 min intervals and 12-lead electrocardiograms were obtained at rest, at the end of each stage, at every event and at the end of the infusion. Stress testing was terminated for significant symptoms, prolonged hypotension, atrial fibrillation or ventricular tachycardia, ST depression >4 mm or akinesis or dyskinesis affecting more than two segments.

A Hewlett Packard Sonos 2000 was used with a 2.5 MHz duplex probe. Two dimensional echocardiography was performed from the parasternal long-and short-axis views and from apical four- and two-chamber views. A full sequence of images was recorded at the end of each 3 min stage. Baseline and peak images were analysed using the 16-segment model of the left ventricle as recommended by the American Society of Echocardiography[6]. Segments were described as normal, hypokinetic, akinetic, or dyskinetic. Ischaemia was defined as worsening of wall motion score or failure of a normal segment to develop hyperkinesis during dobutamine stress. Multivessel involvement was defined as a new wall motion abnormality in an arterial site distant from the resting wall motion abnormality.

Long axis function
Two-dimensional echo guided M-mode recordings were made from the apical four-chamber view with the cursor placed at the septal and lateral sides of the mitral annulus (Figs 1 and 2). Recordings were made at rest and at the end of each stage at a sweep speed of 100 mm . s⁻¹. The amplitude of long axis shortening (cm) was defined as the maximum excursion of the mitral annulus during systole, and the shortening rate (cm . s⁻¹) as the amplitude divided by the time from the start of long axis contraction to maximum excursion. Apical motion was not included in the analysis as the amplitude is less than 1 mm and does not bear any consistent relationship to the electrocardiogram[1,7]. We also measured the time delay from the Q wave to onset of long axis shortening (QOS, ms) on M mode. All measurements were averaged over three beats. All measurements were made by one operator from videotape and averaged over three beats. Intra-observer variability was 6% for QOS and 5% for amplitude of shortening. Inter-observer variability was 9% and 7%, respectively.
Coronary angiography

Coronary angiography was carried out via the right femoral approach using the Judkins technique. Angiograms were reported by an experienced observer blinded to the results of stress testing. Significant disease was defined as ≥70% diameter stenosis in a major epicardial coronary artery estimated by eye. Fourteen (21%) subjects had no significant coronary disease (9 with normal coronary anatomy, 5 with minor atheroma) while 53 (79%) had significant stenoses.

Statistical analysis

Mean values and standard deviations (SD) were calculated for all parameters at rest, at the end of each stage and at individual peak, defined as the highest dose of dobutamine given for each patient. Measurements were always made before atropine was given. Comparison of the differences between means was made using paired and unpaired t-tests. A $P$ value of <0.05 was considered significant. To establish a threshold increase in long axis excursion to define new ischaemia, a receiver operator characteristic curve was constructed against the results of angiography. In patients with a resting wall motion abnormality, the angiogram was only considered positive if there was a stenosis in an artery supplying myocardium distant from the resting abnormality. The incremental value of measurements of long axis function was tested with a stepwise logistic regression.

Results

Heart rate rose from 75 (12) beats . min$^{-1}$ at rest to 134 (12) beats . min$^{-1}$ at peak stress. There was no significant change in blood pressure. Systolic pressure was 130 (20) mmHg at rest and 131 (28) mmHg at peak; diastolic pressure was 80 (12) mmHg at rest and 70 (12) mmHg at peak.

Changes in long axis function with dobutamine stress

In the whole group the amplitude of long axis shortening increased from 1.15 (0.31) cm to 1.29 (0.37) cm at the septal side of the annulus ($P<$0.01) and from 1.28 (0.22) cm to 1.33 (0.33) cm at the lateral side ($P=0.04$). The shortening rate increased from 4.1 (1.6) cm . s$^{-1}$ to 8.3 (3.3) cm . s$^{-1}$ at the septal side ($P<$0.001) and from 5.7 (2.2) cm . s$^{-1}$ to 9.2 (3.8) cm . s$^{-1}$ at the lateral side ($P<$0.001). Time to onset of shortening (QOS) at the septum was 75 (19) ms at rest and 39 (22) ms at peak ($P<$0.001). At the lateral annulus, it was 83 (24) ms at rest and 50 (21) ms at peak ($P<$0.001). Lateral QOS was significantly longer than septal QOS at rest ($P<$0.001) and at peak ($P<$0.05).

There were significant differences in resting indices between patients with coronary artery disease and those without. These differences were maintained throughout stress (Table 1). To determine whether any parameter of long axis function predicted the presence of coronary disease, a stepwise logistic regression analysis was performed with mean change in amplitude, shortening rate and QOS as dependent variables. Only mean change in amplitude (septal and lateral annulus) was an independent predictor of coronary artery disease (odds ratio 0.93, 95% CI 0.893–0.966, $P<$0.001). A receiver operator characteristic curve gave a blunted increase between rest and stress of <0.25 cm as the best discriminator for the presence of significant coronary artery disease.
sensitivity was 85% and the specificity 81%. This cut-off point was then used to compare long axis function and wall motion change.

Comparison of wall motion analysis and long axis function for the detection of coronary artery disease in patients with normal resting wall motion

Forty-four patients had normal resting wall motion, 18 with normal coronary angiograms, 16 with single vessel disease and 10 with multivessel disease. Baseline values did not differentiate those with and without significant coronary artery disease (Table 2). However, at peak, the amplitude of long axis shortening was significantly lower in those with coronary artery disease (Fig. 3) and QOS was significantly longer both septally and laterally. There was a trend towards a lower shortening rate at both sites in patients with coronary disease.

Wall motion changes during dobutamine stress gave a sensitivity of 73% and a specificity of 94% for the detection of significant coronary artery disease. Impaired long axis function, as defined above, gave a sensitivity of 88% and a specificity of 89%. If impaired long axis function was added to wall motion results (by requiring both to be negative to indicate a negative result and either to be positive to indicate a positive result) sensitivity improved to 94% and specificity decreased to 73%.

Of the 16 patients with single vessel disease, 12 had new wall motion abnormalities with dobutamine stress, giving a sensitivity of 75% for the detection of coronary artery disease. Long-axis contraction was abnormal in all the patients with a new wall motion abnormality, as well as in three of the four who had no new wall motion changes (sensitivity 94%, specificity 100%, SE=0·097, 95% CI 0·004–0·379, \( P=0·08 \)).

Patients with resting wall motion abnormalities

In patients with a resting wall motion abnormality (n=26) the amplitude of long axis shortening was lower both at rest and peak than in those with normal resting wall motion (Table 3). QOS and shortening rate were also significantly different in patients with a resting wall motion abnormality (Table 3).

Fourteen patients (54%) with a resting wall motion abnormality had multivessel coronary artery disease. In nine of these patients there were new wall motion abnormalities on stress echocardiography, giving a sensitivity of 64% for detecting multivessel involvement. By comparison, 12 had a blunted mean long axis shortening

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**Table 1  Rest and peak parameters of long axis function in patients with (CAD) and without (NCA) coronary artery disease**

<table>
<thead>
<tr>
<th></th>
<th>NCA Rest</th>
<th>NCA Peak</th>
<th>CAD Rest</th>
<th>CAD Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal amplitude of shortening (cm)</td>
<td>1·34 (0·26)</td>
<td>1·72 (0·23)</td>
<td>1·10 (0·30)*</td>
<td>1·15 (0·38)**</td>
</tr>
<tr>
<td>Lateral amplitude of shortening (cm)</td>
<td>1·38 (0·15)</td>
<td>1·62 (0·30)</td>
<td>1·25 (0·24)</td>
<td>1·24 (0·31)**</td>
</tr>
<tr>
<td>Septal QOS (s)</td>
<td>59 (15)</td>
<td>29 (11)</td>
<td>74 (25)*</td>
<td>43 (24)*</td>
</tr>
<tr>
<td>Lateral QOS (s)</td>
<td>62 (8)</td>
<td>32 (10)</td>
<td>89 (23)**</td>
<td>56 (22)**</td>
</tr>
<tr>
<td>Septal rate of shortening (cm sec(^{-1}))</td>
<td>5·7 (1·6)</td>
<td>10·4 (2·7)</td>
<td>3·7 (1·3)**</td>
<td>7·5 (3·0)*</td>
</tr>
<tr>
<td>Lateral rate of shortening (cm sec(^{-1}))</td>
<td>6·5 (2·7)</td>
<td>10·7 (3·2)</td>
<td>5·4 (1·9)*</td>
<td>7·9 (3·5)*</td>
</tr>
</tbody>
</table>

All \( P \) values compare those with and without coronary artery disease.
*\( P <0·05 \).
**\( P <0·001 \).

**Table 2  Patients with normal resting wall motion (n=44)**

<table>
<thead>
<tr>
<th></th>
<th>NCA Rest</th>
<th>NCA Peak</th>
<th>1VD Rest</th>
<th>1VD Peak</th>
<th>CAD Rest</th>
<th>CAD Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal amplitude of shortening (cm)</td>
<td>1·37 (0·21)</td>
<td>1·69 (0·20)</td>
<td>1·28 (0·22)</td>
<td>1·32 (0·36)**</td>
<td>1·28 (0·20)</td>
<td>1·25 (0·29)**</td>
</tr>
<tr>
<td>Lateral amplitude of shortening (cm)</td>
<td>1·37 (0·13)</td>
<td>1·63 (0·21)</td>
<td>1·32 (0·15)</td>
<td>1·43 (0·22)*</td>
<td>1·32 (0·19)</td>
<td>1·31 (0·26)**</td>
</tr>
<tr>
<td>Septal QOS (ms)</td>
<td>57 (14)</td>
<td>28 (11)</td>
<td>60 (15)</td>
<td>32 (28)*</td>
<td>76 (15)</td>
<td>38 (12)*</td>
</tr>
<tr>
<td>Lateral QOS (ms)</td>
<td>63 (9)</td>
<td>34 (9)</td>
<td>75 (21)</td>
<td>43 (15)*</td>
<td>83 (20)*</td>
<td>51 (17)*</td>
</tr>
<tr>
<td>Septal rate of shortening (cm sec(^{-1}))</td>
<td>5·7 (1·7)</td>
<td>10·6 (3·4)</td>
<td>4·5 (1·2)</td>
<td>8·8 (2·9)</td>
<td>4·4 (1·6)</td>
<td>8·1 (2·9)</td>
</tr>
<tr>
<td>Lateral rate of shortening (cm sec(^{-1}))</td>
<td>6·5 (2·8)</td>
<td>10·8 (3·3)</td>
<td>6·1 (1·8)</td>
<td>9·2 (3·6)</td>
<td>5·6 (1·9)</td>
<td>8·9 (3·6)</td>
</tr>
</tbody>
</table>

NCA=no significant coronary disease; 1VD=single vessel disease; CAD=all patients with coronary disease including single vessel. All \( P \) values are as compared to patients with NCA. *\( P <0·05 \) **\( P <0·001 \).
as defined above, giving a sensitivity of 86% for the detection of multivessel involvement.

**Discussion**

By analysis of long axis function in the whole group, a threshold of <0.25 cm change in long axis shortening during dobutamine stress was identified as the best predictor of coronary artery disease. This value was then used to identify significant coronary artery disease in patients with normal resting wall motion. The sensitivity was 88% and the specificity 89%, comparing favourably with wall motion analysis. A combination of the two methods of analysis gave a sensitivity of 94% and a specificity of 73%. Abnormal long axis function was more sensitive than wall motion change in detecting

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**Figure 3** Septal long axis contraction. The upper panel shows a subject with normal coronary arteries. There is an increase in the amplitude of shortening with stress. The lower panel shows a subject with coronary artery disease in whom there is no significant increase in the amplitude of long axis shortening during stress.

**Table 3 Patients with and without a resting wall motion abnormality (RWMA)**

<table>
<thead>
<tr>
<th></th>
<th>NO RWMA</th>
<th></th>
<th>RWMA</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>Peak</td>
<td>Rest</td>
<td>Peak</td>
</tr>
<tr>
<td>Septal amplitude of shortening (cm)</td>
<td>1.31 (0.20)</td>
<td>1.41 (0.36)</td>
<td>0.93 (0.29)**</td>
<td>1.06 (0.41)**</td>
</tr>
<tr>
<td>Lateral amplitude of shortening (cm)</td>
<td>1.34 (0.17)</td>
<td>1.43 (0.29)</td>
<td>1.17 (0.26)**</td>
<td>1.16 (0.36)**</td>
</tr>
<tr>
<td>Septal QOS (s)</td>
<td>70 (17)</td>
<td>35 (12)</td>
<td>81 (24)*</td>
<td>56 (25) **</td>
</tr>
<tr>
<td>Lateral QOS (s)</td>
<td>76 (19)</td>
<td>45 (17)</td>
<td>98 (24)**</td>
<td>65 (23) **</td>
</tr>
<tr>
<td>Septal rate of shortening (cm . s⁻¹)</td>
<td>4.83 (1.5)</td>
<td>8.9 (3.1)</td>
<td>2.9 (1.1)**</td>
<td>5.8 (2.6)**</td>
</tr>
<tr>
<td>Lateral rate of shortening (cm . s⁻¹)</td>
<td>6.3 (2.3)</td>
<td>9.8 (3.6)</td>
<td>4.5 (1.4)*</td>
<td>6.7 (3.2) **</td>
</tr>
</tbody>
</table>

All P values compare those with and without RWMA.

*P<0.05.

**P<0.001.
single vessel disease (sensitivity 94% vs 75%). In patients in whom the diagnosis of ischaemic heart disease was already apparent due to resting wall motion abnormalities, long axis function identified those with multivessel involvement.

Comparison with the literature

During early contraction, the left ventricle becomes more spherical as the mitral annulus moves towards the apex\[8\]. This motion is dependent on the longitudinal and oblique fibres of the left ventricle, while subsequent transverse shortening is dependent on circumferentially-arranged fibres. The longitudinal fibres are distributed subendocardially which makes them more vulnerable than the circumferential fibres to the effects of myocardial ischaemia. This is due to a combination of increased wall stress during systole and a limited capacity for the subendocardial arterioles to vasodilate compared with those in the intermediate and epicardial layers. Thus, in experimental cats\[3\], occlusion of the circumflex artery and the application of a stenosis to flow into the left main stem artery causes a fall in long-axis shortening of 77% compared with a minor-axis reduction of only 18%. Recovery of function is also slower for the long- compared with the short-axis. In a canine experimental model\[9\], acute coronary occlusion led to an increase in end-diastolic circumference of 30% at the mid-cavity level compared with 58% at the apex. Restoration of normal anatomy after reperfusion was slower at the apex and preceded functional recovery. This may reflect the different contribution of myocardial fibre orientation at each level or higher wall stress at the apex compared with the mid-cavity. This difference in functional impairment and recovery would tend to improve the sensitivity of long axis compared with short-axis function for the detection of ischaemia.

Hoglund et al\[10\] first documented changes in the left ventricular long axis during systole in healthy volunteers and suggested these could be used to assess ventricular function in man. Simonson and Schiller\[11\] showed that a reduction in long axis function, called descent of the base in their study, correlated well with impaired left ventricular ejection fraction. This may reflect the different contribution of myocardial fibre orientation at each level or higher wall stress at the apex compared with the mid-cavity. This difference in functional impairment and recovery would tend to improve the sensitivity of long axis compared with short-axis function for the detection of ischaemia.

Gibson’s group\[11\] confirmed that, in patients with ischaemic disease, long-axis shortening was delayed to 85 ms after the Q wave from a normal mean of 55 ms. There was also a reduction in the amplitude of long axis shortening. Similar results were found by Henein et al\[14\] who further showed that these abnormalities resolved after successful angioplasty. This suggested that long-axis function might be useful for the detection of ischaemia.

Alam et al\[5\], therefore, assessed long axis shortening before and after bicycle exercise and found that there was a blunted increase of long axis shortening in patients with coronary artery disease. They used an upper limit of normal of 3 mm based on inter-observer variability. This gave a sensitivity of 76% for the detection of angiographically significant coronary artery disease and of 88% for the detection of reversible ischaemia on thallium stress imaging. However, the sensitivity was only 50% for single vessel disease, compared with 94% in our study. This discrepancy is unlikely to be explained by different criteria for abnormality, since our threshold of 0.25 cm calculated using a receiver operator characteristic (ROC) curve was similar to that used by Alam et al. It is possible that the time delay after the end of exercise before echocardiography could be completed was the main cause of the discrepancy. Alam et al. did not compare sensitivity of long axis function with wall motion analysis.

Although there was no clear association between the site of the arterial stenosis and mitral annular motion during stress, there were differences at rest between septal and lateral annulus shortening in patients with resting wall motion abnormalities affecting the left anterior descending territory. Other authors have also suggested that long axis function can localise the site of ischaemia\[5,12\].

Clinical significance

Stress echocardiography is highly dependent on observer experience, particularly with single-vessel coronary artery disease and in the presence of a resting wall motion abnormality. In both these situations new wall motion abnormalities may be subtle. A minimum of 100 training studies are therefore recommended before consistent results can be expected\[13\]. An alternative, quantitative measure of ischaemia, without the need for radioactive isotope injection, would therefore be a major advantage.

A number of characteristics make long axis shortening a potentially useful adjunct to wall motion analysis. It is simple to measure even in subjects in whom suboptimal image quality prevents adequate wall motion analysis. It gives a quantifiable measurement which avoids the partial subjectivity of wall motion analysis. Furthermore, abnormalities of long axis function occur early in ischaemia, sometimes in the absence of regional wall motion. We have shown that abnormal long-axis function is more accurate than wall motion analysis in the presence of single-vessel disease or with resting wall motion abnormalities for the detection of ischaemic change. Long-axis function may be useful to corroborate the findings of wall-motion analysis or to alert an observer to the likelihood of a developing wall motion abnormality. It appears from our initial results reported here that, in some cases, long-axis contractile dysfunction may even allow the diagnosis of coronary disease in the absence of abnormal wall motion.

Limitations

Logistic regression analyses must always be tested prospectively and it is therefore too early to apply our
findings in the clinical situation. However, the confirmation of a similar threshold for abnormality as determined by Alam et al.\(^5\) adds weight to the suggestion that this technique will be of clinical use.

There have been few studies on the effects of inotropic stimulation on long axis contractility\(^14\) and we do not know to what extent the complex interaction between the direct haemodynamic effects of dobutamine may modify the effects of ischaemia. Bouki et al.\(^15\) showed that an increase in long axis shortening of >2 mm correlated with viability as assessed by redistribution 201-thallium scanning. However, proof of viability after revascularization was not demonstrated. Furthermore, dobutamine also has effects on afterload which may modify cardiac function although we found little change in blood pressure in the present study. As we were primarily interested in the effects of dobutamine on long axis function, analysis was done at peak dobutamine dose rather than after atropine. As the dobutamine–atropine stress test is now the accepted standard, future studies should analyse long axis function after atropine has been given.

The threshold change in long axis excursion was calculated using patients with both normal and abnormal left ventricular function. A different threshold might have been obtained had the study been confined to patients with normal left ventricles. However this effect will have reduced rather than exaggerated the sensitivity of our results. We chose this method of analysis to make our results more applicable to routine clinical practice where patients do not invariably have normal ventricles, or a resting wall motion abnormality might be missed by an inexperienced operator.

**Conclusion**

A blunted increase in the amplitude of long axis shortening during dobutamine stress can identify patients with coronary artery disease. This technique has a higher sensitivity and specificity than regional wall motion analysis in patients with single vessel disease. In those with a resting wall motion abnormality, long axis function identifies multivessel involvement. Long axis analysis is simple, quick, and reproducible. Whilst further prospective work is necessary, this technique shows promise as an adjunct to conventional wall motion analysis.

**References**