The Potential Value of Ultrasonic Deformation Measurement in Differentiating Regional Ischaemic Substrates During Dobutamine Stress Echocardiography

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The differentiation between differing regional ischaemic substrates is crucial for decision-making in patients with coronary artery disease. This study demonstrates that quantification of dobutamine stress echocardiography using ultrasonic strain measurement has the potential to identify three differing regional ischaemic substrates (ischaemic, stunned and scarred) in the same patient. The data were validated by traditional analysis of dobutamine stress echo, coronary angiography and correlative quantitative positron emission tomography information.

Key Words: dobutamine stress echocardiography; ultrasonic strain imaging; ischaemic substrate.

Introduction

The identification and differentiation between the regional ischaemic substrates (acute or chronic ischaemia, stunning and established infarction) is important for the appropriate diagnosis and management of patients with coronary artery disease. Although differing cardiac imaging modalities have attempted to define these differences, it often remains a clinical challenge.

Prior closed chest experimental investigations have demonstrated the applicability of one-dimensional ultrasonic SR and $\varepsilon$ in the settings of stress echocardiography¹¹ and have shown this method to distinguish between acute or chronically ischaemic myocardium and regional stunning²². To date, it is unknown whether the findings obtained in the ‘pure’ experimental model are mirrored in the potentially more complex clinical situation.

Case Report

History

Dobutamine stress echocardiography was performed in a 62-year-old man to evaluate potential myocardial viability before the patient underwent a second coronary revascularization. Twelve years previously, he had undergone coronary artery bypass grafting with implantation of an internal mammary graft to the left anterior descending coronary artery and saphenous vein grafts to the left circumflex coronary artery (Cx) and the right coronary artery. The recent admission was caused by a return of increasing anginal symptoms.

Dobutamine Stress Echocardiography

Resting wall motion abnormalities were observed in the lateral (akinesia), inferior (hypokinesia) and posterior (hypokinesia) left ventricular walls. Dobutamine stress echocardiography was performed with the patient on standard antianginal treatment (but without beta-blockers), using a standard protocol⁶⁴. At an infusion
Table 1. Summary of the findings of the imaging modalities.

<table>
<thead>
<tr>
<th></th>
<th>Posterior wall</th>
<th>Inferior wall</th>
<th>Anterior wall</th>
<th>Lateral wall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiography</td>
<td>Total occlusion of RCA</td>
<td>Total occlusion of RCA</td>
<td>60% occlusion of the main stem</td>
<td>65% occlusion of the proximal Cx</td>
</tr>
<tr>
<td></td>
<td>Critical occlusion of the RCA venous graft</td>
<td>Critical occlusion of the RCA venous graft</td>
<td>Total occlusion of the mid-LAD</td>
<td>Total occlusion of the lateral branch and of the venous graft</td>
</tr>
<tr>
<td></td>
<td>Ischaemia?</td>
<td>Ischaemia?</td>
<td>PatenLAD arterial graft</td>
<td>Ischaemia?</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Normal?</td>
<td>'Necrotic match’ mid and apically</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Shocking?</td>
<td>'Low flow mismatch’ basally</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>'Mismatch'</td>
<td>Apical and mid infarction</td>
</tr>
<tr>
<td>Positron emission tomography</td>
<td>'Match'</td>
<td>'Match'</td>
<td>Ischaemia viability</td>
<td>Basal ischaemia?</td>
</tr>
<tr>
<td>Dobutamine stress echocardiography (visual)</td>
<td>Improvement in function</td>
<td>Improvement in function</td>
<td>Worsening in function</td>
<td>Akinetic, no response</td>
</tr>
<tr>
<td></td>
<td>Stopping?</td>
<td>Stopping?</td>
<td>Low εL at baseline</td>
<td>Low εL, positive εL at baseline</td>
</tr>
<tr>
<td></td>
<td>PST at baseline</td>
<td>PST at baseline</td>
<td>PSS at baseline</td>
<td>in the basal segment (low dose)</td>
</tr>
<tr>
<td></td>
<td>tεL↑ PST</td>
<td>tεL↑ PSS</td>
<td>tεL↑ PSS</td>
<td>Apical and mid infarction</td>
</tr>
</tbody>
</table>

PST=post-systolic thickening; PSS=post-systolic shortening; RCA=right coronary artery; LAD=left anterior descending coronary artery; εL=radial strain; tεL=longitudinal strain.

rate of 5–10 μg/kg/min, the pronounced akinesia of the entire lateral wall persisted. The hypokinetic inferior and posterior left ventricular walls became hypercontractile, whereas the anterior wall, which had normal contractility at baseline, became hypokinetic (contractility refers to the systolic myocardial function evaluated visually). With increasing dobutamine infusion (30–40 μg/kg/min), there was a further improvement in contractility of the inferior and posterior left ventricular walls and no further deterioration of function in the hypokinetic anterior wall. The contractility of the lateral wall (akinesia) did not change throughout the study. The dobutamine infusion was terminated at an infusion rate of 40 μg/kg/min. A target heart rate was not achieved because of chest discomfort and electrographic signs of ischaemia (2 mm ST depression in leads I, AVL and V5–V6).

Immediately after the dobutamine infusion was stopped, the contractility of the anterior left ventricular wall returned to normal, whereas the contractility of the posterior and inferior wall again deteriorated to baseline levels. These observations are summarized in Table 1.

Analysis of Regional Deformation

DMI data were acquired (Vingmed GE, Vivid Five) at baseline, low dobutamine dose (5–10 μg/kg/min), peak dobutamine dose (30–40 μg/kg/min) and during recovery. To evaluate radial function of the left ventricle, the data was recorded from the basal posterior wall segment (SAX). For longitudinal function, the data were acquired from the septum, lateral, inferior and anterior left ventricular walls divided for analysis into basal, mid and apical segments. The sampling rate for the DMI imaging was never lower than 150 fps. To obtain regional mean velocities, SR and ε, the DMI data were transferred to a workstation for off-line analysis with dedicated software (Speqle-Software Package for Echocardiographic Quantification, University of Leuven). For this study, only changes in peak systolic ε and the time of its occurrence are addressed.

The incremental dobutamine administration resulted in a gradual increase in peak regional ε in the basal segment of the posterior wall (Fig. 1) and also in three segments of the inferior wall (Fig. 2). For both radial and longitudinal deformation, the values of peak ε at peak dobutamine dose were almost three times those recorded at baseline (i.e. radial peak strain 10% — baseline, 19% — low dose, 31% — peak dose, 26% — recovery). Moreover, it is noteworthy, that the delay in peak thickening and shortening occurring after aortic valve closure (i.e. post-systolic thickening/shortening) was decreased in response to the dobutamine infusion. This was particularly prominent for radial deformation (i.e. the time to radial peak strain measured in relation to aortic valve closure: 88 ms, 83 ms, 55 ms, 105 ms, respectively). During recovery, the values of peak strain were lower and the peak deformation was shifted again towards early diastole, indicating an increase in post-systolic thickening/shortening.

The response of the left ventricular anterior wall to the dobutamine infusion was different (Fig. 3). In contrast to the pattern described above, there was no significant increase in peak ε values (note that this value is negative) for the three segments analysed (i.e. mid segment: −10%, −12%, −11%, −11%, respectively).

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In addition, the timing of peak deformation was different. The patterns obtained from mid and apical segments clearly showed that the dobutamine infusion resulted in a delay in peak deformation and an increase in the degree of post-systolic deformation (shortening) (i.e. mid segment — time to peak strain — 29 ms, 33 ms, 67 ms, 27 ms, respectively).

The peak ε values for the lateral wall were low and did not increase significantly throughout the study (Fig. 4). The only response recorded was a rise in the peak ε value obtained from the basal segment at low dobutamine dose. The remainder of the segments showed low or even positive peak ε values without a clear response to the dobutamine infusion.

Table 1 summarizes these results.

**Angiography**

The coronary angiograms were analysed by an investigator blinded to the echocardiographic data. These...
showed a dominant right coronary artery with a total occlusion of its proximal part (100%). A venous graft to the postero-descending branch of the right coronary artery was critically occluded (85%). There was also a 60% narrowing of the main stem of the left coronary artery and a total occlusion of the mid left anterior descending coronary artery. The arterial graft supplying the left anterior descending coronary artery territory was not changed. The remainder of the vessels presented either total occlusion (the second lateral branch of the Cx and the venous graft to the first lateral branch of the Cx) or a less severe lesion (proximal part of Cx — 65%) (Table 1).

**Positron Emission Tomography**

Positron emission tomography study was performed 2 weeks after the dobutamine stress echocardiography. Both $^{13}$N-labelled ammonia (as a perfusion tracer) and $^{18}$F-fluorodeoxyglucose (as a metabolic marker) were used for imaging. A zone showing a ‘mismatch’ pattern with reduced flow and preserved metabolism was identified in the anteroseptal wall extending to the apex (Fig. 5). In the lateral apical and mid segments, a ‘necrotic match’ pattern was found with a concordant reduction in perfusion and in F-fluorodeoxyglucose uptake. In contrast, the basal segment retained signs of metabolism (Fig. 5). In all other segments, both perfusion and metabolism were normal. The positron emission tomography results are displayed in Table 1 and are analysed in the following sections.

**Discussion**

Recently, indices of regional deformation — SR and $\varepsilon$ can be obtained from myocardial Doppler velocity data.
and can detect subtle and transient changes in percentage of wall thickening during dobutamine stress echocardiography. Both indices have been extensively studied in the experimental model of acute ischaemia and stunning.

The differentiation between ischaemic substrates described in this report, although already confirmed in experimental models, has not yet been reported in patients.

Posterior and Inferior Wall: Stunning

An e response, suggestive of the presence of regional myocardial stunning was observed in both the basal segment of the posterior wall (radial deformation) and in the inferior wall (longitudinal deformation). These territories were characterized by baseline wall motion abnormalities (hypokinesia) with low baseline systolic strain values. For the posterior wall and the basal segment of the inferior wall, the majority of baseline deformation occurred after aortic valve closure (i.e. post-systolic thickening/shortening) (Figs 1 and 2). The subsequent dobutamine infusion led to a consistent visual improvement in regional contractility up to the peak dose. This was mirrored by an increase in peak strain values and by a shift of peak deformation from being post-systolic to being systolic. In contrast to earlier experimental studies, the increase in contractile reserve could have been confirmed by peak strain values recorded at not only maximal dobutamine dose but also at low dose. On cessation of dobutamine infusion, this normalization of regional deformation returned to the abnormal baseline profile. The deformation findings were in agreement with the positron emission tomography data, where the inferior and posterior walls showed resting ‘match’ pattern with normal flow and metabolism diagnostic of regional stunning.

Anterior Wall: Ischaemia

An ischaemic response was found in the anterior wall. Although the resting contractility in this territory was normal (below the threshold of visual detection), the systolic e values were low and resting coronary flow measured by 13N-ammonia was compromised (Figs 3 and 5). The contractility in the anterior wall deteriorated progressively throughout the dobutamine infusion. The analysis of strain showed a slight increase in its peak systolic values at low dobutamine dose. This indicated a very limited contractile reserve. Such a minimal increase in peak strain values could not have been detected on visual assessment. A further increase in dobutamine dose resulted in a significant reduction in peak systolic strain. The analysis also showed the development and regression of post-systolic shortening, particularly prominent in the mid and apical segments of the anterior wall. These findings corresponded to a ‘mis-match pattern’ detected by positron emission tomography (Fig. 5) confirming the ischaemic but viable myocardium in these segments.

Lateral Wall: Infarction

Infarcted myocardium was detected in the lateral left ventricular wall. This wall was akinetic at baseline and did not improve its contractility during the dobutamine infusion. Peak strain values were low and (except for the basal segment) did not increase during the study. The value of peak strain recorded in the basal segment increased slightly and although there was no improvement in contractility, this segment could be regarded as viable. These findings were confirmed by positron emission tomography, where substantially reduced flow and metabolism in the apical and mid part of the lateral wall (necrotic ‘match pattern’) shifted into a ‘mismatch pattern’ towards the basal segment, i.e. representing reduced flow and preserved metabolism (Fig. 5). Thus, although a substantial part of the lateral wall appeared to be infarcted, its basal segment met the criteria of hibernating myocardium.

Summary

In this study four differing cardiac imaging modalities were used to evaluate a patient with coronary artery disease and to establish an adequate management. An overview of the results, together with the clinical conclusions extracted, is shown in Table 1.

Coronary angiography documented multivessel coronary artery disease affecting both native coronary arteries and the venous grafts implemented to the coronary vasculature. However, this method was unable to define the differing ischaemic substrates resulting from these coronary lesions. Positron emission tomography information was helpful in identifying viable myocardium, but failed to differentiate between normal and stunned myocardial segments as both situations lead to the same ‘match’ pattern of perfusion and metabolism.

The limitations of visual assessment of dobutamine stress echocardiography are commonly known. The subtle and transient changes in regional contractility remain undetected, which reduces the specificity of such an approach.

In the study described, the strain measurement allowed the clear differentiation between ischaemic, stunned and scarred myocardium. The truly regional information obtained helped to distinguish not only between differing ischaemic substrates (walls) but also between differing segments of the same wall. The quantification of dobutamine stress echocardiography with indices of regional deformation is clinically valuable and may have important therapeutic implications in patients with coronary artery disease.
References


