Low dose dobutamine echocardiography for predicting functional recovery after coronary revascularisation

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Abstract

Objective—To evaluate the effects of chronic coronary occlusion on the accuracy of low dose dobutamine echocardiography in predicting recovery of dysfunctional myocardium after revascularisation.

Design—Retrospective study.

Setting—Tertiary referral centre.

Patients—53 consecutive patients with ≥ 70% stenosis of the left anterior descending coronary artery (LAD) and regional ventricular dysfunction (group 1, non-occluded LAD; group 2, occluded LAD) who underwent dobutamine echocardiography.

Interventions—26 patients underwent coronary artery bypass grafting and 27 had percutaneous transluminal coronary angioplasty.

Main outcome measures—Baseline studies before revascularisation included cross sectional echocardiography at rest and during dobutamine infusion (5–10 µg/kg/min), and coronary angiography. The dobutamine study was performed mean (SD) 35 (28) days before revascularisation. Echocardiography at rest was repeated 90 (48) days after revascularisation.

Results—Of 296 dysfunctional segments, 63 in group 1 (43%; 63/146) and 69 in group 2 (46%; 69/150) improved at follow up. Mean (SD) regional wall motion score index decreased from 1.97 (0.49) (95% confidence interval (CI) 1.01 to 2.93) before revascularisation to 1.74 (0.52) (95% CI 1.30 to 2.98) at follow up in group 1 (p = 0.001), and from 2.12 (0.41) (95% CI 1.30 to 2.98) to 1.88 (0.36) (95% CI 1.16 to 2.60) in group 2 (p = 0.0006). In group 1, sensitivity (87% ± 52%; p < 0.0001), negative predictive value (88% ± 65%; p = 0.001), and accuracy (77% ± 64%; p = 0.01) were all significantly higher than in group 2, despite the angiographic evidence of collaterals in patients with occluded vessels.

Conclusions—Dobutamine echocardiography shows reduced sensitivity in predicting recovery of dysfunctional myocardium supplied by totally occluded vessels. Thus caution should be used in selecting such patients for revascularisation on the basis of a viability assessment made in this way. (Heart 2001;86:679–686)

Keywords: dobutamine; coronary artery disease; viability; chronic occlusion

Dobutamine echocardiography is currently used to predict recovery of regional and global left ventricular systolic function in patients with chronic coronary artery disease. Inotropic stimulation with dobutamine results in a transient amelioration of contractile dysfunction in viable myocardium which is highly predictive of functional recovery following revascularisation.1 4 However, although the specificity of the test is very high its sensitivity has been reported to be suboptimal, especially in the setting of severely dysfunctional myocardium.4 5 It has been shown that enhancement of contractile function by dobutamine relies on preservation of coronary flow reserve, leading to an increase in blood flow in dysfunctional myocardium.5 6 However, coronary reserve is correlated with the severity of coronary artery stenosis and is greatly reduced in territories supplied by occluded vessels.6 9 Thus it is conceivable that the accuracy of the test may vary in relation to the patency of the vessel, but very limited data evaluating such a hypothesis have so far been reported.10

The aim of our present study was to evaluate whether the accuracy of low dose dobutamine echocardiography is influenced by the patency of coronary vessels and by the development of a collateral circulation in patients with chronic coronary artery disease. We selected patients with left anterior descending coronary artery (LAD) disease because revascularisation of the LAD has a greater impact on left ventricular function and prognosis,13 15 and because it minimises the source of overlap among different vascular territories.

Methods

PATIENT POPULATION

Our patient population was selected from a consecutive group of 170 patients who formed part of a prospective protocol at our institution. The criteria for entering the study were first, the presence of ≥ 70% diameter stenosis in the LAD; and second, regional wall motion abnormalities at rest in one or more myocardial segments belonging to the LAD territory, identified on both cross sectional echocardiography and contrast ventriculography.

Patients with myocardial infarction, unstable angina, or congestive heart failure occurring within one month of the study were excluded; additional exclusion criteria were: ≥ 50% left main stenosis, significant valvular disease,
previous coronary artery bypass graft surgery, and technically inadequate echocardiographic images.

One hundred and twenty nine patients (120 men and nine women) met the entry criteria, and 110 of these (85%) had a history of previous myocardial infarction. In 90 of the latter (70%), the infarct occurred in the LAD territory. Among the 129 patients, an occluded LAD was present in 51 and a significantly stenosed LAD in the remaining 78. Sixty patients belonging to this initial population were revascularised. The decision to carry out revascularisation was based on stable angina in 35 patients (58%), angina at rest in nine (15%), positive stress test in 11 (18%), and worsening heart failure in the remaining five (8%), but not on myocardial viability. Seven patients refused to have echocardiographic studies after revascularisation. Therefore the remaining 53 patients (50 men and three women, mean (SD) age 59 (7) years) represent the study population. This was divided in group 1 (non-occluded LAD; 27 patients; mean stenosis 82 (12)% and group 2 (occluded LAD; 26 patients). As detailed in table 1, the two groups did not differ with respect to age, history of anterior infarction, clinical symptoms, prevalence of multi-vessel disease, baseline left ventricular ejection fraction, or preoperative global and regional (LAD territory) wall motion score index (WMSI).

**STUDY PROTOCOL**

Baseline studies before revascularisation included cross sectional echocardiography at rest and during dobutamine infusion. Forty six patients also underwent thallium SPECT and dobutamine echocardiography. 201Thallium images were acquired using the same examination criteria. thallium injection, as previously described. Thirty two images were acquired from a 30° right anterior oblique to a 60° left posterior oblique view in 6° increments.

**CORONARY ANGIOGRAPHY**

All patients underwent cardiac catheterisation. Left ventriculography and coronary angiography were carried out by the Judkins technique. The left and right coronary arteries were imaged in multiple views, including craniocaudal angulations. To minimise the potential effect of coronary vasoconstriction, contrast injection was performed after intracoronary administration of glyceryl trinitrate (200 µg). The number of diseased vessels did not differ significantly between the two groups of patients (table 1).

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**Table 1 Characteristics of the patient population**

<table>
<thead>
<tr>
<th></th>
<th>Non-occluded LAD (group 1, n=27)</th>
<th>Occluded LAD (group 2, n=26)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>59 (6)</td>
<td>58 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>26</td>
<td>24</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9 (31%)</td>
<td>8 (28%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>11 (40%)</td>
<td>10 (37%)</td>
<td>NS</td>
</tr>
<tr>
<td>Previous anterior MI</td>
<td>15 (56%)</td>
<td>16 (61%)</td>
<td>NS</td>
</tr>
<tr>
<td>Q wave</td>
<td>15 (56%)</td>
<td>4 (15%)</td>
<td>NS</td>
</tr>
<tr>
<td>Non-Q-wave</td>
<td>4 (15%)</td>
<td>3 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Angiographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>21 (77%)</td>
<td>20 (78%)</td>
<td>NS</td>
</tr>
<tr>
<td>Proximal stenosis</td>
<td>17 (63%)</td>
<td>16 (62%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diameter stenosis (%)</td>
<td>77 (8)</td>
<td>100</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Collateral channels to LAD</td>
<td>1 (3%)</td>
<td>22 (85%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Echocardiographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>44 (11)</td>
<td>41 (9)</td>
<td>NS</td>
</tr>
<tr>
<td>WMSI</td>
<td>1.68 (0.33)</td>
<td>1.9 (0.37)</td>
<td>NS</td>
</tr>
<tr>
<td>Regional WMSI</td>
<td>1.97 (0.48)</td>
<td>2.12 (0.41)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean (SD) or n (%).

LAD, left anterior descending coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; WMSI, wall motion score index.
Low dose dobutamine echocardiography and coronary revascularisation

Echocardiography. The short axis mid-
the left ventricle was divided into 16 segments
dial motion and wall thickening. For analysis,
and was assessed visually using both endocar-
chordal, papillary muscle, and apical levels,
pre-revascularisation study results.
low up, the operators were not aware of the
echocardiography was performed during fol-
the clinical and angiographic results. When
independent operators who were unaware of
by continuous display. This was done by two
analysed o
Undigitised echocardiographic images were
ECHOCARDIOGRAPHIC ANALYSIS
Figure 1 Pie chart showing the division of left ventricle
into 16 segments in short axis tomograms at chordal (upper), mid-papillary (medium), and apical (lower) levels. White segments were assigned to the left anterior descending coronary artery (LAD) territory.

Undigitised echocardiographic images were
analysed off line from the videotape playback
by continuous display. This was done by two
independent operators who were unaware of
the clinical and angiographic results. When
echocardiography was performed during fol-
low up, the operators were not aware of the
pre-revascularisation study results.

Regional wall motion was evaluated at the
chordal, papillary muscle, and apical levels,
and was assessed visually using both endocar-
dial motion and wall thickening. For analysis,
the left ventricle was divided into 16 segments
as recommended by the American Society of
Echocardiography.16 The short axis mid-
ventricular images at the chordal and mid-
papillary muscle levels were divided into six
myocardial segments, starting at the 3 o’clock
position and proceeding clockwise, represent-
ing posterolateral, inferior, posterosetal, an-
tero septal, anterior, and anterolateral myocar-
dium, respectively. Short axis images at the
apical level were divided into four myocardial
segments, starting at the half past one o’clock
position and proceeding clockwise, represent-
ing lateral, inferior, septal, and anterior apical
myocardium. The LAD territory was defined
as basal, mid, and distal segments of the left
anterior wall, basal and mid segments of the
anterior and posterior septum, and the distal
septum, the total number of segments being
eight (fig 1). To evaluate regional systolic func-
tion, wall motion and thickening were graded
semiquantitatively using a scoring system
where 1 = normal contraction, 2 = hypokinesia
(severely reduced wall thickening and inward
motion), 3 = akinesia (absence of wall motion
and of systolic thickening), and 4 = dyskinesia
(absence of wall thickening and outward
motion). Systolic function was scored at rest
and at each dobutamine dose.

Regional systolic dysfunction was defined
when a score of ≥ 2 was assigned to a myocar-
dial segment in at least two different echocar-
diographic views. Viable myocardium was
defined as an improvement of functional score
of ≥ 1 grade in at least one segment with rest
hypokinesia or akinesia. Myocardial scarring
was identified in segments with resting dys-
function that did not show improvement
during low dose dobutamine echocardi-
ography. Recovery in the LAD territory was
defined as improvement in functional score by
≥ 1 grade of one or more septal or anterior
segments compared with the preoperative rest
study. For both preoperative and postoperative
rest echocardiograms, a WMSI was derived
(the sum of individual wall motion scores
divided by the respective number of segments)
for the entire ventricle (global WMSI) and for
the LAD territory (regional WMSI).

The reproducibility of the echocardi-
graphic analysis in our laboratory has been
reported previously.3 In particular, exact agree-
ment in segmental scores (including function
at rest and during inotropic stimulation) was
82% (κ value 0.62; p < 0.01), and in 97.5% of
all segments analysed the score difference
between two echocardiographic readings was
within 1 point.

Our interobserver and intraobserver repro-
ducibility of the global left ventricular ejection
fraction was analysed by the Bland–Altman
method. This analysis showed no significant
difference for either interobserver variability
(τ = 0.37; NS) or intraobserver variability
(τ = 0.3; NS). According to our variability
methods, a cut off point of 6% was chosen to
distinguish patients with or without a signifi-
cant improvement in postrevascularisation
ejection fraction.

211THALLIUM IMAGING

In each patient, four consecutive mid-
ventricular slices from the short axis series were
considered. Tomograms were then divided into
six sectors of equal arc, representing the poste-
rolateral, inferior, posterosetal, anteroseptal,
anterior, and anterolateral myocardium.4 The
sectors from two consecutive three pixel thick
short axis tomograms were then grouped and
averaged. Thus 12 myocardial regions were
analysed for each patient. Of these segments,
six were assigned to the territory of the LAD,
four (two anterolateral and two posterolateral)
were assigned to the territory of left circumflex
coronary artery, and two inferior segments
were assigned to the territory of the right
coronary artery (fig 1). Alignment and analysis
of the studies were visually made by two opera-
tors unaware of the echocardiographic results.

A cut off point of 65% was used to
distinguish viable from non-viable myocar-
dium.17
CORONARY ANGIOGRAPHY ANALYSIS
All coronary angiograms were analysed by an investigator who had no knowledge of the results of the echocardiograms. Each vessel was visualised in multiple views, and the most severe appearing lesion was selected for analysis. Care was taken to avoid overlap of adjacent branches. Vessel occlusion was defined as a lesion with no anterograde distal flow. Collateral circulation was graded according to the classification of Rentrop and colleagues: 0 = no visible collateral, 1 = collateral filling of the vessel branches without reaching the epicardial artery, 2 = partial filling of the epicardial artery, and 3 = complete filling of the epicardial artery.

STATISTICAL ANALYSIS
Statistical analysis was performed with the SPSS statistical package. Unpaired and paired t tests were used to compare continuous variables. Values are reported as mean (SD) and 95% confidence intervals. Bonferroni’s correction was used for multiple group comparisons.

Results
Angiographic collateral flow to the LAD was present in one patient in group 1 without occlusion (1/27; 3%) and in 22 patients in group 2 (22/26; 85%) with an occluded LAD (p < 0.00001). There were no significant differences in clinical characteristics between the two groups (table 1). The left ventricular ejection fraction was 44 (11)% (95% CI 22% to 66%) in group 1, and 41 (9)% (95% CI 23% to 59%) in group 2 (NS).

Twenty seven patients underwent transluminal coronary angioplasty (PTCA; 11 patients in group 1 and 16 patients in group 2); successful dilatation—defined as a diameter of the residual stenosis not exceeding 30% of the lumen diameter—was achieved in all cases. The remaining 26 patients underwent coronary artery bypass grafting (CABG; 16 in group 1 and 10 in group 2); in all these cases grafting of the LAD was successful. The internal mammary artery was used in 10 patients (six in group 1 and four in group 2). No patients had major complications associated with the revascularisation procedure.

In all, we evaluated 424 myocardial segments belonging to the LAD territory; 296 (70%) of these were dysfunctional, including 146 in group 1 and 150 in group 2. Figure 2 shows the data on systolic function in the segments evaluated.

SEGMENTAL ANALYSIS
In group 1 patients, 79 (54%) of 146 dysfunctional segments were hypokinetic and 67 (46%) were akinetic. In group 2, 60 (40%) of 150 dysfunctional segments were hypokinetic (NS v group 1) and 90 (60%) were akinetic (p = 0.03 v group 1).

The number of dysfunctional segments showing contractile reserve during low dose dobutamine echocardiography was significantly higher in group 1 than in group 2 patients (81 of 146 (55%) v 57 of 150 (38%); p = 0.002; fig 3). This difference was mostly accounted for by the higher percentage of akinetic segments showing contractile reserve in group 1 patients than in group 2 patients, although this difference was not significant (16/67 (24%) v 13/90 (14%), respectively) (fig 3).

A biphasic response was observed in only three segments (1%), one in group 1 and two in group 2.

Of 296 dysfunctional segments in the LAD territory undergoing revascularisation, 132 (44%) improved at follow up. Recovery of regional function was not affected by the patency of the coronary vessel, as it occurred in 63 (43%) of 146 dysfunctional segments in group 1 and 69 (46%) of 150 dysfunctional segments in group 2 (NS). In particular, improvement was observed in 45 (57%) of 79 hypokinetic segments in group 1 and in 35 (58%) of 60 hypokinetic segments in group 2 (NS), as well as in 18 (27%) of 67 akinetic segments in group 1 and 34 (38%) of 90 akinetic segments in group 2 (NS) (fig 4).

Sensitivity, specificity, accuracy, and positive and negative predictive power for dobutamine echocardiography and thallium SPECT in predicting functional recovery after revascularisation are reported in table 2. Low dose

![Figure 2](image-url) Regional systolic function represented as the percentage of segments showing normal contraction, hypokinetic, and akinetic in patients with a non-occluded left anterior descending coronary artery (LAD; white bars) and an occluded LAD (black bars). The percentage of akinetic segments was significantly higher in patients with an occluded LAD.

![Figure 3](image-url) Percentage of dysfunctional segments showing contractile reserve on low dose dobutamine echocardiography in patients with a non-occluded left anterior descending coronary artery (LAD; white bars) and an occluded LAD (black bars).
Low dose dobutamine echocardiography and coronary revascularisation

Table 2 Accuracy of low dose dobutamine echocardiography (LDDE) and ²⁰¹Thallium SPECT in predicting functional recovery after revascularisation in patients with a non-occluded (group 1) and an occluded (group 2) left anterior descending coronary artery

<table>
<thead>
<tr>
<th></th>
<th>LDDE</th>
<th>²⁰¹Thallium SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>87% (55/63)</td>
<td>52% (36/69)***</td>
</tr>
<tr>
<td>Specificity</td>
<td>74% (57/78)</td>
<td>64% (60/98)**</td>
</tr>
<tr>
<td>Accuracy</td>
<td>77% (112/146)</td>
<td>64% (96/150)*</td>
</tr>
<tr>
<td>PPV</td>
<td>68% (55/81)</td>
<td>63% (36/57)</td>
</tr>
<tr>
<td>NPV</td>
<td>88% (57/66)</td>
<td>65% (60/95)**</td>
</tr>
</tbody>
</table>

*p = 0.01; **p = 0.001; ***p < 0.0001 v group 1.
†p < 0.05; ††p < 0.01; †††p < 0.0001 v LDDE.
NPV, negative predictive value; PPV, positive predictive value; SPECT, single photon emission computed tomography.

Table 3 Accuracy of low dose dobutamine echocardiography (LDDE) and ²⁰¹Thallium SPECT in predicting functional recovery after revascularisation of akinetic segments in patients with a non-occluded (group 1) and an occluded (group 2) left anterior descending coronary artery

<table>
<thead>
<tr>
<th></th>
<th>LDDE</th>
<th>²⁰¹Thallium SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>72% (13/18)</td>
<td>26% (9/34)***</td>
</tr>
<tr>
<td>Specificity</td>
<td>94% (46/49)</td>
<td>63% (52/86)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>88% (59/67)</td>
<td>68% (61/90)**</td>
</tr>
<tr>
<td>PPV</td>
<td>81% (13/16)</td>
<td>69% (9/13)</td>
</tr>
<tr>
<td>NPV</td>
<td>90% (46/51)</td>
<td>67% (52/77)**</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01; ***p < 0.001 v group 1.
†p > 0.05; ††p < 0.01; †††p < 0.0001 v LDDE.
NPV, negative predictive value; PPV, positive predictive value; SPECT, single photon emission computed tomography.

Figure 4 Effects of revascularisation on regional systolic function. The percentage of improved hypokinetic and akinetic segments did not differ between patients with a non-occluded left anterior descending coronary artery (LAD; white bars) and an occluded LAD (black bars).

To investigate whether the degree of the collateral circulation influenced the dobutamine echocardiography results, patients with an occluded LAD were further subdivided into group 2A with a well developed collateral circulation (n = 18; Rentrop class III and II), and group 2B with a less well developed collateral circulation (n = 8; Rentrop classes I and 0). In group 2A, the sensitivity and accuracy were significantly reduced compared with group 1 patients (53% v 87%; p < 0.0001; and 65% v 77%; p = 0.036), but not different from group 2B (50% and 60%, respectively). No significant differences in specificity were observed among the three groups of patients. In contrast, recovery of contractile function was not affected by the status of the coronary artery before revascularisation, as regional wall motion improved to a similar degree in the three groups of patients (table 5).

²⁰¹Thallium SPECT data were available on 183 (62%) of 296 dysfunctional segments (93 of group 1 and 90 of group 2). In group 2 (table 2), ²⁰¹thallium SPECT showed a significantly higher sensitivity than low dose dobutamine echocardiography (72% v 52%; p < 0.05), whereas in the same comparison in group 1 there was lower specificity (21% v 60%; p < 0.0001), lower accuracy (59% v 77%; p < 0.01), and reduced negative predictive value (37% v 88%; p < 0.0001). These data were also confirmed when further analysis was restricted to akinetic segments (table 3).

**PATIENT ANALYSIS**

In the whole group of patients, left ventricular ejection fraction increased significantly from 43 (9%) (95% CI 25% to 61%) before revascularisation to 47 (9%) (95% CI 29% to 65%) afterwards (p < 0.001). Left ventricular ejection fraction improved similarly in patients undergoing PTCA (from 43 (10%) (95% CI 23% to 63%) to 47 (10%) (95% CI 27% to 67%)) (p < 0.001) and in those subjected to CABG (from 41 (11%) (95% CI 19% to 63%) to 45 (11%) (95% CI 23% to 67%) (p < 0.001).

Improvement in left ventricular ejection fraction was more pronounced in grouped 2 patients (from 41 (9%) (95% CI 23% to 59%) to 47 (7%) (95% CI 33% to 61%)) (p < 0.001), whereas this did not reach significance in group 1 patients (from 44 (11%) (95% CI 22% to 66%) to 46 (10%) (95% CI 26% to 66%) (NS).

We compared the accuracy of low dose dobutamine echocardiography and ²⁰¹thallium SPECT in predicting global left ventricular function after revascularisation in patients with single vessel revascularisation. These data are reported in table 6. We found a threshold of at least two viable segments conferring optimal values of accuracy. In group 1, low dose dobutamine echocardiography showed a similar value for sensitivity but a higher value for accuracy than ²⁰¹thallium SPECT, whereas in group 2, ²⁰¹thallium SPECT showed better sensitivity (89% v 44%) and accuracy (60% v 57%) than low dose dobutamine echocardiography.
Table 5: Accuracy of low dose dobutamine echocardiography (LDDE) and the effects of revascularisation in patients with a non-occluded left anterior descending coronary artery (LAD) (group 1), an occluded LAD and collaterals of class II–III (group 2A), and an occluded LAD and collaterals of class 0–I (group 2B)

<table>
<thead>
<tr>
<th>Group</th>
<th>LDDE sensitivity</th>
<th>LDDE specificity</th>
<th>LDDE accuracy</th>
<th>Regional WMSI Pre-</th>
<th>Regional WMSI Post-</th>
<th>Regional WMSI change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>87%</td>
<td>69%</td>
<td>77%</td>
<td>1.97 (0.48)</td>
<td>1.74 (0.53)</td>
<td>12</td>
</tr>
<tr>
<td>Group 2A</td>
<td>53%**</td>
<td>73%</td>
<td>65%*</td>
<td>2.26 (0.33)</td>
<td>2.01 (0.30)</td>
<td>9</td>
</tr>
<tr>
<td>Group 2B</td>
<td>50%</td>
<td>75%</td>
<td>60%</td>
<td>1.81 (0.52)</td>
<td>1.50 (0.36)</td>
<td>12</td>
</tr>
</tbody>
</table>

| *p < 0.05; **p < 0.0001 v group 1. |
| †p < 0.05; ††p < 0.01 v regional WMSI pre-revascularisation. |

Table 6: Accuracy of low dose dobutamine echocardiography (LDDE) and ⁹⁹mTc-Tl SPECT in predicting global left ventricular functional recovery after single vessel revascularisation for either a non-occluded (group 1) or an occluded (group 2) left anterior descending coronary artery

<table>
<thead>
<tr>
<th>LDDE</th>
<th>¹⁹⁹mTc-Tl SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Sensitivity 100% (4/4)</td>
<td>44% (4/9)</td>
</tr>
<tr>
<td>Specificity 28% (2/7)</td>
<td>66% (4/6)</td>
</tr>
<tr>
<td>Accuracy 54% (6/11)</td>
<td>57% (8/15)</td>
</tr>
<tr>
<td>PPV 44% (4/9)</td>
<td>66% (4/6)</td>
</tr>
<tr>
<td>NPV 100% (2/2)</td>
<td>44% (4/9)</td>
</tr>
</tbody>
</table>

NPV, negative predictive value; PPV, positive predictive value; SPECT, single photon emission computed tomography.

**Discussion**

**ACCURACY OF LOW DOSE DOBUTAMINE ECHOCARDIOGRAPHY IN PREDICTING REVERSIBILITY OF REGIONAL DYSFUNCTION**

Our main finding in the present study was that low dose dobutamine echocardiography is not very accurate in predicting recovery of dysfunctional myocardium supplied by occluded coronary arteries. In fact, only 52% of segments supplied by an occluded LAD that improved after revascularisation were identified by dobutamine echocardiography. In addition, 35% of the segments supplied by occluded vessels that did not show contractile reserve improved after revascularisation. Sensitivity further decreased in severely dysfunctional myocardium, as only 26% of akinetic viable segments supplied by an occluded LAD were identified by dobutamine echocardiography. Low dose dobutamine echocardiography also showed a lower sensitivity in patients with occluded vessels when global left ventricular functional recovery was analysed.

Various pathophysiological mechanisms may account for this finding. It has been reported that transient amelioration of myocardial dysfunction during inotropic stimulation—the hallmark of viability using dobutamine echocardiography—depends on the recruitment of residual coronary reserve which allows an increase of blood flow in the dysfunctional myocardium. However, when coronary reserve is compromised, recruitment of inotropic reserve is rapidly followed by the development of ischaemia and a deterioration in function, even in the absence of completely occluded coronary vessels. This hypothesis is strengthened by our ⁹⁹mTc-Tl SPECT data, which showed a better sensitivity and accuracy than low dose dobutamine echocardiography only in the patients with occluded vessels.

In patients with occluded coronary vessels, flow reserve has been reported to be greatly attenuated or completely lost during dipyridamole infusion. It is conceivable that in this case the increase in blood flow in the dysfunctional myocardium may be inadequate to cause transient contractile improvement, or it may result in a very mild and transient functional enhancement undetectable by our current semiquantitative analysis of echocardiographic images.

Experimental data further indicate that the accuracy of dobutamine for identifying dysfunctional myocardium is decreased when a substantial amount of necrotic myocardium coexists in the same territory, even when blood flow is restored at reperfusion. In addition, reversible degradation of the cellular contractile apparatus in long standing dysfunctional myocardium may also contribute to the lack of contractile reserve, generating a false negative response.

Thus it is conceivable that different mechanisms may contribute to reducing the accuracy of dobutamine for identifying severely dysfunctional viable myocardium.

**PREVIOUS STUDIES**

Despite the theoretical limitations of the test in the setting of occluded coronary arteries, there are few data on its use in such patients. In a population of 12 patients with a chronically occluded left anterior descending coronary artery and a moderately depressed ejection fraction, Afridi and colleagues reported a positive and negative predictive accuracies for dobutamine echocardiography of 100% and 86%, respectively, for improvement in dysfunctional myocardium after revascularisation, though sensitivity and specificity were not reported. A high negative predictive accuracy is at variance with our findings in the present study, where a suboptimal value was observed, indicating that many akinetic segments defined as non-viable by dobutamine do recover after revascularisation. The short (one month) follow up evaluation in Afridi’s study may partly explain this discrepancy, as it has been reported that a longer time interval may be required for dysfunctional myocardium to recover completely. Thus a longer period of follow up in that study might have allowed recovery of additional dysfunctional segments, so reducing the observed negative predictive value of the test.

**VIABILITY IN COLLATERAL DEPENDENT MYOCARDIUM**

Another important observation of the current study is that recovery of function occurs in about half the dysfunctional segments supplied by occluded vessels, and results in a significant increase in global left ventricular ejection fraction, that is one of the main determinants of survival in patients with coronary artery disease. However, the degree of collateral flow did not predict the occurrence of functional recovery, indicating that viability—at least in terms of the possibility of recovery of contractile function at rest—is not always associated.
with the presence of a collateral circulation on angiography.

This finding supports the observation of Di Carlì and colleagues, who reported that viability evaluated by positron emission tomography is detectable in only 58% of dysfunctional regions supplied by an occluded vessel where there is angiographic evidence of collaterals. It is also consistent with the data of Sabia and associates, who showed a lack of correlation between the degree of wall motion improvement after revascularisation and blood flow supply before revascularisation in patients with recent myocardial infarction.

Taken together, these data indicate that angiographic evaluation of collateral circulation should not be used to predict myocardial viability in patients with chronic coronary artery disease and occluded coronary arteries who are candidates for revascularisation.

STUDY LIMITATIONS

Repeat coronary angiography was not performed in the present study. Thus restenosis at the time of follow up cannot be excluded with certainty. However, no patient developed symptoms or had evidence of ischaemia on investigation, which minimises the likelihood of restenosis. In addition, the observation that most segments with unchanged function after revascularisation were in the same vascular territories as segments that showed improved function reduces this possibility still further.

Another limitation of the study is that recovery of viable dysfunctional segments may not have been complete by three months after revascularisation. However, this would tend to reduce the negative predictive value further, making our results understated.

Visual analysis of regional function may represent a limitation of the echocardiographic technique, especially in large ventricles, whereas in the present study left ventricular function and dimensions were preserved or were only moderately abnormal.

Currently, there are no reliable quantitative methods for evaluating regional function, and such methods as there are do not represent gold standard analyses at present. In addition, visual analyses from videotapes might impair reproducibility. However, data from our laboratory indicate excellent reproducibility for videotape analysis, especially for akinetic myocardium. In the present study only low dobutamine doses were used. However, the biphasic contractile response induced by high dobutamine doses, while being very specific, is less sensitive at predicting functional recovery than the low dose response. By not using high doses, we might have missed a deterioration in the function of akinetic segments that showed improvement at low dosage; in this way we may have included among the viable myocardial segments both those showing sustained improvement (for which the positive accuracy is reduced) and those with a potential biphasic response (for which the positive accuracy is very high). This would tend to maximise sensitivity while reducing specificity. However, the sensitivity of dobutamine was suboptimal in the present study, so the use of only low doses would only diminish the impact of our findings rather than exaggerate it. Moreover, our negative accuracy in akinetic segments was 65%—in other words, 35% of akinetic segments that did not improve with dobutamine recovered after revascularisation. As demonstrated by Afridi and colleagues and Panza and associates, the vast majority of segments showing transient improvement do so at dobutamine doses of 10 µg/kg/min. Thus it is very unlikely that the 35% of segments classified as negative using low doses would improve at higher doses. This gives further support to our conclusion that the use of low dobutamine doses did not affect the main findings of the study.

Finally a factor that may hamper the evaluation of segmental motion is the presence of postsurgical paradoxical septal motion. We do not believe that this could have hampered our results as more than half our patients were treated by PTCA and as a combination of both inward motion and myocardial wall thickness was used in evaluating regional function.

CLINICAL IMPLICATIONS AND CONCLUSIONS

Our study shows that recovery of function occurs in a sizeable number of revascularised dysfunctional segments supplied by occluded coronary arteries. Identification of such myocardial territories remains a problem, as neither the presence of collaterals nor the response to inotropic stimulation using dobutamine echocardiography is sufficiently accurate in predicting the functional effects of revascularisation under these circumstances. However, the limited number of such patients so far reported emphasises the need for further confirmation of our findings.

An unusual hyperkalaemia induced block

The tracing below was recorded from a patient with a DDD pacemaker and hyperkalaemia (7.8 mEq/l) caused by acute renal failure. The atrial mechanism is sinus at a rate of 110/min. Every sinus P wave is followed by a ventricular spike, but several of these fail to depolarise the myocardium. The paced QRS complexes are extremely wide, measuring about 0.38 seconds. There is a basic 2:1 block of artificial stimuli; following a ventricular capture, the ensuing spike falls at the apex of the T wave during the refractory period. This is caused by the extreme prolongation of the ventricular depolarisation and repolarisation process. In addition, spike-to-QRS intervals show a gradual lengthening, ending in block of two consecutive stimuli.

The association of 2:1 block with progressive prolongation of the conduction intervals up to block of two or three consecutive impulses is known as “alternating Wenckebach periodicity”. This phenomenon is well recognised in atioventricular conduction, particularly in atrial flutter, but has not been hitherto observed in conduction between an artificial pacemaker and the ventricular myocardium.

Correction of the hyperkalaemia was followed by normal ventricular capture and narrowing of the QRS complexes.

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Low dose dobutamine echocardiography for predicting functional recovery after coronary revascularisation

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Heart 2001 86: 679-686
doi: 10.1136/heart.86.6.679

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