Value of real-time three-dimensional adenosine stress contrast echocardiography in patients with known or suspected coronary artery disease

Constantina Aggeli, Ioannis Felekos*, George Roussakis, Christina Kazazaki, Staurola Lagoudakou, Panagiota Pietri, Dimitrios Tousoulis, Christos Pitsavos, and Christodoulos Stefanadis

1st Department of Cardiology, University of Athens Medical School, Hippokration Hospital, 63, Kasomouli St, N.Kosmos, 11744 Athens, Greece

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Aim
The aim of this study was to evaluate the feasibility of myocardial wall-motion and perfusion assessment using contrast echocardiography during real-time three-dimensional (RT3D) adenosine stress test, and compare its diagnostic accuracy with the two-dimensional (2D) method using coronary angiography as reference.

Methods and results
Patients with known or suspected coronary artery disease (CAD) have been submitted to adenosine stress contrast echocardiography and coronary angiography, within a 1-month period. Two-dimensional apical four, two, and three chamber, as well as three-dimensional (3D) pyramidal full-volume data sets were acquired at rest and at peak stress. The 17-segment division of the left ventricle was used and each segment was evaluated based on wall motion and perfusion. Sixty patients (age: 60.1 ± 8.5 years, 38 men) were enrolled, i.e. 1020 segments were evaluated at rest and at peak stress. Wall-motion analysis per patient revealed that the sensitivity and specificity of 2D to detect CAD were 80 and 82% and of RT3D echocardiography were 82 and 64%, respectively, whereas in the per patient perfusion analysis the respective percentages were 88, 64% for 2D and 90, 73% for RT3D. Regarding left anterior descending artery and right coronary system, there seems to be no statistical significant difference in terms of wall-motion and perfusion evaluation between the two modalities.

Conclusions
Real-time 3D adenosine stress echocardiography is a feasible and valuable technique to evaluate myocardial wall motion and perfusion in patients with suspected CAD, despite existing problems concerning lower spatial and temporal resolution when compared with 2D echocardiography.

Keywords
Real-time 3D echocardiography • Adenosine stress contrast echocardiography • Coronary artery disease

Introduction
Stress echocardiography is a safe, well-established, and validated non-invasive method for both the diagnosis and prognosis of coronary artery disease (CAD).1,2 Recently, diagnosis of the extent and severity of myocardial perfusion abnormalities has become feasible with the development of myocardial contrast echocardiography (MCE), which enables the assessment of myocardial perfusion, following the intravenous infusion of an ultrasound contrast agent. MCE is being increasingly used for CAD detection, as well as for myocardial viability assessment.3–6

However, the complex anatomy, as well as the sophisticated function of the heart mandates the transition from two-dimensional to three-dimensional approach. Thus, real-time three-dimensional (RT3D) echocardiography has been introduced as a novel technique in clinical practice,7–10 especially after the integration of matrix array technology in modern ultrasound equipment. Concerning stress echocardiography, RT3D has distinct advantages, offering offline manipulation of three-dimensional (3D) images, the ability to obtain multiple and modified sections of any desired segment, virtual elimination of off-axis acquisition, and shorter acquisition time.11,12 Nevertheless, the clinical utility...
and value of RT3D, in stress echocardiography remains yet to be determined.

Therefore, the aims of the current study were: (i) to establish the feasibility of RT3D adenosine stress contrast echocardiography in detecting wall-motion and perfusion abnormalities, (ii) to compare this novel method with the respective 2D technique in terms of wall-motion and perfusion evaluation, and (iii) to validate the data derived from the RT3D echocardiographic study by those of the coronary angiography, used as the reference method for the assessment of CAD.

Methods

Study population

Sixty patients (age 60.1 ± 8.5 years), with known or suspected CAD, were referred to our tertiary hospital for clinically indicated stress echocardiography or coronary angiography. Indications for stress echo were consistent with the 2008 published appropriateness criteria for stress echocardiography and included: 27 (45%) symptomatic patients with intermediate or high-risk factors for CAD, without history of prior myocardial infarction, 6 (10%) patients with uninterpretable ECG, 18 (30%) asymptomatic or symptomatic patients who had undergone percutaneous coronary interventions for revascularization, as well as 9 (15%) high-risk patients with poor functional capacity (<4 METS) who were scheduled for major extracardiac surgery. Exclusion criteria included the following: myocardial infarction, unstable angina, CABC, BMI >30 kg/m², second- or third-degree atrioventricular block, wheezing, systolic blood pressure <90 mmHg, pregnancy or lactation, uncontrolled hypertension, cardiomyopathy, history of cerebellar haemorrhage in the past 2 years. Patients not in sinus rhythm, as well as those with uncontrolled symptoms of congestive heart failure or severe valvular disease were also excluded. Furthermore, patients with known or suspected intracardiac shunting, or documented hypersensitivity to the contrast agent, were not included in our study since the latter conditions constitute absolute contraindications for contrast agent infusion according to the EMEA statement. Participants were asked to abstain from consumption of food and beverages containing xanthine derivatives for >24 h prior to the study and anti-ischaemic therapy (in particular beta-blockers) was withdrawn for 24 h, as it could influence wall-motion interpretation. All of them provided written informed consent prior to adenosine testing. The hospital Ethics Committee has approved the protocol.

Adenosine stress contrast echocardiography

All studies were performed with the Philips iE33 ultrasound machine (Philips Medical Systems, Bothell, WA, USA). Patients were examined in the left decubitus position after establishing an intravenous line for adenosine and echo-contrast agent (sulphur hexafluoride microbubbles, SonoVue, Bracco International B.V.) infusion. Blood pressure and heart rate were closely monitored during the stress protocol, while 12-lead electrocardiograms were obtained before and after adenosine infusion. Adenosine stress contrast protocol was performed as we have previously published. Adenosine was infused intravenously at a rate of 140 μg/kg over 6 min, under continuous electrocardiographic monitoring. Echo-contrast agent was continuously infused through an infusion pump at a rate of 0.8–1.0 mL/min, at baseline and during the last 3 min of adenosine infusion as recommended by the European Association of Echocardiography, in order to opacify the endocardial borders of the left ventricle and to evaluate myocardial perfusion. Two-dimensional images and subsequently the 3D data sets were obtained at baseline and at the end of the adenosine protocol, with a rapid switch between the two modes (2D and RT3D).

The 2D data were acquired using the 2.5 MHz SS-1 transducer. The dynamic range of this system was 40 Db. Digital cineloops of apical four-chamber, two-chamber, and three-chamber views were recorded, using at first left ventricular opacification (LVO) mode with a mechanical index (MI) of 0.25 and afterwards perfusion mode with a MI of 0.10. Transient high MI (1.10 MHz) imaging was used to destroy contrast micro bubbles (flash echocardiography), allowing the assessment of myocardial replenishment. The frame rate varied between 21 and 50 Hz.

RT3D data were recorded using the 3.5 MHz matrix array X3-1 transducer. Two full-volume data sets were acquired from an apical window over seven cardiac cycles, with a breath hold (when possible): first in an LVO mode with an MI of 0.24 and then in low MI mode for perfusion assessment with an MI of 0.14. The data sets were then digitally stored for off-line analysis. The frame rate varied between 10 and 35 Hz, depending on the depth and the mode the operator used. It should be stated at this point that no flash echocardiography was applied, due to unavailability of this method in the setting of the specific 3D technology.

The test was considered positive for ischaemia, if new or worsening wall-motion abnormalities appeared and/or new perfusion abnormalities were observed in two or more consecutive myocardial segments. Pre- and during adenosine infusion MCE perfusion data were compared and graded for each coronary territory.

Echocardiographic image analysis

The left ventricle was divided into 17 segments, according to the American Society of Echocardiography recommendations. Wall-motion segmental score was graded as: 1—normokinetic, 2—mild hypokinetic, 3—severe hypokinetic, 4—akinetic, and 5—dyskinetic. Semi-quantitative perfusion analysis was performed in 2D four-, two-, and three-chamber views. At rest, it normally takes about 5 s to completely replenish the myocardium with microbubbles after their destruction, using a high-MI pulse. When normal hyperaemic response is present, the myocardium fills in just 1 s. Any segment with normal replenishment at rest that did not fill in approximately 1 s after adenosine infusion was considered to demonstrate a reversible perfusion defect. RT3D images were processed off-line using the QLAB (ver.7.1) software. RT3D pyramidal volumetric data sets were cropped in order to reproduce the traditional 2D four-, two-, and three-chamber views. Additional sections were obtained on the reader’s choice, if deemed necessary, by rotating the pyramidal full-volume data sets and cropping along the three rectilinear axes projected by the QLAB software. When a segmental wall-motion abnormality was detected, the reader obtained more sections across this segment in order to ascertain that the observed abnormality was not due to erroneous off-axis cropping (Figures 1 and 2).

Perfusion analysis was also made in 3D images and it was characterized as normal or as myocardial perfusion defect (defined as the complete absence of contrast distribution in a myocardial region). Both 2D and 3D images were independently and blindly interpreted by two echocardiography specialists, who were unaware of the patient’s clinical data or the results of any prior evaluation. Wall-motion abnormalities and myocardial perfusion defects were independently evaluated as well. In case of disagreement the captured images were interpreted by a third reviewer.

Coronary angiography

All sixty patients underwent quantitative coronary angiography by the Judkins technique, within 1 month prior or after stress
echocardiography had been performed. Ventriculography was performed in the 30° right anterior oblique and 60° left anterior oblique views. Eccentric stenoses were evaluated in two orthogonal views. A normal arterial segment was identified immediately proximally and distally to the lesion and measured with an electronic calliper. The minimal stenosis diameter was also measured and its severity was expressed as percent reduction in the normal diameter. A 50% reduction in luminal diameter of at least one major epicardial vessel was considered as significant CAD. The echocardiographers as well as the interventional cardiologists evaluated the respective examinations blindly.

Statistical analysis
Continuous variables were presented as mean and standard error and were compared using the unpaired or paired t-test as suited. Categorical variables and proportions were compared using the χ² test. The agreement between modalities was assessed with the kappa statistic.

Kappa statistic values are expressed as k ± SE. Intervals of agreement are denoted as: kappa value greater than 0.800 denotes excellent agreement, 0.601–0.800 good agreement, 0.401–0.600 moderate agreement, 0.400 or less poor agreement. Sensitivity, specificity, positive predictive value (PPV), negative predictive value, and accuracy of the two modalities for the diagnosis of CAD were presented with 95% confidence intervals and their differences were compared with the McNemar test. Analysis was performed by coronary territory and by patient. A value of P < 0.05 was considered significant in all cases. Data analysis was performed using the SPSS 17.0 statistical package for Windows (SPSS, Inc., Chicago).

Results
Sixty patients (38 men, mean age 60.1 ± 8.5 years old) were enrolled in the study. Baseline characteristics of the studied population are illustrated in Table 1. The mean heart rate before adenosine infusion was 70 ± 5 bpm, lower than that of the end of adenosine infusion 96 ± 3 bpm (P < 0.01). The blood pressure was measured just before performing the stress echo and at the end of adenosine infusion [mean value 115 ± 5 and 124 ± 9 mmHg, respectively, (P = NS)]. All patients completed the stress-contrast protocol uneventfully. Adverse effects concerning

<table>
<thead>
<tr>
<th>Variables</th>
<th>n = 60, patients</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>60.1 ± 8.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.3 ± 2.1</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>38/22</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>29 (48.3)</td>
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<tr>
<td>Diabetes mellitus (%)</td>
<td>12 (20)</td>
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<tr>
<td>Dyslipidaemia (%)</td>
<td>30 (50)</td>
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<tr>
<td>Smoking (%)</td>
<td>36 (60)</td>
</tr>
<tr>
<td>Family history of coronary heart disease (%)</td>
<td>5 (8.3)</td>
</tr>
<tr>
<td>Echocardiographic data</td>
<td></td>
</tr>
<tr>
<td>Mean ejection fraction (%)</td>
<td>58.2 ± 5</td>
</tr>
<tr>
<td>Abnormal WM, n (%) for 2D</td>
<td>41 (68)</td>
</tr>
<tr>
<td>Abnormal WM, n (%) for 3D</td>
<td>44 (73)</td>
</tr>
<tr>
<td>Abnormal perfusion for 2D, n (%)</td>
<td>47 (78)</td>
</tr>
<tr>
<td>Abnormal perfusion for 3D, n (%)</td>
<td>47 (78)</td>
</tr>
<tr>
<td>Angiographic data (%)</td>
<td></td>
</tr>
<tr>
<td>One-vessel disease</td>
<td>21 (35)</td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>25 (41.7)</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>4 (6.6)</td>
</tr>
<tr>
<td>Medication intake (%)</td>
<td></td>
</tr>
<tr>
<td>ACE-inhibitors/ARBs</td>
<td>31 (52)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>45 (75)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>8 (13)</td>
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<tr>
<td>Ca blockers</td>
<td>14 (23)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>38 (63)</td>
</tr>
<tr>
<td>HMGCoA inhibitors</td>
<td>42 (70)</td>
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</tbody>
</table>

Categorical values are presented as number and percentage of patients; continuous variables are presented as mean ± SD.
Adenosine infusion were mainly flushing, noted commonly in the study population. However, no major adverse events which led to test discontinuation were recorded. The mean left ventricular ejection fraction, as evaluated by 2D echocardiography, was 58.2 ± 5%.

**Coronary angiography**

Coronary angiography revealed lesions >50% in 49 patients. Twenty of them had one-vessel disease [13 left anterior descending artery (LAD) and 7 left circumflex artery (LCx)], 25 had two-vessel disease [11 LAD and LCx, 10 LAD and right coronary artery (RCA), 4 LCx and RCA], and 4 had three-vessel disease. Reclassifying analysis per vascular territory, LAD disease was observed in 38 patients (63%), whereas 26 (43%) individuals had LCx lesions and 18 (30%) had RCA stenoses. Angiographically defined stenosis >70% was reported in 40 patients.

**Echocardiographic analysis**

Out of the 1020 segments, wall-motion analysis was feasible, at rest, in 98% and in 97% of 2D and 3D depicted segments, respectively ($P = NS$). Out of 20 segments that could not be analysed with 2D, 4 regarded LAD, 8 LCx, and 8 RCA territory, whereas out of 31 segments that could not be evaluated by 3D, 4 concerned LAD, 14 LCx, and 13 RCA territory. The respective evaluated segments at peak stress were 93% for 2D and 92% for 3D. Out of 71 segments that could not be evaluated using 2D, 10 were related to LAD, 35 were related to LCx, and 26 to RCA region, whereas out of 82 segments that could not be assessed with 3D, 6 were consistent with LAD, 42 with LCx, and 34 with RCA region.

Perfusion could be evaluated, at rest, in 97% and in 96% of 2D and 3D depicted segments, respectively ($P = NS$). With 2D, 31 segments could not be evaluated out of which 3 regarded LAD, 13 LCx, and 15 RCA territory, and with 3D, 41 segments could not be adequately visualized out of which 3 concerned LAD, 21 concerned LCx, and 17 RCA region. At peak stress the evaluated percentages were 92% for 2D and 90% for 3D. Utilizing 2D, 82 segments could not be analysed, out of which 4 regarded LAD, 36 LCx, and 42 RCA territory, whereas out of 102 that could not be evaluated by 3D, 10 were consistent with LAD, 53 with LCx, and 39 with RCA region.

At rest, the agreement between 2D and RT3D wall-motion assessment was 93% (kappa value: 0.689), whereas, at stress, the agreement was 91% (kappa value: 0.629). The corresponding percentages for the assessment of perfusion were 92 and 90% for 2D and RT3D, respectively (kappa value: 0.658). The mean acquisition time for all necessary views to evaluate all 17 segments was 49.4 ± 4.0 s for RT3D and 138 ± 9.0 s for 2D ($P < 0.001$).

**Assessment of wall-motion and perfusion abnormalities by 2D and RT3D echocardiography**

Two of the patients had wall-motion abnormalities at rest. In particular, one had mild hypokinesia in the apical anterior and apical lateral segments of the left ventricle, whereas the other had mild hypokinesia in the apex of the left ventricle. At rest, no perfusion defects were denoted in these two patients. Both were diabetics, with uncontrolled blood glucose levels (Hba 1c levels 8.2 and 8.7 mg/dL, respectively) and without history of known myocardial infarction. In these particular patients, perfusion analysis illustrated perfusion defects at the apex, at peak stress, finding that was in accordance with their coronary angiograms.

New or worsened wall-motion abnormalities at peak stress (sign of ischaemia) were detected in 41 and 44 patients by 2D and RT3D echocardiography, respectively, whereas perfusion defects appeared in 47 patients by both 2D and 3D. In the per patient analysis, the diagnostic parameters for wall motion and perfusion are illustrated in graph 1. In no case did the differences between the two modalities achieve statistical significance.

The combined evaluation of wall motion and, perfusion offered incremental value, (Figure 3) over wall-motion assessment alone in the diagnosis of CAD (coronary artery stenosis >50%) for both 2D and 3D echo. Particularly, sensitivity increased from 80 to 96% ($P < 0.05$), specificity decreased from 82 to 55% ($P < 0.05$) and accuracy increased from 80 to 88% ($P < 0.05$) for 2D. The respective reported values for 3D were: sensitivity increased from 82 to 98% ($P < 0.05$), specificity decreased from 64 to 45% ($P < 0.05$), and

![Figure 3](https://example.com/figure3.png)

**Figure 3** Graph 1: Graph illustrating diagnostic parameters between 2D and RT3D per patient analysis for (A) coronary lesions >50% and (B) lesions >70%. Proportions expressed as percentage.
accuracy increased from 78 to 88% ($P < 0.05$). The corresponding values for stenoses $>70\%$ are presented in graph 2 (Figure 4).

Analysis was reclassified on detection of angiographic single-vessel versus multi-vessel disease and the diagnostic parameters were differentiated as shown in graph 2. Multi-vessel analysis was based on multiregional abnormalities as observed by 2D and 3D echocardiography.

The respective values concerning the per vascular territory analysis are demonstrated in Tables 2 and 3. All rates differences were not statistically significant, apart from those for LCx region where 2D was shown to be more sensitive than 3D in detecting perfusion defects ($P < 0.05$). Regarding the right coronary territories sensitivity, specificity, and accuracy rates were 78, 71, and 75% for 2D perfusion evaluation, whereas the respective values

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**Table 2** Wall-motion diagnostic parameters (CI: 95%)

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>2D echo</td>
<td>79% (68–89)</td>
<td>82% (72–91)</td>
<td>88% (84–92)</td>
<td>69% (63–75)</td>
<td>80% (75–85)</td>
</tr>
<tr>
<td></td>
<td>3D echo</td>
<td>82% (68–89)</td>
<td>86% (77–94)</td>
<td>91% (87–95)</td>
<td>83% (78–88)</td>
<td>85% (80–90)</td>
</tr>
<tr>
<td>RCA</td>
<td>2D echo</td>
<td>72% (61–83)</td>
<td>76% (65–87)</td>
<td>57% (51–63)</td>
<td>76% (71–81)</td>
<td>75% (70–80)</td>
</tr>
<tr>
<td></td>
<td>3D echo</td>
<td>61% (49–73)</td>
<td>74% (63–85)</td>
<td>50% (44–56)</td>
<td>82% (76–88)</td>
<td>70% (64–76)</td>
</tr>
<tr>
<td>LCX</td>
<td>2D echo</td>
<td>69% (58–80)</td>
<td>76% (66–86)</td>
<td>64% (58–70)</td>
<td>76% (70–82)</td>
<td>73% (67–79)</td>
</tr>
<tr>
<td></td>
<td>3D echo</td>
<td>62% (50–74)</td>
<td>76% (50–74)</td>
<td>67% (61–73)</td>
<td>76% (70–82)</td>
<td>70% (64–76)</td>
</tr>
</tbody>
</table>

Diagnostic parameters concerning myocardial perfusion of two- and three-dimensional adenosine stress echocardiography for the detection of coronary artery disease and kappa statistic for agreement with coronary angiography (method of reference; $>50\%$ stenoses were considered to be significant). In all cases, the differences between the two modalities were not statistically significant ($P = NS$).

**Table 3** Diagnostic parameters of myocardial perfusion analysis (CI: 95%)

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>2D echo</td>
<td>87% (68–86)</td>
<td>86% (77–95)</td>
<td>92% (88–96)</td>
<td>79% (74–84)</td>
<td>87% (83–91)</td>
</tr>
<tr>
<td></td>
<td>3D echo</td>
<td>81% (71–91)</td>
<td>91% (84–98)</td>
<td>94% (91–97)</td>
<td>74% (68–80)</td>
<td>85% (80–90)</td>
</tr>
<tr>
<td>RCA</td>
<td>2D echo</td>
<td>78% (68–88)</td>
<td>79% (68–88)</td>
<td>61% (56–67)</td>
<td>89% (85–93)</td>
<td>78% (73–93)</td>
</tr>
<tr>
<td></td>
<td>3D echo</td>
<td>67% (56–78)</td>
<td>76% (66–86)</td>
<td>54% (48–60)</td>
<td>84% (79–89)</td>
<td>73% (67–79)</td>
</tr>
<tr>
<td>LCX</td>
<td>2D echo</td>
<td>61%* (72–90)</td>
<td>88% (80–96)</td>
<td>84% (79–89)</td>
<td>86% (82–90)</td>
<td>85% (76–94)</td>
</tr>
<tr>
<td></td>
<td>3D echo</td>
<td>65% (53–77)</td>
<td>85% (76–94)</td>
<td>77% (72–82)</td>
<td>76% (70–82)</td>
<td>76% (70–82)</td>
</tr>
</tbody>
</table>

Diagnostic parameters concerning myocardial perfusion of two- and three-dimensional adenosine stress echocardiography for the detection of coronary artery disease and kappa statistic for agreement with coronary angiography (method of reference; $>50\%$ stenoses were considered to be significant). In all cases, the differences between the two modalities were not statistically significant, except from the LCx vascular territory $*P = 0.005$. 

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for 3D perfusion evaluation were 81, 71, and 76%. On the other hand, wall-motion evaluation in the same vascular regions reported 75% sensitivity, 71% specificity, and 73% accuracy for 2D, whereas for RT3D the respective rates were 72, 71, and 73%. Combining wall-motion and perfusion assessment together 2D demonstrates 92% sensitivity, 50% specificity, and 75% accuracy, whereas the 3D reports 92% sensitivity, 54% specificity, and 77% accuracy.

Performing segmental analysis 2D assessment revealed 318 segments with new wall-motion abnormalities, out of which 167 segments regarded LAD, 73 RCA, and 78 LCx territory. Three-dimensional wall-motion evaluation reported abnormal 312 segments, out of which 172 referred to LAD, 68 to RCA, and 72 to LCx region. Respectively, perfusion evaluation demonstrated 339 abnormal segments for 2D (179 LAD, 76 RCA, 84 LCx), whereas 3D revealed 313 segments with abnormal perfusion (168 LAD, 71 RCA, 74 LCx).

**Interobserver–intraobserver variability**

The agreement between the two readers (in the per vascular territory analysis) for wall-motion assessment was 92% for 2D and 90% for RT3D. For myocardial perfusion, the agreement was 94% for 2D and 88% for RT3D. The intraobserver variability was for wall motion 95% for 2D and 92% for 3D. The respective percentages for myocardial perfusion were 94% for 2D and 88% for 3D.

**Discussion**

According to our knowledge, this is the first study that evaluates the use of RT3D adenosine stress contrast echocardiography in detecting both perfusion and wall-motion abnormalities in patients with known or suspected CAD and using coronary angiography as the method of reference. The principal finding of this study was that the assessment of wall-motion abnormalities and the evaluation of segmental myocardial perfusion, using RT3D were feasible in a high percentage of the myocardial segments. Compared with 2D stress contrast views concerning wall-motion analysis, the sensitivity, and the specificity were similar. Furthermore, 3D myocardial perfusion analysis revealed high accuracy rates for the diagnosis of LAD disease, perhaps due to the ability of obtaining more sections of the left ventricle and thus avoiding apical foreshortening (a common problem with conventional 2D echo), whereas the method’s diagnostic accuracy for the right coronary circulation was moderate. Interestingly RT3D proved to be as efficient as 2D in the context of single-vessel and multi-vessel disease detection. Last but not least, perfusion evaluation seems to offer an incremental benefit over wall motion alone, for the diagnosis of CAD for both 2D and RT3D modalities. This is of great clinical interest, especially for the right circulation, where the combined assessment of wall motion and perfusion seems to improve the sensitivity of the method. However, the improvement of sensitivity noted is counterbalanced by a significant decline in specificity.

RT3D echocardiography has emerged as a novel technique, although there are few data concerning its incremental value, when compared with the 2D method, in the setting of stress echocardiography. The feasibility of RT3D echocardiography and its good concordance with 2D echo on wall-motion analysis for detection of inducible ischaemia has been reported in several published studies. Although Takeuchi et al.17 and Krenning et al.22 demonstrated only low to moderate sensitivity for the 3D method, other authors12,18 reported high sensitivity rates. A recent study by Badano et al.23, using dipyridamole as stressor, proved that 3D echocardiography is a feasible method for the diagnosis of CAD, based on wall-motion analysis, especially for LAD vascular region. In addition, in studies20,22,24 where contrast agents were utilized, the accuracy of the 3D method to evaluate wall motion was improved. In our previous study, using dobutamine as stressor, the ability of RT3D imaging to overcome left ventricular foreshortening has been reported to improve the detection of apical ischaemia.17

Although all previous RT3D studies11,15–18,23 used wall-motion analysis (with or without contrast agent) as a criterion for detection of CAD, myocardial perfusion analysis has been performed in only few clinical studies. In a study by Bhan,19 full-volume 3D MCE was documented to be feasible concerning myocardial perfusion evaluation, with a good agreement with 2D MCE. Still, 2D echo was assumed as the method of reference for perfusion imaging and the majority of segments assessed was normal. The first pilot study which documented the accuracy of live 3D and full-volume MCE in the setting of myocardial perfusion evaluation during adenosine stress echo was published by Abdelmonem et al.25 However, the study population consisted only of a small number of patients. Furthermore coronary angiography was not undertaken and SPECT was considered the gold standard for the detection of CAD.

In the current study, we demonstrated a high diagnostic value of 2D adenosine stress contrast echo. Specifically, we illustrated high accuracy rates concerning the LAD territory, while the respective rates for the right coronary system were acceptable, a finding which is in accordance with our previous and other author’s reports.14,24 Furthermore, in the context of CAD detection, RT3D adenosine stress echocardiography seems to be highly feasible regarding wall motion and perfusion evaluation with the utilization of contrast agents. Another major reason for the reported high feasibility rates is the negligible increase in the heart rate caused by vasodilators, which in turn overcomes the low frame rates achieved by the available technology. Therefore vasodilator stressors are ideal for RT3D stress echo, in comparison with dobutamine and exercise testing that lead to a marked increase in the heart rate, thus rendering image interpretation quite difficult. Nevertheless a less than optimal acoustic window represents a major impediment for the conduction of RT3D stress echo. In this context extremely obese people and patients with chronic obstructive pulmonary disease were excluded, thus eliminating two major factors for compromised acoustic window.

Our findings suggest that RT3D technique is at least equivalent to 2D adenosine stress contrast echocardiography in detecting CAD, especially in LAD vascular territory. Owing to technical restrictions to properly visualize the basal segments, RT3D perfusion analysis demonstrated moderate sensitivity rates for the assessment of LCx region, although assessment of right coronary territories, were comparative with the 2D method. Moreover, RT3D adenosine stress echo offers a number of advantages
which could be translated into clinical efficacy, including rapid acquisition, as illustrated by the small acquisition times in our study, easier image interpretation, because of the absence of tachycardia and tachypnoea, which result in more image artefacts. Additionally, the simultaneous visualization of the same segments in different planes, contributes to our study’s high intra- and interobserver agreement in assessing LV wall-motion and perfusion analysis, while the acquisition of multiple cross sections of the left ventricle eliminates apical foreshortening. Future advances in technology could probably establish RT3D stress echo as the modality of choice for the conduction of any stress study.

**Study limitations**

In this study, diagnostic limitations, mostly due to technological drawbacks concerning the use of RT3D technology in the setting of stress echocardiography, have to be acknowledged. Inferior spatial resolution and lower frame rates, as compared with 2D echocardiography, as well as the lack of flash echocardiography application are the main disadvantages of RT3D. Therefore, patients with prior myocardial infarction were excluded from the study, due to the inability of current RT3D technology to evaluate myocardial perfusion changes during vasodilator stress echo. In addition, patients who had undergone CABG were excluded due to post-operative changes in vascular anatomy, fact that would prevent proper anatomical correlation of wall-motion and perfusion abnormalities. As a result RT3D failed to demonstrate superior clinical value over conventional 2D echo and cannot be recommended at the moment as the modality of choice for stress echocardiography as it can only be applied in selected cases. Furthermore, the low frame rates achieved by current RT3D technology have a negative impact on feasibility during dobutamine or exercise stress protocols conducted by several echo laboratories. Additionally contrast agents, although safe, have not yet been approved for myocardial perfusion assessment. Consequently in this specific setting their use is not widely adopted. Moreover, the reported PPV values are high due to the high prevalence of CAD in this study population, which in turn can be justified by the enrolment of individuals with major risk factors for CAD.

**Conclusion**

In conclusion, RT3D adenosine stress contrast echo seems to be a promising feasible technique for the detection of CAD, especially LAD disease. The combined evaluation of wall-motion and perfusion offers an incremental value for both 2D and 3D for CAD diagnosis. However, additional data are needed to determine its exact position in clinical cardiology. Moreover, the evolution of 3D technology will alleviate the existing problems concerning the resolution of the current RT3D method, thus enhancing its diagnostic accuracy in the setting of stress echocardiography.

**Conflict of interest:** none declared.

**References**


Tricky image of exuberant accessory mitral valve tissue with partial interchordal space obliteration

Clara Alexandrescu, Stefania L. Negrea*, and Gilles Dreyfus

Cardio Thoracic Center of Monaco, 11 bis, Avenue d’Ostende, 98000 Monaco

*Corresponding author. Tel: +377 92 16 80 00; fax: +377 92 16 82 99. Email: stefiananegrea779@yahoo.com

A 74-year-old man was referred for mitral valve surgery of symptomatic (weakness and fatigue) prolapse-related mitral regurgitation. He had a past medical history of hypertension, dyslipidaemia, and overweight. His initial evaluation consisted in transthoracic echocardiography which documented the presence of severe mitral regurgitation due to posterior leaflet prolapse (Panels A and B; see Supplementary data online, Movie S1). The preoperative transoesophageal echocardiography (TEE) confirmed the limited lesion of the middle scallop of the posterior leaflet (P2) with many ruptured chordae tendinae resulting in posterior mitral valve leaflet prolapse (flail of P2 scallop). TEE examination also showed an unusual more echogenic image that seemed to be a group of chordae tendinae with excess tissue in relation with anterior mitral valve leaflet. This structure had an excessive movement encroaching into the left ventricular outflow tract without causing obstruction (Panel A; see Supplementary data online, Movie S1). The surgical inspection confirmed the presence of excessive tissue (a lacy-like pattern) made by non-differentiated chordae tendinae at the level of anterior mitral valve leaflet with partial interchordal space obliteration (Panel C). In this case with complex lesions (exuberant accessory mitral valve associated with isolated chords rupture), the patient underwent mitral valve repair surgery and resection of the unusual structure related to the anterior mitral valve with a successful surgical result (Panel D). This case illustrates a rare association between exuberant accessory mitral valve tissue and not for ruptured chordae tendinae was the absence of an upward movement back into the left atrium.

Supplementary data are available at *European Journal of Echocardiography* online.

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