Influence of Left Ventricular Hypertrophy and Geometry on Diagnostic Accuracy of Wall Motion and Perfusion Magnetic Resonance During Dobutamine Stress

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Background—The purpose of this study was to determine the influence of left ventricular (LV) hypertrophy and geometry on the diagnostic accuracy of wall motion and additional perfusion imaging during high-dose dobutamine/atropine stress magnetic resonance for the detection of coronary artery disease.

Methods and Results—Combined dobutamine stress magnetic resonance (DSMR)-wall motion and DSMR-perfusion imaging was performed in a single session in 187 patients scheduled for invasive coronary angiography. Patients were classified into 4 categories on the basis of LV mass (normal, ≤81 g/m² in men and ≤62 g/m² in women) and relative wall thickness (RWT) (normal, <0.45) as follows: normal geometry (normal mass, normal RWT), concentric remodeling (normal mass, increased RWT), concentric hypertrophy (increased mass, increased RWT), and eccentric hypertrophy (increased mass, normal RWT). Wall motion and perfusion images were interpreted sequentially, with observers blinded to other data. Significant coronary artery disease was defined as ≥70% stenosis. In patients with increased LV concentricity (defined by an RWT ≥0.45), sensitivity and accuracy of DSMR-wall motion were significantly reduced (63% and 73%, respectively; P<0.05) compared with patients without increased LV concentricity (90% and 88%, respectively; P<0.05). Although accuracy of DSMR-perfusion was higher than that of DSMR-wall motion in patients with concentric hypertrophy (82% versus 71%; P<0.05), accuracy of DSMR-wall motion was superior to DSMR-perfusion (90% versus 85%; P<0.05) in patients with eccentric hypertrophy.

Conclusions—The accuracy of DSMR-wall motion is influenced by LV geometry. In patients with concentric remodeling and concentric hypertrophy, additional first-pass perfusion imaging during high-dose dobutamine stress improves the diagnostic accuracy for the detection of coronary artery disease. (Circ Cardiovasc Imaging. 2010;3:507-514.)

Key Words: coronary artery disease • dobutamine • magnetic resonance imaging • myocardial perfusion imaging • hypertrophy left ventricular • ischemia

Dobutamine stress magnetic resonance (DSMR)-wall motion is established for the evaluation of patients with suspected and known coronary artery disease (CAD).1–5 DSMR-wall motion has been demonstrated to be superior to dobutamine stress echocardiography in unselected patient populations owing to an improved definition of the endocardial border for the detection of stress-inducible wall motion abnormalities (WMA).6 However, despite the consistently high endocardial border visualization achieved with cine MRI, visual identification of developing WMA may be challenging in hypertrophied hearts. Left ventricular (LV) hypertrophy (LVH) and concentric remodeling have been identified as potential causes for both false-negative and false-positive results on dobutamine stress echocardiography.7,8 The influence of LVH and LV geometry on the diagnostic capabilities of DSMR-wall motion has not been evaluated yet. Recently, myocardial perfusion imaging during DSMR (DSMR-perfusion) was introduced as an additional tool to improve the sensitivity for the detection of CAD.9 In the present study, we hypothesized that LVH and LV geometry influence the accuracy of DSMR-wall motion and that additional DSMR-perfusion may be beneficial to detect CAD, particularly in patients with LVH and increased LV concentricity.

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Methods

Patient Population
The study was conducted prospectively in accordance with the Institutional Review Board at the Charité University School of Medicine (Berlin, Germany), and written informed consent was given by all patients. Inclusion criteria were suspected and known
CAD with or without resting wall motion abnormalities in patients who were scheduled for a clinically indicated invasive coronary x-ray angiography. Patients with general contraindications to MRI (eg, noncompatible biomaterial implants, claustrophobia), dobutamine or gadolinium-based contrast agents (glomerular filtration rate, \(<30 \text{ mL/min}\)) and patients with an LV ejection fraction \(<30\%\) were excluded. Hypertension, hypercholesterolemia, diabetes mellitus, family history of premature CAD, and coronary risk factors were defined by published criteria. All patients were instructed to refrain from \(\beta\)-blockers 24 hours before the MRI study.

Between June 2008 and July 2009, we screened 199 consecutive patients to participate in this study. Five patients declined to participate (claustrophobia), 4 had contraindications to dobutamine (3 with severe aortic stenosis, 1 with suspected myocarditis), and 3 had intermittent atrial fibrillation; hence, the final study population consisted of 187 patients.

### MRI

MRI was performed on a 1.5-T scanner (Philips Intera CV). Multiple short-axis cine views covering the LV from base to apex without a gap were acquired for the determination of LV volumes and mass. Cardiac standard geometries (3 short-axis views and a 4-, 2-, and 3-chamber view) were acquired at rest and during each dobutamine stress level according to standard procedure. At maximum dobutamine atropine stress, perfusion imaging also was performed using an IV bolus of 0.1 mmol/kg gadolinium diethylene triamine penta-acetic acid (injection rate, 4 mL/s; saline flush of 20 mL at the same rate). The geometry of the perfusion scan was identical to the 3 cine short-axis views. A second infusion of 0.1 mmol/kg gadolinium diethylene triamine penta-acetic acid was administered immediately after DSMR-perfusion without image data acquisition. Ten to 15 minutes after termination of the dobutamine infusion and routine application of IV esmolol (50 to 100 mg), delayed enhancement (DE) imaging was done using 3D data acquisition with full coverage of the heart in short- and long-axis (4-, 2-, and 3-chamber) orientation. The inversion time was individually adapted (200 to 250 milliseconds [ms]) to optimally null the signal from normal myocardium and was derived from an inversion-prepared cine sequence (Look-Locker).

### MRI Sequence Design

For cine imaging, a steady-state free precession sequence with retrospective gating (50 phases per cardiac cycle) was used during an end-expiratory breath hold (repetition time, 3.4 ms; echo time, 1.7 ms; flip angle, 60°). In-plane spatial resolution was 1.8×1.8 mm with a slice thickness of 8 mm.

For perfusion imaging the balanced steady-state free precession sequence parameters were as follows: repetition rate, 2.8 ms; echo time, 1.4 ms; flip angle, 50°; raw data matrix, 160×143; voxel size, 2.8×3×10 mm³, with acquisition of 3 short-axis views (basal, midventricular, and apical slice). A separate saturation pulse was applied to each slice (delay, 100 ms). For the steady-state free precession magnetization to reach equilibrium, a half- or half-repetition time start-up mode with an additional 8 start-up echoes was applied before image data acquisition.

DE imaging was performed using an inversion-prepared 3D spoiled gradient-echo sequence (repetition time, 3.6 ms; echo time, 1.7 ms; flip angle, 15°; voxel size, 1.5×1.7×5 mm³). The inversion time was determined by analysis of an inversion-prepared cine sequence and was individually adapted (200 to 250 ms) to optimally null the signal from normal myocardium.

### Image Analysis

All image analyses were performed on a commercially available extended workspace station (Philips Medical Systems). Endocardial LV borders were manually traced at end diastole and end systole. The papillary muscles were included as part of the LV cavity volume. LV end-diastolic volume and end-systolic volume were determined using a summation of disks method (Simpson’s Rule). Ejection fraction was computed as (end-diastolic volume–end-systolic volume)/end-diastolic volume. LV septal and inferolateral wall thickness and LV diameter were measured between the interventricular septum and the lateral wall in an end-diastolic short-axis slice immediately basal to the tips of the papillary muscles at end diastole. An increase in septal wall thickness was defined as \(\geq 12\) mm in men and \(\geq 10\) mm in women. Relative wall thickness (RWT) was calculated as the ratio of septal plus inferolateral wall thickness at end diastole/LV end-diastolic diameter. Increased RWT was defined as \(\geq 0.45\), and increased LV mass index was defined as \(\geq 81\) g/m² for men and \(\geq 62\) g/m² for women. Patients were classified into 4 groups according to RWT and LV mass index as follows: normal geometry (normal LV mass, normal RWT), concentric remodeling (normal LV mass, increased RWT), concentric hypertrophy (increased LV mass, increased RWT), and eccentric hypertrophy (increased LV mass, normal RWT).

### Segmental analysis of wall motion and results of the perfusion study and coronary angiography were performed with consensus by 2 observers blinded to all clinical data using a synchronized quad-screen image display and applying a standard 16-segment scoring system (1 = normal; 2 = hypokinetic; 3 = akinetic; 4 = dyskinetic). A 16-segment model was used to compare DSMR-wall motion with DSMR-perfusion because the short-axis orientation of DSMR-perfusion did not allow for imaging of the LV apex. Information on premature stress termination was not given to the observers. A positive DSMR-wall motion was defined as new or worsening WMA in \(\geq 1\) segment.

Perfusion scans were interpreted with consensus by 2 observers blinded to the results of DSMR-wall motion and invasive coronary angiography. The observers were presented with anonymized MRI studies, including perfusion at stress and DE. DE was defined as previously published (ie, as hyperenhanced zones with image intensities \(>2\) SD above the mean of a normal, nonenhanced region). Ischemia on DSMR-perfusion was considered to be present in segments without DE in case a subendocardially arising hypointensity showed \(\geq 25\%\) transmurality for \(\geq 3\) consecutive dynamics or when segments with nontransmural DE demonstrated an additional stress-inducible hypoperfusion for \(\geq 3\) consecutive dynamics.

Each myocardial segment was scored on the basis of the transmural extent of DE (0 = no DE; 1 = 1% to 25%; 2 = 26% to 50%; 3 = 51% to 75%; 4 = 76% to 100%). Summed transmurality scores were calculated by adding the transmural scores of all 16 segments. Diagnostic accuracy was calculated for combining the information from DSMR-wall motion, DSMR-perfusion, and DE. A patient was considered to have CAD if 1 of the tests was positive.

### Coronary Angiography

Invasive coronary angiography was performed in all patients within 30 days after MRI. The angiograms were evaluated visually for the presence of significant stenoses (ie, \(\geq 70\%\) luminal diameter reduction) in the 3 large epicardial coronary arteries and their major branches (ie, vessel diameter \(\geq 2.0\) mm) by highly experienced invasive cardiologists who were blinded to the MRI data.

### Statistical Analysis

Statistical analysis was performed with SPSS release 15.0.1. For all continuous parameters, data are expressed as mean±SD and were compared with 1-way ANOVA using Scheffé post hoc testing where appropriate. Discrete data were analyzed using the \(\chi^2\) and Fisher exact tests when comparing the same method among different groups of patients. McNemar test was applied when comparing different methods for the same group of patients. In case of multiple comparison of discrete data, Kruskal-Wallis and Tukey post hoc testing were done. Sensitivity, specificity, and diagnostic accuracy were calculated according to standard definitions. Similarly, the change in diagnostic accuracy if the information from DSMR-wall motion was coupled with DE (DSMR-wall motion+DE) was calculated. Clinical variables were defined according to the Framingham Risk Score assessment. Univariate logistic regression analysis was performed to assess the relationship between clinical variables (sex, age, body mass index, hypertension, hyperlipidemia, diabetes, current smoking, DSMR-wall motion, DSMR-perfusion) and the presence...
ence of significant coronary artery stenosis. Variables with a \( P < 0.1 \) on univariate analysis were entered into the multiple logistic regression analysis. Statistical tests were 2-tailed; significance was considered \( P < 0.05 \).

## Results

### Clinical and Hemodynamic Characteristics

Demographic and hemodynamic data are shown in Table 1. The mean peak doses of dobutamine and atropine were 34.8 \( \mu g/\text{kg per minute} \) and 0.42 mg, respectively; atropine was given in 91 patients. A total of 163 (87%) patients reached the target heart rate (ie, 85% of maximum age-predicted heart rate). Four patients did not reach target heart rate despite maximal pharmacological infusion. The stress protocol was terminated early due to newly developed WMA (11 patients), severe chest pain or dyspnea (8 patients), and frequent ventricular ectopic beats (1 patient); however, all patients tolerated perfusion imaging and, thus, were able to finish the study protocol.

### Coronary Angiography

Significant CAD (\( \geq 70\% \) stenosis) was present in 105 (56%) patients. Among these patients, 57 (53%) had single-vessel CAD and 48 (47%) multivessel CAD. The remaining 82 (44%) patients had no significant CAD. In patients with single-vessel CAD, 23 had left anterior descending, 19 had left circumflex, and 14 had right-side CAD.

### Results of DSMR-Wall Motion and DSMR-Perfusion

New or worsening WMA and perfusion deficits occurred in 98 (52%) and 113 (60%) patients, respectively. Stress-inducible WMA or perfusion deficit occurred in 127 (68%) patients. Perfusion deficits occurred in the presence of inducible WMA in 84 (86%) of 98 patients and in the absence of inducible WMA in 29 (33%) of 89 patients. Fourteen patients demonstrated normal DSMR-perfusion with abnormal DSMR-wall motion.
Influence of LV Mass and Geometric Pattern on Diagnostic Accuracy

Data on the influence of LV mass and geometric pattern with regard to diagnostic accuracy of DSMR-wall motion, DSMR-perfusion, DE, and the combination of DSMR and DE are summarized in Table 3. The accuracy of DSMR-perfusion versus DSMR-wall motion was higher in patients with concentric hypertrophy (82% versus 71%; \( P=0.04 \)) (Figures 1 and 2) and increased LV concentricity (82% versus 73%; \( P=0.008 \)). In patients with eccentric hypertrophy, accuracy was higher for DSMR-wall motion (90%) compared with DSMR-perfusion (85%; \( P=0.006 \)). The numbers of patients with CAD in each of the 4 geometric groups were 42 (67%) with normal geometry, 15 (39%) with concentric remodeling, 23 (51%) with concentric hypertrophy, and 25 (63%) with eccentric hypertrophy.

Influence of Stress Level on Diagnostic Accuracy

Study participants achieving a high-rate pressure product (\( \geq 18,744 \text{ bpm} \times \text{mm Hg} \)) (ie, 50th percentile) had a trend for higher sensitivities than those achieving a lower-rate pressure product (ie, \( < 18,744 \text{ bpm} \times \text{mm Hg} \)) for both DSMR-wall motion (86% versus 74%) and DSMR-perfusion (94% versus 85%).

Results of DE

Table 2 summarizes data on DE. For all patients, the sensitivity, specificity, and diagnostic accuracy of DE for the detection of significant CAD were 47%, 70%, and 57%, respectively. For each geometric pattern, the incremental change in sensitivity and specificity if the information from DSMR-wall motion was coupled with DE (DSMR-wall motion + DE) is presented in Table 3.
DSMR-perfusion, and DE, the sensitivity, specificity, positive-predictive value, and negative-predictive value were 97%, 42%, 68%, and 92%, respectively.

Factors Associated With CAD
The univariate factors associated with CAD for all patients are shown in Table 4. A significant association was found for male sex, DSMR-wall motion, and DSMR-perfusion. With a multiple logistic regression procedure, the only covariates independently associated with the presence of CAD were abnormal DSMR-wall motion (odds ratio [OR], 10.99; 95% CI, 4.45 to 27.17; *P* < 0.001) and DSMR-perfusion (OR, 14.00; 95% CI, 5.7 to 34.38; *P* < 0.001).

In all geometric subgroups, univariate analysis identified only abnormal DSMR-wall motion and DSMR-perfusion as being significantly associated with the presence of CAD. On multiple logistic regression, inducible WMA was an independent factor associated with CAD in patients with normal geometry (OR, 51.35; 95% CI, 5.46 to 482.66; *P* < 0.001) and eccentric hypertrophy (OR, 74.75; 95% CI, 9.39 to 595.11; *P* < 0.001).

Table 3. Diagnostic Performance According to Geometric Pattern

<table>
<thead>
<tr>
<th></th>
<th>Normal Geometry</th>
<th>Concentric Remodeling</th>
<th>Concentric Hypertrophy</th>
<th>Eccentric Hypertrophy</th>
<th>LHV</th>
<th>Increased LV Concentricity</th>
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<tbody>
<tr>
<td></td>
<td>(n=63)</td>
<td>(n=30)</td>
<td>(n=45)</td>
<td>(n=46)</td>
<td>(n=85)</td>
<td>(n=84)</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSMR-wall motion</td>
<td>37/42 88 75--95†‡</td>
<td>10/15 67 41--78</td>
<td>23/25 92 75--88‡‡</td>
<td>37/48 77 63--87</td>
<td>24/38 63 47--77</td>
<td></td>
</tr>
<tr>
<td>DSMR-perfusion</td>
<td>37/42 88 75--95</td>
<td>14/15 93 68--95</td>
<td>23/25 92 75--98</td>
<td>43/48 90 78--95</td>
<td>34/38 89 76--96</td>
<td></td>
</tr>
<tr>
<td>DE imaging</td>
<td>16/42 38 25--53</td>
<td>8/15 53 26--63</td>
<td>15/23 60 41--77</td>
<td>25/48 52 38--66</td>
<td>18/38 47 32--62</td>
<td></td>
</tr>
<tr>
<td>DSMR-wall motion + DE</td>
<td>39/42 93 81--98</td>
<td>13/15 87 62--96</td>
<td>24/25 96 80--99</td>
<td>42/48 88 75--94</td>
<td>31/38 82 67--91</td>
<td></td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSMR-wall motion</td>
<td>18/21 86 65--95</td>
<td>19/24 79 60--91</td>
<td>13/15 87 62--96</td>
<td>31/37 84 69--92</td>
<td>37/46 80 67--89</td>
<td></td>
</tr>
<tr>
<td>DSMR-perfusion</td>
<td>17/21 81 60--92</td>
<td>18/24 75 55--88</td>
<td>11/15 73 48--89</td>
<td>28/37 76 60--87</td>
<td>35/46 76 62--88</td>
<td></td>
</tr>
<tr>
<td>DE imaging</td>
<td>15/21 71 50--86</td>
<td>8/24 75 55--88</td>
<td>10/15 67 42--85</td>
<td>24/37 85 49--78</td>
<td>32/46 70 55--81</td>
<td></td>
</tr>
<tr>
<td>DSMR-wall motion + DE</td>
<td>12/21 57 37--76</td>
<td>13/24 54 35--72</td>
<td>8/15 53 30--75</td>
<td>19/37 51 36--67</td>
<td>24/46 52 38--66</td>
<td></td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSMR-wall motion</td>
<td>55/63 87 77--83†‡</td>
<td>29/39 74 59--85</td>
<td>36/40 90 77--86‡‡</td>
<td>68/85 80 70--87</td>
<td>61/84 73 62--81</td>
<td></td>
</tr>
<tr>
<td>DSMR-perfusion</td>
<td>54/63 86 75--92</td>
<td>32/39 82 67--91</td>
<td>34/40 85 71--93</td>
<td>71/85 84 74--90</td>
<td>69/84 82 73--89</td>
<td></td>
</tr>
<tr>
<td>DE imaging</td>
<td>31/63 49 37--75</td>
<td>26/39 67 51--79</td>
<td>25/40 63 47--76</td>
<td>49/85 58 47--68</td>
<td>50/84 60 49--81</td>
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<tr>
<td>DSMR-wall motion + DE</td>
<td>51/63 81 70--89</td>
<td>26/39 67 51--79</td>
<td>32/40 80 65--90</td>
<td>61/85 72 61--80</td>
<td>55/84 65 55--75</td>
<td></td>
</tr>
</tbody>
</table>

LVH is defined as LV mass index >81 g/m² for men and >62 g/m² for women. Increased LV concentricity is defined as RWT ≥0.45.

* P < 0.05 vs concentric hypertrophy.
† P < 0.05 vs increased LV concentricity.
‡ P < 0.05 vs concentric remodeling.

Figure 1. False-negative DSMR-wall motion but true-positive results for DSMR-perfusion in a patient with concentric hypertrophy and multivessel CAD (see supplemental Movie 1). A, Normal DSMR-wall motion at rest and during low-dose and maximum dobutamine stress. B, DSMR-perfusion shows perfusion deficits of the anterior and inferior-inferolateral wall. C, DE imaging demonstrates a small subendocardial scar of the inferior wall. D, Coronary angiography with several stenoses of the left anterior descending coronary artery and collateralized occlusion of the right coronary artery.
Similarly, an inducible perfusion deficit was independently associated with the presence of CAD in patients with normal geometry (OR, 36.71; 95% CI, 3.91 to 344.93; \( P = 0.002 \)), concentric remodeling (OR, 29.69; 95% CI, 2.8 to 314.9; \( P = 0.005 \)), and concentric hypertrophy (OR, 19.53; 95% CI, 2.82 to 135.07; \( P = 0.003 \)).

**Discussion**

The main findings of this study were that the sensitivity and diagnostic accuracy of DSMR-wall motion are influenced by the LV geometric pattern (ie, increased LV concentricity impairs DSMR-wall motion test accuracy). Additional stress perfusion imaging, however, is beneficial in patients with concentric remodeling and concentric hypertrophy and compensates for the reduced accuracy.

The assessment of wall motion during dobutamine stress has proven its clinical usefulness for the detection of inducible myocardial ischemia. Several studies using echocardiography have demonstrated that specific morphological patterns of LV hypertrophy have an influence on test accuracy. To our knowledge, the present study is the first to systematically analyze the influence of different LV geometric patterns on accuracy of DSMR-wall motion. Concordant with previous reports, we demonstrated that in patients with normal LV mass and normal geometry, DSMR-wall motion has both high sensitivity and high specificity for the detection of hemodynamically relevant CAD. We could show that an absolute increase in LV mass or septal wall thickness did not adversely affect accuracy of DSMR-wall motion, which is in line with prior studies using echocardiography and cardiovascular MRI (CMR).

Although CMR is regarded for its superior image quality that allows for a consistently high definition of the endocardial border in all LV segments, our study demonstrates that

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**Table 4. Univariate Factors Associated With CAD**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Normal Geometry</th>
<th>Concentric Remodeling</th>
<th>Concentric Hypertrophy</th>
<th>Eccentric Hypertrophy</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>( P )</td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Male sex</td>
<td>3.1</td>
<td>0.1–74.7</td>
<td>0.48</td>
<td>34.6</td>
<td>0.9–122.6</td>
</tr>
<tr>
<td>Age*</td>
<td>1.1</td>
<td>0.9–1.2</td>
<td>0.6</td>
<td>1.0</td>
<td>0.9–1.1</td>
</tr>
<tr>
<td>BMI†</td>
<td>0.9</td>
<td>0.6–1.2</td>
<td>0.41</td>
<td>1.0</td>
<td>0.7–1.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.3</td>
<td>0.01–6.4</td>
<td>0.41</td>
<td>1.1</td>
<td>0.8–1.6</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>7.7</td>
<td>0.2–289.2</td>
<td>0.27</td>
<td>9.4</td>
<td>0.3–34.8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.3</td>
<td>0.1–60.5</td>
<td>0.63</td>
<td>2.4</td>
<td>0.2–33.8</td>
</tr>
<tr>
<td>Current smoking</td>
<td>2.7</td>
<td>0.1–75.2</td>
<td>0.56</td>
<td>2.1</td>
<td>0.2–24.4</td>
</tr>
<tr>
<td>Inducible WMA</td>
<td>175.5</td>
<td>5.4–569.5</td>
<td>0.004</td>
<td>2.4</td>
<td>0.2–27.5</td>
</tr>
<tr>
<td>Inducible perfusion deficit</td>
<td>24.2</td>
<td>2.0–289.6</td>
<td>0.01</td>
<td>55.7</td>
<td>3.4–926.9</td>
</tr>
</tbody>
</table>

BMI indicates body mass index.

*Per decade.
†Per 5 kg/m².
LV geometry may limit the diagnostic capability of wall-motion analysis for the detection of stress-inducible ischemic reactions. The lower accuracy of DSMR-wall motion in patients with increased LV concentricity was largely attributable to an increase in more false-negative cases. Visual assessment of DSMR-wall motion is based on analysis of myocardial thickening and systolic endocardial inward motion at rest and during stress. During the infusion of dobutamine, however, diastolic dysfunction may accentuate to a varying degree even in normal myocardium but has been described to be more pronounced in the presence of concentric hypertrophy compared with eccentric hypertrophy. Consequently, impaired myocardial relaxation results in minimal excursion distances of the endocardial border and together with LV cavity obliteration may serve as a likely explanation for difficulties in recognizing stress-inducible WMA. On the contrary, the detection of a regional perfusion abnormality under these morphological conditions is rather improved. A hypertrophied myocardial wall further eases visual detection of even very small subendocardial perfusion deficits. Indeed, our study showed that the accuracy of DSMR-perfusion in patients with concentric hypertrophy and concentric remodeling was significantly higher, mainly resulting from a decreased number of false-negative cases in both patient subgroups. In a previous study, we have already reported an improved sensitivity of DSMR-perfusion for the detection of CAD in patients with increased septal wall thickness; however, no further classification into different morphological patterns has been performed yet. Interestingly, in the present study, the LV mass index per se did not have a significant influence on the accuracy of DSMR-wall motion and DSMR-perfusion. Recent reports have shown that markers of concentric LV hypertrophy but not ventricular dilatation are associated with the burden of atherosclerosis, and thus, accurate detection of ischemic reactions of the myocardium in such a patient population is clinically important. Furthermore, in patients with a normal stress echocardiography, the risk for future cardiac events is 5 times higher in those with concentric hypertrophy than in those with eccentric hypertrophy, which might reflect the problem of underdiagnosing ischemia in this population. A recently published study demonstrated that patients with LVH and a negative DSMR-wall motion have a poor prognosis relative to patients without LVH. Considering the data from the present study, CMR appears advantageous in these patient subgroups because stress-perfusion MRI can readily be integrated into a standard dobutamine stress protocol.

Overall, there were 19 false-positive cases for DSMR-perfusion compared to 14 false-positive cases for DSMR-wall motion. Although our results did not show statistically significant differences between the specificity of DSMR-wall motion and DSMR-perfusion among patient subgroups, there was an overall trend for more false-positive cases with DSMR-perfusion, which is in line with previous studies comparing stress perfusion with wall motion imaging. Several reasons might explain this finding. Our patient population consisted of a cohort with a high number of patients with prior coronary interventions and previous myocardial infarction who are prone to demonstrate impairment of vasodilator reserve. Similarly, coronary microvascular dysfunction can occur in the presence of LVH without significant obstructive CAD. It can be identified by noninvasive assessment of myocardial blood flow reserve during perfusion imaging and may be severe enough to cause ischemia. Our study showed that in patients with eccentric hypertrophy, the increase in false-positive cases leads to a significant decrease in diagnostic accuracy for DSMR-perfusion versus DSMR-wall motion. Patients with eccentric LVH are known to demonstrate an increase in myocardial wall stress compared to normal hearts, which might explain the more-frequent occurrence of perfusion abnormalities as an indicator of microcirculatory impairment.

More than one third of all patients included in our study had increased LV concentricity, thus, the additional time it takes to perform perfusion imaging (2 to 3 minutes) seems well invested in the era of comprehensive CMR, particularly when taking into account the application of a gadolinium-based contrast agent for DE imaging is part of a routine examination for the detection of CAD in most centers. We thus propose to routinely perform DSMR-perfusion in patients with concentric remodeling and concentric hypertrophy since the diagnostic gain is highest with an improvement in diagnostic accuracy from 74% and 71% to 82%, respectively. Consequently, in patients with concentric remodeling or concentric hypertrophy, the combination of negative wall motion and positive perfusion testing should be interpreted as an ischemia-positive test result. In patients with eccentric hypertrophy, we would not generally recommend the use of DSMR-perfusion, and readers must take into account the significant increase in false-positive results. In patients with normal geometry, there is no need to routinely perform DSMR-perfusion.

Study Limitations
Although the catheterization results of the present study were based on visual analysis and not on quantitative coronary angiography or fractional flow reserve measurements, this closely reflects clinical reality in the majority of centers. A general problem in validating noninvasive techniques for the detection of myocardial ischemia is the lack of an optimal standard of reference. Luminographic assessment of coronary stenoses may not adequately reflect the hemodynamic relevance of CAD, which depends not only on luminal narrowing, but also on localization, length, and vessel size of the coronary lesion as well as on its severity. Furthermore, invasive angiography is inadequate to demonstrate impairment of vasodilator reserve in the absence of a significant major coronary arterial narrowing. We did not acquire long-axis views with DSMR-perfusion, so purely apical perfusion abnormalities may have been missed. The high prevalence of CAD (73%) in this cohort limits the applicability of diagnostic accuracy to the general population of patients referred for DSMR. Some of the subgroup analyses were not powered enough and should be regarded as exploratory. According to previously published criteria from transthoracic echocardiography, we selected a dichotomous variable of <0.45 or ≥0.45 in RWT as 1 of our primary outcome variables. Furthermore, we did not explore the robustness of these findings to other possible cut points or the identification of an optimal RWT cut point. A large number of statistical evaluations were
performed, and the likelihood of type I errors as a result cannot be excluded.

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Disclosures

None.

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CLINICAL PERSPECTIVE

The assessment of regional wall motion during high-dose dobutamine stress magnetic resonance (DSMR-wall motion) is an established clinical method with a generally high diagnostic and prognostic value for the evaluation of patients with coronary artery disease. This study highlighted the influence of different left ventricular geometric patterns on diagnostic accuracy of DSMR-wall motion and the potential benefit of performing additional first-pass DSMR-perfusion imaging. In patients with increased left ventricular concentricity, DSMR-perfusion improved the diagnostic accuracy compared to DSMR-wall motion, especially with regard to sensitivity for the detection of coronary artery disease. In contrast, DSMR-wall motion remains an accurate test in patients with normal geometry and eccentric hypertrophy. We thus recommend adding DSMR-perfusion to a routine stress protocol in patients with increased left ventricular concentricity.
Influence of Left Ventricular Hypertrophy and Geometry on Diagnostic Accuracy of Wall Motion and Perfusion Magnetic Resonance During Dobutamine Stress
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