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Comprehensive Dobutamine Stress CMR Versus Echocardiography in LBBB and Suspected Coronary Artery Disease

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OBJECTIVES This study aimed to compare dobutamine stress cardiac magnetic resonance (DSCMR) with dobutamine stress echocardiography (DSE) in patients with left bundle branch block (LBBB) and suspected coronary artery disease (CAD).

BACKGROUND Noninvasive diagnosis of CAD in patients with pre-existent LBBB is difficult because single-photon emission computed tomography and stress echocardiography both have limitations. We hypothesized that a comprehensive DSCMR examination including cine, perfusion, and late gadolinium enhancement imaging would be more accurate than DSE, thus potentially reducing the number of unnecessary invasive coronary angiograms.

METHODS We prospectively evaluated 82 consecutive patients with LBBB referred to our cardiology clinic for investigation of suspected CAD. All 82 patients underwent DSE, DSCMR, and invasive quantitative coronary angiography within 14 days. We compared the diagnostic accuracy of DSE, CMR cine imaging, the additive value of first-pass perfusion, and late gadolinium enhancement. In the comprehensive examination, a positive result was adjudged as the presence of either subendocardial or transmural late gadolinium enhancement with or without inducible peri-infarct ischemia or an inducible perfusion defect corresponding to an inducible regional wall motion abnormality.

RESULTS CMR cine imaging (regional wall motion abnormalities) had higher specificity, negative predictive value, and overall diagnostic accuracy than did DSE (87.5% vs. 72.9%; 80.8% vs. 67.3%; and 80.4% vs. 72.0%, respectively), although sensitivity was the same (72.0%). The addition of first-pass stress perfusion and late gadolinium enhancement (scar) further improved diagnostic confidence (sensitivity 82.4%, specificity 95.8%, positive predictive value 93.3%, negative predictive value 88.5%, and diagnostic accuracy 90.2%).

CONCLUSIONS DSCMR is a safe procedure and has greater diagnostic accuracy than does DSE in assessing patients with suspected CAD and LBBB. A comprehensive examination with the addition of perfusion and late gadolinium enhancement to CMR cine imaging significantly boosted specificity and sensitivity, making DSCMR a reliable alternative to invasive quantitative coronary angiography in this group of patients. (J Am Coll Cardiol Img 2014;7:490–8) © 2014 by the American College of Cardiology Foundation

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Left bundle branch block (LBBB) is a cardiac conduction abnormality that causes the left side of the heart to contract later than the right side does (1). The prevalence of LBBB increases with age, and coronary artery disease (CAD) is the most common cause, with a prevalence estimated at 30% to 52% (2,3). Perhaps because of this, patients with LBBB have been shown to have significantly increased cardiovascular mortality (4).

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Given this situation, initial investigation of incidental LBBB is often directed toward exclusion of CAD. The majority of these patients have intermediate probability for CAD, and most pathways for investigation of CAD in the intermediate probability group recommend noninvasive functional assessment such as exercise electrocardiography (ECG), single-photon emission computed tomography (SPECT), or stress echocardiography (5,6). Whereas these techniques are robust and well validated in the general population, in patients with LBBB, they have certain limitations (7–11). Cardiac magnetic resonance (CMR) has the ability to overcome some of the disadvantages of other noninvasive investigations; however, its utility and potential superiority in this setting has not yet been established.

We hypothesized that, in patients with LBBB and suspected CAD, a comprehensive dobutamine stress cardiac magnetic resonance (DSCMR) examination including wall motion analysis, perfusion, and late gadolinium enhancement (LGE) imaging would be more accurate in diagnosis of CAD than dobutamine stress echocardiography (DSE) would be when compared to the gold standard of invasive coronary angiography (ICA).

METHODS

Study population. We prospectively investigated 82 consecutive patients with LBBB who were referred to our clinic with suspected CAD over a period of 12 months. All patients underwent DSE, DSCMR, and ICA. All tests were performed within 14 ± 8 days by observers blinded to results of the others. The study protocol is summarized in Figure 1.

We included patients with LBBB and suspected CAD based on clinical judgment of the referring cardiologist. Patients were of intermediate probability of CAD as recommended by current clinical guidelines for investigation of suspected stable angina (5,11–13). The patients were all age ≥40 years and had typical features of angina (exertional chest pain or dyspnea) with 1 or more risk factors. We excluded patients who had a previous history of established CAD, those with renal impairment (estimated glomerular filtration rate <60 ml/min/1.73 m^2), metallic implants incompatible with CMR, uncontrolled arterial hypertension (baseline systolic blood pressure >190 mm Hg or diastolic blood pressure >100 mm Hg), atrial fibrillation with uncontrolled ventricular response, and prior adverse reaction to dobutamine. Antianginal medications, including oral beta-blockers, calcium-channel blockers, and nitrates, were not discontinued before DSCMR. For each examination (DSCMR, DSE, and ICA), analysis was performed by 2 observers blinded to the results of the other investigations. In case of any doubt, a third independent observer was used to adjudicate. All patients provided written informed consent to undergo DSCMR, DSE, and ICA, and the local ethics committee approved the study.

Dobutamine stress echocardiography. Two-dimensional transthoracic DSE was carried out in all patients using an IE33 scanner (Philips, Amsterdam, the Netherlands). All patients were pharmacologically stressed using dobutamine starting at a rate of 10 μg/kg/min and increased at 3-min intervals to 20, 30, and 40 μg/kg/min. If the target heart rate was not reached with dobutamine, intravenous boluses of atropine sulfate (0.25 to 0.5 mg aliquots up to a maximum total dose of 2 mg) were used at 30 or 40 μg/kg/min stages to augment the heart rate response. All studies were carried out with the patient in the left lateral position and with continuous ECG monitoring. Standard echocardiographic views were taken (parasternal long- and short-axis; apical 2-, 3-, 4-, and 5-chamber; and subcostal views). Images were acquired at rest and peak stress. Indications for terminating the dobutamine infusion were the following: the patient reaching target heart rate (i.e., 85% of predicted for age); occurrence of a new wall motion abnormality; development of significant symptoms (e.g., chest pain, dyspnea); or significant ECG changes such as arrhythmias. Intravenous contrast was used for all patients at both rest and stress.

Comprehensive DSCMR. DSCMR was performed with a 1.5-T system (Avanto Magnetom, Siemens, Erlangen, Germany). The order of sequences is summarized in Figure 2, and detailed CMR methods

ABBREVIATIONS AND ACRONYMS

AUC = area under the curve
CAD = coronary artery disease
CMR = cardiac magnetic resonance
DSCMR = dobutamine stress cardiac magnetic resonance
DSE = dobutamine stress echocardiography
ECG = electrocardiography
ICA = invasive coronary angiography
LBBB = left bundle branch block
LGE = late gadolinium enhancement
RWMA = regional wall motion abnormality
SPECT = single-photon emission computed tomography

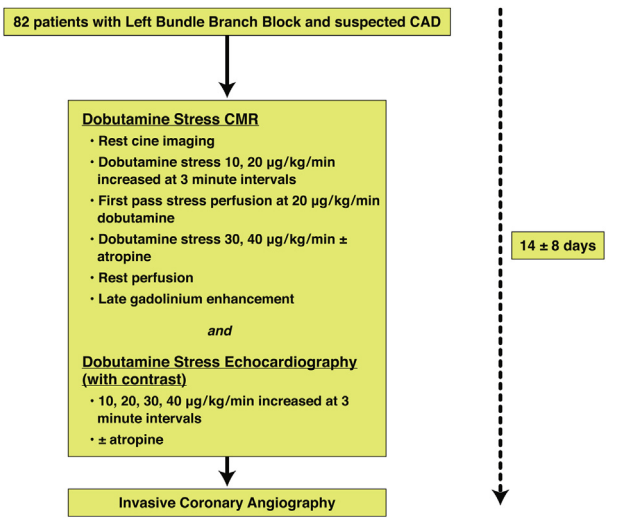

Figure 1. Summary of the Study Protocol

In our study, 82 patients underwent dobutamine stress echocardiography or dobutamine stress cardiac magnetic resonance (CMR) before undergoing invasive coronary angiography. CAD = coronary artery disease.

and analysis are provided in the supplementary methods in the Online Appendix. Dobutamine was infused at progressive 3-min stages of 10, 20, 30, and 40 µg/kg/min. Intravenous boluses of atropine sulfate (0.25 to 0.5 mg aliquots up to a maximum total dose of 2 mg) were used at the 30 or 40 µg/kg/min stages to augment the heart rate response. At the stage of 20 µg/kg/min dobutamine stress (henceforth defined as *intermediate dose*), intravenous gadolinium-tetraazacyclododecanetetraacetic acid (0.1 mmol/kg) was injected and first-pass myocardial perfusion images were acquired. This dose was selected due to our previous clinical experience suggesting that at higher doses of dobutamine, the increase in contractility and heart rate makes it difficult to qualitatively interpret the first-pass perfusion images. Furthermore, there is also some evidence that myocardial perfusion can be accurately assessed at 20 µg/kg/min with a similar increase in myocardial blood flow to adenosine at this dose (14–16). LGE imaging for myocardial infarction was acquired 10 min after intravenous contrast administration by an inversion recovery fast gradient-echo sequence as previously reported (17). Infarcted myocardium was quantitated by semiautomatic detection of any region with signal intensity 2 SD above the mean signal intensity of the remote myocardium as previously validated (17). LGE was counted as positive only if it was in a subendocardial or transmural distribution typical of CAD.

Using CMR cine imaging alone, CMR was judged to be positive if an inducible regional wall motion abnormality (RWMA) was seen. In the comprehensive DSCMR examination, the test was adjudged to be positive: 1) if there was LGE present in a distribution typical of infarction (subendocardial or transmural) with or without evidence of peri-infarct ischemia; or 2) if there was no LGE, if there was an inducible perfusion defect that corresponded to an inducible RWMA.

Invasive coronary angiography. ICA was performed in all 82 patients. An experienced investigator blinded to echocardiographic and CMR findings assessed the presence of coronary stenoses in 2 orthogonal views of each BARI (Bypass Angioplasty Revascularization Investigation)-defined segment by quantitative coronary angiography analysis using GE automated edge detection software, which calibrates using the coronary guide catheter as its reference diameter (Centricity Cardiology CA1000, GE Healthcare, Dornstadt, Germany). Significant stenoses were defined as ≥70% luminal narrowing in the most severe view (≥50% for left main stenosis). Patients were classified as having 1-, 2-, and 3-vessel disease.

Statistical analysis. All continuous variables were expressed as mean ± SD. A 2-tailed p value <0.05 was considered significant. Categorical data are presented as absolute values with percentage in parentheses and were compared by chi-square or Fisher exact test as appropriate. Sensitivities, specificities, positive and negative predictive values, chi-square statistics and the area under the curve (AUC) of stress echocardiography, CMR wall motion analysis, and a comprehensive CMR examination for detection of >70% coronary stenoses by quantitative coronary angiography analysis were calculated. Comparisons between diagnostic techniques were made with the McNemar test. The AUC between the tests was calculated using the method of DeLong et al. (18). All statistics were analyzed using SPSS software (version 19.0, IBM Corporation, Armonk, New York), except for the comparison between the AUC, which was conducted using MedCalc software (version 12.7.0, MedCalc, Ostend, Belgium).

RESULTS

Baseline characteristics. All 82 patients completed the investigations successfully without any complications. There were no patients with suboptimal imaging as judged by the independent observers. There were no major adverse events.

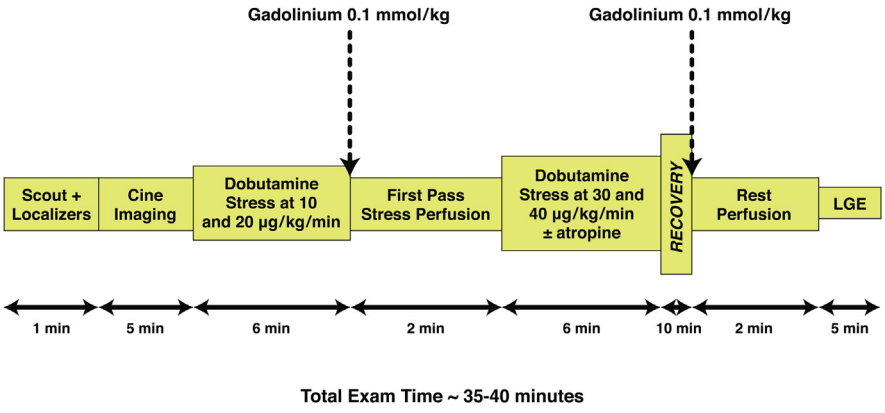

Figure 2. Summary of the CMR Protocol

Protocol for comprehensive dobutamine stress cardiac magnetic resonance (CMR) in which all patients underwent cine imaging at rest and stress, first-pass perfusion at intermediate dose, and late gadolinium enhancement (LGE) imaging.

The mean peak dose of dobutamine given was 35.4 ± 5.7 µg/kg/min and mean peak heart rate was 143.3 ± 10.0 beats/min. Patient characteristics are summarized in Table 1 and hemodynamic parameters are summarized in Table 2.

The mean age of patients with CAD was 57.1 ± 8.9 years, compared with 55.9 ± 6.6 years for patients without CAD. The cohort was typical of a group with intermediate pre-test probability for CAD, with the most common conditions encountered in our patient population being hypercholesterolemia, smoking, hypertension, and family history of CAD. The only significant difference between those with CAD and those without was the presence of hypertension (61.8% in patients with CAD vs. 35.4% in patients without CAD; p = 0.018).

DSE and DSCMR compared with ICA. Following quantitative analysis of ICA, 34 patients were

Table 1. Baseline Characteristics

	All Patients (n = 82)	CAD (n = 34)	No CAD (n = 48)	p Value
Age, yrs	56.5 ± 7.8	57.2 ± 9.2	56.0 ± 6.6	0.50
Male	53 (64.6)	23 (67.6)	30 (62.5)	0.63
QRS duration, ms	133.0 ± 8.1	134.5 ± 7.0	132.2 ± 8.7	0.19
Hypertension	38 (46.3)	21 (61.8)	17 (35.4)	**0.018**
Diabetes mellitus	19 (23.2)	11 (32.4)	8 (16.7)	0.10
Peripheral arterial disease	17 (20.7)	7 (20.6)	10 (20.8)	0.98
COPD	12 (14.6)	6 (17.6)	6 (12.5)	0.54
Hyperlipidemia	39 (47.6)	14 (41.2)	25 (52.1)	0.33
Smoker	33 (40.2)	12 (35.3)	21 (43.8)	0.44
Alcohol excess	9 (11.0)	3 (8.8)	6 (12.5)	0.73
Family history of CAD	37 (45.1)	13 (38.2)	24 (50.0)	0.29
Aspirin	22 (26.8)	9 (26.5)	13 (37.1)	0.34
Beta-blocker	13 (15.9)	6 (17.6)	7 (14.6)	0.71
Oral nitrate	4 (4.9)	0 (0.0)	4 (8.3)	0.14
Statin	32 (39.0)	13 (38.2)	19 (39.6)	0.90
Calcium-channel antagonist	25 (30.5)	14 (41.2)	11 (22.9)	0.08
ACE inhibitor	31 (37.8)	16 (47.1)	15 (31.3)	0.15

Values are mean ± SD or n (%). **Bold** p value is statistically significant.
ACE = angiotensin-converting enzyme; CAD = coronary artery disease; COPD = chronic obstructive pulmonary (airways) disease.

Table 2. Hemodynamic Data for DSCMR

Resting heart rate, beats/min	71 ± 9
Maximal heart rate, beats/min	143.3 ± 10.0
Resting systolic BP, mm Hg	132 ± 20
Peak systolic BP, mm Hg	162 ± 10
Resting diastolic BP, mm Hg	72 ± 9
Peak diastolic BP	71 ± 11
Peak dose of dobutamine, mg	35.4 ± 5.71
Number reaching target HR, 85% of predicted	82 (100.0)
Atropine given	79 (96.3)

Values are mean ± SD or n (%).
BP = blood pressure; DSCMR = dobutamine stress cardiac magnetic resonance; HR = heart rate.

deemed to have significant CAD. For assessment of inducible wall motion abnormalities, DSCMR and DSE had the same sensitivity (70.6%); however, cine imaging had improved specificity (87.5% vs. 72.9%), leading to a higher diagnostic accuracy (80.4% vs. 72.0%). Positive and negative predictive values for wall motion interpretation by CMR were 80.0% and 80.8%, respectively; whereas for echocardiography, values were 64.9% and 77.8% (Table 3). Examples of typical findings using DSCMR are shown in Figures 3 to 5.

There was an incremental benefit in diagnostic accuracy with the addition of stress perfusion imaging and LGE as outlined in Table 3. Eleven patients had LGE; in all patients, this was in an ischemic pattern (subendocardial or transmural). No patients had a subepicardial or midwall pattern of LGE suggestive of an underlying cardiomyopathy. Sensitivity was 82.4%, whereas specificity increased to 95.8%, giving an improved overall diagnostic accuracy of 90.2%. Using the receiver-operating characteristic, the AUC is greatest for a comprehensive DSCMR examination and is significantly better than DSE (AUC: 0.89 vs. 0.72, respectively; $p < 0.05$).

Of the 34 patients with CAD identified by invasive angiography, 14 had left anterior descending disease, 14 left circumflex disease, 5 right coronary artery disease, and 1 had 2-vessel disease. Table 4 summarizes the respective performance of each noninvasive technique in comparison to invasive angiography for determining the affected coronary artery territory. In the left coronary circulation, comprehensive DSCMR had improved sensitivity in comparison to DSE and CMR cine imaging (left anterior descending: 71.4% vs. 64.3% vs. 57.1%; left circumflex: 92.9% vs. 64.3% vs. 78.6%, respectively). Sensitivity for the left-sided circulation was DSE 64.2%, CMR cine imaging 67.9%, and comprehensive DSCMR 82.1%. Both CMR techniques failed to identify 1 RCA lesion that was correctly identified by DSE. All 3 techniques correctly identified the presence of 2-vessel disease in 1 patient.

DISCUSSION

Our study is the first prospective evaluation using a comprehensive DSCMR examination of patients with LBBB for the diagnosis of CAD. Regarding our primary hypothesis, we have shown that DSCMR is a safe procedure that has a higher diagnostic accuracy than DSE does. Additionally, we have shown that there is an incremental benefit in diagnostic accuracy in using a comprehensive examination including CMR cine imaging, first-pass stress perfusion, and LGE over using CMR cine imaging alone.

The prevalence of LBBB increases with age (up to around 17% at the age of 80 years in a Northern European population), and it is known to confer an adverse prognosis, at least in part due to the risk of cardiac death (2–4). The prevalence of CAD in patients with LBBB is thought to be between 30% and 50%; therefore, given the poor prognosis of LBBB, it would be beneficial to identify those who may benefit from revascularization (19).

Presently, however, diagnosis of CAD in patients with LBBB is difficult. Functional noninvasive tests

Table 3. Per-Patient Diagnostic Performance of DSE and CMR

	Sensitivity	Specificity	Accuracy	PPV	NPV	AUC
DSE	70.6 (24/34)	72.9 (35/48)	72.0 (59/82)	64.9 (24/37)	77.8 (35/45)	0.72
CMR cine imaging only	70.6 (24/34)	87.5 (42/48)	80.4 (66/82)	80.0 (24/30)	80.8 (42/52)	0.79
First-pass perfusion	70.6 (24/34)	93.8 (45/48)	84.1 (69/82)	88.9 (24/27)	81.8 (45/55)	0.82
LGE	41.5 (11/34)	100.0 (48/48)	72.0 (59/82)	100.0 (11/11)	67.6 (48/71)	0.66
Comprehensive DSCMR	82.4 (28/34)	95.8 (46/48)	90.2 (74/82)	93.3 (28/30)	88.5 (46/52)	0.89*

Values are % (n/N). *$p < 0.05$ between comprehensive CMR and DSE.
AUC = area under the curve; CMR = cardiac magnetic resonance; DSCMR = dobutamine stress cardiac magnetic resonance imaging; DSE = dobutamine stress echocardiography; LGE = late gadolinium enhancement; NPV = negative predictive value; PPV = positive predictive value.

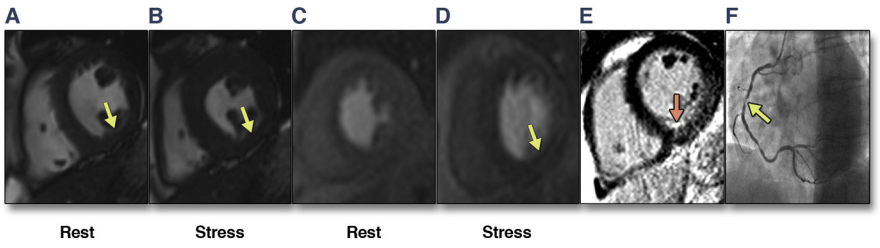

Figure 3. An Example of a Correct Diagnosis of CAD by CMR Cine Imaging, Perfusion, and LGE

A patient with a resting inferior wall motion abnormality **(A and B, arrows)**. There is a subtle inducible perfusion defect at stress but not rest **(C and D, arrow)**. There is subendocardial LGE in the same region; however, the perfusion defect is larger, suggesting peri-infarct ischemia **(E, arrow)**. The comprehensive dobutamine stress CMR is suggestive of CAD affecting the right coronary artery, confirmed by invasive coronary angiography, which revealed a tight stenosis in the right coronary artery **(F, arrow)**. Abbreviations as in Figures 1 and 2.

(exercise ECG, SPECT, and stress echocardiography) are all affected adversely by LBBB (7–9). Cardiac CT angiography has been shown to have good diagnostic accuracy in LBBB; however, in patients with intermediate probability of CAD, such as the population in our study, current guidelines suggest the use of a functional test as first-line (10,11). Due to these limitations and the consequent diagnostic uncertainty, many patients may end up undergoing unnecessary ICA.

Unfortunately, the well-validated noninvasive functional techniques for diagnosis of CAD are not as diagnostically accurate in LBBB. Although the sensitivity of SPECT remains high in patients with LBBB, its specificity decreases, especially in the septum (20). This is mainly due to false positives caused by partial volume effects due to reduced septal thickening. Stress echocardiography provides better results and is presently recommended in patients with LBBB; however, results from published studies are still variable. It has reduced sensitivity, mainly due to false negatives caused by the abnormal resting wall motion and myocardial thickening (9). Geleijnse et al. (9) evaluated 64 patients with LBBB using DSE and reported a sensitivity of 60% in the anterior circulation compared with 67% in the posterior circulation. Other studies have been small and reported mixed results (21,22). The reversible wall motion abnormalities and perfusion defects seen in the left anterior descending territory may also be related to high heart rates during maximal stress, and use of vasodilator stress does seem to provide better results (20,23). These difficulties mean that the ideal noninvasive imaging technique has not yet been found for patients with LBBB. The improved diagnostic accuracy of DSCMR in our study is therefore encouraging.

DSCMR has been shown to have good diagnostic accuracy in patients with suspected CAD, with several studies reporting good sensitivity and specificity (24). In 1 of the largest studies using DSCMR for detection of significant CAD, using CMR cine imaging alone, Gebker et al. (25) reported sensitivity and specificity of 85% and 82%, respectively, with an increase in sensitivity to 91% with the addition of first-pass perfusion, at the cost of a decrease in specificity to 70% in 455 patients (25). The investigators suggested that this was due to the fact that perfusion defects tend to occur before RWMA. The difficulty in assessing RWMA

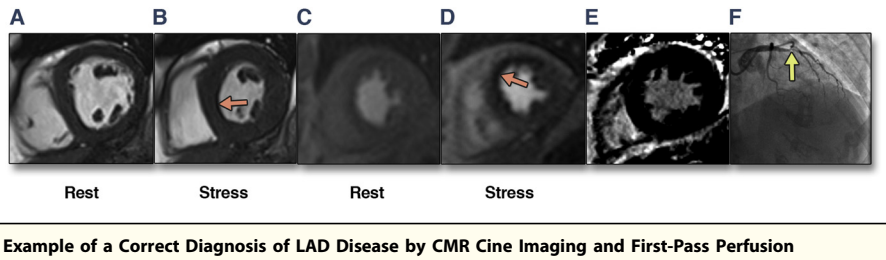

Figure 4. An Example of a Correct Diagnosis of LAD Disease by CMR Cine Imaging and First-Pass Perfusion

A patient with an inducible septal wall motion abnormality **(A and B, arrow)**. An inducible perfusion defect is seen at stress in the septal wall **(C and D, arrow)**. There is no significant late gadolinium enhancement **(E)**. Intensive coronary angiography confirmed a tight stenosis in the left anterior descending (LAD) artery **(F, arrow)**. CMR = cardiac magnetic resonance.

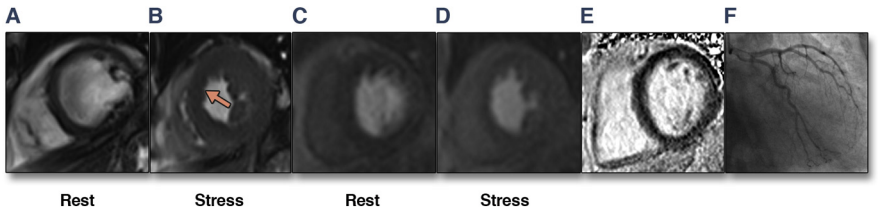

Figure 5. A Typical False Positive Seen by CMR Cine Imaging but Correctly Diagnosed in the Comprehensive Examination

This patient appears to have an inducible septal wall motion abnormality **(A and B, arrow)**. There is no perfusion defect, however **(C and D)**, and no late gadolinium enhancement **(E)**. Intensive coronary angiography revealed no significant coronary artery disease **(F)**. CMR = cardiac magnetic resonance.

in patients with LBBB would explain the lower sensitivity seen in our study, which has reported a similar specificity. The reduced sensitivity of CMR cine imaging alone was also shown in a study by Paetsch et al. (26), who reported a sensitivity of 78.2% and specificity of 87%.

Given the reduced sensitivity of DSCMR due to the resting myocardial abnormalities in LBBB, we also hypothesized that the addition of first-pass stress perfusion and LGE imaging would enhance the diagnostic accuracy of the CMR examination, which was proven to be correct. In a study by Lubbers et al. (27), the investigators found that the addition of first-pass perfusion imaging during dobutamine stress reduced the number of false positives. Indeed, in their study, all 4 patients that had an inducible wall motion abnormality with no perfusion defect had LBBB. Our sensitivity and specificity for DSE corresponds well to a study of 64 patients by Geleijnse et al. (9), also using dobutamine, which reported sensitivity of 68% and specificity of 91%. As one might expect, the sensitivity is similar using CMR cine imaging. The similar number of false negatives may be due to the observer attributing a true RWMA to the dyskinetic motion of LBBB. The higher specificity of CMR cine imaging (reduced false positives) may be due to CMR's increased spatial resolution, allowing for greater diagnostic confidence. In this respect, our results correspond fairly well to those of Nagel et al. (28) in patients without LBBB, who also proposed that the improved diagnostic accuracy using CMR cine imaging alone was due to the increased spatial resolution of CMR.

The addition of first-pass stress perfusion and LGE increased diagnostic accuracy markedly. Cine, perfusion, and LGE imaging are 3 techniques that can each independently diagnose CAD; hence, an examination combining the 3 allows for greater diagnostic confidence. Of clinical importance is the improved performance of the comprehensive DSCMR examination in left-sided coronary disease, where the majority of problems lie with DSE. Sensitivity increased from 64.2% with DSE to 82.1% with the comprehensive examination. One could speculate that this may lead to some prognostic benefit in improved identification of patients who need invasive management. This has been shown in a general population of patients with suspected CAD (29). Similar to other studies, we have shown that a comprehensive CMR examination can be performed safely in routine clinical practice (29).

The additional value of LGE appears to be in its increased specificity and/or positive predictive value. It is important to remember that this may only apply to a cohort with typical anginal symptoms and an intermediate or high probability of CAD. An associated inducible perfusion defect

Table 4. Percentage of Patients Correctly Identified per Vessel by Echocardiography and CMR

	ICA	DSE	CMR Cine Imaging Only	Comprehensive DSCMR
No CAD	48	72.9 (35/48)	87.5 (42/48)	95.8 (46/48)
LAD	14	64.3 (9/14)	57.1 (8/14)	71.4 (10/14)
LCx	14	64.3 (9/14)	78.6 (11/14)	92.9 (13/14)
RCA	5	100.0 (5/5)	80.0 (4/5)	80.0 (4/5)
2-vessel disease	1	100.0 (1/1)	100.0 (1/1)	100.0 (1/1)

Values are n or % (n/N).
ICA = invasive coronary angiography; LAD = left anterior descending; LCX = left circumflex; RCA = right coronary artery; other abbreviations as in Tables 1 to 3.

along with the presence of LGE may indicate peri-infarct ischemia. In other groups of patients, such as those without anginal symptoms, this may not apply as the presence of LGE may be more indicative of a cardiomyopathy, especially if not in a typical coronary distribution, obviating the need for invasive angiography (30). We believe that the increase in sensitivity found by using the comprehensive examination is probably due to the criteria for a positive result, which means that a patient must have either LGE (with or without a perfusion defect) or an inducible RWMA and a perfusion defect, meaning that the criteria are more strict. This combination leads to the overall improved diagnostic performance of the comprehensive DSCMR examination.

We have also found that performing first-pass perfusion at an intermediate dose of dobutamine appears to provide adequate diagnostic confidence for the assessment of inducible perfusion defects by direct comparison against ICA. To the best of our knowledge, there have been no studies that have assessed the performance of first-pass perfusion imaging at different dobutamine doses. However, previous studies suggest that the majority of the increase in myocardial blood flow and vasodilation caused by dobutamine occurs at 20 μg/kg/min; beyond this, there is simply an increase in heart rate and contractility, which in our experience makes it more difficult to interpret perfusion (14–16). Furthermore, the false positive perfusion defects seen in SPECT are most often due to the fast heart rate at peak stress—the rate of false positives reduces significantly in patients with LBBB when vasodilator stress is used rather than dobutamine (23).

Study limitations. Although our study is the first prospective evaluation of DSCMR in patients with LBBB using CMR, there are some limitations. First, although all patients in our study were referred for ICA and this reduced post-test referral bias, we were comparing a functional test (CMR) to an anatomical test. The importance of the functional impact of coronary stenoses has been well established, and we now know that visual assessment of angiographic stenoses is not optimal (31). Results may have been different if we had compared CMR to a functional invasive test such as fractional flow reserve; however, to combat this we only declared a significant stenosis to be over 70% by quantitative coronary angiography analysis rather than 50%, which is most often used.

Our study was also conducted in a single center with high volumes of CMR and angiography. It may be difficult to extrapolate this to lower-volume centers. In addition, the number of patients in our study is relatively small. It is larger, however, than many other diagnostic studies in this area. Further information could be gained by larger, multicenter trials with the potential for obtaining prognostic information.

Last, we did not employ real-time 3-dimensional echocardiography. Whether its addition might improve both sensitivity and specificity of DSE has not been evaluated prospectively in patients with LBBB and suspected CAD. The addition of strain analysis has also been shown to improve diagnostic accuracy of DSE (32).

CONCLUSIONS

Comprehensive DSCMR is a feasible, safe, noninvasive investigation for the exclusion of CAD in patients with LBBB that outperforms DSE. The addition of perfusion and LGE sequences to CMR cine imaging improves sensitivity, specificity, and overall diagnostic accuracy. Comprehensive DSCMR provides a viable noninvasive functional investigation for LBBB and suspected CAD and may overcome some of the disadvantages of DSE in this group.

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Key Words: bundle branch block ■ cardiac magnetic resonance ■ coronary disease ■ stress echocardiography.

▶ APPENDIX

For supplementary methods, please see the online version of this article.