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High-Resolution Versus Standard-Resolution Cardiovascular MR Myocardial Perfusion Imaging for the Detection of Coronary Artery Disease

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Background—Although accelerated high-spatial-resolution cardiovascular MR (CMR) myocardial perfusion imaging has been shown to be clinically feasible, there has not yet been a direct comparison with standard-resolution methods. We hypothesized that higher spatial resolution detects more subendocardial ischemia and leads to greater diagnostic accuracy for the detection coronary artery disease. This study compared the diagnostic accuracy of high-resolution and standard-resolution CMR myocardial perfusion imaging in patients with suspected coronary artery disease.

Methods and Results—A total of 111 patients were recruited to undergo 2 separate perfusion-CMR studies at 1.5 T, 1 with standard-resolution (2.5×2.5 mm in-plane) and 1 with high-resolution (1.6×1.6 mm in-plane) acquisition. High-resolution acquisition was facilitated by 8-fold *k-t* broad linear speed-up technique acceleration. Two observers visually graded perfusion in each myocardial segment on a 4-point scale. Segmental scores were summed to produce a perfusion score for each patient. All patients underwent invasive coronary angiography and coronary artery disease was defined as stenosis $\geq 50\%$ luminal diameter (quantitative coronary angiography). CMR data were successfully obtained in 100 patients. In patients with coronary artery disease (n=70), more segments were determined to have subendocardial ischemia with high-resolution than with standard-resolution acquisition (279 versus 108; *P*<0.001). High-resolution acquisition had a greater diagnostic accuracy than standard resolution for identifying single-vessel disease (area under the curve, 0.88 versus 0.73; *P*<0.001) or multivessel disease (area under the curve, 0.98 versus 0.91; *P*=0.002) and overall (area under the curve, 0.93 versus 0.83; *P*<0.001).

Conclusions—High-resolution perfusion-CMR has greater overall diagnostic accuracy than standard-resolution acquisition for the detection of coronary artery disease in both single- and multivessel disease and detects more subendocardial ischemia. (***Circ Cardiovasc Imaging***. 2012;5:306-313.)

Key Words: cardiovascular MRI ■ coronary artery disease ■ high spatial resolution ■ myocardial perfusion imaging

Cardiovascular MR (CMR) myocardial perfusion imaging is a highly accurate method of detecting significant coronary artery disease (CAD) in single- and multivessel disease.[1–3] Recent comparative studies have suggested a higher diagnostic accuracy of CMR compared with single photon emission CT (SPECT).[3] This increase in accuracy is thought to relate in part to the higher spatial resolution of CMR compared with SPECT (typically 2–3 mm versus 5–10 mm).

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With recently developed spatiotemporal undersampling methods such as *k-t* broad-use linear acquisition speed-up technique (*k-t* BLAST) and *k-t* sensitivity encoding, the in-plane spatial resolution of perfusion-CMR can be improved further, from 2 to 3 mm to 1 to 2 mm.[4] The feasibility and clinical applicability of high-resolution perfusion-CMR has been demonstrated in a number of studies[5–8]; but to date, only 1 small-scale study in volunteers has directly compared high-resolution and standard-resolution acquisition. In their study, Maredia et al[8] demonstrated a reduction in endocardial dark-rim artifact and improved image quality of high-resolution perfusion images.

We hypothesized that in patients with CAD, high-spatial-resolution perfusion-CMR would improve detection of subendocardial ischemia and thus the overall diagnostic accuracy compared with standard-resolution perfusion-CMR.

Figure 1. Dark-rim artifact: Case Example 1. This example shows a midventricular slice during standard-resolution perfusion-CMR. Dark-rim artifact (DRA; arrows) is a frequent finding and relates to several factors including cardiac motion, Gibb's ringing, susceptibility, and partial volume cancellation between the myocardium and blood pool. Although dark-rim artifacts may mimic perfusion defects, they can be distinguished by characteristic features: they occur at the arrival of contrast in the left ventricular cavity and before its arrival in the myocardium (Frame 1); they tend to disappear within 8 to 10 frames (Frame 7); their location is usually typical for a particular pulse sequence; and their width roughly equates to the in-plane spatial resolution, which was 2.5 mm in this example (Frame 3). See also Figure 3 (Case Example 3). CMR indicates cardiovascular MR.

Methods

Population

A total of 111 patients with suspected CAD were recruited. Each patient's pretest probability of CAD was calculated based on their age, sex, and symptoms.[9] All had undergone or were scheduled to undergo diagnostic coronary angiography within the previous/next 30 days as part of routine clinical care. No coronary intervention or clinical events occurred between angiography and recruitment. Exclusion criteria were contraindications to CMR, adenosine, or gadolinium contrast agents; a history of recent (within 6 months) myocardial infarction or unstable angina; or poorly controlled arrhythmias. Patients were instructed to refrain from caffeine for 24 hours before their CMR study but continue cardiac medications as normal. All patients gave written consent to participate and the study was approved by the regional ethics committee.

CMR Protocol

Studies were carried out on a 1.5-T CMR system (Philips Healthcare, Best, The Netherlands) using a 5-element cardiac phased array receiver coil for signal reception. All patients underwent 2 CMR studies on separate days within 4 weeks. For the same patient, both scans were performed before or after coronary angiography. On 1 occasion, a "standard" perfusion pulse sequence was used, and on the other, a high-resolution method accelerated with *k-t* BLAST was used. The order of methods was randomly chosen.

For both techniques, perfusion data were acquired in 3 short-axis slices (basal, mid, and apical) in each R-R interval. The standard pulse sequence was a saturation recovery gradient echo method accelerated with sensitivity encoding (acceleration factor 2, partial Fourier sampling, partial echo, repetition time 2.7 ms, echo time 1.0 ms, flip angle 15°, image acquisition time per slice 136 ms, single saturation prepulse per R-R interval shared over 3 slices, matrix 144×144, median field of view 360 mm, 2.5×2.5-mm in-plane spatial resolution). The high-resolution pulse sequence used a similar saturation recovery gradient echo method but was accelerated with *k-t* BLAST (acceleration factor 8 with 11 training profiles, no partial Fourier or partial echo acquisition, repetition time 3.4 ms, echo time 1.7 ms, flip angle 15°, 1 saturation prepulse per slice, image acquisition time per slice 103 ms, matrix 192×192, median field of view 310 mm, and 1.6×1.6-mm in-plane spatial resolution).

For both studies, stress perfusion started after 4 minutes of an intravenous adenosine infusion (140 μg/kg/min) during an intravenous bolus injection of dimeglumine gadopentetate (Magnevist; Schering AG, West Sussex, UK) and a 15 mL saline flush delivered at 5 mL/s at the time the patient held their breath in end-expiration. For the standard-resolution method, a contrast agent dose of 0.05 mmol/kg body weight was used during perfusion data acquisition like in previous studies with this pulse sequence.[3] To compen-

sate for the lower signal-to-noise ratio associated with the smaller voxel size, a contrast agent dose of 0.1 mmol/kg body weight was used for the high-resolution method, consistent with previous reports.[7,10,11] Rest perfusion imaging was performed 15 minutes later using identical imaging parameters. Late gadolinium-enhanced imaging was performed in all patients on their first visit using conventional methods (1.6×1.6-mm in-plane spatial resolution) with a cumulative contrast agent dose of 0.2 mmol/kg body weight (the same for both protocols).[12] During standard-resolution perfusion CMR scans, this cumulative dose was achieved by administration of an additional bolus of 0.1 mmol/kg body weight of contrast agent immediately after rest perfusion.

CMR Analysis

CMR images were interpreted in random order by 2 observers (S.P., M.M.; 10 years and 1 year experience in CMR) acting in consensus and blinded to all clinical information (QMASS 6.1.6; Medis, Leiden, The Netherlands). Visual analysis used a 16-segment American Heart Association model.[13] Perfusion in a segment was considered abnormal if signal intensity was reduced compared with remote myocardial segments or an endocardial to epicardial perfusion gradient within a segment was present.[6] Additionally, any perfusion defect was required to persist longer than the contrast media first pass to distinguish it from artifact. Corresponding late gadolinium-enhanced images were reviewed side by side with the perfusion data. Perfusion defects present at stress but not rest and occurring outside any hyperenhanced myocardial tissue on late gadolinium-enhanced images were considered as inducible defects according to the Duke algorithm.[14] Perfusion in each myocardial segment was graded on a 4-point scale (transmural ischemia index) from 0 to 3 (0=normal, 1=inconclusive, 2=subendocardial defect, 3=transmural defect). All segmental scores were summed to produce a perfusion score (0–48) for each patient. In addition, perfusion scores were calculated for the left anterior descending, left circumflex, and right coronary artery territories according to the 16-segment American Heart Association model adjusted for arterial dominance.[13,15] Image quality was graded 1 to 4 (1=unusable, 2=poor, 3=adequate, 4=excellent) by consensus of the 2 observers. Occurrence of artifacts related to *k-t* reconstruction, respiratory motion, electrocardiographic gating, and endocardial dark-rim artifact was scored between 0 and 3 (0=none, 1=minor, 2=moderate, 3=severe). Dark-rim artifacts were recorded if an endocardial dark-rim appeared at the arrival of contrast in the left ventricular cavity and before contrast arrival in the myocardium (Figure 1). Where present, the maximum width of dark-rim artifact was measured with electronic calipers at standardized window settings.

Quantitative Coronary Angiography

Quantitative coronary angiography was performed (QCAPlus; Sanders Data Systems, Palo Alto, CA) on all x-ray angiography images by

an experienced observer blinded to clinical and CMR data (M.M.; 6 years of experience in coronary angiography). Each myocardial segment was ascribed a coronary artery territory according to the standard American Heart Association 16-segment model adjusted for arterial dominance.[13,15] Significant CAD was defined angiographically as stenosis ≥50% diameter in any of the main epicardial coronary arteries or their branches with a diameter of ≥2 mm.

Statistical Analysis

Analysis was performed using SPSS 17.0 (SPSS, Chicago, IL). Data are presented as mean±SD or median, as appropriate. Group means were compared using the paired Student t test. Ordinal data were compared using χ^2 or Wilcoxon signed-rank tests as appropriate. All statistical tests were 2-tailed and a probability value <0.05 was considered significant.

Receiver operating characteristic analysis was performed on a per-patient basis using summed perfusion scores to determine the diagnostic accuracies of standard and high-resolution acquisition to detect coronary stenosis of ≥50% on quantitative coronary angiography. A secondary analysis using a stenosis severity of ≥70% was also performed. Optimal perfusion score cutoff values were determined as the values that maximized the sum of sensitivity and specificity. Diagnostic accuracies are presented as areas under the curve (AUCs) and compared using the methods described by Delong and Delong.[16] The study was designed to have a statistical power of 80% to detect a 10% difference in AUC with an α level of 0.05. Sensitivity, specificity, and positive/negative predictor values were also calculated for each technique but these values were not directly compared because the study was not statistically powered for such analyses.[17]

Results

Study Population

A total of 111 patients were enrolled in the study. In 5 patients, both standard and high-resolution CMR scans could not be completed (3 patients were claustrophobic and 2 patients declined to return for a second visit). Three patients successfully completed both scans but x-ray angiography was cancelled for clinical reasons unrelated to the CMR findings. Three patients had to be excluded due to technical problems on either one of their visits. Therefore, 100 patients (90% of the cohort) were included in the final analysis. In these patients, all images were of analyzable quality. Clinical details of the 100 study patients (74% men; mean age, 61±7 years) are summarized in Table 1. Quantitative coronary angiography confirmed significant CAD in 70 patients (70%). Thirty-two patients (32%) had single-vessel disease and 38 patients (38%) had multivessel disease (2- or 3-vessel disease; Table 1). In terms of anatomic location of coronary artery stenoses, 46 patients (46%) had significant left anterior descending stenoses, 42 patients (42%) had significant left circumflex stenoses, and 43 patients (43%) had significant right coronary artery stenoses. Typical examples of patients with ischemia are shown in Figures 2 and 3 and in online Video 1 (http://circimaging.ahajournals.org). The hemodynamic stress response achieved with adenosine during standard and high-resolution imaging was similar (rate-pressure product, mm Hg×beats/min: 10 262±2491 versus 10 247±2279; P=0.90). All patients were in sinus rhythm and heart rate allowed acquisition at each R-R interval in all. All 12 patients with a clinical history of myocardial infarction but no additional patients had evidence of hyperenhancement on late gadolinium-enhanced imaging imaging.

Table 1. Patient Characteristics (n=100)

Age, y±SD	61±7
Male, no. (%)	74 (74)
Medical history, no. (%)	
Hypertension	67 (67)
Hypercholesterolemia	65 (65)
Diabetes mellitus	18 (18)
Smoking	42 (42)
Family history of CAD	37 (37)
Previous MI	12 (12)
Previous PCI	8 (8)
Atrial fibrillation	2 (2)
LV ejection fraction, %	58±9
Pretest likelihood of CAD, % (IQR)*	51 (31–65)
Presenting cardiac symptoms, no. (%)	
Nonanginal chest pain	22 (22)
Atypical angina	37 (37)
Typical angina	32 (32)
Dyspnea	9 (9)
Angiography findings, no. (%)†	
No significant disease	30 (30)
One-vessel disease	32 (32)
Two-vessel disease	14 (14)
Three-vessel disease	24 (24)
LAD disease	46 (46)
LCX disease	42 (42)
RCA disease	43 (43)

CAD indicates coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; LV, left ventricular; IQR, interquartile range; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery.

*Pretest likelihood of CAD is expressed as median percent (interquartile range).

†Significant disease defined as coronary stenosis ≥50% on quantitative coronary analysis.

Detection of CAD

The diagnostic accuracy (AUC) of standard-resolution perfusion-CMR for the detection of CAD ≥50% was 0.83 (Table 2; Figure 4). The optimal perfusion score cutoff value was determined as ≥4, which resulted in a sensitivity and specificity of 84% and 73%, respectively (Table 3).

The diagnostic accuracy of high-resolution perfusion-CMR to detect was significantly higher with an AUC of 0.93 (P<0.001; Table 2; Figure 4). The optimal perfusion score cutoff value was also ≥4 with this technique, which resulted in a sensitivity and specificity of 91% and 80%, respectively (Table 3). Similar diagnostic performance was seen using a CAD threshold ≥70% and the diagnostic accuracy of high-resolution perfusion-CMR remained significantly higher than standard-resolution acquisition (AUC, 0.92; 95% CI, 0.87–0.97 versus 0.83; 95% CI, 0.75–91; P<0.001). The statistical power for the comparison of AUCs was 0.93 (α 0.05, β 0.07).[18]

The diagnostic performance of high-resolution acquisition to detect CAD ≥50% was significantly greater than standard-
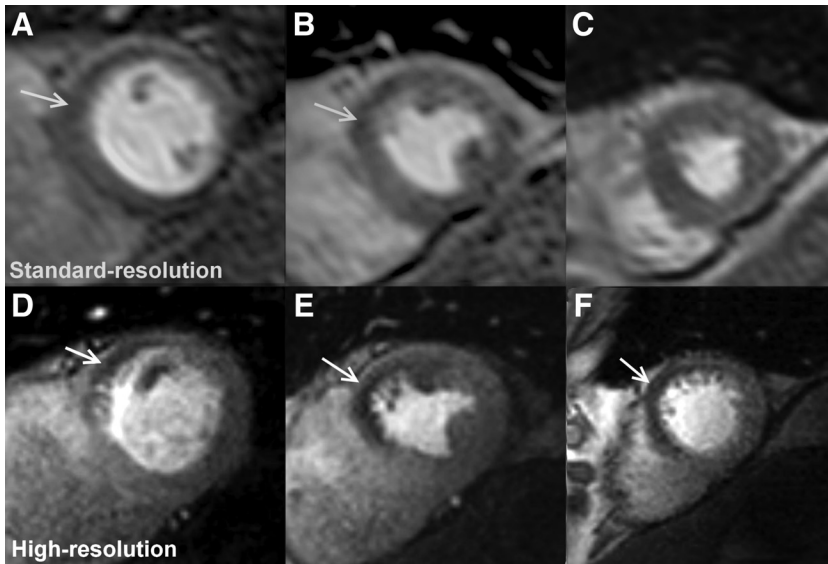
Figure 2. Stress perfusion-CMR: standard versus high-resolution: Case Example 2. This patient had left anterior descending artery disease. Standard resolution (A–C) shows an inconclusive perfusion defect in the basal anterior segment (arrow, A) and transmural perfusion defects in the mid-anterior (arrow, B) and apical septal segments (arrow, C) (total perfusion score=7). High resolution (D–F) shows definite perfusion defects in the same distribution (D–E) plus additional ischemia in the mid-anterior and apical anterior segments (E and F; total perfusion score=13). The perfusion defects and their transmural extent are better delineated with high-resolution acquisition (eg, ischemia is determined as subendocardial in E). CMR indicates cardiovascular MR.

resolution for both single-vessel disease (AUC, 0.88 versus 0.73; P<0.001) and multivessel disease (AUC, 0.98 versus 0.91; P=0.002; Table 2).

Detection of Anatomic Location of CAD

High-resolution acquisition had a significantly higher diagnostic accuracy than standard-resolution in the left anterior descending and left circumflex territories for the detection of CAD ≥50% (AUC, left anterior descending, 0.92 versus 0.81; left circumflex, 0.87 versus 0.73; both P values

<0.001). Differences for the right coronary artery territory did not reach statistical significance (AUC, 0.88 versus 0.80; P=0.08; Table 2).

In single-vessel disease (n=32), both standard and high-resolution imaging identified perfusion defects in only 1 territory in a similar number of patients (25 [78%] versus 27 [84%]; P=0.75). However, in multivessel disease, high-resolution imaging identified perfusion defects in >1 territory in significantly more patients than standard resolution (32 [84%] versus 23 [61%]; P=0.04).
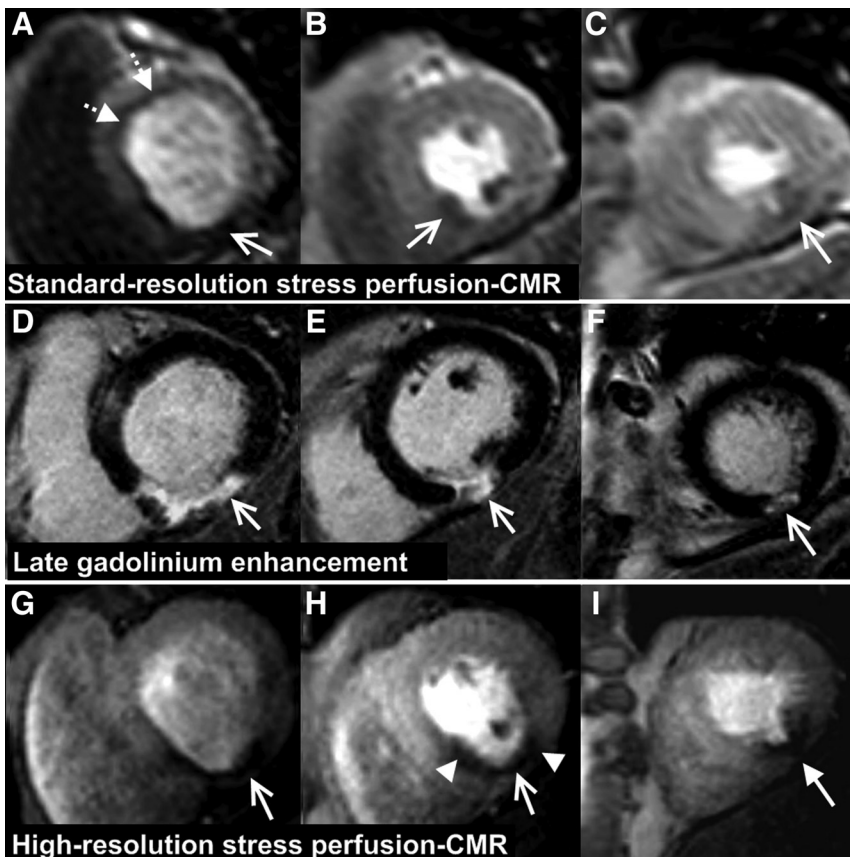
Figure 3. Standard versus high-resolution perfusion-CMR: Case Example 3. An inferior scar with thinning of the myocardium is seen in all images (open arrows, A–I). Dark-rim artifact seen on the basal slice (dashed arrows, A) at standard resolution (2.5 mm in-plane spatial resolution) is not present at high resolution (G). By virtue of their identical spatial resolution, LGE imaging and high-resolution perfusion-CMR allow for a better correlation between scar and perfusion than LGE imaging and standard resolution perfusion-CMR. An area of peri-infarct ischemia (small arrows, H) is therefore more clearly identified at high resolution. In this patient, coronary angiography showed a chronic total occlusion of the right coronary artery and the patient's symptoms were relieved by subsequent PCI. CMR indicates cardiovascular MR; LGE, late gadolinium-enhanced imaging; PCI, percutaneous coronary intervention.

Table 2. Diagnostic Accuracy of Standard-Resolution and High-Resolution Perfusion-CMR for the Detection of Coronary Artery Disease

	Area Under Receiver Operator Characteristic Curve		
	Standard Resolution	High Resolution	P Value
Overall	0.83 (0.75–0.91)	0.93 (0.88–0.98)	<0.001
Single-vessel disease	0.73 (0.60–0.86)	0.88 (0.79–0.97)	<0.001
Multivessel disease	0.91 (0.83–0.99)	0.98 (0.95–1.00)	0.002
LAD disease	0.81 (0.71–0.90)	0.92 (0.86–0.97)	<0.001
LCX disease	0.73 (0.64–0.83)	0.87 (0.79–0.94)	<0.001
RCA disease	0.81 (0.72–0.90)	0.88 (0.81–0.95)	0.08

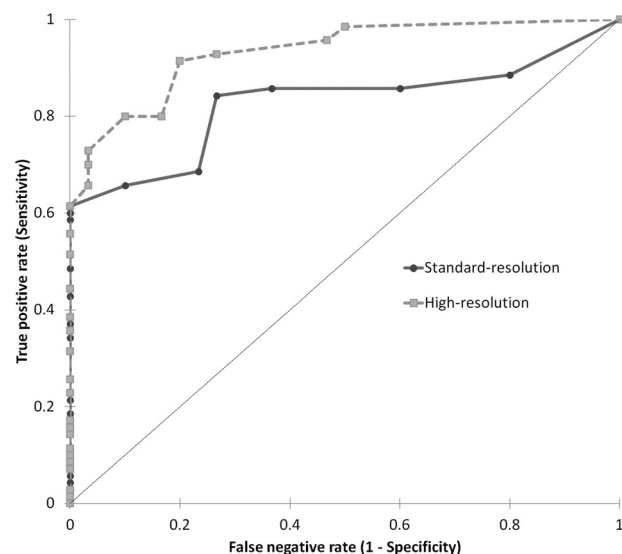Values expressed as mean (95% CI). Coronary artery disease defined as stenosis ≥50%.

CMR indicates cardiovascular MR; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery.

Subendocardial Ischemia

Using the 16-segment model, 1120 myocardial segments were available from the 70 patients with CAD for further analysis. With high-resolution acquisition, significantly more segments were determined as having subendocardial ischemia (transmural index score of 2) than with standard resolution (279 versus 108; $P<0.001$); and there was a significant reduction in the number of segments determined as being normal (692 versus 831; $P<0.001$) or inconclusive (47 versus 70; $P=0.04$; Figure 5). By contrast, the number of segments assessed as having transmural ischemia was similar with both techniques (102 versus 111; $P=0.56$).

Image Quality

Overall image quality (median score=3 for both; $P=0.58$) and artifact score (median score=0 for both; $P=0.10$) were
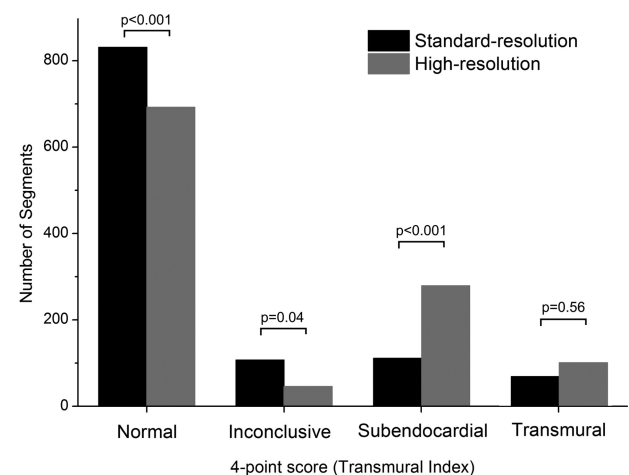
Table 3. Sensitivity, Specificity, and Predictive Values for Standard-Resolution and High-Resolution Perfusion-CMR for the Detection of Coronary Artery Disease

	Standard Resolution	High Resolution
Overall		
Sensitivity, %	84 (74–91)	91 (82–96)
Specificity, %	73 (55–86)	80 (62–91)
PPV, %	88 (77–94)	91 (82–96)
NPV, %	67 (48–82)	80 (61–92)
Single-vessel disease		
Sensitivity, %	78 (61–89)	88 (71–96)
Specificity, %	73 (55–86)	80 (62–91)
PPV, %	76 (57–88)	82 (65–93)
NPV, %	76 (56–89)	86 (67–95)
Multivessel disease		
Sensitivity, %	84 (69–93)	95 (82–99)
Specificity, %	93 (73–97)	97 (82–100)
PPV, %	91 (76–98)	97 (85–99)
NPV, %	82 (64–93)	94 (78–99)

Values are expressed as percentage (95% CI) and are quoted at optimal perfusion score cutoff thresholds (determined by receiver operator curve analysis). Coronary artery disease defined as ≥50% stenosis.

CMR indicates cardiovascular MR; PPV, positive predictive value; NPV, negative predictive value.

similar for both standard and high-resolution techniques. However, dark-rim artifact was significantly less frequent with high resolution (8% versus 30%; $P<0.001$) and when it did occur, it was less marked than with standard resolution (1.7±0.3 versus 3.3±0.8 mm; $P<0.001$). Fifteen high-resolution data sets (15%) were affected by *k-t* reconstruction artifacts at stress and/or rest due to respiratory motion, but this did not affect myocardial contrast passage and generally occurred at the end of a breath hold.

Figure 4. Receiver operator characteristic curves. Standard and high-resolution perfusion-CMR both had a high diagnostic accuracy for the detection of coronary artery disease (≥50% stenosis) but the high-resolution technique was superior. The areas under the curve were 0.83 for standard resolution and 0.93 for high resolution ($P<0.001$). CMR indicates cardiovascular MR.

Figure 5. Distribution of transmural ischemia index. In patients with coronary artery disease (≥50% stenosis), high-resolution perfusion-CMR determined significantly more segments as having subendocardial ischemia than the standard resolution technique and fewer as normal or inconclusive. CMR indicates cardiovascular MR.

Discussion

This study has demonstrated a high diagnostic accuracy for both standard and high-resolution perfusion-CMR. However, the high-resolution technique outperformed the standard-resolution technique with greater diagnostic accuracy in single-vessel disease, multivessel disease, and overall. In particular, high-resolution acquisition was better at distinguishing a multivessel pattern of disease. These benefits are likely to be derived from better detection of subendocardial ischemia at greater spatial resolution. Our findings may therefore have important implications for the noninvasive assessment of myocardial ischemia and for defining the role of high-resolution perfusion-CMR in current clinical practice.

CMR perfusion imaging requires rapid data acquisition, which necessitates a tradeoff among spatial resolution, temporal resolution, signal-to-noise, and spatial coverage. *k-t* BLAST exploits correlations in time and space to accelerate data acquisition and the speed-up afforded can be used to improve spatial resolution with relatively preserved signal-to-noise.[6,19,20] Although the clinical feasibility of *k-t* BLAST and similar acceleration techniques such as *k-t* sensitivity encoding has been demonstrated, their advantages over commonly used standard-resolution methods has not been defined in a clinical setting.[5–8] In particular, there has been no previous direct comparison between standard and high-resolution techniques in a patient population.

In this study, the overall diagnostic accuracy of standard-resolution perfusion-CMR for detecting angiographically defined CAD was within the range of previous studies with an AUC of 0.83 compared with 0.86 by Schwitter et al,[1] 0.78 by Cheng et al,[21] and 0.89 in the perfusion analysis of the Clinical Evaluation of Magnetic Resonance Imaging in Coronary Heart Disease (CE-MARC) study.[3] Similarly, the overall diagnostic accuracy of high-resolution perfusion-CMR was within the range of previous studies using *k-t* sensitivity encoding or *k-t* BLAST with an AUC of 0.93 compared with 0.94 by Manka et al[11] and 0.85 by Plein et al.[6]

We speculate that the demonstrated superiority of high-resolution acquisition relates to a better specificity due to reduction in subendocardial dark-rim artifacts and a greater sensitivity due to better detection of subendocardial ischemia (Table 3). Previous work investigating dark-rim image artifacts has shown the prominent role of spatial resolution on the occurrence and extent of this artifact.[10,22] The significant reduction in both frequency and severity of dark-rim artifact with high-resolution acquisition seen in this study confirms similar findings in a previous volunteer study.[8]

In this study, high-resolution perfusion-CMR detected more segments with subendocardial ischemia than the standard-resolution method. The 2 possible explanations for this observation are that standard-resolution acquisition failed to detect subendocardial ischemia in some patients or that high-resolution acquisition overestimated ischemia in normal segments. Without an available reference standard for determining subendocardial ischemia, this question cannot be conclusively resolved. However, given that the overall diagnostic accuracy for detection of CAD was significantly better with high resolution than standard resolution, the more plausible explanation is that high-resolution acquisition leads to better detection of subendocardial ischemia. As well as the benefits this provides in typical CAD detection, high-resolution perfusion-CMR could potentially provide an improved tool for the evaluation of conditions in which there are microvascular perfusion abnormalities at the subendocardial level such as syndrome X, hypertensive heart disease, or hypertrophic cardiomyopathy.[23]

In this study, contrast agent dose was optimized for visual analysis. However, quantitative methods for the estimation of myocardial blood flow based on myocardial perfusion CMR data have been validated in animal models and applied to clinical studies.[24–26] High-resolution perfusion-CMR offers further intriguing opportunities for quantitative analysis such as sharper delineation of transmural perfusion gradients.[27] However, the algorithms applied for the reconstruction of high-resolution perfusion-CMR data acquired with spatio-temporal undersampling methods give rise to a degree of low-pass temporal filtering, posing additional challenges to quantitative assessment. Recent developments such as *k-t* principal component analysis are likely to overcome some of these challenges and will require evaluation in future studies.[28]

One of the limitations of myocardial perfusion imaging and visual analysis is the dependence on a reference area of normal perfusion. This is a particular impediment in diffuse or multivessel disease, the group of patients who are at greatest risk and would benefit most from accurate diagnosis and correct risk-stratification.[29] The ability of high-resolution perfusion-CMR to adequately resolve subendocardial ischemia and transmural perfusion gradients should therefore be a major advantage because it reduces the need for an intrapatient comparison. Our study demonstrated this advantage because 84% of patients with multivessel disease were correctly identified as having perfusion defects in >1 territory compared with only 61% with standard resolution. This finding is of considerable significance because the assessment of multivessel disease has long been recognized as a weakness of myocardial perfusion imaging. With single photon emission CT, as few as 29% of patients with known angiographic 3-vessel disease are recognized as having inducible perfusion abnormalities in all 3 coronary artery territories.[30] Similarly, in the only study that has evaluated standard-resolution perfusion-CMR specifically in the setting of angiographic 3-vessel disease, the detection of a 3-vessel disease pattern was only 57%.[31] Therefore, the demonstrated ability of high-resolution acquisition to more accurately identify the extent of ischemia in multivessel disease may represent a significant step forward in noninvasive imaging with potential implications for correctly stratifying and managing this high-risk group (Case Example 4, Video 1).

Study Limitations

k-t BLAST adds complexity to the acquisition of perfusion data. In particular, the method is sensitive to respiratory motion and cardiac arrhythmia. In our study, respiratory artifacts affected 15% of high-resolution studies, which is similar to previous studies.[6,7] For this reason, overall image quality and artifact scores for both techniques were similar, despite the significant reduction of dark-rim artifact seen at

high resolution. Newer spatiotemporal undersampling methods for high-resolution acquisition are less susceptible to respiratory motion but were not available at the time of this study.[28] Potentially these techniques could offer the demonstrated benefits of high-resolution acquisition without the respiratory artifact tradeoff, but this is yet to be investigated.

This study was powered to detect a difference in overall diagnostic performance as defined by the AUC of receiver operating characteristic analysis but not to compare individual sensitivity or specificity values in a dichotomous model because this would have required a very large sample size.[17] Such large comparative studies pose considerable logistic challenges and are unlikely to be conducted for incremental optimizations of an established imaging test such as perfusion-CMR. The presented diagnostic accuracies must also be interpreted within the context of referral bias because all patients had been clinically preselected for coronary angiography. We also acknowledge that because transmural ischemic index can only be assessed at a segmental level, data clustering may affect the analysis of its distribution, but because each patient contributed the same number of segments, the presented estimates should remain valid.

Finally, similar to the majority of previous perfusion-CMR studies, a limitation of this work was the use of x-ray coronary angiography to determine the presence of significant CAD because this only provides an anatomic rather than functional assessment of a coronary artery stenosis. However, x-ray coronary angiography remains the most widespread investigation in clinical decision-making and thus relates this study to real-world practice.

Conclusions

This study showed that accelerated, high-resolution perfusion-CMR imaging has higher diagnostic accuracy than standard-resolution acquisition for the detection of CAD in both single- and multivessel disease. Dark-rim artifact is reduced and the extent of multivessel disease is better identified at high resolution. High-spatial-resolution perfusion-CMR may also provide an improved tool for identifying subendocardial ischemia.

Disclosures

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CLINICAL PERSPECTIVE

Coronary artery disease is the leading cause of death worldwide and accurate methods of detection are therefore important. Furthermore, the detection of ischemia in patients with known coronary artery disease is increasingly used to guide revascularization decisions, particularly in complex cases. Myocardial perfusion cardiovascular MR (CMR) has emerged as a highly accurate modality to detect ischemia, and the recent CE-MARC study demonstrated a higher diagnostic accuracy compared with single photon emission CT. Myocardial perfusion CMR offers significantly greater spatial resolution than single photon emission CT without any ionizing radiation exposure. In this study of 100 patients, we used a new technique to increase the spatial resolution of myocardial perfusion CMR even further (<2 mm in-plane). The results showed that overall diagnostic accuracy as measured by the area under the receiver operator curve was better with the high spatial resolution technique. In addition, high-resolution myocardial perfusion CMR allowed better detection of subendocardial ischemia and better correlation with scar on late gadolinium-enhanced CMR. We propose that high-resolution myocardial perfusion CMR shows promise for the screening of patients with suspected coronary artery disease and as a guide to management in cases of established coronary artery disease, in particular as part of a comprehensive CMR assessment of myocardial function, viability, and perfusion.

SUPPLEMENTARY MATERIAL

Video 1 - Stress Perfusion-CMR: Standard vs. High-Resolution: Case Example 4

This 52-year old patient had significant three-vessel coronary artery disease on coronary angiography. Standard-resolution (first movie) shows perfusion defects in the basal inferior, mid inferior, mid inferoseptal, apical anterior and apical inferior segments. High-resolution (second movie) shows a similar distribution of perfusion defects but demonstrates additional ischemia in the basal lateral, mid anterior and mid anterolateral segments with a circumferential defect in the apical slice. Perfusion defects are also better delineated at high-resolution and the transmural extent of ischemia more clearly seen.