Three-dimensional whole-heart vs. two-dimensional high-resolution perfusion-CMR: a pilot study comparing myocardial ischaemic burden

Adam K. McDiarmid¹, David P. Ripley¹, Kevin Mohee¹, Sebastian Kozerke², John P. Greenwood¹, Sven Plein¹, and Manish Motwani¹*

¹ Division of Cardiovascular and Diabetes Research, Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds, UK; and ²Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland

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Aims
Typically, myocardial perfusion imaging with two-dimensional (2D) cardiovascular magnetic resonance (CMR) acquires data in three to four myocardial slices at a spatial resolution of 2–3 mm. However, accelerated data acquisition can facilitate higher spatial resolution (<2 mm) or three-dimensional (3D) whole-heart coverage (up to 16 slices). This study aims to compare image quality, diagnostic confidence, and quantitation of myocardial ischaemic burden (MIB) between 2D high-resolution and 3D whole-heart perfusion-CMR.

Methods and results
Twenty-seven patients with stable angina underwent both high-resolution 2D and whole-heart 3D perfusion-CMR. Total perfusion defect (TPD) and total scar burden (TSB) areas were contoured and expressed as percentage myocardium. MIB was calculated by subtracting TSB from TPD. Image quality, artefact, and diagnostic confidence scores were similar for both techniques (P > 0.05). The mean MIB from high-resolution and 3D acquisition was similar (4.3 ± 5.2% vs. 4.1 ± 4.9%; P = 0.81), with a strong correlation between techniques (r = 0.72; P < 0.001). There was no systematic bias for estimates of MIB between techniques [mean bias = −0.17%, 95% confidence interval (CI): −1.7 to −1.3%] and the 95% limits of agreement were −7.5 to 7.2%. When used to categorize MIB as >10% or <10%, there was only fair agreement between the two techniques (κ = 0.29, 95% CI: −0.12 to 0.70).

Conclusion
There is strong correlation and broad agreement between estimates of MIB from both techniques. However, the 95% limits of agreement are relatively wide and therefore a larger comparative study is needed before they can be considered interchangeable—particularly around the clinically relevant 10% threshold.

Keywords
coronary artery disease • magnetic resonance imaging • ischaemia • myocardial perfusion imaging

Introduction
Myocardial ischaemic burden (MIB) is an important prognostic marker and can help identify patients most likely to benefit from revascularization compared with medical therapy alone. It is most commonly assessed with single-photon emission computed tomography (SPECT) or positron emission tomography (PET), as these techniques offer whole-heart coverage.¹,² Myocardial perfusion imaging with cardiovascular magnetic resonance (CMR) is a highly accurate method for diagnosing coronary artery disease (CAD), but its role in quantifying MIB is less certain.³,⁴ The lack of complete left ventricular (LV) coverage with standard two-dimensional (2D)-perfusion-CMR (three to four short-axis slices only) means that any estimate of MIB is an extrapolation. However, the introduction of accelerated data acquisition using spatio-temporal undersampling methods has led to the development of three-dimensional (3D) whole-heart perfusion-CMR, or alternatively 2D-perfusion-CMR with higher spatial resolution (<2 mm).⁵ Potentially, 3D-perfusion-CMR presents a direct alternative to SPECT or PET for measurement of MIB—without inter-slice assumptions.⁶ A further...
advantage of 3D acquisition is that all slices are acquired at the same selected point in the cardiac cycle which facilitates better inter-slice comparison.\textsuperscript{5,6} On the other hand, higher spatial resolution acquisition has also been shown to have several benefits including greater detection of subendocardial ischaemia and reduced dark-rim artefact (DRA).\textsuperscript{8–11} Although both methods have high diagnostic accuracy and have been validated against fractional flow reserve (FFR), it is not known how their estimates of MIB compare.\textsuperscript{12–15} Therefore, this pilot study directly compared image quality, diagnostic confidence, and quantification of MIB between 3D whole-heart and 2D high-resolution perfusion-CMR.

**Methods**

**Patient population**

Thirty patients with stable angina and scheduled for coronary angiography on a clinical basis were recruited to undergo both a 2D high-resolution and a 3D whole-heart perfusion-CMR scan on two separate days within 8 weeks. The order of methods was randomly chosen. No clinical events occurred between the two scans. The presence or absence of significant CAD was defined by quantitative coronary angiography (QCA). Exclusion criteria were contra-indications to CMR, adenosine, or gadolinium contrast agents; a history of recent (<6 months) myocardial infarction or unstable angina; or poorly controlled arrhythmias. Patients were instructed to refrain from caffeine for 24 h prior to scans, but continue cardiac medications as normal.\textsuperscript{16} Patients gave written consent and the study was approved by the regional ethics committee.

**CMR protocol**

All studies were performed on a 3.0 T scanner (Achieva-TX, Philips Healthcare, Best, The Netherlands) equipped with dual-source parallel radiofrequency transmission and a 32-channel cardiac coil.

2D high-resolution and 3D-perfusion-CMR acquisitions used the optimal imaging parameters derived from previous studies (Figure 1).\textsuperscript{6,10,13,15} High-resolution acquisition used a spoiled saturation-recovery fast gradient-echo sequence [repetition time (TR)/echo time (TE)/flip angle: 2.7 ms/1.0 ms/15°; saturation pre-pulse delay 120 ms, 1 saturation pre-pulse per slice, acquisition time per slice 134 ms; no partial Fourier or partial echo acquisition; field-of-view 340 × 340 mm; five-fold k-t BLAST (broadcast-use linear acquisition speed-up technique) acceleration with 11 interleaved training profiles; three short-axis slices (basal, mid, and apical using ‘3 of 5’ positioning\textsuperscript{17}) with 10 mm thickness and 1.2 × 1.2 mm acquired in-plane spatial resolution]. 3D-perfusion-CMR used a spoiled fast saturation-recovery gradient-echo sequence [TR/TE/flip angle 1.8 ms/0.7 ms/15°; saturation pre-pulse delay 150 ms; acquisition timed to end-systole; linear k-space encoding; 70% partial Fourier acquisition in two dimensions; field-of-view 350 × 350 mm; 10-fold k-t acceleration and 11 training profiles leading to 7-fold net acceleration; typical acquisition duration 192 ms; k-t BLAST reconstruction to 12 contiguous short-axis slices (planned from long-axis cines to ensure coverage from apex to below LV-outflow-tract in systole) with voxel size 2.3 × 2.3 × 5 mm\textsuperscript{3}]. Stress-perfusion images were acquired during intravenous adenosine-induced hyperaemia administered for 4 min at 140 mcg/kg/min. Consistent with previous k-t BLAST facilitated perfusion-CMR studies, an intravenous bolus of 0.075 mmol/kg of gadobutrol (Gadovist, Bayer Healthcare, Berlin, Germany) was administered at 4.0 mL/s followed by a 20 mL saline flush. Stress perfusion-CMR was followed by cine-imaging covering the LV in 10–12 short-axis sections. Rest perfusion-CMR was performed 15 min after stress, using identical imaging parameters. Late-gadolinium enhancement (LGE) imaging was performed on the first visit, after an additional 10–15 min using a 2D T1-weighted segmented inversion-recovery gradient-echo method (TR/TE/flip angle 4.9 ms/1.9 ms/15°; inversion time adjusted according to Look-Locker; spatial resolution 1.35 × 1.35 × 10 mm; same short-axis geometry as cine-imaging to cover same LV volume). Case examples are shown in figures 2 and 3.

**CMR analysis**

**Visual analysis for ischaemia**

Perfusion-CMR images were anonymized, randomly ordered, and reported by two observers (S.P. and A.K.M.; >10 years and 2 years of experience, respectively) (Qmass MR 7.5, Medis, Leiden, The Netherlands). Anonymization involved removal of all identifying data—including dates of acquisition. For random order review, both patient order and acquisition type were shuffled. The presence or absence of a perfusion defect was recorded by both observers acting independently. In case of disagreement, arbitration from a third observer was sought (J.P.G., >10 years of experience). A perfusion defect was defined as an area of reduced signal intensity on stress perfusion images compared with remote myocardium or the presence of an endocardial-to-epicardial perfusion gradient.\textsuperscript{8} Additionally, any perfusion defect was required to persist longer than the myocardial contrast first-pass to distinguish it from artefact. Corresponding LGE images were reviewed side-by-side with the perfusion data. Perfusion defects present at stress but not rest and occurring outside any hyper-enhanced myocardial tissue on LGE images were considered as inducible defects (ischaemia).\textsuperscript{10} Image quality and diagnostic confidence were graded by both observers in consensus. Image quality was graded 0–3 (0 = interpretable, 1 = poor, 2 = adequate, 3 = high). Occurrence of artefacts related to k-t reconstruction, respiratory motion, electrocardiographic gating, and DRA was scored 0–3 (0 = none, 1 = minor, 2 = moderate, 3 = severe). Using the AHA 17-segment model (minus apical cap for 2D high-resolution three-slice technique), diagnostic confidence was recorded for each perfusion territory (0 = uncertain, 1 = low-confidence, 2 = high-confidence).\textsuperscript{18}

**Assessment of perfusion defect size**

**Total perfusion defect**

For both high-resolution and 3D acquisitions, total perfusion defect (TPD) as percentage myocardium was determined by dividing the area of any perfusion defect by the area of total myocardium (both contoured on stress-perfusion images), and multiplying by 100. All manual contouring was performed by an experienced observer (A.K.M., 2 years of experience) using the same software, same workstation, and standardized zoom and window settings. Perfusion defects were contoured at the frame of maximal myocardial signal intensity determined by a region of interest drawn in remote myocardium. Contiguous perfusion defects across different perfusion territories were contoured as a whole; non-contiguous perfusion defects were contoured separately and the areas summed.

**Total scar burden**

Total scar burden (TSB) in percentage myocardium was determined by dividing the total area of any hyper-enhancement by the area of total myocardium (both contoured on full short-axis stack of LGE images) and multiplying by 100. Myocardial hyper-enhancement for LGE images was defined as areas with signal intensity ≥2 SD above the mean signal intensity of remote myocardium.\textsuperscript{19}

**Myocardial ischaemic burden**

For each acquisition, MIB as percentage myocardium was calculated by subtracting TSB from TPD. Any negative values for MIB were normalized to zero (no ischaemia). To determine the reproducibility of MIB...
assessments, the analysis was repeated in 10 randomly selected patients 1 month later by the same observer (A.K.M.), and by a second observer (D.P.R., >3 years of experience) blinded to the results of all previous analyses.

**Quantitative coronary angiography**

QCA was performed (QCAPlus, Sanders Data Systems, Palo Alto, CA, USA) on anonymized X-ray angiography images (M.M., 8 years of experience). Significant CAD was defined as luminal stenosis ≥ 70% diameter in any of the main epicardial coronary arteries or their branches with a diameter ≥ 2 mm.

**Statistical analysis**

Data are presented as mean ± SD. Group means were compared using paired Student’s t-tests. Ordinal data were compared using the Wilcoxon signed-rank test. Linear correlations were assessed using Pearson correlation coefficients. All statistical tests were two-tailed and P < 0.05 was considered significant. Agreement between high-resolution and 3D-perfusion-CMR measurements for TPD and MIB was assessed using Bland–Altman analysis. The categorization of MIB as <10% or >10% by both techniques was compared using Cohen’s k statistic. To assess reproducibility, coefficients of variation (CoVs) were calculated.

**Results**

**Study population**

Of the 30 recruited patients, 28 completed both perfusion-CMR acquisitions (2 patients did not return due to claustrophobia). Data

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**Figure 1** 2D high-resolution and 3D whole-heart techniques. In 2D-perfusion-CMR (A), three non-contiguous slices are acquired in different phases of the cardiac cycle in order to maximize spatial coverage (positioned from long-axis cines using ‘3 of 5’ technique). Each slice is acquired after a saturation pre-pulse (black bar). In 3D-perfusion-CMR (B), a single saturation pre-pulse is followed by a saturation-recovery time (TSR) and undersampled 3D-perfusion data readout. The use of advanced spatio-temporal undersampling allows sufficient data acquisition to reconstruct 12–16 contiguous slices, i.e. whole-heart coverage (positioned from long-axis cines to ensure coverage from below LVOT to apex in end-systole). The ‘training data’ is acquired with the undersampled data in an interleaved fashion. As all perfusion data in the 3D technique are acquired at the same point in the cardiac cycle, reconstructed slices all appear in the same cardiac phase (end-systole here). Modified and reprinted with permission from Motwani et al.5
Case Example 1. A 45-year-old man with previous PCI to the LAD presented with significant angina. The top-panel shows 3D-perfusion-CMR (12 slices) at stress; the middle-panel shows LGE imaging; and the bottom-panel shows high-resolution (1.1 mm in-plane) perfusion-CMR at stress. 3D-perfusion-CMR shows stress-induced hypoperfusion throughout the anterior wall from base to apex, well beyond the area of scar seen in the mid-anterior wall on LGE imaging (solid arrows = scar; dashed arrows = ischaemia beyond scar). The three-slice 2D high-resolution technique did not demonstrate any significant ischaemia beyond the established scar in the mid-ventricle. X-ray angiography confirmed a subtotal occlusion of a large diagonal branch. VLA, vertical long axis.
Figure 3  Case Example 2. A 57-year-old man with prior MI presented with recurrent angina. The top-panel shows 3D-perfusion-CMR (12 slices) at stress; and the bottom-panel shows 2D high-resolution (1.1 mm in-plane) perfusion-CMR at stress. Both perfusion techniques show an inferior perfusion defect from base to apex consistent with the infarct seen on LGE imaging (middle-panel). This example shows the benefit of high-resolution acquisition as the perfusion defects are better delineated compared with 3D acquisition, and therefore a small amount of additional peri-infarct ischaemia can be seen in each of the three slices (arrows) beyond the area of established scar. Overall, the extent of ischaemia is better seen with 2D high-resolution acquisition and there is more confident correlation with LGE imaging which is acquired at a similar spatial resolution (1.2 mm in-plane). With 3D acquisition, the lower spatial resolution (2.5 mm in-plane) means that the borders of the perfusion defect within each slice are less distinct and are more difficult to distinguish from DRA in the mid-to-apical anteroseptal regions (endocardial border opposite dashed lines). VLA, vertical long axis. Reprinted with permission from Motwani et al.5
from one patient were excluded due to a mistimed contrast injection during their high-resolution perfusion acquisition. Therefore, paired perfusion-CMR scan data from 27 patients were available for the final analysis. All 27 patients underwent coronary angiography within 6 weeks of their second scan (8 patients before; and 19 patients after), and all had evidence of significant CAD defined by QCA.

Table 1 summarizes further clinical details. The mean interval between perfusion-CMR scans was 17 ± 38 days. There was no significant difference in the haemodynamic stress response during 2D high-resolution and 3D-perfusion-CMR imaging (rate–pressure product, mmHg × beats/min: 10 274 ± 2246 vs. 10 219 ± 2259; P = 0.89).

Diagnostic confidence and image quality
No images were graded unusable and therefore there were no further exclusions for either technique. Image quality (median score = 2 for both; P = 0.52) and artefact scores (median = 1 for both; P = 0.87) were similar for both techniques. Diagnostic confidence was high for both techniques in all three perfusion territories (all median scores = 2; all P values between methods > 0.05).

Total perfusion defect
All 27 patients (100%) were found to have perfusion defects (inducible or fixed) by both observers. TPD by 2D high-resolution and 3D whole-heart acquisition showed strong positive correlation (r = 0.75; P < 0.001) and there was no significant difference in mean TPD values (9.1 ± 5.7 vs. 7.8 ± 5.8%, respectively; P = 0.12). There was no systematic bias for estimates of TPD between techniques [mean bias = −1.26%, bias 95% confidence interval (CI): −2.8 to 0.4%] and the 95% limits of agreement were −9.3 to 6.8% (Figure 4).

Myocardial ischaemic burden
MIB by 2D high-resolution and 3D-perfusion-CMR showed strong positive correlation (r = 0.72; P < 0.001) and there was no significant difference in mean MIB values (4.3 ± 5.2 vs. 4.1 ± 4.9%, respectively; P = 0.81) (Figure 5). There was no systematic bias for estimates of MIB between techniques (mean bias = −1.26%, bias 95% CI: −1.7 to 1.3%) and the 95% limits of agreement were −7.5 to 7.2% (Figure 6).

Out of the 27 patients, MIB was found to be >10% by both methods in 3 patients; and <10% by both methods in 17 patients (including 4 patients with an MIB of 0% by both methods). In 7 of the 27 patients, the two methods disagreed at the 10% threshold: in 3 patients, the high-resolution method estimated MIB as >10% but 3D acquisition estimated it as <10% (MIB difference = 4.1 ± 2.6%); and in 4 patients, the high-resolution method estimated MIB as <10%, but 3D acquisition estimated it >10%
Influence of prior MI

All 16 patients with prior history of MI had evidence of hyper-enhancement on LGE imaging. There were no cases of LGE hyper-enhancement without a clinical history of MI. In 8 of the 16 patients (50%) with prior MI, a negative MIB value was determined with both 2D and 3D methods (normalized to zero for subsequent agreement analyses). There were no cases where only one of the techniques determined a negative MIB value.

After categorizing patients into prior MI (n = 16) or no MI (n = 11), there were no significant differences in mean MIB values between 2D and 3D methods for either group (MI: 1.9 ± 3.9 vs. 1.4 ± 3.3%, P = 0.55; no MI: 8.4 ± 4.7 vs. 8.6 ± 3.7%, P = 0.93). Similarly, there was no systematic bias for estimates of MIB between techniques for either the MI group (mean bias = 0.41%, bias 95% CI: −1.8 to 1.0%, 95% limits of agreement: −5.7% to 5.0%) or the no MI group (mean bias = 0.23%, bias 95% CI: −3.5 to 4.0%, 95% limits of agreement: −10.0 to 10.5%).

Reproducibility

The intra-observer CoVs for MIB estimates from high-resolution and 3D perfusion-CMR were 9 and 12%, respectively. Corresponding CoVs for inter-observer reproducibility were 14 and 15%, respectively.

Discussion

The main findings of this study are (i) image quality and diagnostic confidence scores are similar for both 2D high-resolution and 3D whole-heart perfusion-CMR; and (ii) although there is strong correlation and broad agreement between estimates of MIB from both techniques, the 95% limits of agreement are relatively wide and therefore a larger comparative study is needed before they can be considered interchangeable—particularly when categorizing MIB as either side of 10%.

An accurate assessment of MIB is important because the extent of ischaemia is a marker of patient prognosis. In the nuclear imaging sub-study of COURAGE, patients with an MIB > 10% had a lower risk of death or MI if they underwent revascularization rather than optimal medical therapy alone.

Most data on MIB have been derived from SPECT studies, but with advances in accelerated data acquisition, 3D whole-heart perfusion-CMR has become feasible and its role in assessing MIB has also been evaluated in a number of recent studies. In the first study, 3D-perfusion-CMR was shown to perform better than conventional 2D acquisition in estimating the size of perfusion defects in phantoms. Since then several clinical studies have demonstrated its feasibility and high level of reproducibility for measuring MIB. In particular, estimates of MIB from 3D-perfusion-CMR have been used to confirm a reduction in ischaemic volume following percutaneous coronary intervention, have shown strong correlation with the Duke Jeopardy Score (an invasive index of ischaemic burden), and have also been validated against FFR for the detection of significant CAD.

A recent study by Jogiya et al. found strong correlation between estimates of MIB from 3D-perfusion-CMR and SPECT in 38 patients with confirmed perfusion defects on both modalities. Although the latter study found no systematic bias between MIB estimates from

(MIB difference = 9.3 ± 1.2%). Overall, when used to categorize MIB as >10% or <10%, there was only fair agreement between the two techniques (κ = 0.29, 95% CI: −0.12 to 0.70) (Figure 5).
the two techniques, and therefore suggested potential interchangeability, the 95% limits of agreement were relatively wide (−14.3 to 13.1%). Considering that a 10% MIB threshold is often used to direct clinical management, this caution is particularly relevant at the lower end of the MIB spectrum given the clinical impact of even a 5–10% absolute difference. Nonetheless, disagreement between 3D-perfusion-CMR and SPECT estimates of MIB at the 10% threshold only occurred in 3 of 38 cases in the latter study.6

On the other hand, investing acceleration into high-resolution 2D-perfusion-CMR rather than 3D whole-heart coverage, also has potential benefits for MIB estimation compared with standard 2D acquisition (Figure 3). As well as being less susceptible to DRA and having better in-slice correlation with LGE (which is acquired at a similar spatial resolution), high-resolution perfusion-CMR has also been shown to detect greater amounts of subendocardial ischaemia compared with standard-resolution 2D acquisitions—with particular benefit in patients with multi-vessel disease.10,11 In one direct comparison, in 35 patients with angiographically confirmed 3-vessel CAD, only 24 patients were found to have an MIB > 10% with a 2D standard-resolution perfusion-CMR method compared with 33 with the high-resolution technique.11 However, unlike 3D whole-heart perfusion-CMR, the 2D high-resolution method has not yet been compared with SPECT or angiographic scores for MIB estimation.

As both 3D and high-resolution 2D-perfusion-CMR offer competing benefits in MIB estimation, their comparison in the current study is well justified. Although there has been no previous direct comparison of 3D whole-heart and 2D high-resolution perfusion-CMR, the study by Jogiya et al.6 did compare MIB estimates from 3D acquisition with estimates from three slices selected from the same 3D whole-heart dataset. The authors explicitly acknowledged the limitations of such an extrapolation, including the impact of resolution and timing of acquisition in the cardiac cycle, but the data did offer some insight into the impact of three-slice vs. whole-heart estimates of MIB. Although MIB estimates in Jogiya et al.’s study6 were smaller from the three-slice analysis compared with whole-heart analysis (5.7 vs. 6.8%, P = 0.03), there was no difference in assigning patients to either medical or revascularization therapy when using a clinical threshold of 10% MIB.

In our study, which is the first direct comparison of high-resolution 2D and whole-heart 3D-perfusion-CMR acquisition, there was only fair agreement across the 10% MIB threshold (κ = 0.29). In 4 of 27 cases, 3D-perfusion-CMR identified an MIB > 10%, but estimates with 2D high-resolution perfusion-CMR were < 10%; and conversely there were three cases where MIB was > 10% with 2D high-resolution perfusion-CMR but not with 3D acquisition. These differences with potential clinical impact likely relate to the competing merits of both techniques, i.e. complete spatial coverage for ischaemia detection including the apical cap with 3D acquisition vs. better detection of subendocardial ischaemia with high-resolution acquisition. As these factors are likely to affect individual patients differently according to their specific distribution of CAD, a single-best approach is difficult to define. Furthermore, with similar image quality, artefact and diagnostic confidence scores for both 3D and high-resolution perfusion-CMR, it remains difficult to conclude on the preferred approach for MIB estimation—particularly in the absence of a true reference standard.

An additional finding in this study was a negative MIB value, with both techniques. This was seen in 50% of patients with prior MI, and for the purpose of analysis was considered to represent no inducible ischaemia. A potential reason for the occurrence of negative MIB values may be an issue of inadequate co-registration between perfusion and LGE imaging slices. Such misregistration would be expected to have most impact on the 2D perfusion technique in which only 3 perfusion slices must be related to 12 LGE imaging slices. However, whilst 3D-perfusion-CMR may offer better slice-to-slice registration with LGE imaging by virtue of greater spatial coverage, the 2D high-resolution perfusion technique offers better intra-slice registration by virtue of the similar spatial resolution as LGE (1.2 vs. 1.3 mm). Which of these effects is the most important in an individual patient, for an individual perfusion defect, cannot be predicted, and depends on the precise intra-slice and inter-slice extent of any perfusion defect, as well as the relative contributions of scar and ischaemia. However, both effects clearly have the potential to lead to the scenario where quantified TSB from LGE imaging is larger than the TPD from either the 2D high-resolution or 3D-perfusion-CMR sequence. Furthermore, it is recognized that an infarct detected on LGE imaging may sometimes be underestimated or not seen on perfusion imaging as a result of small size, heterogeneous infarct tissue characteristics, or recanalization of the culprit vessel.22 The findings in this study highlight the difficulties in reliably assessing peri-infarct ischaemia which ideally requires intimate registration of perfusion and LGE images in terms of both spatial coverage and spatial resolution—and not just one variable in isolation.

Finally, the relatively wide 95% limits of agreement between 3D and high-resolution estimates of MIB in this study (overall, and for both MI and non-MI subgroups) suggest that estimates of MIB may not be used interchangeably at present—particularly when categorizing patients either side of the 10% threshold. We would also apply the same argument to previous comparisons of MIB by SPECT and 3D-perfusion-CMR. Instead, there is a need for larger comparative studies to define the optimal prognostic MIB threshold for each of these techniques separately.

**Study limitations**

We acknowledge this is a pilot study and only a larger study with prognostic outcomes will determine whether the differences seen in MIB between techniques are clinically meaningful. Nonetheless, the findings from this exploratory data are a reminder of the heterogeneity of available perfusion-CMR methods and the need for greater standardization given the potential influence of factors such as spatial resolution, temporal resolution, and spatial coverage.23

This study investigated a population with a relatively high prevalence of previous MI (n = 16), but we were primarily interested in the assessment of inducible ischaemia. In some cases, the presence of scar may have limited the detection of superimposed inducible ischaemia, and it is possible that the assessment of ischaemia may have been more accurate in populations without previous MI. Similarly, although a population with a broader spectrum of MIB would have been more comprehensive, our focus at the lower end around the 10% threshold is the most clinically relevant.

We acknowledge the use of QCA is an imperfect reference standard for ischaemia. However, our main aim was to compare the size of perfusion defects in patients with CAD between...
techniques, rather than re-examine their diagnostic accuracy which has been done previously. Although FFR is clearly a better endpoint for perfusion studies, we considered QCA an adequate endpoint for this purpose. Following this initial pilot study, a larger study with an FFR endpoint is planned.

**Conclusion**

This study adds to the ongoing debate about the comparative benefits of either higher spatial resolution or greater spatial coverage in perfusion-CMR—and where the optimal trade-off lies. Although estimates of MIB from high-resolution and 3D perfusion-CMR are strongly correlated, the 95% limits of agreement are relatively wide and therefore a larger comparative study is needed to determine if they can be considered freely interchangeable—particularly around the clinically relevant 10% threshold. Moreover, there is a need to define the optimal prognostic MIB threshold for each of these techniques separately.

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