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Quantitative myocardial perfusion imaging versus visual analysis in diagnosing myocardial ischaemia: a CE-MARC sub-study

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Abstract

Objectives: To compare the diagnostic accuracy of visual and quantitative analyses of myocardial perfusion cardiovascular magnetic resonance (CMR) against a reference standard of quantitative coronary angiography.

Background: Visual analysis of perfusion CMR studies for assessing myocardial perfusion has been shown to have high diagnostic accuracy for coronary artery disease. However, only a few small studies have assessed the diagnostic accuracy of quantitative myocardial perfusion.

Methods: This retrospective study included 128 patients randomly selected from the CE-MARC population such that the distribution of risk factors and disease status was proportionate to the full population. Visual analysis results of CMR perfusion images, by consensus of two expert readers, were taken from the original study reports. Quantitative myocardial blood flow (MBF) estimates were obtained using Fermi-constrained deconvolution. The reference standard for myocardial ischaemia was a quantitative coronary X-ray angiogram (QCA) stenosis severity of ≥70% diameter in any coronary artery of >2mm diameter, or ≥50% in the left main stem. Diagnostic performance was calculated using receiver operator characteristic (ROC) curve analysis.

Results: The AUC for visual analysis was 0.88 (95% confidence interval: 0.81, 0.95) with a sensitivity of 81.0% (95% confidence interval: 69.1%, 92.8%) and specificity of 86.0% (95% confidence interval: 78.7%, 93.4%). For quantitative stress MBF the AUC was 0.89 (95% confidence interval: 0.83, 0.96) with a sensitivity of 87.5% (95% confidence interval: 77.3%, 97.7%) and specificity of 84.5% (95% confidence interval: 76.8%, 92.3%). There was no statistically significant difference between the diagnostic performance of quantitative and visual analyses (p=0.72). Incorporating rest MBF values to generate an MPR did not significantly increase the quantitative analysis AUC (p=0.79).

Conclusions: Quantitative perfusion has a high diagnostic accuracy for detecting coronary artery disease, but is not superior to visual analysis. The incorporation of rest perfusion imaging does not improve diagnostic accuracy in quantitative perfusion analysis.

Key words: cardiovascular magnetic resonance, myocardial ischaemia, quantitative myocardial perfusion, diagnostic accuracy

Abbreviations

AHA = American heart association
AIF = arterial input function
AUC = area under the curve
CAD = coronary artery disease
CMR = cardiovacular magnetic resonance
LGE = late gadolinium enhancement
LMS = left main stem
MBF = myocardial blood flow
MPR = myocardial perfusion reserve
QCA = quantitative coronary angiography
ROC = receiver operator characteristic
SR-TFE = saturation recovery turbo field echo

Introduction

Cardiovascular Magnetic Resonance (CMR) is a well-established technique for the assessment of patients with coronary artery disease (CAD), being diagnostically superior (1,2), cost effective (3,4) and a better predictor of cardiovascular events (5) than myocardial perfusion scintigraphy by single-photon emission computed tomography (SPECT). CMR compares favourably with positron emission tomography (PET) (6), has higher image resolution, is more widely available, does not use ionizing radiation; and can evaluate function, perfusion and viability in the same investigation. Perfusion CMR requires the passage of a contrast agent bolus through the heart to be visualised over time. Typically a saturation prepared single-shot readout sequence is used to achieve adequate coverage and spatial and temporal resolution (7,8). Post-processing of CMR perfusion images can generate estimates of absolute myocardial blood flow (MBF). Absolute MBFs provide an objective measure of perfusion which does not require a healthy region of myocardium for visual comparison. They have been used to show diffuse perfusion changes due to smoking (9) and type 2 diabetes mellitus (10) and there is evidence to suggest that these measurements may bring improvements in diagnostic performance (11). However assessments of the diagnostic accuracy of MBF estimates have been limited to small studies (typically <50 patients) (11–15). Perfusion is often expressed as myocardial perfusion reserve (MPR = stress MBF / rest MBF). However, it is unknown whether the use of MPR values improves diagnostic performance over stress perfusion measurements alone. If not, the time consuming rest perfusion scan could potentially be removed from the acquisition protocol without reducing the performance of the test (16,17).

The primary objective of this study was to compare the sensitivity, specificity and diagnostic accuracy of expert visual analysis and MBF estimates against a reference standard of quantitative

coronary angiography (QCA). This was done using a large representative subsample of the CE-MARC (clinical evaluation of magnetic resonance imaging in coronary heart disease) study (2). We hypothesised that quantitative CMR would have a higher diagnostic accuracy than visual analysis for identifying significant coronary artery stenosis. A secondary objective was to compare the diagnostic accuracy of MPR measurements, which use both rest and stress MBF data, with stress MBF measurements only.

Methods

Patients: The study protocol was approved by the national research ethics service. CE-MARC recruited patients with suspected angina pectoris, of which 676 had assessable CMR and angiography (2,18). For this sub-study 128 cases were randomly selected by an independent statistician from the CE-MARC population, such that the distribution of risk factors (hypertension, diabetes, smoking, age) and disease status (normal, single, double or triple vessel disease) was proportionate to those in the full population. This sub-sample contained 50 patients that have been included in a previous study (16).

Image acquisition: Myocardial perfusion CMR and QCA data were acquired from each patient as previously described (2,18). All patients underwent invasive quantitative coronary angiography (QCA) within 32 days of their CMR examination. Adenosine (140 μg/kg/min) induced stress imaging was performed at least 15 minutes before rest imaging. Myocardial perfusion CMR was performed using a bolus intravenous injection of 0.05 mmol/kg dimeglumine gadopentetate (Magnevist®, Schering AG, West Sussex, UK) through an arm vein at an injection rate of 5ml/s. CMR imaging was carried out on 1.5T Philips Intera (Best, The Netherlands) equipped with 'Master' gradients (30 mT/m peak gradients and 150 mT/m/ms slew rate) using a 5-element cardiac phased-array coil and triggering performed by the

vectorcardiographic method. Three short axes images were acquired using a T1-weighted saturation recovery turbo field echo (SR-TFE) imaging sequence. A shared (non-slice selective) saturation pulse was used giving pre-pulse delay times to the centre of k-space of 126ms, 272ms and 418ms for the basal, middle and apical slices respectively. The image acquisition parameters were: TE 1.0 ms, TR 2.7 ms, flip angle 15°, SENSE factor 2, matrix 144 × 144, field of view 320–460 mm, pixel size 2.2-3.2mm, slice thickness 10 mm and partial Fourier 0.67 giving a readout window of 130.2ms per slice. Imaging continued until the first pass had been observed to pass through the myocardium. The average number of frames in the perfusion series was 56 (range 26, 78).

Late gadolinium enhanced CMR was performed between 10-15 minutes after the rest perfusion study with a T1-weighted, segmented inversion-recovery gradient echo sequence; pulse sequence parameters: TE 1.9 ms, TR 4.9 ms, flip angle 15°, 10–12 short axis slices, single slice per breath-hold, matrix 240 × 240, field of view 320–460 mm as per patient size. The optimal inversion time to null signal from normal myocardium was determined prior to the scan using a Look-Locker approach (19).

Image Analysis: Quantitative CMR analysis was performed blinded to the results of all other investigations. Contours describing the myocardium and a region within the left ventricular blood pool, avoiding papillary muscles, were drawn using dedicated cardiac image analysis software (Mass 7.0, Medis, Leiden University, Leiden, The Netherlands). Contours were copied to all time frames and manually adjusted for motion. Adjustments were limited to rigid translations only. Manual contouring took around one hour per patient. The myocardium was subdivided into 6 circumferentially equidistant regions in the basal and mid slices and 4 in the apical slice according to the AHA standard (20). Individual perfusion data sets exhibiting

excessive (more than one frame) through plane motion (typically due to ECG gating failure) were visually identified and excluded prior to MBF quantitation. Signal versus time curves from the myocardium and blood pool were converted to contrast agent concentration curves assuming a linear signal response to contrast agent as described previously (16). All pre-contrast signal estimates were taken from the stress study. Values of 1435ms and 4.3 $s^{-1}.mM^{-1}$ were used for the blood T1 and contrast agent relaxivity respectively. To avoid remnant contrast agent from the stress perfusion scan affecting the rest perfusion analysis the pre-contrast signal intensity was subtracted from the rest perfusion curves prior to analysis. Myocardial blood flow (MBF) values were estimated using Fermi-constrained deconvolution (16,21). The arterial input function was taken from the basal slice. The pre-contrast baseline signal, end of first pass time point and the bolus arrival time delay between the blood pool and myocardial curves were calculated using previously described automated methods (16,22)

Visual CMR perfusion images were jointly reported by two cardiologists (JPG, SP) with >6 years' experience in CMR at the time, and who were blind to the results of all other investigations. This was a perfusion only assessment that did not take into account cine, LGE or angiography images sets. Scores for hypoperfusion (ischaemia) of 0 (normal), 1 (equivocal), 2 (subendocardial ischaemia), or 3 (transmural ischaemia) were given by visual comparison of stress and rest CMR perfusion scans (16 segments of the 17 segment AHA model, excluding the apical cap segment). To generate the receiver operator characteristic (ROC) curve the summed scores over all AHA segments were used. Diagnostic performance was ascertained from the ROC curve as the area under the curve (AUC) value. The cut-off value that generated the optimal sensitivity and specificity for the test was determined by maximising the Youden index

(23). A separate assessment of LGE was performed with a score of 0 (none), 1 (1–25%), 2 (26–50%), 3 (51–75%) or 4 (>75%) allocated to each segment of the AHA model.

All x-ray angiograms were performed after CMR. Quantitative coronary angiography (QCA) analysis was performed off-line by a cardiologist blinded to the CMR results using QCAPlus software (Sanders Data Systems, Palo Alto, California, USA). Significant CAD was defined as ≥70% diameter stenosis of a first order coronary artery measuring ≥2mm in diameter, or left main stem stenosis ≥50%. Single, double and triple vessel disease was defined as significant stenosis affecting one, two or three vessels respectively. Both visual CMR perfusion and QCA scores were taken from the original CE-MARC reports and were not reanalysed for this sub-study.

All perfusion results were compared to QCA on a per-patient basis. MPR values were calculated as the stress MBF estimate divided by the resting MBF estimate. To generate the ROC curve the AHA segment with the lowest perfusion measure (MPR or stress MBF) was used as the quantitative measure.

Diagnostic performance was evaluated using ROC curve analysis taking the QCA diagnosis as the reference standard. Diagnostic performance was first assessed in terms of the ability of the perfusion index to detect disease in any coronary artery. A separate assessment of the diagnostic performance for detecting disease in each individual coronary artery was performed using the AHA segmentation recommendations to map myocardial segments to individual coronary arteries. The number of detected perfusion defects that correctly corresponded to disease in the coronary artery specified by the AHA mapping was then assessed.

Statistical Analysis: Categorical variables are expressed as numbers and percentages. Continuous variables are expressed as mean ± standard deviations unless otherwise stated. With

a sample size of 128 and using a correlation between the scores of r=0.45, the study was powered to detect a difference of 0.15 in the AUC values between ROC curves with a power of 80% at the 5% significance level (24). ROC curves were generated using Analyse-it (Analyse-it Software Ltd. UK). All other statistical analysis was carried out using SPSS (version 21.0, Chicago, IL). Comparison of ROC curves was performed using the DeLong method (25). There was no correction for multiple comparisons of AUC curves. Normally distributed data were compared using Student's t-test.

Results

Baseline patient characteristics are summarised in Table 1. The study consisted of 128 patients (mean age 61 years; age range 37-77 years). 77 (60%) were male (mean age 61 years; age range, 45-76 years) and 51 were female (mean age, 60 years; age range, 37-77 years). There was no significant age difference between male and female groups (p=0.33). 42 patients had significant coronary artery disease as assessed by QCA and 86 did not. Four whole patient perfusion data sets (3%) were excluded from the study because of severe through plane motion caused by electrocardiographic (ECG) triggering failures (3 stress scans and 1 rest scan). These consisted of one patient with single vessel disease, one with double vessel disease and two healthy patients as assessed by QCA. Post-exclusion, 40 patients with significant coronary heart disease and 84 without remained for analysis. Analysis of late gadolinium enhancement images showed 33 patients had evidence of myocardial scaring (infarct pattern).

Mean global (i.e. mean MBF per slice averaged over all three slices) myocardial blood flow values over all three slices are shown in Table 2. Mean MBFs from healthy patients for each slice are shown in Table 3. Perfusion was significantly lower in ischaemic patients than in normal; Stress MBF 2.16 (0.70) ml/min/g vs. 3.00 (0.81) ml/min/g, ($p<0.001$) and MPR 1.86

(0.57) vs 2.31 (0.67), ($p<0.001$). Receiver operator characteristic curves for visual and quantitative perfusion analysis are shown in

Figure 1. The sensitivity, specificity, area under the curve (AUC) and optimal cut-off values are shown in Table 4 and Table 5 shows the respective contingency tables The highest diagnostic accuracy was achieved using MPR measurements. There was no statistically significant difference in diagnostic performance between visual (AUC 0.88, cut-off 2.0) and quantitative analysis for MPR (AUC 0.89, cut-off 1.11; $p=0.72$) or stress MBF (AUC 0.87, cut-off 1.27 ml/min/g; $p=0.54$). There was no significant difference in diagnostic accuracy between MPR and stress MBF quantitative ROC curves ($p=0.79$).

Separate assessments for single, double and multi (double or triple) vessel disease patients are shown in Table 6. There was no significant difference between the diagnostic accuracy of visual and quantitative analysis in single, double or multi vessel disease groups. In 28 (70%) out of 40 cases the minimum quantitative perfusion score mapped correctly to a coronary artery territory that contained a significant stenosis according to the AHA segmentation model. 8 out of 9 (89%) defects correctly corresponded to a stenosis in the LCX, 12 out of 19 (63%) correctly corresponded to a stenosis in the LAD and 8 out of 12 (70%) correctly corresponded to a stenosis in the RCA. Separate assessments for the individual coronary arteries are shown in Table 7. Quantitative measures (stress MBF or MPR) did not perform significantly better than visual analysis for any of the coronary arteries.

Discussion

The primary finding of this study is that quantitative myocardial perfusion analysis has a high diagnostic accuracy but does not out-perform expert visual analysis. In addition, diagnostic performance of quantitative perfusion was not significantly improved by including rest perfusion

measurements. This suggests that the rest perfusion acquisition may not be necessary for quantitative analysis, potentially saving time, expense (less contrast) and patient inconvenience. To the author's knowledge this is the largest investigation into the diagnostic performance of quantitative CMR perfusion to date, around twice as large as the previous largest study with n=67 (11).

The presence of myocardial infarction can make visual diagnosis of superimposed ischaemia challenging. In this study quantitation achieved a high diagnostic accuracy even though a significant number (thirty three) of cases in the study had myocardial infarction as assessed by LGE imaging. Therefore the quantitative diagnostic accuracy reported in this study supports the robustness of this technique in 'real-world' clinical cases.

Our data showed comparable diagnostic accuracy in single and multi-vessel disease with visual or quantitative analysis implying that there was no advantage in quantitative analysis in patients with different extents of CAD. Furthermore, we found similar diagnostic accuracies for the ability of visual or quantitative analysis to detect perfusion defects in the three coronary arteries (LCX, LAD and RCA). Although MPR appears to perform slightly better than visual or stress MBF analysis, especially at sensitivities above 80% (Figure 1), these differences were not statistically significant. The high diagnostic accuracy observed using stress MBF alone agrees well with previous studies that analysed stress only images using semi-quantitative, (6,26,27) visual (28,29) and quantitative analyses. These observations demonstrate that stress data alone can yield excellent diagnostic performance and a rest perfusion study may not be necessary in a standard protocol to detect or exclude CAD. MPR is a measure of the potential flow increase the myocardium has in reserve before maximal vasodilation occurs. Whereas stress perfusion is uncoupled from oxygen demand resting perfusion is not (6), so factors influencing resting

myocardial oxygen demand cannot be controlled for in a clinical setting. This uncontrolled aspect of the rest perfusion measurement may account for the fact that dividing by the rest MBF measurement did not improve diagnostic accuracy in our quantitative data.

Our finding that the diagnostic performance of quantitative perfusion is comparable to, but not significantly better than, visual analysis is consistent with previous, smaller studies (13,15). However, Mordini at al. (11) did report a diagnostic advantage using quantitation. This may be due in part to the fact that Mordini measured the ratio between the endocardial segment and the median epicardial value and required at least two segments to fall below the threshold before a patient was classed as ischaemic, whereas our study used the minimum segmental MBF score. Our study did not replicate this transmural subdivision strategy due to concerns over increasing the noise in the signal versus time curves.

MBF values in patients without ischaemia were comparable with those published in studies of healthy volunteers (30,31). At 1.23ml/min/g the resting MBF is somewhat higher than most studies, due to non-linearity effects in the AIF, but still well within the range of MBF values quoted in the literature. The total exclusion rate was 3% (4/128). This compares favourably with other quantitative studies.; for instance, Patel et al (9) excluded 23% of patients and Costa et al (6) excluded 16%.

The optimal threshold for abnormal perfusion from the ROC analysis was set at an MPR of 1.11 and a stress MBF of 1.27 ml/min/g. The MPR threshold is somewhat lower than other studies (Huber at al. 1.54 (17), Patel et al 1.55, (13)) possibly due to the high rest MBF measurements in our study. The stress MBF threshold of 1.27 ml/min/g was somewhat lower than that of Mordini et al. at 1.58 ml/min/g (11), possibly because their model required two AHA segments below the cut-off threshold whereas our model only required one.

Limitations

Perfusion CMR assesses myocardial ischaemia, whereas QCA is a measure of coronary artery stenosis, which is itself an imperfect reference standard. Thus, false-negative results could occur if lesions not causing ischaemia (as assessed by CMR) were judged clinically significant on the basis of angiographic stenosis severity. Invasive measurement of fractional flow reserve is now the reference standard for the measurement of haemodynamic significance of a coronary artery stenosis, but was not routinely performed at the time of recruitment to the CE-MARC study.

The combination of a 0.05mmol/kg contrast dose and a pre-pulse delay of 126ms yields a non-linear signal response to contrast agent concentration in the AIF, resulting in an over-estimate of MBF. The lack of a linear AIF measurement constitutes a limitation to this retrospective dataset. This could potentially diminish the range of MBF estimates and reduce the performance of quantitative perfusion, including the benefits of rest perfusion. However, our analyses achieved a high sensitivity and specificity in agreement with other studies employing dual-bolus techniques implying that non-linearity errors have not profoundly affected the results. This agrees with previous work directly comparing dual and single bolus strategies and finding no significant difference in diagnostic performance (32).

The use of a shared pre-pulse to acquire all three perfusion slices results in different T1 contrast between the three image slices. This has been addressed by using the basal AIF for all three slices and by applying a linear correction to the myocardial curves. This approach may be subject to errors if the myocardial signal to concentration relationship is sufficiently non-linear, although there were no significant differences in MBF between the three slices in the study population (Table 3).

Manual correction for breathing motion introduces an extra source of error into the measurements as the signal curves can be contaminated by high signal blood pixels in the LV or other surrounding tissues deteriorating the results of MBF quantitation. Although care was taken to avoid these errors an automated, non-rigid registration might have improved our quantitative results. The use of quantitative perfusion analysis in clinical practice requires a known healthy/diseased threshold value. Currently this value may vary between studies because of variations in MBFs due to differing methodologies. Before MBF measurements can be used widely standardisation of these methods and multi-centre studies are necessary to show that a single cut-off across different sites and CMR vendors is suitable and can still achieve the high diagnostic accuracies reported in this study. This is even more relevant if the rest perfusion measurement is to be discarded because expressing perfusion as a ratio can normalise systematic shifts in MBF, due to differences in methodology, that remain if a stress only perfusion measurement is used. It also noteworthy that quantitative perfusion can impose limits on the acquisition such as lower contrast dose and reduced image T1-weighting that can force a reduction in image quality and or heart coverage, which may adversely affect visual assessment.

Conclusions

Quantitative myocardial perfusion has a high diagnostic accuracy for detecting coronary artery disease, but is not superior to expert visual analysis, even in multi-vessel disease. Rest perfusion data acquisition does not increase the diagnostic accuracy of quantitative myocardial perfusion and could be eliminated from the imaging protocol.

Perspectives

Competency in Medical Knowledge

This work has shown that quantitative myocardial perfusion estimates obtained from CMR have a high diagnostic accuracy equivalent to, but not better than, that of expert visual analysis. In addition, the use of a rest perfusion measurement did not improve diagnostic performance above stress perfusion quantitation alone. The clinical implications are that these observations support removal of rest perfusion imaging from the acquisition protocol.

Translational Outlook

For quantitative perfusion estimates to be accepted as a standard clinical tool a number of obstacles need to be overcome. Firstly, the time consuming analysis needs to be streamlined so that quantitative estimates are easily available to a non-expert user within a reasonable time frame. Secondly, diagnosis using quantitative measurement requires a known healthy/diseased cut-off value. These cut-off points vary between studies because of the variation in quantitative values due to the wide range of methods used. These include differences in contrast dose administered, CMR acquisition sequence, methods for correcting non-linearity between contrast agent concentration and signal intensity, motion correction and modelling methods used to generate the final flow value. If these measurements are to be used widely standardisation of these methods is required in order to reduce these variations. Multi-centre studies would then be necessary to show that a single cut-off across different sites and CMR vendors is suitable and can still achieve the high diagnostic accuracies reported in this study.

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Figure 1 ROC curves for quantitative and visual analyses. ROC curves for visual analysis, myocardial perfusion reserve (MPR) and stress myocardial blood flow (MBF) showing diagnostic accuracy for detecting significant stenosis as assessed by QCA. There was no statistically significant difference in diagnostic performance between visual and MPR (p=0.72) or stress MBF (p=0.54).

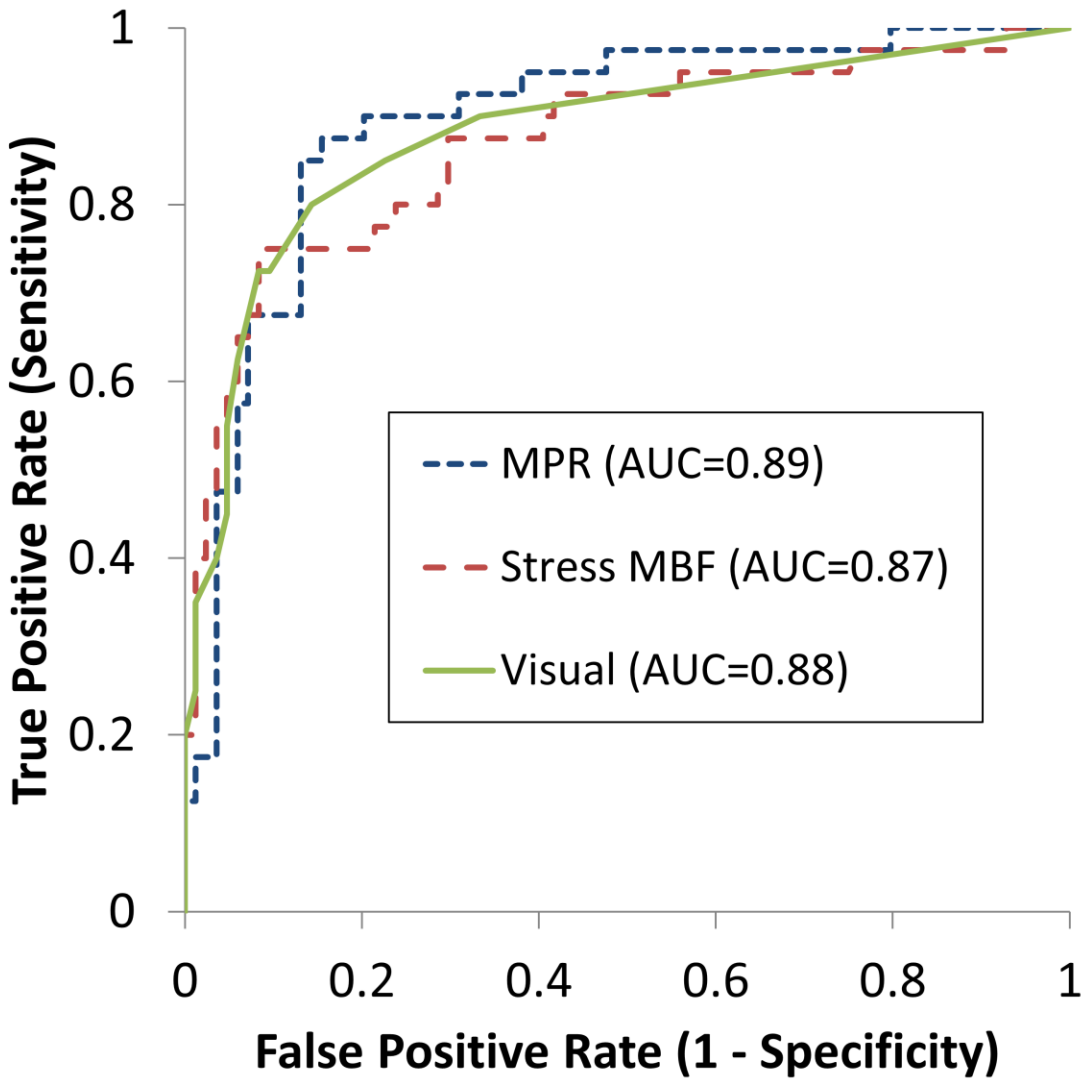

Table 1- Patient Characteristics

Age [years]	61 ± 9
Female	51 (40)
Hypertension	65 (51)
Diabetes	17 (13)
Smoking	16 (13)
1 vessel disease	23 (18) (1 excluded)
2 vessel disease	15 (12) (1 excluded)
3 vessel disease	4 (3) (0 excluded)
Total patients with CAD	42 (33) (2 excluded)

Data are mean ± SD or number of cases (%)

Table 2: Quantitative perfusion results for ischaemic and non-ischaemic groups

	Number of cases	Stress MBF [ml/min/g]	Rest MBF [ml/min/g]	MPR
Ischaemic	40	2.16 ± 0.70	1.23 ± 0.41	1.86 ± 0.57
Non Ischaemic	84	3.00 ± 0.81	1.37 ± 0.39	2.31 ± 0.67
All	124	2.73 ± 0.87	1.32 ± 0.40	2.17 ± 0.67

Data are mean ± SD.

MBF = myocardial blood flow, MPR = myocardial perfusion reserve

Table 3: Quantitative perfusion values by slice in healthy cases

Slice	Stress MBF [ml/min/g]	Rest MBF [ml/min/g]	MPR
1	2.81 ± 0.75	1.29 ± 0.27	2.25 ± 0.73
2	3.15 ± 0.65	1.41 ± 0.38	2.34 ± 0.55
3	3.04 ± 0.98	1.40 ± 0.48	2.33 ± 0.74

Data are mean ± SD.

MBF = myocardial blood flow, MPR = myocardial perfusion reserve

Table 4: Diagnostic performance of quantitative and visual methods to detect stenosis as measured by QCA. Scores need to be greater than the optimal cut-off value to classify the patient as ischaemic.

	AUC	Sensitivity (%)	Specificity (%)	Optimal cut-off
Stress MBF [ml/min/g]	0.87 (0.80, 0.94)	75.0 (61.6, 88.4)	91.7 (85.8, 97.6)	1.27
MPR	0.89 (0.83, 0.96)	87.5 (77.3, 97.7)	84.5 (76.8, 92.3)	1.11
Visual	0.88 (0.81, 0.95)	81.0 (69.1, 92.8)	86.0 (78.7, 93.4)	2.00

Data are value (95% confidence interval)

AUC = area under the curve, MBF = myocardial blood flow, MPR = myocardial perfusion reserve

Table 5: Contingency tables for Stress MBF, MPR and visual analysis

a)

CAD as assessed by:		X-ray (QCA)	
		+	-
MRI (MPR)	+	35; 0.67 (0.21)	13; 0.75 (0.18)
	-	5; 1.39 (0.24)	71; 1.61 (0.39)

b)

CAD as assessed by:		X-ray (QCA)	
		+	-
MRI (stress MBF)	+	30; 0.76 (0.29)	7; 0.94 (0.23)
	-	10; 1.99 (0.54)	77; 2.17 (0.62)

c)

CAD as assessed by:		X-ray (QCA)	
		+	-
visual	+	34; 11.71 (6.59)	12; 6.58 (4.10)
	-	8; 0.75 (0.89)	74; 0.31 (0.64)

Contingency tables showing number of cases, mean value and standard deviation of the values for a) MPR, b) stress MBF and c) visual analysis.

Data values are: number of cases; mean (standard deviation). Symbols '+' and '-' correspond to positive and negative assessments for coronary artery disease respectively.

Table 6: Area under the curve (AUC) values for single, double and multiple vessel disease.

	Single vessel disease	Double vessel disease	Multiple vessel disease
Stress MBF	0.93 (0.85, 1.0)	0.81 (0.67, 0.95)	0.83 (0.71, 0.95)
MPR	0.88 (0.78, 0.98)	0.94 (0.84, 1.00)	0.91 (0.82, 1.00)
Visual	0.89 (0.80 , 0.98)	0.85 (0.72, 0.98)	0.87 (0.76, 0.98)
No. of cases	22	14	18

Data are values (95% confidence interval)

MBF = myocardial blood flow, MPR = myocardial perfusion reserve.

Multiple vessel disease is defined as a patient with either double or triple vessel disease.

Table 7: Area under the curve (AUC) values for quantitative perfusion for individual coronary arteries

	LCX	LAD	RCA
Stress MBF	0.75 (0.62, 0.89)	0.76 (0.64, 0.89)	0.83 (0.69, 0.97)
MPR	0.74 (0.60, 0.87)	0.77 (0.65, 0.89)	0.73 (0.56, 0.89)
Visual	0.69 (0.56, 0.83)	0.77 (0.64, 0.88)	0.73 (0.57, 0.89)

Data are value (95% confidence interval)

LCX = left circumflex, LAD = left anterior descending, RCA = right coronary artery, MBF = myocardial blood flow, MPR = myocardial perfusion reserve.