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Quantitative myocardial perfusion imaging by cardiovascular magnetic resonance and positron emission tomography

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Abstract

Recent studies have demonstrated that a detailed knowledge of the extent of angiographic coronary artery disease (CAD) is not a prerequisite for clinical decision making, and the clinical management of patients with CAD is more and more focused towards the identification of myocardial ischemia and the quantification of ischemic burden. In this view, non-invasive assessment of ischemia and in particular stress imaging techniques are emerging as preferred and non-invasive options. A quantitative assessment of regional myocardial perfusion can provide an objective estimate of the severity of myocardial injury and may help clinicians to discriminate regions of the heart that are at increased risk for myocardial infarction. Positron emission tomography (PET) has established itself as the reference standard for myocardial blood flow (MBF) and myocardial perfusion reserve (MPR) quantification. Cardiac magnetic resonance (CMR) is increasingly used to measure MBF and MPR by means of first-pass signals, with a well-defined diagnostic performance and prognostic value. The aim of this article is to review the currently available evidence on the use of both PET and CMR for quantification of MPR, with particular attention to the studies that directly compared these two diagnostic methods.

Keywords

Cardiac magnetic resonance (CMR); positron emission tomography (PET); quantitative perfusion imaging

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Introduction

Until recently decision on revascularization of a coronary artery stenosis has been frequently based on the angiographic appearance of the coronary lesions, without a concomitant assessment of the functional severity of the stenosis and of the resulting ischemic burden, despite the well-established knowledge that the percentage of stenosis is a poor predictor of the functional severity of the lesion, in particular intermediate cases.[1-3]

Supportive evidence on the role of non-invasive imaging for the stratification of patients with stable coronary artery disease (CAD) came from the nuclear sub study of the COURAGE trial,[4] which examined a subgroup of patients tested with single photon emission computed tomography (SPECT), exploring the effects of optimal medical treatment (OMT) vs percutaneous coronary intervention (PCI) on the ischemic burden and patients' outcome. This study demonstrated that the combination of PCI and OMT was more effective in reducing the total ischemic burden than OMT alone and that the antiischemic effect of PCI was greater for patients with moderate to severe pre-treatment ischemia. The reduction of the ischemic burden was associated in a non risk-adjusted model with freedom from events. These trends constituted an important indication confirming the value of ischemia assessment to guide therapeutic decision making.

These findings confirmed a previous landmark study by Hachamovitch et al,[5] who sought to show the survival benefit associated with revascularization vs medical therapy, stratifying the patients based on the extent of the ischemic burden detected by SPECT. In a large retrospective population of 10,627 patients, it was demonstrated that those with no or very low amounts of inducible ischemia (<10%-12%) were at very low risk and did not require invasive treatment, while for increasing amounts of ischemic myocardium there was a significant prognostic benefit by PCI.

The functional significance of coronary stenoses has also been assessed invasively. The usefulness of fractional flow reserve (FFR) in guiding revascularization procedures has been determined by a few cornerstone studies that compared FFR-guided revascularization with decision making guided by angiographic data. The DEFER Study demonstrated that PCI of coronary artery lesions with non-significant FFR is not of benefit.[5] The FAME[6] and the FAME 2[7] studies demonstrated that FFR-guided PCI in patients with multi-vessel CAD allows a functionally complete revascularization in these patients using a lower number of stents and with a significantly reduced event-rate in comparison to patients managed on the basis of their angiographic findings.

These studies delineated that a detailed knowledge of the extent of angiographic CAD is not a prerequisite for clinical decision-making and that functional measurements of the ischemic burden, a marker available using non-invasive techniques, is sufficient for decision making and provides prognostic information. On the basis of these scientific evidences, the clinical management of patients with CAD is progressively moving away from merely assessing the presence or absence of coronary artery lesions and is more and more focused towards the identification of myocardial ischemia and the quantification of ischemic burden.

In this view, non-invasive assessment of ischemia and in particular stress imaging techniques are emerging as preferred and non-invasive options. Most clinical perfusion imaging techniques only assess relative differences in myocardial perfusion. Non-quantitative methods might substantially underestimate perfusion compared to quantitative methods,[8,9] especially when the appreciation of three-vessel disease[10,11] and microcirculation[12,13] are challenged. A quantitative estimate of regional myocardial perfusion can provide an objective measure of the severity of myocardial injury and may help clinicians to discriminate regions of the heart that are at increased risk for myocardial infarction. Myocardial perfusion reserve (MPR),[14] defined as the ratio of the maximum myocardial blood flow (MBF)15 to the baseline, is an indicator of epicardial CAD as well as myocardial microvascular function abnormalities.

Experimental and clinical studies have shown that the functional severity of a coronary stenosis can be determined by measuring MBF and MPR. Positron emission tomography (PET) has established itself as the reference standard for MBF and MPR quantification.[16-18] Cardiac magnetic resonance (CMR) is increasingly used to measure MPR by means of first-pass signals.[19-21] The aim of this article is to review the evidence currently available on the use of both PET and CMR for quantification of MPR, with particular attention to the studies that directly compared these two diagnostic methods.

CMR Quantitative Perfusion Imaging

In the past two decades, first-pass perfusion cardiovascular magnetic resonance (CMR) has rendered an indispensable tool for the non-invasive detection of myocardial ischemia. By taking advantage of its high spatial resolution, non-invasive and non-toxic nature CMR perfusion imaging has achieved an improvement in sensitivity and specificity for the detection of CAD and has given further insights into the understanding of ischemic heart disease.[22]

In CMR perfusion studies, a paramagnetic gadolinium (Gd) containing contrast agent is injected during vasodilator-induced (adenosine or dipyridamole) stress and repeated app 15 minutes later at rest. The spatiotemporal distribution of Gd within the heart can be measured dynamically and the resultant blood and tissue enhancement data can be analyzed to estimate the rate of perfusion to each region of the myocardium.[23,24]

A potential advantage of perfusion CMR is its ability to quantify perfusion reserve within a myocardial segment. Although time-demanding, compared to visual interpretation, quantitative evaluation of myocardial perfusion properties with CMR, as expressed semi-quantitatively by MPR index and fully-quantitatively by absolute MBF, may provide additional clinically relevant information and an objective, stepwise correlation of myocardial perfusion impairment to the severity of coronary artery status.

A semi-quantitative analysis of myocardial perfusion is based on the assessment of the signal intensity changes over the course of the first pass of the contrast through the myocardium. The upslope integral technique has been the most effective semi-quantitative method that was studied and yields a high diagnostic accuracy in patients with suspected

CAD.[25,26] The accuracy of the upslope analysis may, however, be affected by differences in the contrast agent's pharmacodynamics and pharmacokinetic properties. The use of fully quantitative perfusion analysis helps to avoid these problems.

In order to perform absolute quantification of MBF, a quantifiable relationship must exist between the signal intensity changes in the image and underlying blood flow. Most quantitative analysis methods require that the measured blood (arterial input function, AIF) and tissue (tissue function, TF) enhancement data are calculated and mathematically deconvolved in order to estimate the system impulse response function, from which myocardial perfusion can be computed.

There are two main deconvolution techniques: compartment kinetic modeling and Fermi-function deconvolution. With compartmental kinetic models, the forward flux of Gd from the blood to the myocardium is taken to represent absolute MBF.[27,28] Fermi-function method is based on the calculation of the amount of Gd present within a region of myocardium.[29] This technique is relatively robust to the effects of extracellular accumulation of the contrast agent during first pass of the contrast. Both of the techniques described above have been shown to correlate with myocardial perfusion over a wide range of flow. Multiple other techniques have been used for deconvolution, and are currently under validation.[30]

Quantitative CMR perfusion imaging has been validated against microspheres in animals,[15] more established non-invasive imaging modalities (echocar-diography,[31] SPECT,[32,33] PET[34-38]) and invasive, catheter-based techniques[39,40] for functional appreciation of coronary flow. The above research and clinical evidence demonstrated a strong correlation between quantitative CMR values and coronary artery status, and highlighted the prognostic value of the method in patients with CAD.[41-44]

PET Quantitative Perfusion Imaging

PET is considered the current gold standard technique for quantitative perfusion imaging, and has contributed substantially to the understanding of cardiac physiology and pathophysiology. Myocardial PET myocardial perfusion imaging improves diagnostic accuracy[45] and provides a useful adjunct to assessment of regional perfusion abnormalities.[46]

With the use of suitable tracers and appropriate mathematic models, PET has been successfully applied in regional quantification of absolute MPR,[3,47] and has been used for the sensitive detection of early abnormalities in coronary vascular function associated with CAD.[48] Currently, $^{13}NH_3$, H_2, ^{15}O, and ^{82}Rb are the most widely used PET perfusion tracers. ^{82}Rb is most widely used in clinical practice MBF tracer because it does not require a cyclotron on site and has a very short half-life. Several tracer kinetic models for quantification of PET-MBF have been successfully validated against the radiolabeled microsphere gold standard in animals. These models have to compensate for underestimation of radiotracer concentration due to the partial-volume effect, limited spatial resolution and motion of the heart.[49]

Quantitative perfusion indices measured by PET correlates inversely with the degree of coronary artery stenosis at angiography.[3] Furthermore, recent studies have demonstrated that PET-derived MPR is an independent predictor of outcome, predicts major adverse cardiac events and cardiac death in patients with myocardial ischemia,[50] reduced survival in patients with left ventricular systolic dysfunction[51] and provides incremental risk stratification among diabetic patients without CAD.[52]

Because of its ability to provide non-invasive regional absolute quantification of MBF, PET has been widely used to assess myocardial perfusion pattern in a wide range of the cardiac pathology.

In healthy humans, PET has demonstrated significant variation in regional CFR related to parameters like gender and age, a finding that has important clinical implications.[53,54] In asymptomatic subjects with cardiovascular risk factors, PET allows the early detection of functional coronary flow impairment, irrespective of any vessel structural alterations.[55,56]

However, PET has proven more clinically useful in the appreciation of functional significance of epicardial coronary lesions. In chronic stable angina, perfusion PET successfully distinguished between segments perfused to the normal and diseased vessels.[57] Although affected by a certain degree of variation, PET-MPR is linearly related to the severity of CAD. The extent and severity of ischemia on PET provides incremental risk estimates of cardiac death and all-cause death compared with traditional coronary risk factors.[58] Furthermore, the accurate study MBF by PET permitted an insight into the understanding and estimation of myocardial perfusion in human hibernating myocardium and its response to the available therapeutic options.[59,60]

In parallel, the feasibility of PET to assess MBF and MPR has offered an effective assessment of microvas-cular function, a parameter otherwise unable to exam by direct methods. This feature of PET permitted the demonstration of abnormal in a wide range of primary and secondary cardiomyopathies. In patients with hypertrophic cardiomyopathy (HCM), with the use of PET, it has been demonstrated impaired MPR corresponding to microvascular dysfunction and affecting both the hypertrophied and the non-hypertrophied segments.[61] MBF and MPR impairment in context of HCM, detected with the use of PET, has allowed the assessment of response to the different therapeutic interventions,[62-64] and has proven to be an independent predictor of pejorative outcome.[65] Similarly, in patients with dilated cardiomyopathy (DCM), abnormal perfusion pattern demonstrated in multiple PET studies[66-68] has been shown to be an independent predictor of subsequent cardiac events and clinical deterioration.[69]

CMR vs PET Quantification Perfusion Imaging

PET is well accepted as a validated technique for non-invasive quantitative measurements of myocardial perfusion using either $^{15}O_2$-labeled water or $^{13}NH_3$. CMR has demonstrated potential for clinical quantitative perfusion imaging and might be a good alternative for non-invasive quantitative evaluation of the myocardial perfusion and detection of CAD.[70]

Semi-quantitative perfusion CMR methods estimating MPR have proven effective in the appreciation of CAD. Myocardial perfusion ratio index has been shown to be closely related to the degree of stenosis.[23,25] Initial studies comparing CMR semi-quantitative analysis methods with PET have shown good correlation in patients with CAD.[34,35]

In a pivotal prospective study by Schwitter et al,[34] the quality of a multislice CMR approach was determined and compared with PET and quantitative coronary angiography (QA). A total of 48 patients and healthy subjects were studied by dipyridamole first-pass CMR using a multislice hybrid echo-planar pulse sequence and segmental signal intensity upslope quantitative measurements were compared to $^{13}NH_3$ PET. Receiver-operator characteristic analysis of subendocardial upslope data revealed a sensitivity and specificity of 91% and 94%, respectively, for the detection of CAD as defined by PET (mean coronary flow reserve minus 2 SD of controls) and a sensitivity and specificity of 87% and 85%, respectively, in comparison with QA (diameter stenosis ≥50%). The number of pathological sectors per patient on PET and MR studies correlated linearly (slope, 0.94; $r = 0.76$). The presented MR approach identified patients with coronary artery stenoses and provided information on the amount of compromised myocardium, with best results being obtained when perfusion indices were assessed in the subendocardial layer, which is most sensitive to an ischemic challenge.

In another study comparing semi-quantitative adenosine perfusion CMR with quantitative measures of QA and PET in healthy volunteers and patients with CAD, Ibrahim et al[35] compared upslope and peak-intensity indices, measured with the use of a multislice ultra-fast hybrid sequence to $^{13}NH_3$ PET flow reserve measurements. Localization of coronary artery stenosis, based on the upslope index, yielded sensitivity, specificity and diagnostic accuracy of 69%, 89%, and 79%, respectively. Upslope index correlated with PET flow reserve (r: 0.70). A reduced coronary flow reserve (PET: 2.0, MRI: 1.3) was detected by the upslope index with sensitivity, specificity, and diagnostic accuracy of 86%, 84%, and 85%, respectively. Although MPR was underestimated by CMR as compared to PET, a close relationship was observed between MRI upslope index and PET estimates of flow reserve, yielding acceptable diagnostic performance for localization of CAD.

Improvement in imaging acquisition and post-processing methods permitted the development of quantitative algorithms in perfusion CMR. Few studies have examined its accuracy and diagnostic value against PET perfusion. Parkka et al[36] studied the accuracy of first-pass CMR and kinetic modeling for quantitative analysis of MBF and MPR during dipyridamole infusion, compared to PET, in 18 healthy males. Using a perfusion-related parameter, the unidirectional influx constant (Ki), MBF was computed in three coronary artery territories. There was a significant correlation for both dipyridamole-induced flow and MPR between CMR and PET. However, in accordance with previous studies, MPR values provided with MRI were lower compared to PET (2.5 ± 1.0 vs 4.3 ± 1.8).

In the same concept, Fritz-Hansen et al[38] assessed quantitative CMR with the Ki perfusion method in healthy volunteers, using $^{13}NH_3$ PET as a reference method. Ten healthy males were examined with combined PET and CMR dipyridamole perfusion imaging in order to determine absolute MPR. CMR-derived myocardial and blood time concentration curves

were fitted by a two-compartment perfusion model. A linear relationship was observed between CMR- and PET-derived MPR for regional and global data (Figure 1). A good agreement between the two methods to determine low or high perfusion reserves was found (Figure 2; Table 1).

These studies, with the use of quantitative CMR methods in healthy humans, enforced previous evidence that Ki constant can identify myocardial regions of occluded infarct-related arteries.[71] CMR perfusion data were similar between the two studies, indicating that both saturation- and inversion-recovery imaging sequences are useable and that the method seems robust for use. However, the method seems to underestimate perfusion at stress compared to PET.

In parallel, model-independent analysis methods tested at 3 T CMR have provided similar results. Pack et al[72] applied in five normal subjects adenosine perfusion CMR imaging with the use of a saturation recovery turboFLASH sequence and subsequent PET perfusion imaging. Regional and pixelwise quantitative perfusion estimates correlated with dynamic $^{13}NH_3$ PET (r = 0.85) and were similar to results from other validated CMR studies. The authors succeeded to demonstrate that a model-independent analysis method can be used to quantify myocardial perfusion with dynamic contrast-enhanced perfusion CMR.

More recently, Morton et al compared MBF and MPR with CMR and PET in a cohort of 41 patients with known or suspected CAD. Patients underwent quantitative $^{13}NH_3$ PET and adenosine CMR perfusion imaging before coronary angiography.[37] CMR-derived indices correlated well with PET-derived measurements (r: 0.75). MBF and MPR for the 2 lowest scoring segments in each coronary territory also correlated strongly between the two techniques (*r*: 0.79). Absolute CMR perfusion values correlated significantly, but weakly, with PET values both at rest (*r*: 0.32) and during stress (*r*: 0.37). An MPR by PET < 1.44 predicted significant CAD with 82% sensitivity and 87% specificity, and MPR by CMR < 1.45 predicted significant CAD with 82% sensitivity and 81% specificity (Figure 3). This has been the single study so far to compare fully quantitative CMR against PET perfusion imaging in patients with CAD. Quantitative indices derived by the two techniques correlated strongly, and both techniques proved comparable and accurate. However, the correlation between the absolute perfusion values from PET and CMR was relatively weak, suggesting that a single absolute stress perfusion cutoff value is not superior for the detection of CAD for the moment. Interestingly, there was not any incremental value in combining MPR data from both PET and CMR for the diagnosis of CAD.

Overall, although bibliographic evidence is poor, a good correlation has been steadily confirmed for relative and absolute quantitative perfusion CMR methods, when PET quantification techniques are considered as the reference standard. Both techniques have proven useful for the detection and estimation of coronary artery stenosis. The tendency to measure lower stress perfusion with CMR than with PET, observed in all studies, could in part be explained by the different methods used in both the acquisition and the post-processing of the exams. Different contrast agents with particular pharmacodynamic and pharmacokinetic properties, differences among stressors as well as difference in the

mathematical models used for exam analysis, could partially explain this difference. Further research in this area will be needed.

CMR vs PET Spatial Resolution

In order to appreciate and compare the efficacy of CMR and PET perfusion imaging, special consideration should be given to the spatial resolution of each technique.

Improvements in hardware, pulse sequence development, and image reconstruction algorithms have enabled high-resolution imaging of first-pass myocardial perfusion with CMR, with spatial resolution of approximately 1 mm which is around 10× better than with nuclear perfusion imaging and 2-3 times better than with conventional perfusion CMR.[73] In addition, perfusion studies have been performed at 3 T scanners and have demonstrated improved signal-to-noise ratio (SNR).[74] Spatial coverage has also been improved by adopting 3D encoding methods combined with parallel imaging using either 3D SSFP or 3D FLASH.[75]

Although the spatial resolution of PET is generally better than SPECT (typically 4-7 mm with PET and 1015 mm with SPECT),[76] it is ultimately dependent on the distance traveled by the positron between its point of emission and annihilation in tissue (positron range). Resolution is also determined by the residual kinetic energy at the time of annihilation event, random counts, and the detectors' thickness.[77] Compared to the conventional PET scanners crystals, novel PET crystals possess higher light outputs leading to improved energy and spatial resolution.[78]

Myocardial ischemia affects the subendocardial layers of the left ventricular myocardium earlier and more severely than the outer layers.[79] The detection of subendocardial ischemia is considered a sensitive endpoint for the diagnosis of pathological alterations of myocardial blood supply.[80-83] Due to the relatively low spatial resolution of nuclear myocardial perfusion imaging, SPECT and PET techniques have been limited to patients with LV hypertrophy.[84-86] Only a few studies using ^{15}O-labeled water PET reported a transmural perfusion ratio in normal hearts in animal experiments and in healthy volunteers,[87] confirming the existence of transmural perfusion inhomogeneities also in normal hearts, with higher rest MBF in the subendocardium and a homogeneous MBF during stress.

The high spatial resolution of myocardial perfusion CMR, in comparison to PET, allows the visualization of subendocardial ischemia as a delayed wash-in of the contrast agent.[40,80,87] Post-processing of perfusion CMR data can be used to quantify the imbalances between subendocardial and subepicardial myocardial perfusion and thus improving the diagnostic accuracy of ischemia.

Current Limitations and Future Perspectives

While PET and CMR offer an accurate, reproducible, and efficient appreciation of myocardial perfusion, which could potentially guide therapeutic stratification and management, they suffer from certain drawbacks that preclude their establishment as exams of choice for ischemia assessment at the moment.

PET is well accepted as a validated technique for non-invasive quantitative measurements of myocardial perfusion using either $^{15}O_2$-labeled water or $^{13}NH_3$. However, it has a relatively low spatial resolution, is associated with radiation exposure, and it is not widely available for clinical use.

CMR has higher spatial and temporal resolution, uses non-ionized tracers, and is more widely available. On the other hand, CMR cannot be used in patients with iatrogenic devices incompatible with the MRI environment. CMR might be a good alternative for non-invasive quantitative evaluation of the myocardial perfusion and detection of CAD.

Both perfusion techniques are limited by significant variability in post-processing quantification analysis. It is also possible that systematic errors could relate to the fact that PET[88,89] and particularly CMR[90] have only moderate inter-study reproducibility. The findings that MPR, a ratio of stress and rest perfusion values, correlates well but that the absolute perfusion values correlate relatively poorly suggests that the errors in quantification have a similar influence on both rest and stress perfusion values and were subsequently canceled by the calculation of MPR. These errors might be a result of either methodological or physiological factors.

This variation is potentially attributed to a combination of factors including variation in stress test response, image acquisition/quality, and variation in measurements at the time of post-processing. Reproducibility may also differ due to inherent pitfalls, such as differences in the expertise between centers. Therefore, any study must reasonably account for factors that systematically alter its accuracy and reproducibility. Defining these factors is a necessary prerequisite to their broad clinical application.

The final barrier is to demonstrate that perfusion quantification has additional benefit over visual analysis or semi-quantitative techniques. One of the justifications for absolute quantification has been improved detection of three-vessel disease.[91] The incremental benefit of absolute quantification still needs to be established in larger clinical studies.

Nonetheless, the above limitations reflect the practical challenges encountered in both clinical practice and research. No quantitative perfusion analysis technique has been adopted in clinical practice at this time, and visual inspection performed by an experienced reporter remains the mainstay of clinical reporting.

Ongoing technical innovation with the development of improved hardware, software and novel technical approaches, such as novel spatial-temporal acceleration techniques,[92,93] introduction of novel contrast media,[94] and radiotracers[95] promise improved diagnostic performance for the assessment of coronary artery status and myocardial ischemic burden and offer the potential for the exams to being employed as a clinical endpoint. Further development of each exam will substantially define each one’s distinct role in improving clinical care.

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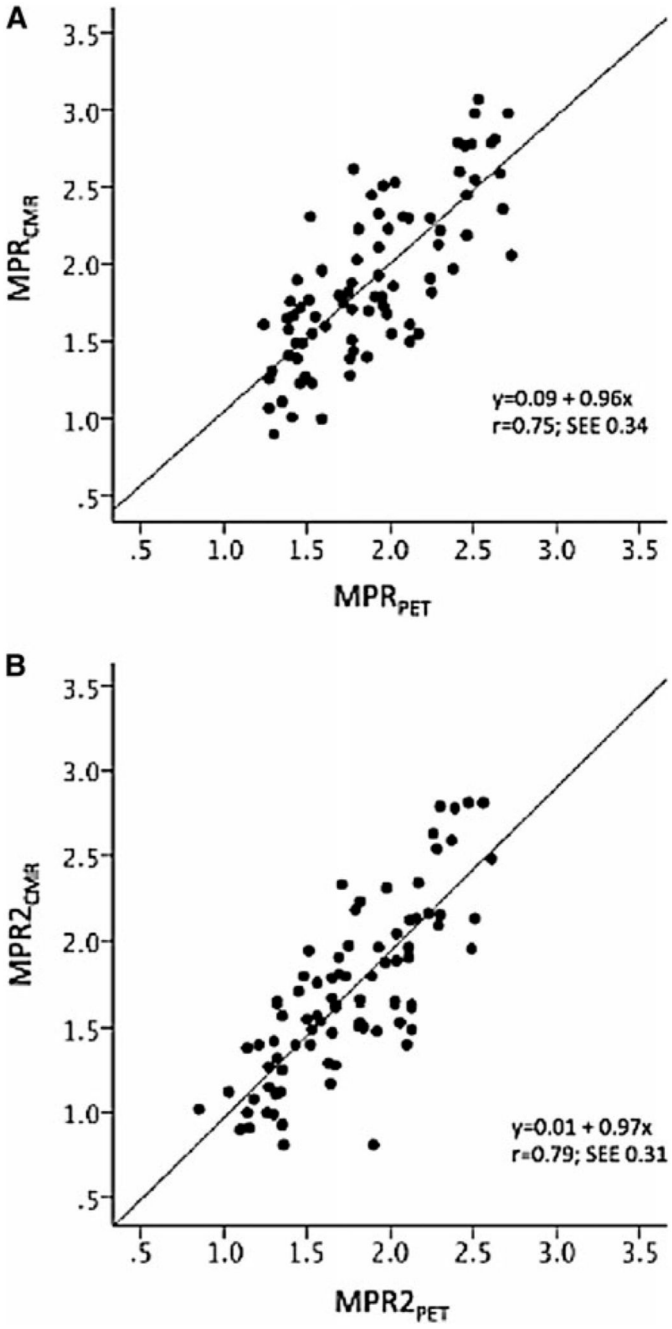

Figure 1.

Scatter plots with fit lines comparing myocardial perfusion reserve (MPR) values from cardiac magnetic resonance (MPR_{CMR}) and positron emission tomography (MPR_{PET}) for the entire myocardial territory (**A**) and the mean of the lowest 2 segments in each territory (MPR2) (**B**) (Courtesy of Morton et al[37]).

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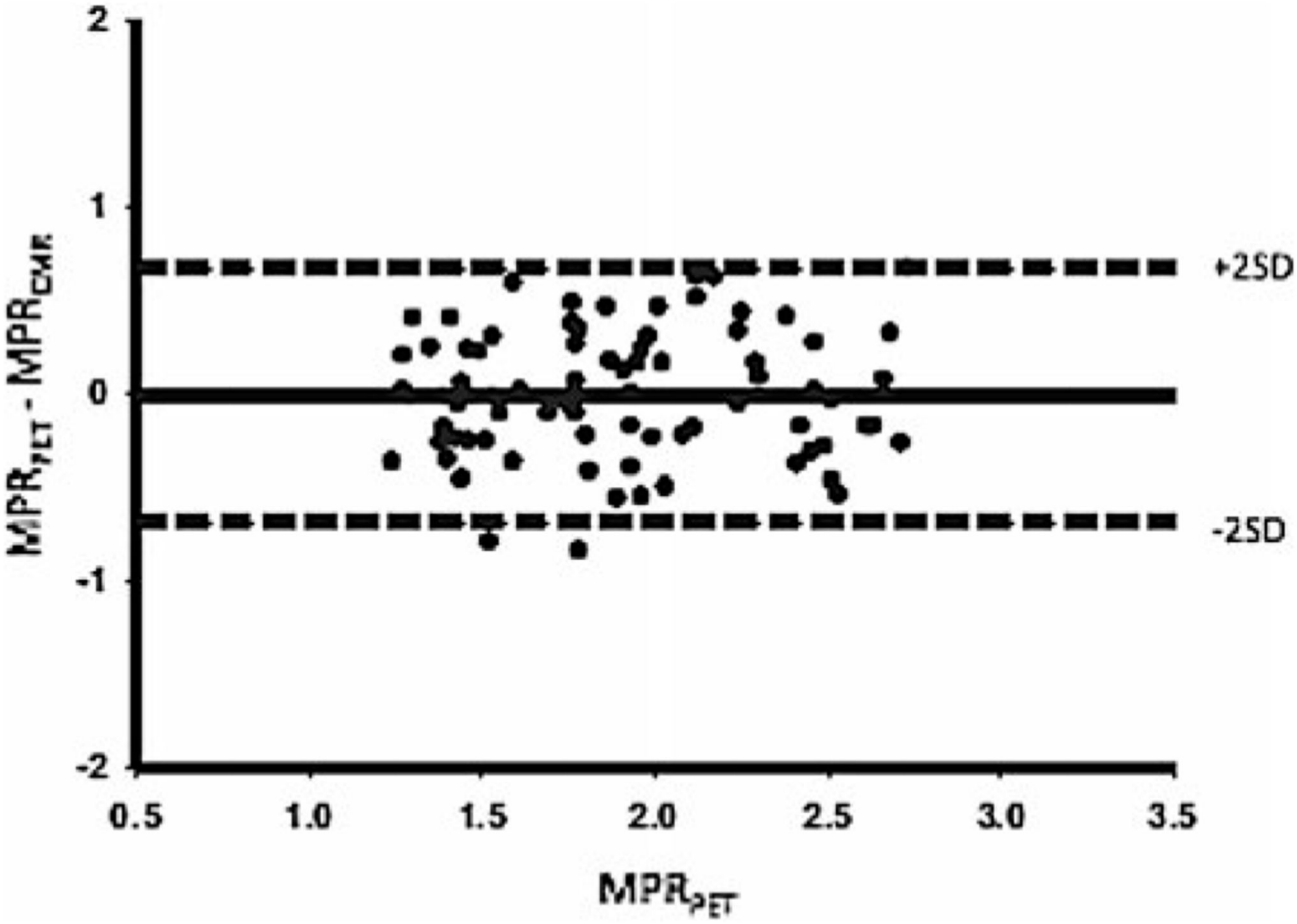

Figure 2.
Bland-Altman plot showing the agreement between CMR- and PET-derived absolute MPR measurements (Courtesy of Morton et al[37]). Abbreviations as in Table 1.

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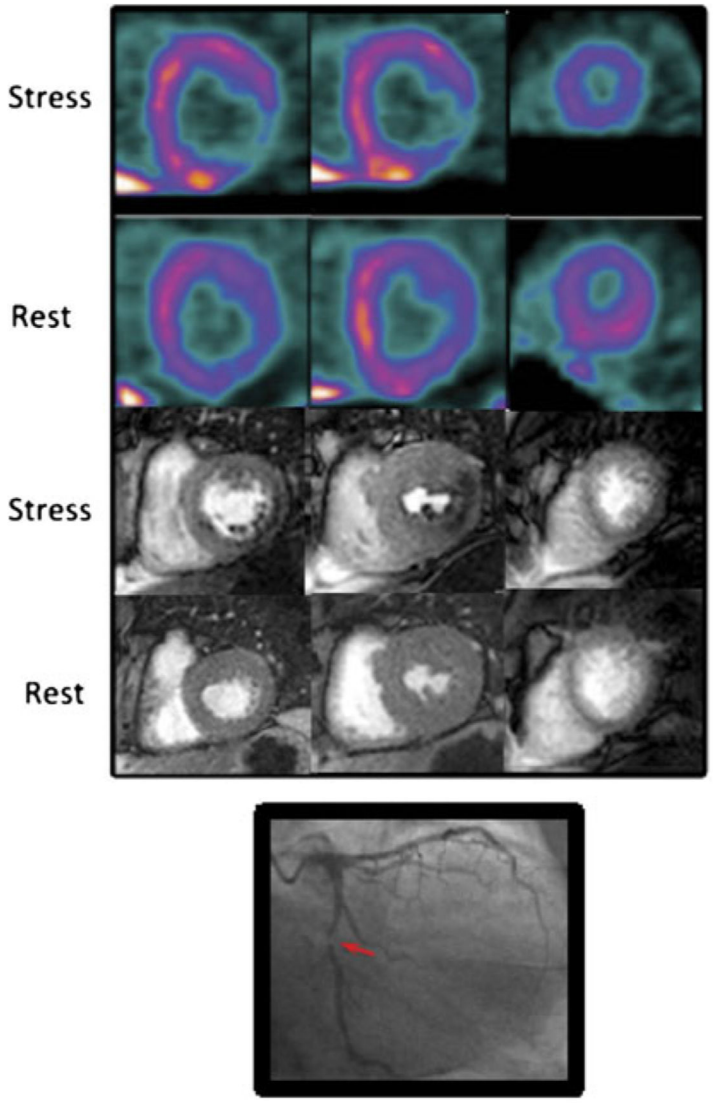

MPR2	LAD	CX	RCA
PET	1.7	1.3	1.97
CMR	1.9	1.42	1.87

Figure 3.

PET *(top)*, CMR *(middle)*, and the x-ray angiogram of the left coronary artery of a 54-year-old patient with diabetes and exertional angina. Basal, mid, and apical slices have been taken from the PET study, which approximately correspond to the CMR slices. There is a stress-induced perfusion defect in the infero-lateral region from base to apex visible on both PET and CMR images. There is a corresponding severe stenosis of the proximal Cx. There was no other significant angiographic disease. Myocardial perfusion reserve of the lowest 2 segments (MPR2) for each territory are shown in the table. The MPR2 for the circumflex

artery is below the cutoff of 1.44 and 1.45 for both PET and CMR, respectively (Courtesy of Morton et al[37]). *PET*, Positron emission tomography; *CMR*, cardiac magnetic resonance; *Cx*, circumflex coronary artery; *LAD*, left anterior descending coronary artery; RCA, right coronary artery.

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Table 1

Published evidence comparing CMR and PET quantitative perfusion imaging: principal methodological characteristics and results

Year	Author	Reference	n	Type of participants	CMR perfusion protocol	Stressor	Quantitative analysis CRM method	PET radiotracer	Quantitative angiography (% significant stenosis)	Sensitivity*	Specificity*	Agre bet CI P de indi
2001	Schwitter J	34	66	Healthy volunteers [18] and CAD [48]	1.5 T mulislice hybrid echo-planar pulse sequence	Dipyridamole	Semi-quantitative	$^{13}NH_3$	Performed (>50%)	91%	94%	MI not MI 0.
2002	Ibrahim T	35	44	Healthy volunteers [19] and CAD [25]	1.5 T, Multislice ultra-fast hybrid sequence	Adenosine	Semi-quantitative	$^{13}NH_3$	Performed (>50%)	86%	84%	MI not MI 0
2006	Pärkkä JP	36	18	Healthy volunteers	1.5 T, saturation recovery turboFLASH sequence	Dipyridamole	Quantitative	$(^{15}O)H_2O$	Not performed	-	-	MI 0.70 *r.*
2008	Fritz-Hansen	38	10	Healthy volunteers	1.5 T, ECG-triggered saturation recovery turboFLASH sequence	Dipyridamole	Quantitative	$^{13}NH_3$	Not performed	-	-	MI 0.79 *r.* st
2008	Pack N	72	5	Healthy volunteers	3 T, saturation recovery turboFLASH sequence	Adenosine	Quantitative	$^{13}NH_3$	Not performed	-	-	MI 0.85 r: st
2012	Morton G	37	38	CAD	1.5 T, k-t balanced turbogradient echo sequence	Adenosine	Quantitative	$^{13}NH_3$	Performed (>70%)	-	-	MI 0.32 *r.*

n, Number of patients; *CAD*, coronary artery disease; *CMR.*, cardiac magnetic resonance; *PET*, positron emission tomography; *MBF*, myocardial blood flow; *MPR*, myocardial perfusion reserve

*Detection of CAD by CMR-derived MPR. against PET-derived MPR.

**Correlation coefficient