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Fractional Flow Reserve and Myocardial Perfusion Imaging in Patients With Angiographic Multivessel Coronary Artery Disease

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Objectives The aim of this study was to investigate the correlation between myocardial ischemia detected by myocardial perfusion imaging (MPI) with single-photon emission computed tomography with intracoronary pressure-derived fractional flow reserve (FFR) in patients with multivessel coronary disease at angiography.

Background Myocardial perfusion imaging can underestimate the number of ischemic territories in patients with multivessel disease. However, there are limited data comparing MPI and FFR, a highly accurate functional index of myocardial ischemia, in multivessel coronary disease.

Methods Sixty-seven patients (201 vascular territories) with angiographic 2- or 3-vessel coronary disease were prospectively scheduled to undergo within 2 weeks MPI (rest/stress adenosine) and FFR in each vessel.

Results In 42% of patients, MPI and FFR detected identical ischemic territories (mean number of territories 0.9 $\pm$ 0.8 for both; $p = 1.00$). In the remaining 36% MPI underestimated (mean number of territories; MPI: 0.46 $\pm$ 0.6, FFR: 2.0 $\pm$ 0.6; $p < 0.001$) and in 22% overestimated (mean number of territories; MPI: 1.9 $\pm$ 0.8, FFR: 0.5 $\pm$ 0.8; $p < 0.001$) the number of ischemic territories in comparison with FFR. There was poor concordance between the ability of the 2 methods to detect myocardial ischemia on both a per-patient ($\kappa = 0.14$ [95% confidence interval: -0.10 to 0.39]) and per-vessel ($\kappa = 0.28$ [95% confidence interval: 0.15 to 0.42]) basis.

Conclusions Myocardial perfusion imaging with single-photon emission computed tomography has poor concordance with FFR and tends to underestimate or overestimate the functional importance of coronary stenosis seen at angiography in comparison with FFR in patients with multivessel disease. These findings might have important consequences in using MPI to determine the optimal revascularization strategy in patients with multivessel coronary disease. (J Am Coll Cardiol Intv 2010;3:307–14)

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There is increasing evidence to demonstrate that in patients with stable coronary artery disease (CAD) the functional significance of the coronary stenosis determines the potential benefit of the revascularization procedure (1–4). Consequently, diagnostic coronary angiography is often accompanied by a functional investigation such a myocardial perfusion scan or derivation of fractional flow reserve (FFR) in the diseased artery/arteries to help decide the requirement and most suitable mode of coronary revascularization.

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Myocardial perfusion imaging (MPI) techniques, such as technetium-99m-labeled sestamibi single-photon emission computed tomography (SPECT), use the principle of flow reserve by comparing hyperemic flow in the myocardial territory supplied by the stenotic artery with hyperemic flow in a myocardial territory subtended by a nonstenotic vessel to detect perfusion defects that correspond to areas of myocardial ischemia (5–7). However, the requirement of at least 1 nonstenotic coronary artery for accurate interpretation of results is an important limitation of perfusion imaging, especially in patients with multivessel CAD (5–7). For example, in a study by Lima et al. (8) in a group of patients with proven angiographic 3-vessel CAD, MPI with SPECT demonstrated no significant perfusion defect or a single-vessel pattern of disease in 54% of patients.

Abbreviations and Acronyms

CAD = coronary artery disease
CI = confidence interval
FFR = fractional flow reserve
MPI = myocardial perfusion imaging
NPV = negative predictive value
PCI = percutaneous coronary intervention
PET = positron emission tomography
PPV = positive predictive value
SPECT = single-photon emission computed tomography

Fractional flow reserve is an alternative, well-established index for investigating the physiological significance of a coronary stenosis (9–12). Fractional flow reserve expresses the maximum achievable blood flow to the myocardium supplied by a stenotic artery as a fraction of the normal maximum flow in that vessel (9,10). Fractional flow reserve is simply derived from the ratio of distal (post stenotic) to proximal coronary pressure and can be measured as part of a diagnostic and/or interventional cardiac catheterization procedure. An FFR ≥0.80 across a coronary stenosis is indicative of the absence of reversible ischemia in the myocardial territory supplied by that artery (9–13). The ischemic threshold of FFR has been replicated independently with different noninvasive functional tests in numerous studies (including exercise electrocardiography, dobutamine stress echocardiography, and MPI) as well as alongside one another in the same population (14,15). Multiple randomized and observational studies have also confirmed the clinical utility of FFR in the context of single-vessel/multivessel as well as left main stem CAD (3,16–18). However, unlike MPI, derivation of FFR in a given artery does not require comparison with a nonstenotic vessel. Therefore, FFR maintains its diagnostic accuracy in assessment of patients with multivessel CAD.

Considering the important limitations of myocardial perfusion techniques in patients with multivessel CAD this group of functional tests are commonly used in conjunction with FFR to guide revascularization in patients with stable 2-/3-vessel disease. The aim of this study was to prospectively compare the ability of MPI with SPECT (based on detection of myocardial perfusion defects) and FFR (based on FFR <0.80) to detect evidence of myocardial ischemia in patients with angiographically defined multivessel CAD.

Methods

Sixty-seven patients (a total of 201 vessels) with stable 2- or 3-vessel CAD, who were deemed suitable to undergo percutaneous coronary intervention (PCI), were recruited. Potential participants were identified during elective diagnostic angiography. Individuals who consented to partake in the study underwent MPI followed by FFR-guided PCI in all 3 coronary vessels within a 2-week period of one another. Markers for myocardial ischemia represented by perfusion defects in each myocardial territory as detected by MPI and abnormal flow reserve in each epicardial vessel as detected by FFR were compared per-patient and per-vascular territory.

Inclusion criteria included presence of stable angina and angiographic evidence of at least 2-vessel CAD. The CAD was detected by visual analysis of diagnostic angiographic images and defined as ≥50% stenosis in the proximal and/or mid-segment of a given epicardial vessel. Patients with a recent acute coronary syndrome, confirmed old myocardial infarction, previous coronary artery bypass surgery, left main stem artery stenosis, left ventricular (LV) systolic function <50% and/or LV regional wall motion abnormality (RWMA), arrhythmia, and poorly controlled airways disease (partial contraindication to administration of adenosine) were excluded. The exclusion of patients with impaired LV function, RWMA, and previous acute coronary syndrome (giving rise to myocardial fibrosis) was designed to reduce confounders during MPI and FFR measurements. The study had local ethics committee approval, and all patients gave written informed consent before recruitment to the study.

Adenosine/rest MPI with SPECT. All perfusion scans were performed before FFR-guided PCI according to a 2-day stress/rest protocol with 900 MBq (25 mCi) of technetium-99m sestamibi. Intravenous infusion of adenosine was used

to induce stress (140 μg/kg/min). Antianginal medication was discontinued 48 h before the study, and patients refrained from drinking caffeine for 24 h before the study. All scans were performed after an overnight fast. The SPECT acquisition was performed over 180° in step-and-shoot mode with 2-headed SPECT cameras (Philips Adac Vertex and Cardio MD cameras, Philips Medical Systems, Cleveland, Ohio) equipped with low-energy, high-resolution collimators. Acquisitions were gated for 16 frames/cardiac cycle. There was a 20% acceptance window around the 140 keV photon peak. Attenuation correction was not performed. The raw gated SPECT data were ungated and reconstructed with iterative reconstruction. The images were processed with Autoquant software (version 6.5, Cedars-Sinai, Los Angeles, California) and were scored both visually and semi-quantitatively. The American Heart Association semi-quantitative 5-point scoring system was used to report on both adenosine/rest images with a 17-segment model as previously described (19,20). Myocardial perfusion studies were scored visually as normal (no defect or ischemia), ischemic (when showing reversibility in ≥1 segment), or as a fixed defect. All fixed defects in this study were treated as nonreversible. The angiographic dominance of the vascular territories was used for designation of territories during SPECT as previously described (19,21). In patients with left coronary dominance the inferior and infero-lateral segments were assigned to the left circumflex territory, and all 4 apical segments were assigned to the left anterior descending territory (21). In the event of right coronary (RCA) dominance the inferior, infero-lateral, and apical inferior segments were assigned to the RCA territory, with the remaining 3 apical segments assigned to the left anterior descending coronary artery territory (21). In addition the patients' body mass index was taken into account when reporting scans. Two experienced nuclear physicians (P.D. and O.D.), who were blinded to angiographic (with the exception of coronary dominance) and FFR data, reported all scans with consensus.

Cardiac catheterization. Cardiac catheterization was performed within 2 weeks of MPI after an overnight fast. All medication and caffeinated drinks were discontinued for 24 h before the procedure. Catheterization was performed through the femoral route with standard 6-F guiding catheters. The procedure was covered with a weight-adjusted dose (100 U/kg) of unfractionated heparin. A commercially available intracoronary pressure/temperature sensor-tipped guide wire (Certus Wire, Radi Medical Systems, Uppsala, Sweden) was used to derive FFR values as previously described (9,14,15). The pressure-monitoring wire was calibrated and advanced to the tip of the guiding catheter for equalization of pressure/temperature signals. The wire was then introduced into the distal third of the study artery. The FFR was derived online within the Radi Analyzer Unit from the ratio of mean distal (P_d, derived from the distal pressure sensor) to proximal (P_a, derived from aortic pressure as detected by the guide-catheter) pressures at maximal steady state hyperemia. A weight-adjusted central infusion (through femoral vein) of adenosine (140 μg/kg/min) was used to achieve maximal steady state hyperemia (22). An FFR ≥0.80 was accepted as a negative result indicative of the absence of reversible myocardial ischemia in the myocardial territory subtended by the study artery. In every patient FFR was measured in all 3 main coronary vessels. Exceptions were totally occluded arteries and vessels with an entirely normal and smooth angiographic appearance. An FFR value of 0.50 was given to totally occluded vessels, because this value is believed to account for potential contribution of the collateral circulation in the distal vessel (15). Entirely smooth vessels were given an FFR of 0.95, which is accepted to be within the middle of the range for a normal FFR (23). We did not routinely measure the reproducibility of FFR, because FFR has been shown to be a highly reproducible index across a range of physiological conditions (24). The PCI was performed in all vessels with an FFR ≤0.80 with the pressure-monitoring wire as angioplasty guide-wire.

Angiographic analysis. Angiographic criteria were analyzed offline at the end of the study. Coronary dominance was designated on the basis of the origin of the posterior descending artery. Patients where the posterior descending artery originated from the RCA were designated right dominance, and patients where it originated from the left circumflex coronary artery were designated left dominance. None of the patients had a co-dominant circulation. Standard quantitative coronary angiographic criteria were used to derive the percent stenosis of each lesion where FFR had been measured. Entirely smooth and occluded arteries were allocated 100% and 0% stenosis, respectively.

Statistical analysis. Data analysis was performed with SPSS for Windows statistics software version 14.0 (SPSS Inc., Chicago, Illinois). Continuous variables were presented as mean ± SD. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to predict the ability of MPI to identify myocardial ischemia (represented by perfusion defects) in comparison with a positive FFR (FFR ≤0.80) on a per-patient and per-vascular territory basis. The κ statistic values were derived to investigate per-patient and per-vessel concordance between FFR- and MPI-derived evidence for ischemia (a κ statistic of +1 indicating perfect agreement, 0 indicating agreement as expected by chance, and −1 indicating complete disagreement). The Mann-Whitney *U* test was used to compare the mean number of ischemic territories detected by MPI and FFR. Spearman's correlation was calculated to investigate the relationship between FFR values and the reversibility extent of ischemia per-vessel as detected by MPI. Statistical significance was accepted at $p < 0.05$.

Results

Two hundred one vascular territories were studied in 67 patients. Tables 1 and 2 summarize the clinical and angiographic characteristics of patients, respectively. Thirteen patients were diabetic. At angiography 35 patients had 2-vessel disease, with 1 entirely normal, smooth coronary artery (Fig. 1). An FFR value of 0.95 was allocated to normal vessels. Thirty-two patients had 3-vessel disease, and FFR was measured in all 3 vessels (Fig. 1). Twelve patients had 1 occluded artery. An FFR value of 0.50 was allocated to these vessels. No patient had 2 occluded arteries.

Comparison of MPI, FFR, and coronary angiography. MPI demonstrated 1 perfusion defect in 24 patients, 2 perfusion defects in 13 patients, and 3 perfusion defects in 4 patients. No perfusion defects were detected in 26 patients. FFR was <0.80 in 1 vessel in 20 patients, in 2 vessels in 24 patients, and in 3 vessels in 3 patients. In 20 patients FFR was >0.80 in all 3 vessels (Fig.1).

In 28 patients (42%) both MPI and FFR identified identical ischemic territories (mean number of ischemic territories; 0.9 ± 0.8 for both; p = 1.00). In 24 patients (36%) MPI underestimated the number of ischemic territories as compared with FFR (mean number of territories: MPI: 0.4 ± 0.6; FFR: 2.0 ± 0.6; p < 0.01). In 15 patients (22%) MPI overestimated the number of ischemic territories as compared with FFR (mean number of territories: MPI: 1.9 ± 0.8; FFR: 0.5 ± 0.8; p < 0.01).

In patients in whom MPI was abnormal in only 1 vascular territory and FFR <0.80 in more than 1 vessel, the perfusion defect was always seen in the territory with lowest FFR.

Out of the 39 vascular territories studied in diabetic patients a false positive result was only seen in 6 vascular territories where MPI was positive for ischemia but FFR >0.80. In 28 vascular territories, both MPI and FFR identified identical abnormalities, and a false negative result was seen in 6 vascular territories.

Table 1. Baseline Characteristics of Patients

Age (yrs)	64 ± 10
Male	42 (62)
Anthropomorphic measurements	
Weight (kg)	81.6 ± 19.0
Height (m)	1.70 ± 0.10
BMI (kg/m^2)	27.6 ± 4.6
Cardiovascular risk factors	
Smoking	15 (22)
Abnormal lipids	34 (51)
Hypertension	36 (54)
Diabetes	13 (19)
Family history	29 (43)
Left ventricular parameters	
Ejection fraction (%)	68 ± 15
End-diastolic pressure (mm Hg)	16 ± 6

Data presented as mean ± SD or n (%).
BMI = body mass index.

Table 2. Angiographic Characteristics of Patients With 2- and 3-Vessel CAD Presented as % QCA-Derived Stenosis

	2-Vessel Disease	3-Vessel Disease
LAD	50 ± 15	50 ± 15
LCx	49 ± 17	50 ± 17
RCA	59 ± 24	60 ± 25

CAD = coronary artery disease; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; QCA = quantitative coronary angiographic; RCA = right coronary artery.

Concordance between MPI and FFR in multivessel disease. On a per-patient basis, there was poor concordance between the ability of the 2 methods to detect similar abnormalities suggestive of ischemia (κ = 0.14 [95% confidence interval (CI): 0.10 to 0.39], level of agreement = 0.61 ± 0.12) (Fig. 2A). In comparison with FFR, the sensitivity, specificity, PPV, and NPV of MPI being able to detect myocardial ischemia was 76%, 38%, 66%, and 50%, respectively.

In patients with no or only 1 ischemic territory based on an FFR <0.80, the concordance rate was higher than for the entire study group (κ = 0.19, 95% CI: 0.10 to 0.49), whereas in patients with 2 or 3 territories with an FFR <0.80, the concordance rate was markedly lower (κ = 0.00), suggestive that any level of agreement between FFR and MPI might be entirely attributable to chance.

On a per-vessel basis, there was poor concordance between the ability of MPI and FFR to detect similar abnormalities

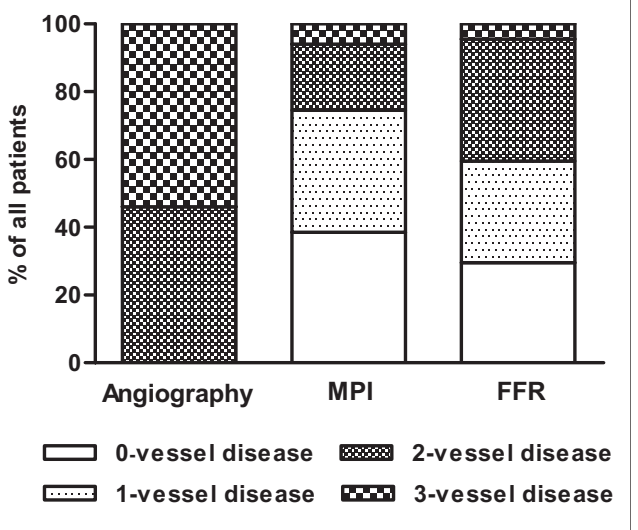

Figure 1. Respective Proportion of Number of Vascular Abnormalities as Described at Coronary Angiography, MPI, and FFR

FFR = fractional flow reserve; MPI = myocardial perfusion imaging.

A

FFR	MPI positive	MPI negative
< 0.80	31	16
> 0.80	10	10

B

FFR	MPI positive	MPI negative
< 0.80	38	42
> 0.80	24	97

Figure 2. Per-Patient and Per-Vessel Concordance Between MPI and FFR

Concordance for detection of ischemia between myocardial perfusion imaging (MPI) (as demonstrated by a myocardial perfusion defect) and fractional flow reserve (FFR) (as demonstrated by FFR <0.80) on a per-patient **(A)** and per-vessel **(B)** basis.

suggestive of ischemia in a given territory (κ = 0.28 [95% CI: 0.15 to 0.42], level of agreement = 0.67 ± 0.07) (Fig. 2B). In comparison with FFR the sensitivity, specificity, PPV and NPV of MPI being able to detect myocardial ischemia was 61%, 69%, 47%, and 80%, respectively.

In addition, the concordance between MPI and FFR continued to remain poor when the association was examined on the basis of FFR quartiles (First quartile [FFR 0.34 to 0.50]: κ = 0, 95% CI: 0 to 0.67; Second quartile [FFR 0.51 to 0.67]: κ = 0, 95% CI: 0 to 0.58; Third quartile [FFR 0.68 to 0.84]: κ = 0.06, 95% CI: 0 to 0.23; Fourth quartile [FFR 0.84 to 1.00]: κ = 0, 95% CI: 0 to 0.39) and main vascular territories (left anterior descending coronary artery: κ = 0.27, 95% CI: 0.05 to 0.50; left circumflex coronary artery: κ = 0.25, 95% CI: 0 to 0.49; RCA: κ = 0.14, 95% CI: 0 to 0.39).

The relation between FFR and MPI in all vascular territories is summarized in Figure 3. The mean FFR value in territories with a normal myocardial perfusion on MPI was similar to mean FFR in territories with a fixed defect on MPI (FFR; normal perfusion: 0.84 ± 0.12, fixed defect: 0.80 ± 0.16; p = 0.21) and higher than mean FFR in territories with a reversible defect on MPI (FFR; normal perfusion: 0.84 ± 0.12, reversible defect: 0.71 ± 0.18; p < 0.01). However, a large overlap of the individual data existed.

Severity of myocardial ischemia. There was a weak correlation in the reversibility extent of ischemia per-vascular territory as assessed by MPI (r = −0.29; p < 0.01) and actual FFR values (Fig. 4).

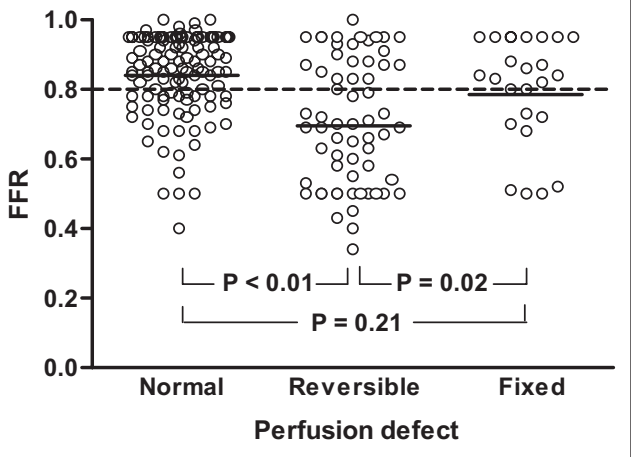

Figure 3. Relation Between FFR and Types of Defect Detected by MPI in all Vascular Territories

FFR = fractional flow reserve; MPI = myocardial perfusion imaging.

Discussion

The present study showed the following: 1) in only a minority of patients (42%) with angiographic 2- or 3-vessel CAD, MPI with SPECT (on the basis of perfusion defects) and pressure-derived FFR (on the basis of FFR <0.80) identify the same territories as being ischemic; and 2) in

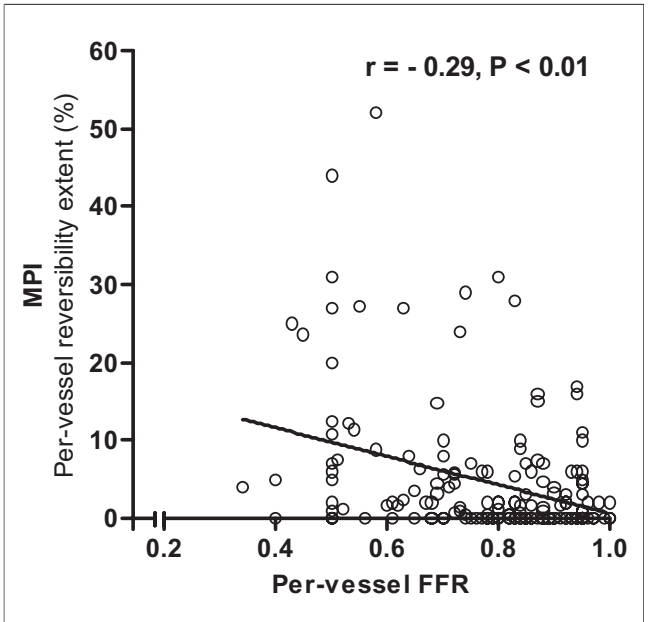

Figure 4. Correlation Between and Reversibility Extent of Ischemia Per-Vascular Territory as Assessed by MPI and Actual FFR Values

FFR = fractional flow reserve; MPI = myocardial perfusion imaging.

most patients (58%) in whom SPECT and FFR are discordant, SPECT often tends to underestimate the extent and severity of the ischemia.

MPI and detection of myocardial ischemia in multivessel CAD. The role of myocardial perfusion techniques, such as SPECT, as a tool to examine the functional significance of coronary stenoses in single-vessel CAD is well-established (5). Perfusion scans are also commonly used as a screening tool to identify patients who might benefit from further investigation and coronary imaging (5). Large meta-analyses have shown that perfusion techniques have a high NPV for primary and secondary cardiac events with annualized event rates after a normal scan being low at 0.45% per annum (25,26). In addition there is increasing evidence that the level of perfusion defect identified in a perfusion scan might be predictive of future risk of cardiovascular events (5,27). However, as outlined previously, the reliance of SPECT and other perfusion techniques on identifying relative differences in perfusion between 2 myocardial territories limits the accuracy of this technique in patients with multivessel and/or main stem CAD. In such cases, where there is widespread myocardial ischemia, perfusion imaging techniques preferentially only identify the myocardial perfusion defect in the most ischemic territory. Such discrepancies limit the clinical utility of MPI to guide revascularization in patients with multivessel/left main CAD.

Although the overall pooled sensitivity of MPI with SPECT for detection of ischemia is reported to be approximately 85% to 90%, these studies have important weaknesses (26,28). Most used coronary angiography, which has well-recognized limitations in accurate identification of functionally significant coronary stenoses, as the reference investigation (29). Furthermore, the majority of patients investigated had single-vessel CAD where MPI has been shown to be highly sensitive. In addition, as seen in our study, in patients with proven 3-vessel disease only a minority had perfusion defects detected reliably in all 3 myocardial territories (6,8). It has been proposed that the diagnostic accuracy of MPI with SPECT might be increased by combining perfusion data with regional and/or global changes in LV function before and after stress, where patients with multivessel disease are more likely to have fixed or transient LV ischemic dilation (30,31).

However, there is increasing evidence that alternative MPI techniques, such as positron emission tomography (PET), might be more sensitive and specific at identifying ischemic territories in patients with multivessel CAD (32). The potential technical advantages of PET, which contribute to its increased accuracy, include the ability to measure absolute myocardial blood flow (in milliliters/minute/gram of myocardium), coronary vasodilator reserve and to assess LV function at rest and during peak stress (as opposed to after stress with SPECT) (32). Although an increasing number of centers use PET as the MPI technique of choice, the overall numbers are small (32). The PET scanners and positron-emitting radiotracers remain significantly more expensive and are much less widely available than SPECT scanners and imaging radiotracers.

FFR in patients with multivessel disease. The utility of FFR for clinical decision-making in patients with multivessel disease has been suggested in both nonrandomized studies, such the DEFER (Deferral versus Performance of PCI of Non-Ischemia-Producing Stenoses) trial (3,23,33), and the recently published multicenter FAME (Fractional Flow Reserve vs. Angiography for Multi-Vessel Evaluation) trial (17). As a functional index of epicardial vessel stenosis, FFR is unique to each and every vessel, and its value is not influenced by the presence and/or absence of stenoses in adjacent vessels. Therefore, FFR is ideally suited to the functional assessment of coronary stenoses in patients with multivessel CAD. In addition, the spatial resolution of FFR is on the order of magnitude of a few millimeters, because the exact position of the pressure wire sensor can be assessed on fluoroscopy at any level through each of the main coronary arteries and/or a side branch (15). In comparison, the spatial resolution of MPI is at the level of a perfusion territory, and that of an exercise electrocardiogram is at the level of the entire heart. As demonstrated in our study, in the presence of discordant results (as seen in 58% of cases), MPI often underestimated the functional severity of ischemia in a given territory as compared with FFR. Only in one-third of discordant cases did MPI overestimate the value of FFR.

In our study an FFR ischemic threshold of 0.80 was used to denote reversible ischemia. This is in contrast to earlier research and clinical studies where a more restrictive threshold of 0.75 is used. More recent studies have shown that a significant proportion of patients with an FFR value within the "grey zone" (range, 0.75 to 0.80) often have an abnormal noninvasive functional test that normalizes after revascularization (13). Consequently, it is recommended that, in the 3 main epicardial vessels—where revascularization might be of prognostic benefit—a more inclusive FFR ischemic threshold of 0.80 should be used with the more restrictive threshold of 0.75 reserved for branch vessels, where revascularization often only confers a symptomatic benefit (15). Large clinical trials such as the FAME trial have also adopted the more inclusive FFR threshold of 0.80 in main epicardial vessels (17). Furthermore, analysis of our data with an FFR ischemic threshold of 0.75 on a per-vessel and per-patient basis did not alter our conclusions (data not presented).

As outlined, MPI and FFR use different physiological concepts to identify the functional significance of epicardial stenoses. However, on the basis of our findings and already known limitations of perfusion imaging, the appropriateness of revascularization strategies based on the combination of coronary angiography and MPI in patients with multivessel

CAD remains under question. Outcome data from future prospective randomized studies of perfusion- and FFR-guided revascularization in this group of patients will help clarify the clinical significance of the discrepancies identified in our study.

Induction of hyperemia during MPI and FFR. Multiple protocols including exercise/rest and adenosine/rest can be used to induce ischemia during MPI. The reported sensitivity and specificity for the 2 techniques are similar, with pooled results indicating a sensitivity of 86% to 90% and specificity of 70% to 75% for the exercise/rest, and sensitivity of 90% and specificity of 75% to 80% for the adenosine/rest protocols (26). The gold standard hyperemic stimulus for derivation of FFR remains weight-adjusted (140 μg/kg/min) central infusion of adenosine (22). In our study the same central infusion of adenosine was used to ensure an identical stimulus during perfusion scanning and FFR measurements.

Ragosta et al. (6) have also compared, as in our study, the ability of SPECT and FFR to identify myocardial ischemia in patients with multivessel CAD. Although in principle both studies reach a similar conclusion, there are important differences. Unlike our study, Ragosta et al. (6) only investigated patients who had been referred for cardiac catheterization subsequent to an abnormal perfusion scan without an attempt to standardize referral criteria for catheterization. This approach might have biased recruitment of patients toward individuals in whom a perfusion defect was present and excluded a small but important sub-group of patients with balanced ischemia who might have presented with a negative scan. To avoid such a bias, in our study patients with multivessel CAD were initially identified on the basis of standard angiographic criteria before undergoing serial MPI and FFR measurements within a 2-week period of one another. In addition, to standardize the stress/hyperemic stimulus we used an identical pharmacological stimulus during MPI and FFR measurements, in contrast to the study by Ragosta.

Study limitations. The presence of additional data on LV wall motion abnormalities at rest and functional changes in LV function at stress might improve the diagnostic accuracy of MPI in patients with multivessel CAD (30,31). Our analysis did not account for LV parameters. However, we excluded, as outlined previously, all patients with impaired LV function, RWMA, and previous acute coronary syndrome (which might result in myocardial fibrosis) to reduce confounders during MPI and FFR measurements.

A proportion of patients in our study had an occluded vessel, where distal passage of the pressure wire in order to measure FFR would not have been possible. These vessels were arbitrarily given a positive FFR value 0.50. Ideally a true FFR should have been measured in all vessels. However, considering all occluded vessels subtended a myocardial territory with contractile function, it is unlikely that an FFR of 0.50 would have been an overestimation of the functional severity of the epicardial vessel occlusion.

Conclusions

This study demonstrates that, although MPI with SPECT detected perfusion defects indicative of myocardial ischemia in a proportion of patients with stable multivessel CAD, its spatial accuracy in comparison with FFR in correctly detecting both the number and position of ischemic territories is poor. In contrast, FFR is an ideal companion to diagnostic angiography, especially in patients with multivessel CAD, where both accurate functional and anatomical information can be obtained during a single catheterization procedure. Considering that a majority of patients who are discovered to have multivessel disease during coronary angiography have not initially had a functional test, assessment of FFR as part of routine cardiac catheterization will allow a 1-stop, combined diagnostic and interventional visit, obviating the need for repeated invasive tests.

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Key Words: coronary revascularization ■ FFR ■ fractional flow reserve ■ MPI ■ myocardial perfusion imaging.