Mismatch Between Results of Myocardial Fractional Flow Reserve (FFR) Measurements and Myocardial Perfusion SPECT for Identification of the Severity of Ischemia

Pitfall of FFR in Patients With Prior Myocardial Infarction

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SUMMARY

We experienced two rare cases of mismatch between the results of FFR and myocardial perfusion SPECT for identification of myocardial ischemia after myocardial infarction. If a FFR cutoff value of 0.75 is applied as in angina patients to patients with myocardial infarction, the severity of ischemia may be underestimated. (Jpn Heart J 2004; 45: 867-872)

Key words: FFR (fractional flow reserve), Myocardial perfusion SPECT, Myocardial infarction

MYOCARDIAL fractional flow reserve (FFR) is an indicator of the level of coronary vascular function, and differs from the coronary flow reserve. Although the latter is defined as the ratio of coronary blood flow at maximum load to coronary blood flow at rest, FFR is calculated as the ratio of the distal coronary pressure to the aortic pressure during maximal hyperemia, and serves as an indicator of the functional severity of coronary artery stenosis.1)

The presence of previous myocardial infarction (MI), however, may blunt the maximal hyperemic response, which has been attributed to infarct-related microvascular dysfunction.4) In such cases, the FFR may not accurately reflect the degree of ischemia.

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Received for publication December 5, 2003.
Revised and accepted March 22, 2004.
We report here on two cases of myocardial infarction, in whom a mismatch was observed between the results of FFR measurements and rest $^{201}$thallium / stress $^{99m}$technetium-tetrofosmin myocardial perfusion SPECT (MPS) for identification of the severity of myocardial ischemia.

CASE REPORT

**Patient 1:** A 75-year-old woman with hyperlipidemia was admitted to our hospital for inferior wall MI. Coronary angiography (CAG) performed 3 weeks after the onset of MI revealed 73% stenosis in the mid segment of the right coronary artery, and coronary pressure measurement showed an FFR of 0.89 (Figure 1). Left ventriculography (LVG) showed a slight decrease in contractility in the inferior wall area. The left ventricular ejection fraction (LVEF) was relatively good (64%). Furthermore, MPS induced inferior wall ischemia and associated chest pain (Figure 4, upper panel). Based on these findings, balloon angioplasty was performed to recanalize the narrowed right coronary artery.

**Patient 2:** The patient was a 71-year-old man, an ex-smoker, who had hyperlipidemia. He was diagnosed with anterior wall MI and thrombolytic therapy was performed. CAG revealed that the patency was restored to myocardial infarction (TIMI) grade III flow in the mid segment of the left anterior descending artery. The maximal serum creatine kinase level was 500 IU. CAG performed 3 weeks

![Figure 1](image1.png)

**Figure 1.** Coronary angiograms and pressure waveforms obtained using the pressure guidewire. Patient 1 had 73% stenosis of the right coronary artery (segment 2). The Pd/Pa value before induction of hyperemia was 0.96 (upper panel), and the distal pressure drop during maximal hyperemia induced by papaverine chloride administration via the coronary arteries was only slight (FFR = 0.89) (lower panel).
Figure 2. Patient 2 had 68% stenosis of the LAD (segment 7). The Pd/Pa value at baseline was 0.93 (upper panel). In this patient also, as in Patient 1, the pressure gradient during maximal hyperemia showed no significant increase (FFR = 0.87).

Figure 3. Electrocardiograms in the two MI patients.
The ECG showed a negative T wave in lead aVR in patient 1 (left). A negative T wave was seen from leads V1 to V5 in patient 2 (right) in lead II, III, and aVF in patient 1. No abnormal Q waves were observed in any lead in either case.

after the onset showed 68% stenosis of the same arterial segment. Although the FFR was 0.87, MPS revealed anterior wall ischemia (Figure 2, Figure 4 lower panel). Therefore, stent implantation was carried out. LVG revealed a region of slightly reduced contractility in the anterior wall area of the left ventricle. The LVEF was 60%.
DISCUSSION

It has been demonstrated that when a cutoff value of 0.75 was applied, the sensitivity and specificity of FFR compared to the results of thallium myocardial scintigraphy and dobutamine echocardiography in angina patients with single-vessel disease were 88% and 100%, respectively. 1) Other studies have also indicated a good correlation between the FFR values and the findings from noninvasive tests. 2, 3) Therefore, FFR measurement has come to be widely employed for the evaluation of ischemia in the clinical setting. However, in the presence of microvessel dysfunction, intracoronary adenosine or papaverine does not induce a sufficient hyperemic response to convert a small pressure gradient to a large pressure gradient in a stenosed vessel. 4) Thus, for a similar degree of stenosis, the FFR values tend to be higher for an infarct-related artery in MI patients than for a noninfarct-related artery in angina patients 5) (Figure 5). The mechanism underlying the reduced hyperemic response in the infarct-related artery remains speculative, but it may be explained as being due to the decreased oxygen consumption by the residual viable myocardium, microvessel stunning, and dyssynergy between the epicardial and resistance vessels in the infarcted area. 6)

Interventionalists employ a pressure-sensor-tipped angioplasty-style guidewire to measure the FFR in the target coronary artery, and if the FFR value

Figure 4. Myocardial perfusion SPECT.
Small size non-reversible perfusion defect in the basal inferior wall with a small amount of ischemia in the base to mid inferior in the RCA distribution (upper panel, patient 1). Moderate amount of ischemia in the mid to distal septum wall and apex in the LAD distribution (lower panel, patient 2).
is < 0.75, they can switch to revascularization of the stenosed vessel with the same guidewire. In patients with previous MI, however, the FFR appears to underestimate the severity of the stenosis, as mentioned above, and use of the FFR cut-off value of 0.75 does not allow reliable separation from ischemia. De Bruyne examined patients 6 days after the onset of myocardial infarction and reported that the FFR was 0.75 in 8 of the 47 MIBI SPECT-positive cases. When he compared FFR with myocardial SPECT used for the evaluation of ischemia, evaluation with FFR at a cutoff level of 0.75 was found to have a sensitivity of 82% and a specificity of 87%. The overall accuracy was thus obviously lower than that in angina patients.

Recent studies have indicated that the FFR is inversely correlated with the amount of viable myocardium in the infarcted area in patients with MI, and the LVEF. In the two cases presented, the infarction size was considered to be relatively small with much residual viable myocardial tissue, however, the FFR values were higher than expected. As shown in animal models of MI, there is a transient dysfunction of the myocardium at the infarct site and the surrounding area. This transient myocardial dysfunction might attenuate the maximal hyperemic response in the infarct-related area. If this were the case, the FFR value is expected to decrease with resolution of the microvessel damage with time.
Furthermore, it remains uncertain why FFR underestimates the severity of ischemia in some MI patients, as in the two cases presented here, but not in others. FFR measurements may be influenced by several factors, as described above, including time after the onset of MI, myocardial stunning\(^{10}\) or hibernation,\(^{11}\) severity of the stenosis, infarct size, and the presence of collateral blood flow. It has also been reported that statins can affect the FFR through their reserve-flow-improving activity.\(^{12,13}\) Since both cases presented in this paper were treated with statins, we cannot rule out the possibility that the FFR of these patients was affected by the statins used.

In summary, FFR values are likely to be overestimated in the culprit coronary artery in patients with prior MI as compared to those in patients with angina pectoris without prior MI, even for a similar degree of stenosis. If an FFR cutoff value of 0.75 is applied as in angina patients to patients with prior MI, the severity of ischemia may be underestimated. Therefore, FFR measurements using a pressure guidewire in the residual stenosis of the culprit lesion after MI must be interpreted with caution.

**REFERENCES**