Coronary artery disease (CAD): Fractional Flow Reserve (FFR) for Pilots Risk Assessment

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Disclosure Information

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I have no financial relationships to disclose

I will not discuss off-label and/or investigational use in our presentation
Risk assessment in Pilots with CAD

• Clinically significant CAD is defined as one or more lesions with > 50% stenosis (diameter reduction)

• Gold standard is coronary angiography, in most cases the qualitative evaluation is based on visual estimation of the study

• High degree intraobserver and interobserver variability (1,2,3,4)

• The target of revascularisation therapy is myocardial ischaemia, not the epicardial coronary disease itself (5)

1: Morton, JACC 2010; 55:173-185
2: Topol, Circulation 1995;92: 2333-42
3: Meijboom, JACC 2008; 636-43
4: Mintz, Circulation 199693 924-931
5: ESC/EACTS Guidelines, EHJ 2010; 31:2501-55
Case report

Pilot, male,
year of birth 1958,
no chest pain

60% stenosis
Detection of ischaemia:

Exercise ECG testing (200 Watt)  
normal

Stress imaging techniques:

Stressechocardiography  
normal
Perfusion scintigraphy  
normal
Cardiovascular magnetic resonance imaging  
normal

Consequences:

EF 60%, no scar, no segmental wall-motion abnormalities
Holter-ECG no SVTS, no VTs or sVTs
aviation medicine rules

1.4.11
Stenosis > 30 per cent in any major vessel should predicate a restriction to multi-crew operation, while stenosis > 50 per cent is disbarring.
When the left main-stem or proximal left anterior descending vessels are involved, pilots with lesions > 30 per cent should be denied certification.

Decision of the primary interventional cardiologist according ESC Guidelines on myocardial revascularisation:

• Normal functional tests are linked with excellent prognosis
• No limiting symptoms (even on oral med. treatment):
  • Class III
  • Level C

denied

III-1-16 Manual of Civil Aviation Medicine

no indication for revascularisation
aviation medicine rules

**FAA** uses a conservative figure of approximation 50% stenosis, FAA certification may depend on the presence or absence of reversible ischemic defects on radionuclide imaging in the area of myocardium supplied by the stenotic vessel.

**EASA** AMC1 MED.B.010 (k)
There should be no stenosis more than 50% in any major untreated vessel, in any vein or artery graft or at the site of angioplasty/stent, except in a vessel subtending a myocardial infarction. More than two stenoses between 30% and 50% within the vascular tree should be not acceptable.

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Decision of the primary interventional cardiologist according ESC Guidelines on myocardial revascularisation:

- Normal functional tests are linked with excellent prognosis
- No limiting symptoms (even on oral med. treatment):
  - Class III
  - Level C

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denied

no indication for revascularisation
Consequences for that pilot:

AeMC / AMS Decision: no waiver possible

Cardiologist: all is fine, go back to work
Methods:

Database (medline) and literature search

• “Outcome after deferral of PCI of an intermediate coronary stenosis”

and

• “Risk of cardiac death or myocardial infarction related to this stenosis”
Conclusions

Five-year outcome after deferral of PCI of an intermediate coronary stenosis based on FFR $\geq 0.75$ is excellent.

The risk of cardiac death or myocardial infarction related to this stenosis is $<1\%$ per year and not decreased by stenting.

(J Am Coll Cardiol 2007;49:2105–11)
Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis
5-Year Follow-Up of the DEFER Study

Objectives
The purpose of this study was to investigate the appropriateness of stenting a functionally nonsignificant stenosis.

Background
Percutaneous coronary intervention (PCI) of an intermediate stenosis without evidence of ischemia is often performed, but its benefit is unproven. Coronary pressure-derived fractional flow reserve (FFR) is an invasive index used to identify a stenosis responsible for reversible ischemia.

Methods
In 325 patients scheduled for PCI of an intermediate stenosis, FFR was measured just before the planned intervention. If FFR was ≥ 0.75, patients were randomly assigned to deferral (Defer group; n = 91) or performance (Perform group; n = 90) of PCI. If FFR was < 0.75, PCI was performed as planned (Reference group; n = 144). Clinical follow-up was 5 years.

(J Am Coll Cardiol 2007;49:2105–11)
Pressure-Wire
0.014 inch
electronic equipment:
double pressure measurement

1. Aorta
2. in coronary vessel
   use as a normal guide wire for PCI
   no exchange of the wire necessary

Characteristics of FFR

• FFR is not influenced by changes in blood pressure, heart rate, or contractility

• FFR has a unique normal value of 1.0 in every patient and every coronary artery

• FFR incorporates the contribution of collateral flow to myocardial perfusion

Jan Willem Bech, MD, PhD
Aorta

P_a

\[ P_a \rightarrow P_d \]

\[ Q_{\text{normal}} \rightarrow \]

Myocardium

\[ P_d \rightarrow 0 \rightarrow Q_{\text{normal}} \]

Normal perfusion pressure

Stenosis

\[ P_d \leftarrow P_a \]

\[ Q_{\text{stenosis}} \rightarrow \]

Stenotic perfusion pressure

under condition of max. hyperemia!

\[ FFR = \frac{Q_{\text{stenosis}}}{Q_{\text{normal}}} \]

Stenotic perfusion press.

Normal perfusion press.

Pijls, JACC 2012;59:1046 – 1057
FFR threshold for ischemia

- FFR < 0.75 → inducible ischemia (spec. 100%)
- FFR > 0.75 → no inducible ischemia (sens. 90%)

For safety reasons: cut off: FFR =/ > 0.8

"FFR and prognosis, intermediate stenosis, single vessel"

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<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Design</th>
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<tr>
<td>DEFER (1)</td>
<td>2001 + 7</td>
<td>325</td>
<td>Multicenter, random.</td>
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<tr>
<td>Legalery (2)</td>
<td>2005</td>
<td>407</td>
<td>Monocenter, not rand.</td>
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<tr>
<td>Ntalianis (3)</td>
<td>2010</td>
<td>296</td>
<td>Monocenter, not rand.</td>
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“FFR and prognosis, intermediate stenosis, single vessel and multivessel“

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<tr>
<td>Berger (4)</td>
<td>2005</td>
<td>102</td>
<td>Monocenter, not rand.</td>
</tr>
<tr>
<td>FAME (5,6)</td>
<td>2010</td>
<td>1005</td>
<td>Multicenter, random.</td>
</tr>
<tr>
<td>FAME II (7)</td>
<td>2012</td>
<td>1220</td>
<td>Multicenter, random.</td>
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</tbody>
</table>

**FAME:**
PCI performed on indicated lesions only if FFR ≤ 0.80

4: Berger JACC 2005; 46: 438-42
5: Torino NEJM 2009; 360: 213-24
6: JACC 2010;56:177–84
7: De Bruyne NEJM 2012; 367.991-1001
Conclusions:

Routine measurement of FFR in patients with multivessel CAD undergoing PCI with drug-eluting stents significantly reduces mortality and myocardial infarction at 2 years when compared with standard angiography-guided PCI.

(J Am Coll Cardiol 2010;56:177–84)
Conclusions:

In patients with stable coronary artery disease, FFR-guided PCI, improves patient outcome as compared with medical therapy alone.

This improvement is driven by a dramatic decrease in the need for urgent revascularization for ACS.

*In patients with functionally non-significant stenoses medical therapy alone resulted in an excellent outcome, regardless of the angiographic appearance of the stenoses.*
„FFR and CT, FFR and Perfusion Scan“

A  Computed Tomography Coronary Angiography Versus Conventional Coronary Angiography and Correlation With Fractional Flow Reserve in Patients With Stable Angina

(J Am Coll Cardiol 2010;56:177–84)

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

(J Am Coll Cardiol Intv 2010;3:307–14)
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<tr>
<th></th>
<th>kappa</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Diagnostic Accuracy, %</th>
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<tbody>
<tr>
<td>FFR &lt;0.75 (n=16)</td>
<td></td>
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<tr>
<td>CT coronary angiography, visual score</td>
<td>0.16</td>
<td>97 (82-100)</td>
<td>40 (29-51)</td>
<td>49 (39-60)</td>
</tr>
<tr>
<td>Quantitative CT coronary angiography</td>
<td>0.20</td>
<td>50 (26-75)</td>
<td>75 (65-85)</td>
<td>71 (61-80)</td>
</tr>
<tr>
<td>Conventional coronary angiography, visual score</td>
<td>0.15</td>
<td>63 (39-86)</td>
<td>60 (49-72)</td>
<td>61 (51-71)</td>
</tr>
<tr>
<td>Quantitative coronary angiography</td>
<td>0.25</td>
<td>69 (46-91)</td>
<td>67 (56-78)</td>
<td>67 (58-77)</td>
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</table>
Computed Tomography Coronary Angiography versus Conventional Coronary Angiography and Correlation with Fractional Flow Reserve in Patients With Stable Angina

Conclusions:

The anatomical assessment of the hemodynamic significance of coronary stenoses determined by visual CTCA, CCA, or QCT or QCA does not correlate well with the functional assessment of FFR.

Determining the hemodynamic significance of an angiographically intermediate stenosis remains relevant before referral for revascularization treatment.

(J Am Coll Cardiol 2008;52:636–43) © 2008 by the American College of Cardiology Foundation
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)
Our Conclusions 1/2:

Visual-functional mismatch between coronary angiography and fractional flow reserve (FFR)

Park SJ

Lesions with angiographic diameter stenosis (DS) ≥50% and FFR >0.80 ("mismatches") were seen in 57% of non-left main lesions (p = 0.032).

Conversely, among the lesions with DS <50% and FFR <0.80 ("reverse mismatches") 16% were found in the non-left main lesions (p < 0.001).

Our Conclusions 2/2:

Decision making in pilots with CAD and stenosis
- visual estimation -
> 30% and <70% remains challenging

Surprising that FFR is not more widely applied to improve the decision process

It might be reasonable to introduce FFR

1. intermediate stenoses single vessel disease
2. multivessel diseases

Foundation of a working group of Aviation Medicine Specialists might be reasonable
Long-Term Clinical Outcome After Fractional Flow Reserve-Guided Percutaneous Coronary Intervention in Patients With Multivessel Disease

Objectives
In the present study, we analyzed the clinical outcome of patients with multivessel coronary artery disease in whom at least one vessel was treated by percutaneous coronary intervention (PCI) and at least one other vessel was deferred on the basis of fractional flow reserve (FFR) measurements during the same session.

Background
Myocardial FFR is an established tool for assessing the severity of epicardial stenoses. It has been shown that it is safe to defer an intervention in single vessel disease patients when FFR >0.75.

Methods
One hundred two patients (66 ± 10 years) with multivessel coronary artery disease were included in the study. In all patients, PCI of at least two vessels was contemplated. Yet in all of them at least one vessel was treated by PCI, whereas at least one other vessel was deferred based on an FFR > 0.75. Major adverse cardiac events (MACE) were recorded during an average follow-up of 29 ± 18 months.

(J Am Coll Cardiol 2007;49:2105–11)
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Long-Term Clinical Outcome After Fractional Flow Reserve-Guided Percutaneous Coronary Intervention in Patients With Multivessel Disease

Results
In 102 patients, 113 coronary arteries underwent PCI. In these arteries FFR was 0.57 ± 0.13 and mean diameter stenosis was 68 ±14%. One hundred twenty-seven coronary arteries had an FFR > 0.75 and PCI was deferred. In these arteries FFR was 0.86 ± 0.06 and mean diameter stenosis was 47 ± 12%. No death occurred during the follow-up. A MACE occurred in 9% and 13% of patients after 12 and 36 months, respectively. These MACE were related to 22 (9.2%) arteries. Among them, 8 (6.3%) MACE were related to one of the initially deferred vessels, whereas 14 (12.3%) MACE were related to one of the initially treated coronary artery.

Conclusions
In patients with multivessel disease, PCI of hemodynamically non-significant stenoses can be safely deferred, even if initially planned on the basis of the angiogram.

(J Am Coll Cardiol 2005;46:438–42)
© 2005 by the American College of Cardiology Foundation
FAME study: CONCLUSIONS

Routine measurement of FFR during DES-stenting in patients with multivessel disease is superior to current angiography guided treatment.

It improves outcome of PCI significantly.

It supports the evolving paradigm of “Functionally Complete Revascularization”, i.e. stenting of ischemic lesions and medical treatment of non-ischemic ones.

Background

The angiographic severity of a coronary stenosis correlates poorly with its ischemic potential.

The current strategy of performing PCI based on the angiographic appearance of a lesion may not be the most effective or efficient technique.

Measuring fractional flow reserve (FFR) to help identify which lesions warrant PCI may be a superior method for achieving a “functionally” complete revascularization.

William F. Fearon, Pim A.L. Tonino, Bernard De Bruyne, Uwe Siebert and Nico H.J. Pijls, on behalf of the FAME Study Investigators
Absolute Difference in MACE-Free Survival

- **30 days**: 2.9%
- **90 days**: 3.8%
- **180 days**: 4.9%
- **360 days**: 5.1%

William F. Fearon, Pim A.L. Tonino, Bernard De Bruyne, Uwe Siebert and Nico H.J. Pijls, on behalf of the FAME Study Investigators
2 Year Survival Free of MI

FFR-Guided

Angio-Guided

730 days
3.6%

William F. Fearon, Pim A.L. Tonino, Bernard De Bruyne, Uwe Siebert and Nico H.J. Pijls, on behalf of the FAME Study Investigators
2 Year Survival Free of Death/MI

William F. Fearon, Pim A.L. Tonino, Bernard De Bruyne, Uwe Siebert and Nico H.J. Pijls, on behalf of the FAME Study Investigators
Conclusions

At 2 years, there is now a significant decrease in the rate of MI in the FFR-guided arm. There continues to be a significant decrease in death and MI favoring the FFR-guided approach. Lastly, there is a strong trend towards a lower rate of death, MI or the need for repeat revascularization in the FFR-guided arm.

There is no signal to suggest that deferred lesions are likely to be responsible for late myocardial infarctions or to progress and require repeat revascularizations.

William F. Fearon, Pim A.L. Tonino, Bernard De Bruyne, Uwe Siebert and Nico H.J. Pijls, on behalf of the FAME Study Investigators
Limitations determination grade of coronary stenosis