During Maximal Vasodilatation

\[ \text{FFR}_{\text{myo}} = \frac{P_d}{P_a} = 0.70 \]
FRACTIONAL FLOW RESERVE:

- has a sound scientific basis
- has been well validated experimentally
- is the only functional parameter which has been validated clinically versus a true gold standard
- facilitates decision-making in PCI
- and improves outcome of angioplasty
experimental validation of FFR in dogs
Volumetric coronary blood flow

\[ Q_{\text{phasic}} \]

200 ml/min

\[ Q_{\text{mean}} \]

20 sec occlusion

Constant pressure \[ R \sim 1 / \text{Flow} \]
Experimental basis of FFR

**Horizontal axis:**
FFR measured by true flow

**Vertical axis:**
FFR measured by Hyperemic pressure ratio

_Pijls et al, Circulation 1993_
Threshold value of FFR to detect significant stenosis in humans

FFR is the **only** functional index which has ever been validated versus a true gold standard. *(Prospective multi-testing Bayesian methodology)*

*ALL* studies ever performed in a wide variety of clinical & angiographic conditions, found threshold between 0.75 and 0.80

**Sensitivity** : 90%

**Specificity** : 100%


*Circulation* 2010
**FFR has been validated in almost all clinical and Angiographic conditions:**

- multivessel disease
- left main and ostial stenosis
- diffuse disease
- bifurcation lesions
- tandem lesions
- unstable angina, NSTEMI
- previous myocardial infarction
- etc.

- ....but not to be used in acute STEMI

(more than 1500 publications)
FFR and Clinical Outcome: Evidence from randomised controlled trials

- Is it safe to defer PCI if FFR is negative?
- Is it indicated to perform PCI if FFR is positive?
- Does systematic use of FFR improve outcome of PCI?
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**DEFER: Cardiac Death And Acute MI After 5 Years**

- non-ischemic stenosis, R/x
- non-ischemic stenosis, R/x + stent
- ischemic stenosis, R/x + stent

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DEFER-study, JACC 2007; 49 : 2105-2111
DEFER: Cardiac Death And Acute MI After 5 Years

- non-ischemic stenosis, R/x
- non-ischemic stenosis, R/x + stent
- ischemic stenosis, R/x + stent

DEFER-study, JACC 2007; 49 : 2105-2111
Stenting a functionally non-significant (FFR-negative) stenosis does NOT make any sense.

*It is unnecessary, expensive, and increases the risk of death and MI without any symptomatic benefit*

DEFER, FAME, Nuclear; Prospect
FFR and Clinical Outcome: 
*Evidence from randomised controlled trials*

- Is it safe to defer PCI if FFR is negative?
- *Is it indicated to perform PCI if FFR is positive?*
- Does systematic use of FFR improve outcome of PCI?
FUNCTIONALLY SIGNIFICANT STENOSIS

a functionally significant (“FFR-POSITIVE”) stenosis generally gives symptoms (angina) (“ischemic” stenosis, hemodynamically significant stenosis)

PCI and stenting is extremely effective in relieving symptoms (angina) in such patients

(and much more effective than medical treatment)

DEFER, COURAGE, SYNTAX, FAME
freedom from chest pain

DEFER-study, JACC 2007; 49 : 2105-2111

Ischemic lesions (FFR < 0.75) treated by stenting
FUNCTIONAL CLASS
in COURAGE - SYNTAX – 3VD and FAME

% free of angina at 1 year

<table>
<thead>
<tr>
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FUNCTIONALLY SIGNIFICANT STENOSIS

stenting a *functionally significant* stenosis is justified, when technically feasible
FFR and Clinical Outcome:
Evidence from randomised controlled trials

• Is it safe to defer PCI if FFR is negative?

• Is it indicated to perform PCI if FFR is positive?

• Does systematic use of FFR improve outcome of PCI? (decrease of Myocardial Infarction & death)
FFR and Clinical Outcome: Evidence from randomised controlled trials

- Is it safe to defer PCI if FFR is negative?
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FAME studies
FAME: FFR-guided PCI in MVD is Superior to Standard Angiography-guided PCI

Tonino et al, NEJM 2009; Pijls et al, JACC 2010
Patient with stenoses ≥ 50% in at least 2 of the 3 major epicardial vessels

Indicate all stenoses ≥ 50% considered for stenting

Randomization

Angiography-guided PCI
Stent all indicated stenoses

FFR-guided PCI
Measure FFR in all indicated stenoses
Stent only those stenoses with FFR ≤ 0.80

follow-up at 1, 2, 5 year
DEATH & MI in the FAME study after 2 years

Angio-guided: angiographically complete PCI

FFR-guided: functionally complete PCI (“ischemia-driven”)

P= 0.03

12.7% 9.5%
12.7% 9.5%

2 year 2 year (excl small periprocedural infarction)
FFR – guided PCI:

- improves outcome
- improves quality of life
- is cost-saving
- reduces radiation and contrast exposure
- does not prolong time of procedure

Tonino et al, NEJM 2009; Pijls et al, JACC 2010
FAME-2: FFR-guided PCI in Coronary Artery Disease is Superior to Optimum Medical Therapy
Multivessel PCI vs Medical Treatment:

**COURAGE study:**

*Negative bias for PCI in COURAGE trial:*

1. PCI was angio-guided, not FFR-guided

2. A number of ischemic lesions were not treated, because they were angiographically mild

3. And a number of non-ischemic lesion were unnecessarily treated because they looked angiographically more severe

> FAME – 2 Study
FAME 2 Trial Flow Chart

Stable patients scheduled for one-, two- or three-vessel DES stenting

FFR in all indicated target lesions

There is at least one stenosis With an FFR ≤ 0.80

Randomisation 1:1

PCI + OMT

OMT

Cohort A

There is at no stenosis With an FFR ≤ 0.80

OMT

Cohort B

Follow-up after 1, 6 months, 1, 2, 3, 4, and 5 years
70% of the patients

Stable patients scheduled for one-, two- or three vessel DES stenting

FFR in all indicated target lesions

30% of the patients

There is at least one stenosis
With an FFR ≤ 0.80

Randomisation 1:1

PCI + OMT

OMT

Cohort A

Follow-up after 1, 6 months, 1, 2, 3, 4, and 5 years

There is at no stenosis
With an FFR ≤ 0.80

OMT

Cohort B
FAME 2 Trial Primary End-Points

The primary end-point of the FAME 2 trial is the 24-month major adverse cardiac event rate defined as:

- All cause death
- Myocardial infarction
- Unplanned hospitalisation leading to urgent revascularisation

as adjudicated by the Clinical Event Committee (CEC)
On recommendation of the independent Data and Safety Monitoring Board enrollment was halted on January 15, 2012 due to a significantly increased patient risk of major adverse cardiac events (MACE) among patients randomized to OMT alone compared to patients randomized to OMT plus FFR-guided PCI.

**Timeline of results of FAME-2:**

- **PCR** May 2012 Paris: preliminary results of cohort A
- **ESC** Aug 2012 Munich: late-breaking trial
- **Publication of the study:** September 2012
- **TCT** Oct 2012 Miami: large perspective of study
In summary:

**EVIDENCE FROM RANDOMIZED TRIALS:**

FFR guidance of PCI facilitates decision making whether to stent or not to stent and where to stent.

FFR-guided PCI is superior to guidance by angiography alone **AND** superior to optimal medical treatment, both with respect to improving symptoms but also with respect to decreasing myocardial infarction rate and death.

*Use of FFR makes PCI to a better treatment modality of CAD and will further expand the patient populations in whom PCI is a beneficial treatment.*
10 – Procedural aspects of PCI

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<tr>
<th>Specific PCI devices and pharmacotherapy</th>
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<tr>
<td><strong>FFR-guided PCI is recommended for detection of ischemia-related lesion(s) when objective evidence of vessel-related ischemia is not available</strong></td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>DES* are recommended for reduction of restenosis/reocclusion, if no contraindication to extended DAPT</td>
<td>I</td>
<td>A</td>
</tr>
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<td>Distal embolic protection is recommended during PCI of SVG disease to avoid distal embolisation of debris and prevent MI</td>
<td>I</td>
<td>B</td>
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<td>Rotablation is recommended for preparation of heavily calcified or severely fibrotic lesions that cannot be crossed by a balloon or adequately dilated before planned stenting</td>
<td>I</td>
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