What is the best way to assess coronary perfusion?

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Coronary Ischemia and nonobstructive coronary artery disease by angiography is common and is associated with cardiovascular events.
Coronary Microcirculation

High oxygen extraction 60-80% vs. 20-30% in skeletal muscle: coronary perfusion is flow dependent.
Functional Angiogram Protocol

- Diagnostic angiography
- Adenosine IC 24-72 µg
- CFR: Non endothelium microcirculation
- Acetylcholine (endothelium dependent vasodilator)
  Epicardial
- Microcirculation
50-Year-Old Female With Chest Pain

Baseline

Acetylcholine 10-4M
50-Year-Old Female With Chest Pain

Baseline

Acetylcholine

Nitroglycerine
Prevalence of Microvascular Dysfunction in Patients With Non-Obstructive CAD

1,439 patients with chest pain and non-obstructive CAD at coronary angiography underwent invasive coronary microvessel assessment.

The majority of the patients with chest pain and non-obstructive CAD have microvascular dysfunction.
Coronary endothelial function in response to acetylcholine

Eighty lead body surface ECG

Coronary Endothelial Dysfunction in Humans Is Associated With Myocardial Perfusion Defects

David Hasdai, MD; Raymond J. Gibbons, MD; David R. Holmes, Jr, MD; Stuart T. Higano, MD; Amir Lerman, MD
## Association Between Noninvasive Tests and Coronary Microvascular Flow Reserve

### Test Results

<table>
<thead>
<tr>
<th>Test</th>
<th>% (+)</th>
<th>(95% CI)</th>
<th>(95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Exercise Echo</td>
<td>100</td>
<td>40.0 (28 - 57)</td>
<td>62 (47 - 75)</td>
<td>52 (38 - 65)</td>
<td>53 (36 - 68)</td>
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<tr>
<td>Dobutamine Echo</td>
<td>21</td>
<td>38.1 (2 - 52)</td>
<td>40 (12 - 74)</td>
<td>31 (9 - 61)</td>
<td>25 (3 - 65)</td>
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<tr>
<td>Exercise SPECT</td>
<td>131</td>
<td>38.2 (26 - 50)</td>
<td>61 (48 - 73)</td>
<td>48 (37 - 60)</td>
<td>50 (36 - 64)</td>
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<tr>
<td>Vasodilator SPECT</td>
<td>63</td>
<td>50.8 (42 - 78)</td>
<td>59 (41 - 76)</td>
<td>61 (42 - 78)</td>
<td>59 (41 - 76)</td>
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<tr>
<td>Vasodilator PET</td>
<td>33</td>
<td>36.4 (4 - 48)</td>
<td>50 (26 - 74)</td>
<td>43 (22 - 66)</td>
<td>25 (5 - 57)</td>
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<tr>
<td>All imaging</td>
<td>365</td>
<td>41.6 (34 - 49)</td>
<td>58 (50 - 65)</td>
<td>49 (42 - 56)</td>
<td>50 (42 - 58)</td>
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<tr>
<td>Exercise ECG</td>
<td>233</td>
<td>15.5 (12 - 27)</td>
<td>78 (69 - 85)</td>
<td>51 (43 - 59)</td>
<td>61 (43 - 77)</td>
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<tr>
<td>All imaging + ECG</td>
<td>365</td>
<td>6.3 (4 - 12)</td>
<td>90 (85 - 94)</td>
<td>50 (45 - 56)</td>
<td>61 (39 - 80)</td>
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</tbody>
</table>

### Imaging Stress Tests

- **Endothelial function**
  - Negative: [Data Points]
  - Positive: [Data Points]

- **Non-endothelial CFR**
  - Negative: [Data Points]
  - Positive: [Data Points]

*Cassar: Circ, 2009*
Case: 52 year old accountant with chest pain

CFR, epicardial stenoses and microcirculation

CFR provides insight into the overall impairment in flow in the coronary circulation, regardless of its origin in the epicardial vessels (focal or diffuse stenoses), or in the microcirculation.

Many patients with microcirculatory dysfunction present also epicardial stenoses
How do we make resistance stable?

Pharmacological    Physiological
Coronary Stenoses Resting and hyperemic Flow

Hyperemia “uncover” the true gradient across the lesion

• Myocardial Fractional Flow Reserve during hyperemia

\[ FFR: = \frac{P_d}{P_A} \]
Fractional Flow Reserve to Determine the Appropriateness of Angioplasty in Moderate Coronary Stenosis

RANDOMIZED TRIAL

Brynsy, MD, PhD; Nico H.J. Pijs, MD, PhD;

Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis
5-Year Follow-Up of the DEFER Study

Nico H.J. Pijs, MD, PhD,* Pepijn van Schaardenburgh, MD,∗ Ganesh Man Eric Boema, PhD; Jan-Willem Bech, MD, PhD; Marcel van't Veer, MD; Jan Hoooren, MD, PhD; Jacques Koole, MD, PhD;∗ William Wijns, MD, Bernard de Bruyne, MD, PhD;

Eindhoven, Rotterdam, Maastricht, and Zwolle, the Netherlands; and Aalst, Belgium

ORIGINAL ARTICLE

Fractional Flow Reserve–Guided PCI for Stable Coronary Artery Disease

Bernard De Bruyne, M.D., Ph.D., William F. Fearon, M.D., Nico H.J. Pijs, M.D., Ph.D., Emanuele Barbato, M.D., Ph.D., Pim Tonino, M.D., Ph.D., Zsolt Piroth, M.D., Nikola Jagic, M.D., Sven Möbius-Winkler, M.D., Gilles Rioufol, M.D., Ph.D., Nils Witt, M.D., Ph.D., Petr Kala, M.D., Philip MacCarthy, M.D., Thomas Engstrom, M.D., Keith Oldroyd, M.D., Kretan Mavromatis, M.D., Ganesh Manoharan, M.D., Peter Verlee, M.D., Ole Frobert, M.D., Nick Curzen, B.M., Ph.D., Jane B. Johnson, R.N., B.S.N., Andreas Limacher, Ph.D., Eveline Nüesch, Ph.D., and Peter Jüni, M.D., for the FAME 2 Trial Investigators*

ABSTRACT

Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease

Bernard De Bruyne, M.D., Ph.D., Nico H.J. Pijs, M.D., Ph.D., Bindu Kaleas, M.P.H., Emanuele Barbato, M.D., Ph.D., Pim A.L. Tonino, M.D., Ph.D., Zsolt Piroth, M.D., Nikola Jagic, M.D., Sven Möbius-Winkler, M.D., Gilles Rioufol, M.D., Ph.D., Nils Witt, M.D., Ph.D., Petr Kala, M.D., Philip MacCarthy, M.D., Thomas Engstrom, M.D., Keith G. Oldroyd, M.D., Kretan Mavromatis, M.D., Ganesh Manoharan, M.D., Peter Verlee, M.D., Ole Frobert, M.D., Nick Curzen, B.M., Ph.D., Jane B. Johnson, R.N., B.S.N., Peter Jüni, M.D., and William F. Fearon, M.D., for the FAME 2 Trial Investigators*

ABSTRACT
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."

Pijls: JACC, 2007
Event-Free Survival 18 Months
Absolute Difference in MACE-Free Survival

Survival free from death, MI, revascularization

Days from randomization

1 mo 2.9% 3 mo 3.8%
6 mo 4.9%
12 mo 5.1%
18 mo 5.3%
Functional SYNTAX Score Recalculated Counting only Lesions With an FFR <0.8

Only 14% of patients with angiographic 3VD had functional 3VD

Only 43% of patients with angiographic 2VD had functional 2VD

J Am Coll Cardiol 55(25):2816, 2010
Outlining the involvement of epicardial and microcirculatory domains in ischaemic heart disease

Normal FFR / Decreased CFR / Increased HMR (microcirculatory resistance)
How do we make resistance stable?

Pharmacological  Physiological
Contraindications to adenosine

- Bronchospasm
- Heart block
- Dipyramidole can potentiate adenosine effect and cause prolonged heart block
- Patients taking inhibitors of adenosine may require higher doses
  - Theophylline
  - Chocolate
  - Caffeine

Measure during a wave-free portion of diastole (microvascular resistance constant and minimal)
iFR and Clinical Outcome

Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI


iFR-SWEDEHEART

Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI

Background: FFR- and iFR-based deferral of coronary revascularisation

- The DEFINE FLAIR (DF) and iFR SWEDHEART (SH) trials demonstrated that iFR is as safe as FFR in guiding myocardial revascularisation.

- Yet, it is unknown if this is valid for patients in whom revascularisation is deferred.

- The pooled population of both studies (4529 patients) provides a unique opportunity to investigate the discussed aspects of revascularisation deferral in contemporary clinical practice.
MACE in iFR and FFR guided revascularisation (all patients)

HR = 1.03  95% CI: (0.81, 1.31)  p = 0.81

MACE similar and low at 1 year after iFR- and FFR-based revascularisation decision-making
Unadjusted outcomes after deferral by clinical presentation and iFR or FFR

**FFR**
- HR 0.52 (0.27-1.00); p<0.05

In FFR-deferred patients, MACE is significantly higher in ACS than SCD

**iFR**
- HR 0.74 (0.38-1.43); p=0.37

In iFR-deferred patients, MACE is similar in ACS and SCD
64 year old male, non-smoker, inactive, admitted with IWMI

54 year old male, smoker, admitted with AWMI
• intracoronary Doppler flow velocity was measured in the infarct-related artery, as well as in a reference vessel to determine reference vessel CFVR

Conclusions

• Microvascular dysfunction, determined after primary percutaneous coronary intervention for acute anterior wall ST-segment–elevation myocardial infarction both at the IRA and the remote area are associated with a significantly increased long-term cardiac mortality
Microvascular Obstruction in Non-Infarct Related Coronary Arteries

- 199 patients followed PCI for STEMI
- Cardiac MRI within one week
- IRA and non-IRA segments (AHA)

MACE-Free Survival (cumulative %)

HR=2.27

Hazard ratio 2.15 (95% CI, 1.06-4.35), P=0.029
PET MPI with N-13 ammonia and MBF

<table>
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<th>Stress</th>
<th>Rest</th>
<th>MFR</th>
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<td>2.11</td>
<td>0.95</td>
<td>2.22</td>
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<tr>
<td>LCx</td>
<td>1.92</td>
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<td>RCA</td>
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<td>0.88</td>
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<td>1.58</td>
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<tr>
<td>LCx</td>
<td>1.98</td>
<td>0.95</td>
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<tr>
<td>RCA</td>
<td>1.73</td>
<td>0.85</td>
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• 157 patients, evaluated by FFR and CFVR
• Long-term follow-up was performed to document the occurrence of major adverse cardiac events: cardiac death, myocardial infarction, or target vessel revascularization. Discordance between FFR and CFVR occurred in 31% and 37% of stenoses at the 0.75, and 0.80 FFR cut-off value
• Discordance of CFVR with FFR originates from the involvement of the coronary microvasculature