Noninvasive testing: still needed?

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Disclosures

• **Speaker honoraria:**
  - Astra Zeneca, Abbott Vascular, GE Healthcare, Guerbet

• **Research grant:**
  - Abbott Vascular
Evolution in the concept of ischemia-guided coronary revascularization: from the early 80’s to the present time

**The «patient-based» approach**

Exercise test
- Normal
- Abnormal

Angina
- Class 0, I, II
- Class III, IV

Figure 3: Extension of survival after 10 years of follow-up in various subgroups

**The «vessel-based» approach**

Guidelines on myocardial revascularization
The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

**The «lesion-based» approach**

Predominant form of revasc:
- CABG
- CABG+PCI
- PCI

Predominant form of revasc:
Controversial issues in stable CAD patients

• Which functional technique is better for assessing flow-limiting coronary artery disease? FFR or noninvasive imaging?

• Among noninvasive imaging, which technique is the most accurate? SPECT? CMR? PET? CT? Stress Echo?

• How to implement noninvasive imaging techniques in diagnostic algorithms with FFR?

• Is noninvasive imaging outdated in the era of FFR?
Duality of Coronary morphology and function

Two faces of the same disease

"different techniques... ...same results"

White CW. NEJM 1984
Intraoperative Doppler flow

Uren NG. NEJM 1994
$^{15}$O-H$_2$O PET

Tonino PA et al. JACC 2010
Fractional flow reserve
Coronary Stenosis ≠ Myocardial Ischemia

The functional significance of coronary lesions is determined by many factors:

- **Lesions-specific factors**
  - Severity of diameter stenosis
  - Lesion length
  - Reference vessel diameter
  - Lesion morphology
  - Plaque burden and plaque rupture
  - Eccentricity
  - Viscous friction, flow separation, turbulence and eddies
  - Surface roughness

- **Factors that affect myocardial blood flow**
  - Collaterals
  - Microvascular Resistance

Factors that affect myocardial blood flow include:

- Viscous friction, flow separation, turbulence, eddies, and surface roughness.
- Collaterals and microvascular resistance.

The functional significance of coronary lesions is determined by many factors.
Prognostic role of perfusion imaging (SPECT)

Follow-Up 2-3 years

Iskander, JACC 1998; 32: 57-62
Survival benefit in patients undergoing revascularisation compared to medical treatment based on the presence and magnitude of ischemia

0.7 1.0 1.8 2.9 3.7 4.8 3.3 2.0
0% 1-5% 5-10% 11-20% >20%

Cardiac death rate (%)

6.3 6.7

% Total Myocardium Ischemic

Medical Revasc

10627 pts No Prior MI
Short term Follow up: 1.9 yrs

log Hazard Ratio

p<0.001

The role of coronary morphology and function in treatment of stable CAD patients

The COURAGE study and COURAGE Nuclear substudy

Survival free of death

PCI + OMT

Optimal Medical Therapy (OMT)

Hazard ratio: 1.05
95% CI (0.87-1.27)
P = 0.62

Cumulative Event-free Survival

≥5% Ischemia Reduction (n=68)
Unadjusted p=0.001
Risk-Adjusted p=0.082

<5% Ischemia Reduction (n=37)

Circulation 2008;117
Economic consequences of Available Diagnostic Strategies

The Economics of Noninvasive Diagnosis (END) Multicenter study

Groups matched for pretest likelihood

Direct angiography n=5,423

MPS + selective angiography n=1,981

US$

<table>
<thead>
<tr>
<th>Pretest clinical risk</th>
<th>Diagnostic Cost</th>
<th>Follow-Up Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>$2,900</td>
<td>$2,000</td>
</tr>
<tr>
<td>Int</td>
<td>$4,200</td>
<td>$2,400</td>
</tr>
<tr>
<td>High</td>
<td>$4,800</td>
<td>$2,800</td>
</tr>
</tbody>
</table>

No CAD
1-V-CAD
MVD

Shaw LJ et al.
JACC 1999;33:661-9

University Hospital Zurich

2013 ETP, European Heart House, Sophia-Antipolis, France, Page 12
Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Table 8: Indications for revascularization in stable angina or silent ischaemia

<table>
<thead>
<tr>
<th>Subset of CAD by anatomy</th>
<th>Classa</th>
<th>Levelb</th>
<th>Ref.c</th>
</tr>
</thead>
<tbody>
<tr>
<td>For prognosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main &gt;50%</td>
<td>I</td>
<td>A</td>
<td>30, 31, 54</td>
</tr>
<tr>
<td>Any proximal LAD &gt;50%</td>
<td>I</td>
<td>A</td>
<td>30–37</td>
</tr>
<tr>
<td>2VD or 3VD with impaired LV function</td>
<td>I</td>
<td>B</td>
<td>30–37</td>
</tr>
<tr>
<td>Proven large area of ischaemia (&gt;10% LV)</td>
<td>I</td>
<td>B</td>
<td>13, 14, 38</td>
</tr>
<tr>
<td>Single remaining patent vessel &gt;50% stenosis</td>
<td>I</td>
<td>C</td>
<td>—</td>
</tr>
<tr>
<td>1VD without proximal LAD and without &gt;10% ischaemia</td>
<td>III</td>
<td>A</td>
<td>39, 40, 53</td>
</tr>
<tr>
<td>For symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any stenosis &gt;50% with limiting angina or angina equivalent, unresponsive to OMT</td>
<td>I</td>
<td>A</td>
<td>30, 31, 39–43</td>
</tr>
<tr>
<td>Dyspnoea/CHF and &gt;10% LV ischaemia/viability supplied by &gt;50% stenotic artery</td>
<td>IIa</td>
<td>B</td>
<td>14, 38</td>
</tr>
<tr>
<td>No limiting symptoms with OMT</td>
<td>III</td>
<td>C</td>
<td>—</td>
</tr>
</tbody>
</table>

aClass of recommendation.
bLevel of evidence.
cReferences.

With documented ischaemia or FFR <0.80 for angiographic diameter stenoses 50–90%.

CAD = coronary artery disease; CHF = chronic heart failure; FFR = fractional flow reserve; LAD = left anterior descending; LV = left ventricle; OMT = optimal medical therapy; VD = vessel disease.
How does FFR compare to noninvasive imaging of perfusion (SPECT)

Concordance between MPI and FFR is quite poor!*
In **42%** of patients there was concordance between FFR and MPI
In **36%** of patients MPI **underestimated** the number of ischemic territories
In **22%** of patients MPI **overestimated** the number of ischemic territories

*Concordance was better if no or only 1 territory were ischemic by FFR
## Validation of FFR

<table>
<thead>
<tr>
<th>Ref</th>
<th>N</th>
<th>Population</th>
<th>Ref method</th>
<th>Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Bruyne et al. Circ 1985</td>
<td>60</td>
<td>1-VD</td>
<td>Bicycle ECG</td>
<td>0.72*</td>
</tr>
<tr>
<td>Pijls et al. Circ 1995</td>
<td>60</td>
<td>1-VD, pre+post PCI</td>
<td>Bicycle ECG</td>
<td>0.74*</td>
</tr>
<tr>
<td>Pijls et al. NEJM 1996</td>
<td>45</td>
<td>1-VD, intermediate Stenoses</td>
<td>Bicycle ECG + TI SPECT + Stress Echo†</td>
<td>0.75*</td>
</tr>
<tr>
<td>Bartunek et al. JACC 1996</td>
<td>75</td>
<td>1-VD</td>
<td>Stress Echo</td>
<td>0.78*</td>
</tr>
<tr>
<td>Chalumeau et al. JACC 2000</td>
<td>127</td>
<td>MVD</td>
<td>MIBI SPECT</td>
<td>0.74**</td>
</tr>
<tr>
<td>Abe et al. Circ 2000</td>
<td>46</td>
<td>1-VD</td>
<td>TI SPECT</td>
<td>0.75*</td>
</tr>
<tr>
<td>De Bruyne et al. Circ 2001</td>
<td>57</td>
<td>Post MI</td>
<td>MIBI SPECT</td>
<td>0.75 – 0.80*</td>
</tr>
</tbody>
</table>

* 100% specificity; ** Optimal cut-off value, † With reversibility after revasc
Fundamental differences between FFR and functional noninvasive imaging

- **Functional noninvasive imaging**
- **FFR**

### Microvasculature
- **Epicardial arteries** (3.5-1mm)
- **Perforating branches** (>400μm)
- **Arterioles** (100-400μm)
- **Capillaries**

**Epicardial Conduit**

**Microvasculature**
Conceptual Plot of CFR and FFR regions

Johnson & Gould. JACC Cardiovasc Imaging 2012
Discordant CFR (noninvasive perfusion) and FFR results:

- reflect divergent extremes of focal (epicardial) versus diffuse (macro + microvascular) disease
- Reflect clinically relevant basic coronary pathophysiology, not methodology
Possible algorithm integrating noninvasive imaging and FFR

Patient with suspected or known CAD

Noninvasive (anatomo-)functional Imaging

Ischemia +

Angio + FFR

Ischemia overestimated by Imaging

Ischemia confirmed by FFR

Ischemia underestimated by Imaging

Ischemia -

«FINETUNING» → «lesion risk»

High risk nonperfusion variables*

Treat accordingly; Decide on optimal revascularization based on FFR («functional SYNTAX score?»)

Consider Microvascular dysfunction

«GATEKEEPER» → Patient risk

Treat conservatively

*High-risk nonperfusion variables:
High CACS
TID
Reduced post-stress EF
Reduced CFR
The role of cardiac imaging in the FFR era

• Ischemia testing is crucial for the appropriate management of stable CAD patients

• Cardiac noninvasive functional imaging is a (cost-)effective gatekeeper of invasive angiography in patients with stable CAD

• Perfusion imaging (ideally with assessment of CFR) and FFR are not competing techniques, but complementary methodologies to assess a varying spectrum of focal epicardial versus diffuse (macro- and microvascular) disease in CAD patients, and to decide on the most appropriate treatment strategy (medical versus revascularization)
Thank You

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