Non-Invasive Imaging in Interventional Cardiology

Insights from anatomical-functional-morphological and molecular imaging techniques

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BIOMEDICAL RESEARCH FOUNDATION, ACADEMY OF ATHENS
I have no conflicts of interest to declare
## Indications for revascularization in patients with stable angina or silent ischaemia

<table>
<thead>
<tr>
<th>Extent of CAD (anatomical and/or functional)</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>For prognosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main disease with stenosis &gt;50%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Proximal LAD stenosis &gt;50%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Two- or three-vessel disease with stenosis &gt;50% with impaired LV function (LVEF ≤35%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Large area of ischaemia detected by functional testing (&gt;10% LV) or abnormal invasive FFR&lt;sup&gt;d&lt;/sup&gt;</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Single remaining patent coronary artery with stenosis &gt;50%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>For symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemodynamically significant coronary stenosis&lt;sup&gt;c&lt;/sup&gt; in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy&lt;sup&gt;e&lt;/sup&gt;</td>
<td>I</td>
<td>A</td>
</tr>
</tbody>
</table>

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<sup>a</sup> Class: I: class I, IIa: class IIa, IIb: class IIb, III: class III.

<sup>b</sup> Level: A: level A, B: level B, C: level C, D: level D.
13 555 patients [35% with Hx of known CAD, 61% male, age 66±12
F/u :12–18 months for early revascularization and at 7 years for all-cause death (mean follow-up 8.7+3.3 years

Hachamovitch R
et al. EHJ 2011
1,381 randomized patients (OMT n = 699, PCI + OMT n = 682) underwent baseline stress myocardial perfusion SPECT imaging. Extent of ischemia = number of ischemic segments using a 6-segment myocardial model. Patients: no to mild (<3 ischemic segments) ischemia, moderate to severe ischemia (≥3 ischemic segments).
Fractional Flow Reserve and Cardiac Events in CAD

IRIS-FFR Registry
5846 pts patients with ≥1 coronary lesion with FFR measurement
Primary end point: a composite of death from any cause, MI, or urgent revascularization

Five-Year Outcomes with PCI Guided by FFR
Primary end point: a composite of death from any cause, MI, or urgent revascularization

Hazard ratio, 0.46 (95% CI, 0.34–0.63)
P < 0.001


Gaps in the evidence:

Current techniques rely on coronary angiography and the detection of ischaemia-producing lesions. However, future adverse events are related at least in part to non-flow limiting, vulnerable plaques. Better identification of vulnerable plaques and the development of appropriate treatment strategies is needed.

2018 ESC/EACTS Guidelines on myocardial revascularization
18F-fluoride PET for identification of ruptured and high-risk coronary atherosclerotic plaque

Patients with recent acute myocardial infarction (n=40) and stable angina (n=40)

In 37 (93%) patients with myocardial infarction, the highest coronary 18F-NaF uptake was seen in the culprit plaque (median maximum TBR: culprit 1.66 vs. highest non-culprit 1.24, p<0.001).

Does NaF provide incremental prospective prediction of cardiovascular events compared to conventional risk scores and CT imaging? *Prospective, multicenter PREFFIR trial (NCT02278211)*
Vulnerable plaque or total disease burden?

**Vulnerable plaque**
- In pts with ACS, plaque ruptures are frequently found apart from the culprit lesions, indicating that vulnerability is disseminated throughout the coronary tree.

- Of the many plaque ruptures occurring in patients with atherosclerotic disease, very few will trigger symptomatic events.

? Perform a comprehensive risk assessment that integrates specific information on the atherosclerotic plaque burden/health of the coronary tree and systemic factors that increase the risk for disease activity.
Stress Rest

<table>
<thead>
<tr>
<th></th>
<th>LAD</th>
<th>RCA</th>
<th>LCX</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRESS</td>
<td>1.7</td>
<td>1.9</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td>REST</td>
<td>1.0</td>
<td>1.2</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>MFR</td>
<td>1.7</td>
<td>1.6</td>
<td>1.7</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Anagnostopoulos...Nekolla Int J Cardiol 2013
Global CFR is Associated With Adverse Cardiovascular Events Independently of Luminal Angiographic Severity and Modifies the Effect of Early Revascularization

329 consecutive pts referred for ICA post stress MPI PET Median f/u: 3.1 years
End point: cardiovascular death and CHF admission

Early revasc: within 90d from PET: High CFR: ≥ 1.6, Low CFR<1.6
High CADPI: ≥ 37, Low CADPI<37

Taqueti VR et al. Circulation 2015
In cases of regional wall motion abnormalities in the territory of the CTO, objective evidence of viability should be sought.

2018 ESC/EACTS Guidelines on myocardial revascularization
Conclusion

How might non-invasive imaging assist the interventional cardiologist?

- Functional imaging
  - Gate-keeper to invasive angiography
  - Identifies patients with high but reversible risk

- Vulnerable plaque assessment
  - Need to optimise imaging techniques and assess more reliably plaque pathophysiology and total disease burden

- Carefully designed prospective randomized multimodality imaging studies are needed to define the most appropriate strategies for management decisions and improved outcomes in patients with suspected or known CAD
Thank you

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Prognostic Determinants of Coronary Atherosclerosis in Stable Ischemic Heart Disease


Andrews JPM et al. Atherosclerosis 2018
Ischemia Change in Stable Coronary Artery Disease Is an Independent Predictor of Death and Myocardial Infarction

Sub study of Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation

<table>
<thead>
<tr>
<th>Symptomatic patients</th>
<th></th>
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<tbody>
<tr>
<td>Coronary angiography is recommended in patients with intermediate- to high-risk findings at stress testing.</td>
<td>I C</td>
</tr>
<tr>
<td>An imaging stress test should be considered in patients with prior revascularization over stress ECG.</td>
<td>IIa B</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Asymptomatic patients</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Surveillance by non-invasive imaging-based stress testing may be considered in high-risk patient subsets 6 months after revascularization.</td>
<td>IIB C</td>
</tr>
<tr>
<td>After high-risk PCI (e.g. unprotected LM stenosis), late (3–12 months) surveillance angiography may be considered, irrespective of symptoms.</td>
<td>IIB C</td>
</tr>
<tr>
<td>Routine non-invasive imaging-based stress testing may be considered 1 year after PCI and &gt;5 years after CABG.</td>
<td>IIB C</td>
</tr>
</tbody>
</table>

Worsening of ischaemia on serial MPS Is an independent predictor of death or MI

Farzaneh-Far A et al J ACC Img 2012;5:715–24
Taqueti VR et al. Circulation 2015
104 patients with 30%–70% pretest likelihood of CAD, PET imaging during adenosine stress using $^{15}$O-water
Stenoses with FFR <0.8 were classified as significant
For PET: cutoff between normal and pathological MBF is <2.5 mL · g · $^{-1}$min$^{-1}$

Improved Cardiac Risk Assessment With Noninvasive Measures of Coronary Flow Reserve

2783 pts referred for rest/stress PET f/u for a median of 1.4 years
Primary end point: cardiac death

<table>
<thead>
<tr>
<th>Tertile</th>
<th>0%</th>
<th>1-9%</th>
<th>≥10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Tertile</td>
<td>0.1%</td>
<td>1.8%</td>
<td>2.2%</td>
</tr>
<tr>
<td>Middle Tertile</td>
<td>4.5%</td>
<td>9.1%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Lower Tertile</td>
<td>232</td>
<td>234</td>
<td>119</td>
</tr>
</tbody>
</table>

VL Murthy et al. Circulation 2011
Computed Tomographic Angiography Characteristics of Atherosclerotic Plaques Subsequently Resulting in Acute Coronary Syndrome

1,059 pts CT angiography because of suspected or known CAD

Assessment of positive vessel remodeling (PR) and low-attenuation plaques (LAP)

S Motoyama J Am Coll Cardiol 2009;54:49–57

PET/CT Imaging of aortic valve stenosis

SALTIRE 2 study is assessing the effects of bisphosphonates and Denosumab on calcification activity in aortic stenosis (NCT 02132026).
Effectiveness of zoledronate on the inhibition of aortic valve calcification

16 New Zealand rabbits were placed on vitamin D-enriched diet for 3 weeks. PET/CT with 18F-NaF at baseline and before euthanasia for calcification. AVs of 8 animals treated with 500 μg/l zoledronate. Placebo mixture in remaining 8 animals.

Zoledronate

Controls

Synetos A et al. J Cardiovasc Transl Res 2018
Shaw LJ et al J Nucl Cardiol 2012

Nuclear sub-study
1.505 pts

Median % ischemic myocardium: 2% (interquartile range: 2%–10%) for the MED group vs. 0% (interquartile range: 0%–7%) for the revascularized patients (P<.0001).
Inducible Myocardial Ischemia and Outcomes in Patients with CAD and LV Dysfunction

STICH ischaemia-substudy

Patients with CAD and EF ≤35% vs. CABG or medical therapy. MPS or DSE. A test was positive for ischemia by MPS if summed difference score ≥4 or if ≥2 of 16 segments were ischemic during DSE. Follow-up 56 months.
International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial

GAPS IN EVIDENCE:
It remains to be determined whether revascularization by PCI improves prognosis in patients with SCAD.

2018 ESC/EACTS Guidelines on myocardial revascularization

GAPS IN EVIDENCE:... future adverse events are related at least in part to non-flow limiting, vulnerable plaques. Better identification of vulnerable plaques and the development of appropriate treatment strategies is needed.

2018 ESC/EACTS Guidelines on myocardial revascularization

Hachamovitch R Circ Cardiovasc Imaging 2015