Risk stratification in CAD: Role of hybrid/fusion imaging

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BIOMEDICAL RESEARCH FOUNDATION ACADEMY OF ATHENS
I HAVE NO CONFLICTS OF INTEREST
Combined non invasive cardiac imaging

Combined information on anatomy and function

• Advantages
  – Potential to assess the entire spectrum of disease: from sub-clinical atherosclerosis to IHD
  • Coronary anatomy, perfusion and function in the same session
  • Calcium score
  – Integration of structural, functional and molecular imaging

• Limitations
  – Radiation dose
  – Cost
  – No large series published
PET/CT Perfusion Imaging followed by angiography
MPS-CTA hybrid image

80 year old man with exertional chest pain

## Indications for diagnostic testing in patients with suspected CAD and stable symptoms

<table>
<thead>
<tr>
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<th>Asymptomatic&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Symptomatic</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Class&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Level&lt;sup&gt;d&lt;/sup&gt;</td>
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<tr>
<td><strong>Anatomical detection of CAD</strong></td>
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<tr>
<td>Invasive angiography</td>
<td>III</td>
<td>A</td>
</tr>
<tr>
<td>CT angiography&lt;sup&gt;f,g&lt;/sup&gt;</td>
<td>III</td>
<td>B</td>
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<tr>
<td><strong>Functional test</strong></td>
<td></td>
<td></td>
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<tr>
<td>Stress echo</td>
<td>III</td>
<td>A</td>
</tr>
<tr>
<td>Nuclear imaging</td>
<td>III</td>
<td>A</td>
</tr>
<tr>
<td>Stress MRI</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>PET perfusion</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Combined or hybrid imaging test</td>
<td>III</td>
<td>C</td>
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</table>
4,897 symptomatic patients without a history of CAD referred for SPECT and CAC scoring
MACEs: late revascularization (>90 days after scanning), nonfatal myocardial infarction, and all-cause mortality

Multivariate analysis: SPECT and CAC score were independent predictors of MACE
(CAC score ≥1000: hazard ratio, 7.7; \( p<0.001 \), large perfusion defect on SPECT: hazard ratio, 3.7; \( p<0.001 \))
Interrelation of Coronary Calcification, Myocardial Ischemia and Outcomes in Patients With Intermediate Likelihood of CAD
A Combined Positron Emission Tomography/Computed Tomography Study

695 consecutive patients (mean age 61.3±13.1 years, 40.9% male)

Schenker MP et al. Circulation 2008
Prognostic interplay of coronary artery calcification and underlying vascular dysfunction

901 consecutive patients investigated for CAD with a CAC scan and a normal Rubidium-82 MPI PET, F/U for a median of 1.53 years. Primary endpoint; a composite of MACE: cardiac death, nonfatal myocardial infarction, late revascularization, and admission for heart failure.

Risk-adjusted annual MACE by Extent of Coronary Calcification and Coronary Flow Reserve (CFR)

Risk-adjusted annual MACE by Extent of Coronary Calcification and Coronary Flow Reserve (CFR)

M Naya J Am Coll Cardiol 2013;61: 2098–106
Complimentary roles of SPECT MPI and Coronary CTA

335 consecutive patients (suspected or known CAD), 1-day stress/rest $^{99m}$Tc-tetrofosmin SPECT & CCTA, acquired on stand-alone scanners and fused to obtain cardiac hybrid images, f/u 2.8y

End points: death, MI, unstable angina requiring hospitalization, coronary revascularizations

A matched hybrid image finding was associated with a significantly higher death/MI incidence and proved to be an independent predictor for MACE

Kaplan–Meier survival curves showing the prognostic value of cardiac hybrid imaging

Pazhenkottil A P et al. Eur Heart J 2011
Incremental prognostic value of sequential imaging of SPECT and CTA in patients with suspected CAD

Retrospective study, 1295 patients
MACE: cardiac death, non-fatal myocardial infarction, unstable angina, and late (>90 days of imaging tests) revascularization

Incremental prognostic value of SPECT to clinical parameters according to coronary artery stenosis on CCTA.

Incremental prognostic value of CCTA to clinical parameters according to SSS on SPECT.

HL Kim et al Cardiovasc Imaging 2014
Prognostic Value of CCTA with Sequential, Selective PET Perfusion Imaging in CAD

**CCTA≥50% diameter stenosis**: +ve for obstructive stenosis.

**PET perfusion**: absolute myocardial stress perfusion < 2.4 ml/g/min at least in 1 of the 17 myocardial segments = abnormal

**MACEs**: all-cause mortality, myocardial infarction and unstable angina

T Maaniitty et al J Am Coll Cardiol Img 2017
impact of cardiac hybrid imaging-guided patient management on clinical long-term outcome

Retrospective study, 414 patients referred for evaluation of known or suspected CAD with CCTA/SPECT hybrid imaging.

CCTA: no CAD, non-high-risk CAD and high-risk CAD.

Patients with CAD (n=329): matched finding = a reversible perfusion defect in a territory subtended by a coronary artery with disease (70 pts).

MACE: Death, myocardial infarction, unstable angina requiring hospitalization, and late coron. revasc. (>90d)

![Graph showing survival and MACE rates](image)

DC Benz et al. Int J cardiol 2018
EVINCI OUTCOMES STUDY

430 Patients, Median Follow-up time: 52 months

Primary composite end-point: all cause mortality, MI or UA, hospital admission because of CHF

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Early coronary revascularization (<90 days) was not an independent predictor of outcome

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D Neglia et al. ESC 2017
New directions in Hybrid imaging

CT-FFR

Taylor CA et al. J Am Coll Cardiol 2013

Abnormal vFAI

\[ \Delta P_1 = 6.6 \text{ mmHg} \]
\[ \Delta P_1 = 36 \text{ mmHg} \]

\[ vFAI = 0.75 \]

\[ vFAI = 0.75 \]

\[ P_d/P_a \]

\[ Q (\text{ml/s}) \]

Siogkas P...Anagnostopoulos CD ESC 2016,2017

\(^{18}\text{F}-\text{fluoride PET for identification of ruptured and high-risk coronary atherosclerotic plaque} \]
1. Obstructive, Ischemic lesion with high risk features ++++

2*. Obstructive, non-ischemic lesion with high risk features +++

3. Non obstructive, non ischemic lesions with high risk features ++
   Can go through rapid progression and become part of group 1 and 2

4. Non obstructive, ischemic lesions with high risk features +++

5. Non obstructive, ischemic lesions with no high risk features, likely long lesion length +

6. Obstructive, ischemic, no high risk features, likely fibrous plaque +

7. Obstructive, non ischemic, no high risk features, likely fibrous plaque +

SUMMARY

• Hybrid imaging improves risk stratification, however, 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 CAD.

• The value of an approach combining imaging with serum biomarkers for risk stratification should be tested in well designed prospective studies.

• PET/MRI or other options of fused imaging (e.g. CTA with speckle tracking) are in their infancy with no outcome data yet.

Thank you

cdanagnostopoulous@bioacademy.gr
Cardiac SPECT/CCTA hybrid imaging

52-year-old male patient (body mass index: 23.5 kg/m²) without known CAD presents with chest pain

CACS 0.66 mSv, CCTA 0.47 mSv, CZT SPECT 2.8 mSv, total 3.93 mSv

$^{99m}$Tc SPECT MPI stress (143 MBq)–rest (276 MBq)

Benz DC et al. Eur Heart J 2015
Improved Cardiac Risk Assessment With Noninvasive Measures of Coronary Flow Reserve

2783 consecutive patients referred for rest/stress positron emission tomography were followed up for a median of 1.4 years
Primary end point: cardiac death

Highest tertile of CFR (values > 2), lowest tertile (values <1.5)

<table>
<thead>
<tr>
<th>tertile</th>
<th>≥10% (n)</th>
<th>1-9% (n)</th>
<th>0% (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Tertile</td>
<td>2.2% (50)</td>
<td>1.1% (197)</td>
<td>0.1% (681)</td>
</tr>
<tr>
<td>Middle Tertile</td>
<td>4.2% (119)</td>
<td>3.3% (234)</td>
<td>1.8% (575)</td>
</tr>
<tr>
<td>Lower Tertile</td>
<td>8.5% (232)</td>
<td>9.1% (298)</td>
<td>4.5% (397)</td>
</tr>
</tbody>
</table>

VL. Murthy et al. Circulation 2011;124:2215-2224
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
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 years
End point: cardiovascular death and CHF
Early revasc: within 90d from PET
High CFR: ≥ 1.6, Low CFR<1.6
High CADPI: ≥ 37, Low CADPI<37

Adjusted Annualized Event Rate (%)
Integrated non-invasive physiological assessment of coronary circulatory function and impact on cardiovascular mortality in patients with CAD

Myocardial blood flow (MBF) and coronary flow reserve (CFR) were quantified in 4,029 consecutive patients (median age 66 years, 50.5% women) referred for rest/stress myocardial perfusion PET scans, median f/u 5.6y
Maximal MBF<1.8 ml/g/min and CFR<2 were considered impaired
Primary outcome: Cardiovascular mortality

CFR, stress MBF, traditional cardiovascular risk factors, LVEF, myocardial scar, ischemia, rate-pressure-product were predictors of death.

Gupta et al. Circulation 2017
Predicting Outcome in the COURAGE Trial

621 patients from the COURAGE with SPECT and quantitative coronary angiography

Interaction between anatomic and ischemic burden

Most patients with ischaemia <10% of the LV

P=0.03

Mancini GB et al. J Am Coll Cardiol Intv 2014
Non-invasive quantification of coronary artery disease based on CCTA images and Computational Fluid Dynamics: Comparison to quantitative PET perfusion

Criterion of abnormality for $^{15}$O-water PET studies: regional myocardial flow reserve (MFR) $\leq 2.5$ in individual coronary territories based on a hybrid imaging approach.

|$\begin{array}{cc}
\text{vFAI} \geq 0.8 & \text{vFAI} < 0.8 \\
\hline
\text{MFR} \geq 2.5 & 61\% \\
& (N=97) \\
& 5\% \\
& (N=8) \\
\text{MFR} < 2.5 & 18.2\% \\
& (N=29) \\
& 15.7\% \\
& (N=25) \\
\end{array}$

$\kappa=0.43, p<0.001$

Relationship between MFR & vFAI

Agreement between MFR & vFAI

For submission
Median % ischemic myocardium: 2% (interquartile range: 2%–10%) for the MED group vs. 0% (interquartile range: 0%–7%) for the revascularized patients ($P<.0001$).
Clinical Outcomes Utilising Revascularization and Aggressive drug Evaluation (Nuclear sub-study)

314 of 2287 patients, stable angina randomised to OMT or PCI+OMT

<table>
<thead>
<tr>
<th>Residual Ischemia on 6- to 18-Month F/U MPS</th>
<th>PCI+OMT</th>
<th>OMT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (n=314)</td>
<td>n=159</td>
<td>n=155</td>
<td>0.047</td>
</tr>
<tr>
<td>No ischemia</td>
<td>15.2%</td>
<td>8.8%</td>
<td></td>
</tr>
<tr>
<td>Minimal ischemia</td>
<td>40.0%</td>
<td>39.8%</td>
<td></td>
</tr>
<tr>
<td>Mild ischemia</td>
<td>29.0%</td>
<td>24.4%</td>
<td></td>
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<tr>
<td>Moderate to severe ischemia</td>
<td>15.8%</td>
<td>27.0%</td>
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Ischemia reduction > 5% (n=82)

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<tr>
<th></th>
<th>PCI+OMT</th>
<th>OMT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ischemia</td>
<td>31.4%</td>
<td>17.8%</td>
<td></td>
</tr>
<tr>
<td>Minimal ischemia</td>
<td>26.6%</td>
<td>28.5%</td>
<td></td>
</tr>
<tr>
<td>Mild ischemia</td>
<td>36.5%</td>
<td>43.0%</td>
<td></td>
</tr>
<tr>
<td>Moderate to severe ischemia</td>
<td>5.5%</td>
<td>10.7%</td>
<td></td>
</tr>
</tbody>
</table>

13555 patients, mean f/u 8.7yr, subset with <10% scar

Stress-rest SPECT MPI

Impact of imaging on outcomes


3121 patients


Yao SS et al. J Am Soc Echocardiogr. 2010
Risk assessment by functional and anatomical imaging

Risk of CAD death or MI for Moderate-Severe Ischemia

- 10003 pts (4996 CTCAs)
- Stress imaging in 90% of the rest
- 10% CAD prevalence

Event rate ≈
1.6% year in CTCA
vs
1.5% year in Functional

LJ Shaw et al JACC Cardiovasc Imaging 2014

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

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

Farzaneh-Far A et al J Am Coll Cardiol Img 2012;5:715–24
## Diagnostic Performance of CT-FFR and CTA Compared With Invasive FFR Gold Standard

![Diagram](image)

<table>
<thead>
<tr>
<th>Study/y Design</th>
<th>n Screened</th>
<th>Pt/V</th>
<th>Modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>DISCOVER-FLOW 2011 Prospective Single center&lt;sup&gt;31&lt;/sup&gt;</td>
<td>NA</td>
<td>103/159</td>
<td>CTA</td>
<td>94&lt;sup&gt;Pt&lt;/sup&gt; 91&lt;sup&gt;V&lt;/sup&gt;</td>
<td>25&lt;sup&gt;Pt&lt;/sup&gt; 40&lt;sup&gt;V&lt;/sup&gt;</td>
<td>58&lt;sup&gt;Pt&lt;/sup&gt; 47&lt;sup&gt;V&lt;/sup&gt;</td>
<td>80&lt;sup&gt;Pt&lt;/sup&gt; 89&lt;sup&gt;V&lt;/sup&gt;</td>
</tr>
<tr>
<td>DeFACTO 2012 Prospective Multicenter&lt;sup&gt;32&lt;/sup&gt;</td>
<td>285</td>
<td>252/615</td>
<td>CTA</td>
<td>84&lt;sup&gt;Pt&lt;/sup&gt; NA&lt;sup&gt;V&lt;/sup&gt;</td>
<td>42&lt;sup&gt;Pt&lt;/sup&gt; NA&lt;sup&gt;V&lt;/sup&gt;</td>
<td>61&lt;sup&gt;Pt&lt;/sup&gt; NA&lt;sup&gt;V&lt;/sup&gt;</td>
<td>72&lt;sup&gt;Pt&lt;/sup&gt; NA&lt;sup&gt;V&lt;/sup&gt;</td>
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<tr>
<td>NXT 2014 Prospective Multicenter&lt;sup&gt;34&lt;/sup&gt;</td>
<td>357</td>
<td>254/484</td>
<td>CTA</td>
<td>94&lt;sup&gt;Pt&lt;/sup&gt; 83&lt;sup&gt;V&lt;/sup&gt;</td>
<td>34&lt;sup&gt;Pt&lt;/sup&gt; 60&lt;sup&gt;V&lt;/sup&gt;</td>
<td>40&lt;sup&gt;Pt&lt;/sup&gt; 33&lt;sup&gt;V&lt;/sup&gt;</td>
<td>92&lt;sup&gt;Pt&lt;/sup&gt; 92&lt;sup&gt;V&lt;/sup&gt;</td>
</tr>
<tr>
<td>Renker et al&lt;sup&gt;37&lt;/sup&gt; Retrospective Single center</td>
<td>61</td>
<td>53/67</td>
<td>CTA</td>
<td>94&lt;sup&gt;Pt&lt;/sup&gt; 90&lt;sup&gt;V&lt;/sup&gt;</td>
<td>32&lt;sup&gt;Pt&lt;/sup&gt; 34&lt;sup&gt;V&lt;/sup&gt;</td>
<td>38&lt;sup&gt;Pt&lt;/sup&gt; 37&lt;sup&gt;V&lt;/sup&gt;</td>
<td>92&lt;sup&gt;Pt&lt;/sup&gt; 89&lt;sup&gt;V&lt;/sup&gt;</td>
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<td>Kruk et al&lt;sup&gt;38&lt;/sup&gt; Prospective Single center</td>
<td>NA</td>
<td>90/96</td>
<td>CT-based FFR</td>
<td>76&lt;sup&gt;Pt&lt;/sup&gt; 76&lt;sup&gt;V&lt;/sup&gt;</td>
<td>71&lt;sup&gt;Pt&lt;/sup&gt; 72&lt;sup&gt;V&lt;/sup&gt;</td>
<td>69&lt;sup&gt;Pt&lt;/sup&gt; 67&lt;sup&gt;V&lt;/sup&gt;</td>
<td>78&lt;sup&gt;Pt&lt;/sup&gt; 80&lt;sup&gt;V&lt;/sup&gt;</td>
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*PPV* = Positive Predictive Value, *NPV* = Negative Predictive Value

*Circ Res. 2016;119:300-316*
Virtual functional index (vFAI)- a simplified CT FFR

1. Steady state simulations are carried out on the 3D models
2. **Inlet**: a pressure value of 100 mmHg is used
3. **Outlet**: two separate flows of 1ml/s and 3ml/s are applied.
4. The artery-specific pressure gradient (ΔP)-flow relationship for each case is constructed and is defined as:
   \[
   \frac{P_d}{P_a} = 1 - f_v \frac{Q}{P_a} - f_s \frac{Q^2}{P_a}
   \]
   Q is the flow rate, \(f_v\) is the coefficient of pressure loss due to viscous friction and \(f_s\) is the coefficient of pressure loss due to flow separation
5. The virtual functional assessment index (vFAI) is then calculated as the ratio of the area under the artery-specific \(P_d/P_a\) vs. flow curve to the reference area

\[\text{ESC 2016}\]
No ischemia, mild lesion
30% stenosis
Silent plaque rupture & healing
High-Risk lesion
± Ischemia
≥ 50% stenosis
Rapid lesion progression
Ablunt thrombosis
Chronic ischemia
90% stenosis

HIGH-RISK PLAQUE IMAGING
• Plaque burden, serial progression
• Ischemia testing (FFR, non-invasive)
• Plaque composition
• WSS
• ? Intraplaque hemorrhage

Coronary vasodilator reserve

$r^2 = 0.69$
$P < 0.001$
Myocardial perfusion scintigraphy (MPS)

Stress
Rest
Stress Perfusion (%)
Rest Perfusion (%)
Reversibility Perfusion (%)

anterior
septum
lateral
inferior
apex
apical septum
apical lateral
basal septum
basal lateral
basal anterior
apical anterior
basal inferior
apical inferior
High risk imaging variables

- Extensive reversibility of a perfusion defect even $\geq 10\%$ of the LV myocardium (ESC, annual CV mortality $> 3\%$ year)
- Multiple perfusion defects in $>1$ coronary territories
- Transient ventricular cavity dilatation
- Multiple regional wall motion or thickening abnormalities
- EF $< 35\%$
- Increased end-diastolic or end-systolic volume on gated SPECT
- Increased lung uptake
Prognostic Value of MPS

$n = 12\ 000\ pts$

Annual cardiac event rate %

<table>
<thead>
<tr>
<th></th>
<th>normal</th>
<th>abnormal</th>
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<tbody>
<tr>
<td>P</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

Iskander S et al. JACC 1998;32:57
Determinants of risk and its temporal variation in patients with normal MPS

7,376 patients (ex or adenosine)
Follow-up 665 ± 200 days

Hachamovitch R et al JACC 2003
Extensive myocardial ischaemia
Stenosis Severity and Associated Risk for Coronary Occlusion and MI

* Data from 4 different studies in approximately 200 MI patients

MECHANISMS OF PROGRESSION IN NATIVE CORONARY ARTERY DISEASE: ROLE OF HEALED PLAQUE DISRUPTION

31 men aged 51-69 dying suddenly of ischaemic heart disease
39 coronary arteries were studied containing 256 separate plaques

Stenosis $\geq$ 51% by diameter was present in 71 plaques, 52 (73.2%) of which showed a healed disruption pattern: $p < 0.001$, compared to stenoses $< 50$

Subclinical episodes of plaque disruption followed by healing are a stimulus to plaque growth that occurs **suddenly** and is a major factor in causing chronic high grade coronary stenosis
Process of Progression of Coronary Artery Lesions From Mild or Moderate Stenosis to Moderate or Severe Stenosis

36 vessels were anlayised retrospectively

The degree of progression in percent diameter stenosis in each of the 3 intervals of the 4 serial CAGs (between each of 2 serial CAGs) was classified as marked progression (≥15%), slight progression (5% to 14%) and no progression (N: <5%)

MI occurred in 71% of type I lesions but only in 13% of type II lesions

1stCAG : 58%, 3rd CAG: 59%, final CAG: 94%

first, second, third, and final CAGs: 38%, 45%, 58%, and 67%, respectively

Evaluation of Integrated Cardiac Imaging for the Detection and Characterization of Ischemic Heart Disease

**Population**
Patients with anginal-like chest pain

**Clinical Evaluation and Enrollment**
- Intermediate pre-test probability of CAD (20-90%)
- Fulfilling inclusion/exclusion criteria
- Signed informed consent, filling of appropriate questionnaires

**Blood Sample**
- Aliquots of plasma and sera
- Whole blood

**Non-Invasive “Anatomic” Imaging**
- CT calcium score and CT Angiography (CTA)

**Non-Invasive “Functional” Imaging**
- Stress test: (SPECT or PET) and/or (MRI or ECHO)

**Invasive “Anatomo-Functional” Imaging**
- Invasive coronary angiography (ICA)

- **No stenosis or < 50% stenosis**
- ** ≥75% stenosis**
  - Pressure or Doppler flow wire (FFR or CFR)
  - IVUS

**Treatment**
- Revascularization or medical therapy (according to invasive results)

**Follow-up**
- Clinical evaluation and questionnaires
Angiographic Disease Progression and Residual Risk of Cardiovascular Events While on Optimal Medical Therapy

**Observations From the COURAGE Trial**

205 patients assigned to OMT plus percutaneous coronary intervention (PCI) and 284 patients assigned to OMT only had symptom-driven angiograms suitable for analysis.

The only angiographic predictor of myocardial infarction or acute coronary syndrome was the number of lesions originally 50% DS that had not been revascularized (OR, 1.15; CI: 1.01–1.31; P0.04)

Interrelation between calcium score and MBF

Per-vessel CAC scores were correlated marginally with peak MBF ($r=−0.26$, $p<0.0001$), CFR ($r=−0.20$, $p<0.0001$)

* $P < 0.05$ on pair-wise comparison

Eur J Nucl Med MI 2009

P < 0.05 on pair-wise comparison
New directions in Hybrid imaging

CT-FFR

Taylor CA et al. J Am Coll Cardiol 2013

Abnormal vFAI

Siogkas P...Anagnostopoulos CD ESC, 2017

$^{18}$F-fluoride PET for identification of ruptured and high-risk coronary atherosclerotic plaque

Joshi NV, Lancet 2013

<table>
<thead>
<tr>
<th>vFAI ≥ 0.8</th>
<th>vFAI &lt; 0.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFR≥2.5</td>
<td>61% (N=97)</td>
</tr>
<tr>
<td>CFR&lt;2.5</td>
<td>18.2% (N=29)</td>
</tr>
</tbody>
</table>
Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis

325 patients, elective PCI for intermediate stenosis

5-Year Follow-Up of the DEFER Study

5 year cardiac death or MI

![Graph showing the comparison of DEFER, PERFORM, and REFERENCE groups with FFR ≥ 0.75 and FFR < 0.75.]

Pijls NHJ et al. JACC 2007; 49: 2105-11
Combined Assessment of High-Sensitivity Troponin T and Noninvasive Coronary Plaque Composition for the Prediction of Cardiac Outcomes

(A) ROC analysis for calcium score, hsTnT, plaque volume, and Duke clinical score to evaluate accuracy of the prediction of hard cardiac events, (B) total x-squared and IDI values.

Source: G Gitsioudis et al Radiology 2015
Complimentary roles of SPECT MPI and Coronary Calcium Score

1,126 asymptomatic subjects without previous cardiovascular disease CACS and stress SPECT scans were performed within a close time period, median follow-up: 6.9y

End points: Total cardiac events and all-cause death/myocardial infarction (MI)

Annualized Event Rates Based on CACS and SPECT Results

Event Rates in Subjects With a Normal SPECT Result Based on CACS Severity

SM Chang J Am Coll Cardiol 2009
Coronary CT angiography ...beyond lumenography

Long-Term Prognostic Effect of Coronary Atherosclerotic Burden
1196 patients, (mean follow-up of 52±22 months), end points: cardiac death and nonfatal acute coronary syndromes

Components of CTA–adapted Leaman score:

1) localization of the coronary plaques, accounting for dominance,
2) type of plaque, with a multiplication factor of 1 for calcified plaques and 1.5 for noncalcified and mixed plaques,
3) degree of stenosis, with a multiplication factor of 0.615 for nonobstructive (<50% stenosis) and a multiplication factor of 1 for obstructive (≥50% stenosis) lesions.

Mushtaq S et al Circ Cardiovasc Imaging. 2015
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.

Zadeh AA, Fuster V, J Am Coll Cardiol 2015
Risk assessment by functional and anatomical imaging

PROMISE trial
10,003 symptomatic pts randomised to: CCTA or functional testing (90% with imaging)
Composite primary end point: death, myocardial infarction, hospitalization for unstable angina, or major procedural complication.

CAD prevalence 10%

Anatomical vs. functional testing
Hazard ratio, 1.04 (95% CI, 0.83–1.29)
P=0.75

Factors affecting prognosis

- Severity of symptoms
  - Severe PVD, diabetes, renal disease, and uncontrolled CAD risk factors

- Presence of co-morbidities

- Number of diseased vessels, more proximal locations of coronary stenoses, greater severity of lesions

- Total ischaemic burden

- Degree of LV dysfunction

Califf RM, J Am Coll Cardiol. 1996

Stable angina pectoris with no obstructive CAD is associated with increased risk of MACE

Obstructive CAD: at least 1 stenosis of ≥50% , MACE: cardiovascular death, hospitalization for myocardial infarction, heart failure, and stroke.

Age-adjusted event-free survival rates for 4,711 women and 6,512 men who underwent invasive coronary angiography for evaluation of stable angina according to the presence and extent of coronary atherosclerotic disease.
Goals of risk stratification

a) To identify patients at high risk
   • for cardiac death
   • or non fatal MI

b) To develop management strategies to reduce the risk

c) To identify those patients with a less severe form of disease and a good prognosis, thereby avoiding unnecessary invasive and non-invasive tests and revascularization procedures