Role of imaging in acute coronary syndromes and complications

Ioannis Iakovou, MD, PhD
Interventional Cardiology
Onassis Cardiac Surgery Center
Athens, Greece
ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Data from the Thrombolysis In Myocardial Infarction (TIMI)-3B\textsuperscript{42} and Fragmin during Instability in Coronary Artery Disease-2 (FRISC-2)\textsuperscript{43} studies show that 30–38% of patients with unstable coronary syndromes have single-vessel disease and 44–59% have multivessel disease (>50% diameter stenosis). The incidence of left main narrowing varies from 4% to 8%.
Complete revascularization

<table>
<thead>
<tr>
<th>Study ID</th>
<th>RR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTS I CABG</td>
<td>0.57 (0.19, 1.72)</td>
<td>0.53</td>
</tr>
<tr>
<td>ARTS I PCI</td>
<td>0.49 (0.17, 1.43)</td>
<td>0.56</td>
</tr>
<tr>
<td>ARTS II PCI</td>
<td>0.63 (0.32, 1.24)</td>
<td>1.25</td>
</tr>
<tr>
<td>Asian Medical Center CABG cohort</td>
<td>1.39 (0.81, 2.39)</td>
<td>1.72</td>
</tr>
<tr>
<td>Asian Medical Center PCI cohort</td>
<td>0.69 (0.47, 1.02)</td>
<td>2.58</td>
</tr>
<tr>
<td>SYNTAX CABG</td>
<td>0.86 (0.52, 1.43)</td>
<td>1.86</td>
</tr>
<tr>
<td>SYNTAX PCI</td>
<td>0.74 (0.49, 1.14)</td>
<td>2.32</td>
</tr>
<tr>
<td>MASS II CABG</td>
<td>0.84 (0.51, 1.39)</td>
<td>1.89</td>
</tr>
<tr>
<td>MASS II PCI</td>
<td>0.66 (0.37, 1.17)</td>
<td>1.60</td>
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<tr>
<td>Jones et al.</td>
<td>0.56 (0.47, 0.68)</td>
<td>4.40</td>
</tr>
<tr>
<td>Scott et al.</td>
<td>0.64 (0.57, 0.71)</td>
<td>5.09</td>
</tr>
<tr>
<td>BARI</td>
<td>0.84 (0.62, 1.13)</td>
<td>3.29</td>
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<tr>
<td>Kleiisi et al.</td>
<td>0.37 (0.29, 0.48)</td>
<td>3.76</td>
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<tr>
<td>Rastan et al.</td>
<td>0.93 (0.81, 1.07)</td>
<td>4.84</td>
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<tr>
<td>Kozower et al.</td>
<td>0.81 (0.71, 0.93)</td>
<td>4.87</td>
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<tr>
<td>Caputo et al.</td>
<td>0.43 (0.27, 0.66)</td>
<td>2.23</td>
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<tr>
<td>Oswald et al.</td>
<td>0.60 (0.42, 0.85)</td>
<td>2.87</td>
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<tr>
<td>Mohammadi et al.</td>
<td>0.90 (0.67, 1.21)</td>
<td>3.37</td>
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<tr>
<td>BARI trial and registry</td>
<td>0.78 (0.54, 1.13)</td>
<td>2.73</td>
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<tr>
<td>BARI Bourassa et al.</td>
<td>0.77 (0.55, 1.08)</td>
<td>3.02</td>
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<tr>
<td>Ijsselmuiden et al.</td>
<td>2.74 (0.75, 10.06)</td>
<td>0.40</td>
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<tr>
<td>New York State registry I</td>
<td>0.78 (0.71, 0.85)</td>
<td>5.25</td>
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<tr>
<td>New York State registry II</td>
<td>0.67 (0.58, 0.79)</td>
<td>4.57</td>
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<tr>
<td>Velent et al.</td>
<td>0.37 (0.21, 0.64)</td>
<td>1.66</td>
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<tr>
<td>AQUITY Rosner et al.</td>
<td>0.70 (0.45, 1.11)</td>
<td>2.14</td>
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<td>Nikolsky et al.</td>
<td>0.42 (0.21, 0.86)</td>
<td>1.15</td>
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<tr>
<td>Tamburino et al.</td>
<td>0.39 (0.15, 0.84)</td>
<td>0.81</td>
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<tr>
<td>Mariani et al.</td>
<td>0.64 (0.03, 13.11)</td>
<td>0.08</td>
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<tr>
<td>NHLBI dynamic registry</td>
<td>1.18 (0.65, 2.14)</td>
<td>1.50</td>
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<td>Kloster et al.</td>
<td>0.21 (0.01, 4.02)</td>
<td>0.08</td>
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<tr>
<td>CABRI</td>
<td>1.07 (0.36, 3.00)</td>
<td>0.61</td>
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<tr>
<td>Jones et al. II</td>
<td>0.80 (0.71, 0.89)</td>
<td>5.08</td>
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<tr>
<td>New York State registry III</td>
<td>0.89 (0.82, 0.98)</td>
<td>5.25</td>
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<tr>
<td>Yang et al.</td>
<td>1.10 (0.29, 4.18)</td>
<td>0.38</td>
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<tr>
<td>McNeer et al.</td>
<td>0.71 (0.56, 0.89)</td>
<td>3.99</td>
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<tr>
<td>Norwa-Otto et al.</td>
<td>0.94 (0.69, 1.30)</td>
<td>3.16</td>
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<tr>
<td>Appleby et al.</td>
<td>0.57 (0.53, 0.66)</td>
<td>5.10</td>
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<tr>
<td>Tyras et al.</td>
<td>0.69 (0.44, 1.01)</td>
<td>3.28</td>
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<tr>
<td>Deligonul et al.</td>
<td>0.93 (0.37, 2.35)</td>
<td>0.73</td>
</tr>
<tr>
<td>Overall (I-squared = 71.8%, p = 0.000)</td>
<td>0.71 (0.66, 0.78)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis.
The SMILE trial

584 NSTEMI patients were randomly assigned in a 1:1 manner to 1S-PCI or MS-PCI

Usually we have no ischemia information at time of culprit PCI

Sardella et al, JACC 2016;67:264

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We’re not very good at guessing the physiology from the angiogram

213 patients with an angiographically equivocal left main coronary artery stenosis

Figure 4. Relation between FFR values and the 2 reviewers’ visual estimations (lesions were classified as significant, nonsignificant, and unsure).

Hamilos M et al. Circulation 2009;120:1505-1512
Coronary Angiography

Limitations

Luminogram


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Limitations of Coronary Angiography

Coronary Cross-section

Angiogram Silhouette

75%

25%
Limitations of Coronary Angiography

Focal Disease

Diffuse Disease

50% Lesion

50% Lesion

Angiogram Silhouette

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Intravascular Imaging Modalities

- **Intravascular Ultrasound**
  - IVUS grey scale
  - IVUS-VH or iMAP
  - Palpography
  - IVUS-Near-Infra Red Spectroscopy (Apollo catheter)

- **Angioscopy**
- **Optical Coherence Tomography**
  - 1st generation OCT systems (Time-domain OCT)
  - 2nd generation OCT system (Fourier-domain OCT)
## Comparison of Imaging Modalities

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Resolution</th>
<th>Fibrous Cap</th>
<th>Lipid Core</th>
<th>Calcium</th>
<th>Thrombus</th>
</tr>
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<tbody>
<tr>
<td>IVUS</td>
<td>100μm</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Angioscopy</td>
<td>Unknown</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>OCT</td>
<td>10μm</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Spectroscopy</td>
<td>not applicable</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
</tbody>
</table>

+++ = Sensitivity >90%; ++ = Sensitivity 80~90%; + = Sensitivity 50~80%; − = Sensitivity <50%

Arterioscler Thromb Vasc Boil. 2003;23:1333-1342

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Clinical questions in ACS

• Pre-intervention lesion assessment (ie., what is the culprit?)

• What is the likelihood of embolization during stent implantation?

• Is this “other” lesion a vulnerable plaque that is at risk for future events?

• How do I optimize acute stent results (size, length, expansion, edge coverage)?

• Why did this stent thrombose or restenose?
Intravascular Ultrasound (IVUS)

**Advantage:**
- Reveals the morphology of the plaque
- Differs between soft (hypo-echoic) and Hard (hyper-echoic) plaques

**Disadvantages:**
- Doesn’t give information about plaque inflammation or thrombus
- Low spatial resolution (~ 200 μm)
Basic IVUS Measurements

- **External elastic membrane CSA** (equivalent to the total arterial CSA, measured by tracing the leading edge of the hyper echoic adventitia)
- **Reference lumen CSA**
- **Final lumen (stent) CSA**
- **Cross-sectional narrowing** (plaque burden or %plaque area) = $P+M/EEM$ CSA, [$plaque+media$ ($P+M$) CSA = $EEM -$ stent CSA].
- **Area Stenosis** = (reference - lesion) lumen CSA / reference lumen CSA
- **Arc of calcium**
Assessment of unusual lesion morphology

Case 1

56 y-Female, UA, Scleroderma, PHT, MR 3+, CRF, Euroscore=36

CSA: 9.2 mm²

CSA: 11.12 mm²
Stent underexpansion as a cause of ISR, ACS

Case 2

Baseline/ISR of a Cypher 2.5/33

Post Promus 3.5 x 32
Evaluation of vessel size and fine-tuning of the final result
Case 2

Baseline

CSA: 2.8 mm$^2$

Final result

CSA: 8.8 mm$^2$, %stent exp=95%

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1-year Cumulative Outcome

- MACE (%): 25.6 (CSA<70%), 20.7 (CSA 70-100%), 14.5 (CSA>100%), P=0.01
- Any MI (%): 8.3 (CSA<70%), 2.9 (CSA 70-100%), 4.9 (CSA>100%), P=0.03
- Death (%): 8.6 (CSA<70%), 4.3 (CSA 70-100%), 3.5 (CSA>100%), P=0.07
- TLR (%): 18.7 (CSA<70%), 17.1 (CSA 70-100%), 11.3 (CSA>100%), P=0.04

WHC database

Iakovou et al. JACC 2004
IVUS Guided LM-Bifurcation PCI
Case 3

62 y, male, with ACS
IVUS Guided Bifurcation PCI
Case 3 provisional stenting

- IVUS (Atlantis pro 40 MHz) in both vessels
- Predilatation: Across HP 3.0 x 15 (16)
- Promus 4.0 x 24 (16)
- Post stenting IVUS → Postdilatation → Quantum 4.0 x 12 (16-18)
- FKBI
IVUS Guided Bifurcation PCI
Case 3
Final result

@1 y-FU pt is asymptomatic with neg EST
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## Predictors of DES Thrombosis & Restenosis

<table>
<thead>
<tr>
<th></th>
<th>DES Thrombosis</th>
<th>DES Restenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>(CSA &lt;5 mm²)</td>
<td>• Okabe et al., Am J Cardiol. 2007;100:615-20</td>
<td>• Hong et al. Eur Heart J 2006;27:1305-10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• TAXUS IV, V, VI meta-analysis</td>
</tr>
<tr>
<td>(geographic miss,</td>
<td>• Okabe et al., Am J Cardiol. 2007;100:615-20</td>
<td>• Liu et al, Am J Cardiol, in press</td>
</tr>
<tr>
<td>secondary lesions,</td>
<td></td>
<td>• Costa et al, Am J Cardiol, 2008;101:1704-</td>
</tr>
<tr>
<td>large plaque burden)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ADAPT DES
Relationship between IVUS Use and Definite or Probable ST within 1 Year

- 8,583 consecutive pts at 11 international centers, IVUS was used in 3,349

HR: 0.50 [95% CI: 0.29, 0.86]  
P = 0.01
Compared with angiographic guidance, IVUS-guided DES implantation was associated with reduced rates of:

- Death HR 0.58 (0.47-0.71), p<0.001
- MACE HR 0.85 (0.76-0.95), p=0.005
- ST HR 0.62 (0.46-0.83), p=0.002

Note: TLR HR 0.90 (0.73, 1.11) all studies; 0.63 (0.46, 1.14) propensity adjusted studies

Zhang Y et al. EuroInt 2012;8:855-65
Gray Scale vs. Virtual Histology

Color Coding Scheme

Calcified  Fibrous  Fibro-Lipidic  Lipidic-Necrotic
Change in non-culprit lesion phenotype in 106 pts (201 lesions) with plaque burden >40% from the Global VH Registry with baseline and 8-month F/U

75% of TCFAs healed, 25% remained unchanged (mostly proximal in location), and 12 new TCFAs were noted.

Kubo et al. AHA 2008
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Near-infrared Spectroscopy for VP Detection

- NIR spectroscopy is a well-validated method frequently used to assess chemical composition.

- Laser, fiber-optic, and chemometric technologies make intra-coronary use feasible.

- 3.2Fr IVUS-like rapid-exchange coronary catheter

- Can scan artery through blood

- 5 msec spectra acquisition

- Identifies chemical composition of vessel wall
  - TCFA sensitivity and specificity > 85% in autopsy specimens
  - In 2006 lipid spectra detected in an MI patient and in HC Swine studyaria
Advantage:
- Chemical compounds

Disadvantage:
- Based on statistical analysis and calibration is always an issue
- Still not proven to be able to distinguish vulnerable plaques from stable ones
Intravascular Palpography

Palpography assesses the local mechanical properties of tissue using its deformation caused by the intraluminal pressure.

**Advantages:**
- Provides novel information, showing arterial stiffness
- Small added cost to IVUS

**Disadvantage:**
- Does not give any chemical – compositional data, nor shows inflammation
Sequential changes in compliance, as assessed by palpograph after scaffold (ABSORB BVS 1.1 Generation) implantation

- **Pre-implantation**: high compliance (red) in either the proximal/distal or scaffolded segment
- **After scaffold implantation**: the scaffolded segment exhibits low compliance (blue) with an evident mismatch compared to the proximal and distal edges
- **At 12-month follow-up**: the scaffolded segment still shows low compliance, with the mismatch in compliance in the adjacent segments disappearing

Brugaleta et al CJ 2012
Angioscopy

• Perhaps the best technique for assessing thrombus
• Also useful for assessing stent neointimal coverage

(Kubo et al. J Am Coll Cardiol 2007;50:933-9)
What is OCT?

Optical Coherence Tomography (OCT) is a high-resolution imaging technology that employs near-infrared light to probe micrometer-scale structures inside biological tissues.
Optical Coherence Tomography (OCT)

Advantage:
- Very high-resolution

Disadvantages:
- Limited penetration
OCT
- Indications in ACS treatment

- Stent evaluation:
  - **Immediate**: malaposition, dissections / ruptures, thrombus, protrusion...
  - Mid-long term: thrombus, endothelization, intimal hyperplasia
OCT IVUS-like guidance Bifurcation PCI

Proximal dissection

Taxus 3.5/20 mm

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OCT in ACS pts treated with 2nd gen DES

Prospective Registry

13 pts treated with 19 stents for ACS with MV disease

- Xience V: N=11
- Biomatrix: N=3
- Nobori: N=2
- Resolute: N=3

Primary end-point: proportion of stent struts uncovered and/or malapposed in OCT at 110 (48-343) days (staged procedure)

QCA @ baseline, and OCT @ staged procedure by 2 independent readers (AA & KI)

* All patients in dual antiplatelet therapy
1841 struts were included in the analysis after exclusion of struts overlying side branches (n=45). A total of **1278 struts (69.4%) were covered** with neointima whereas **563 struts (30.6%) were uncovered**. There were **1755 struts (95.3%) with complete apposition** and **86 struts (4.7%) with incomplete apposition**.
Representative Case of OCT-Defined Erosion

Eun-Seok Shin et al. JIMG 2015;8:1059-1067
Characteristics of Spasm Sites as Assessed by OCT in Patients With Vasospastic Angina

Fibrous Cap Disruption: Fibrous cap discontinuity with or without a cavity formed inside the plaque

OCT-defined Erosion: Underlying visualized plaque with intact fibrous cap, lumen irregularity and thrombus

Luminal irregularity

No luminal irregularity or thrombus

Eun-Seok Shin et al. JIMG 2015;8:1059-1067
Cholesterol Crystals Images

80-year-old female patient with hypertension and hypercholesterolemia who presented with a NSTEMI

Hannah Sinclair et al. JIMG 2015;8:198-209
Relationship of Fibrous Cap Thickness to Macrophage Infiltration

Cell mean for % KPI positive

- < 65 µm
- 66 to 200 µm
- 201 - 300 µm
- > 300 µm

P = 0.03
P = 0.06

Renu Virmani et al. Circ
OCT for Vulnerable Plaque Detection

Intimal Rupture
OCT for Vulnerable Plaque Detection

Vulnerable Plaque

Thrombus

Thin cap

Necrotic Core

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• The resolution of OCT is 10 times higher than that of IVUS.
• OCT is capable of providing accurate coronary measurements.
• OCT is more accurate than IVUS in detecting subtle stent morphologies including malapposition, residual thrombus, plaque prolapse, and residual dissections.
• Further studies are needed to define the clinical value of OCT.

Eur Heart J. 2014;35:2541-2619
Conclusions

• Complete revascularization is the goal in ACS
• Ischaemia information is usually lacking at time of PCI
• Any physiology is better than none – but FFR remains the ‘Gold Standard’
• If using physiological indices – be aware of what they tell you and the clinical data supporting their use
Conclusions

• Angiography has limitations
• Intravascular imaging has become an integral part of interventional cardiology and is used frequently in ACS
• Choice of imaging modality is dependent upon the lesion and the question to be answered
• Comprehensive lesion assessment requires multimodality imaging
In clinical medicine when faced with a diagnostic or therapeutic decision, we must always choose the right tool for the right job. Invasive imaging is no different. None of the available tools is a single, all-in-one solution. All of them are important in specific situations. Physicians must learn to interpret and use these techniques correctly. The issues with IVUS – time, cost, expertise, etc – apply to all of the new modalities.
Thank you!!!

Email: ioannis.iakovou@gmail.com