Plaque Imaging in 2019: Will Plaque Characterization Add to the Success of FFR?

Jagat Narula MD PHD MACC
Mount Sinai Heart, New York

NO DISCLOSURES
ECSS: Revascularization Based on Anatomical Stenosis is Superior to (Time-Appropriate) OMT

Source: Varnauskas et al. ECSS Lancet 1980; X-ECC 1988
Prognostic Utility of Anatomical and Physiological Characteristics

The Stenosis-Ischemia Relationship is Far From Perfect

IWOS: Ischemia WithOut Stenosis  SWOI : Stenosis WithOut Ischemia

Park JACC 2012; Tonino JACC 2010; Ahmadi/Narula JAMA Cardiol 2016
FFR Guided Revascularization is a Reference Standard: How can it Predict Adverse Events?

Comparison of Per Lesion MI in Angiography Guidance Vs FFR Guidance: The FAME Study

- 1237 Lesions, 49 MI (3.9% MI rate)
- 816 Lesions, 31 MI (3.7% MI rate)
- 513 Lesions, 1 MI (0.2% MI rate)

Pijls, Fearon, De Bruyne, et al. FAME Family; NEJM
FAME-2
5-YEAR FOLLOW-UP: Kaplan–Meier Curves for the PEP
[Death from Any Cause, MI, Urgent Revascularization]

FFR+ Patients Treated with Revascularization + OMT

- **92.90%** MI-FREE SURVIVAL
- **7.10%** DEATH/MI

FFR+ Patients Treated with OMT

- **91.40%** MI-FREE SURVIVAL
- **8.60%** DEATH/MI

Data from FAME 2 Study
2 Year Follow-up, NEJM 2014
ACS & PLAQUE MORPHOLOGY

Observational study
ACS 38
Stable CAD 33

Motoyama, Narula et al. JACC 2007
IS HRP REALLY STENOTIC?

N=3000+
Follow Up to 10 Yrs.
Endpoint: MACE

Motoyama, Narula, et al. JACC August 2015
Importance of the number of APC & AHC and Outcomes

Lee, Akasaka et al. JACC 2019;73:2413-24

722 vessels/299 patients
5-Year Follow up
## Lesion-Specific and Vessel Related Determinants of Fractional Flow Reserve

<table>
<thead>
<tr>
<th>Feature</th>
<th>Estimate</th>
<th>SE</th>
<th>P</th>
<th>Model 1: Vessel with 1 Lesion only N=128</th>
<th>Estimate</th>
<th>SE</th>
<th>P</th>
<th>Model 2: All Vessels (≥1 lesion per vessel) n=383</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.006</td>
<td>0.0202</td>
<td>&lt;0.0001</td>
<td>1.044</td>
<td>0.020</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Luminal Stenosis by CTA-QCA</td>
<td>-0.001</td>
<td>0.0003</td>
<td>&lt;0.0353</td>
<td>-0.002</td>
<td>0.0002</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAP Volume</td>
<td>-0.002</td>
<td>0.0003</td>
<td>&lt;0.0001</td>
<td>-0.001</td>
<td>0.0003</td>
<td>0.0006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vessel Territory (LAD vs. RCA/LCX)</td>
<td>-0.076</td>
<td>0.0158</td>
<td>&lt;0.0001</td>
<td>-0.065</td>
<td>0.011</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion Location (Proximal vs. Mid/Distal)</td>
<td>-0.0206</td>
<td>0.0129</td>
<td>0.1152</td>
<td>-0.024</td>
<td>0.010</td>
<td>0.0174</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of segments</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.019</td>
<td>0.006</td>
<td>0.0020</td>
<td></td>
</tr>
<tr>
<td>Lesion Length (mm)</td>
<td>-0.0011</td>
<td>0.001</td>
<td>0.2771</td>
<td>0.0002</td>
<td>0.001</td>
<td>&lt;0.7762</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ahmadi, Nogaard, Leipsic, Narula et al. JACC Imaging 2018
## Plaque Characteristics and Fractional Flow Reserve

### Quantitative plaque characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal stenosis, %</td>
<td>–</td>
<td>&lt;0.001* (overall)</td>
</tr>
<tr>
<td>No stenosis</td>
<td>0 (reference)</td>
<td>–</td>
</tr>
<tr>
<td>0–50</td>
<td>3.9 (1.2–12.3)</td>
<td>0.021*</td>
</tr>
<tr>
<td>50–70</td>
<td>12.2 (4.3–34.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>&gt;70</td>
<td>35.4 (12.4–101.2)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Plaque length, mm</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Plaque volume (per 10 mm²)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Calcified plaque volume (per 10 mm²)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Noncalcified plaque volume (per 10 mm²)</td>
<td>1.05 (1.01–1.09)</td>
<td>0.010*</td>
</tr>
<tr>
<td>Lumen area, mm²</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Wall area, mm²</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Maximal plaque burden, %</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

### Qualitative plaque characteristics

- Noncalcified plaque
- Partially calcified plaque
- Calcified plaque
- Low-attenuation plaque
- Positive remodeling
- Spotty calcification
- Napkin ring sign

---

Knaapen, Leipsic, Ahmadi, Narula, et al. JACC 2018;71:499-509
## Coronary Stenosis Severity, FFR, and Underlying Pathologic Features

<table>
<thead>
<tr>
<th>Angiographic Diameter Stenosis Severity, %</th>
<th>FFR</th>
<th>No. of Lesions (% in Subgroup) (% in Entire Cohort)</th>
<th>Possible Histologic Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&gt;0.80</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>50-70</td>
<td>&gt;0.80</td>
<td>402 (65) [33]</td>
<td>2FNP with moderate luminal stenosis</td>
</tr>
<tr>
<td></td>
<td>≤0.80</td>
<td>218 (35) [18]</td>
<td>2FPP with moderate luminal stenosis</td>
</tr>
<tr>
<td>71-90</td>
<td>&gt;0.80</td>
<td>104 (20) [8]</td>
<td>2FNP with moderate to severe luminal stenosis</td>
</tr>
<tr>
<td></td>
<td>≤0.80</td>
<td>409 (80) [33]</td>
<td>2FPP with moderate to severe luminal stenosis</td>
</tr>
</tbody>
</table>

**Histological features:**
1. Coronary artery lumen
2. Fibrous part of the plaque (entire navy blue area)
3. Necrotic core (entire yellow area) that includes neovascularization (small red lines), red blood cell leakage (red dots), macrophages (black stars), and intraplaque hemorrhage (4)

Ahmadi, Narula, JAMA Cardiology 2016
High Coronary WSS in Patients with Stable CAD Predicts MI
A FAME-2 Sub-Study

Kumar, Bruyne, Samady et al. JACC 2018
Five-Year Outcomes with PCI Guided by Fractional Flow Reserve

FFR+ HRP-?
Safe to Defer

100% of Anatomically Significant Lesions be Revascularized

FFR assessment of functional significance

All FFR+ Lesions to be Revascularized

CT assessment of HRP characteristics

FFR+ Lesions are Safe to Defer

What We Thought?

COURAGE Trial demonstrated that revascularization based on anatomical stenosis alone is not indicated

What We Think?

FAME Trial demonstrated safety of deferral of FFR- lesion, regardless of degree of luminal stenosis

What Should We Think?

FAME-2: Approximately 50% of FFR+ lesions on medical therapy alone remain event-free with no difference in rate of death, MI, no need for revascularization and no difference in angina.

Ahmadi, Nogaard, Narula. JACC [Editorial] 2019
CT Coronary Angiography - one stop assessment

Anatomy

Physiology

Courtesy: Brian Ko MD, Monash University, Australia
FFR derived from CT Coronary Angiography (CT-FFR)

1. From typical CCTA
2. No radiation
3. No $\Delta$ image protocols
4. No medications
5. No added contrast
Clinical Utility: $\text{FFR}_{\text{CT}}$

$\text{FFR}_{\text{CT}}$ minimizes patients with non-obstructive coronary artery disease referred for invasive coronary angiography.

Douglas et al. EHJ 2015; Douglas et al. NEJM 2015; Lu et al. JACC imaging 2017
CT Myocardium at Risk: Approach Score

Approach Score:

- Estimate of anatomical myocardial territory at risk during STEMI
- Based on vessel dominance + site of lesion in main vessel + size side-branches

Strongly correlated with myocardial territory infarcted on cardiac MRI (r=0.90)

Ihdayhid et al. ESC 2019
Pre-procedural planning using PCI Planner accurately predicts the hemodynamic result of PCI in single and serial lesions.
Focal Stenosis

Model haemodynamic benefit of PCI and length of treatment required

Diffuse Disease

Minimal haemodynamic benefit in PCI to borderline lesions/diffuse disease
**FFR<sub>CT</sub> Guided PCI Planning in Tandem Lesions**

**Pre PCI**
Distal LAD FFR = 0.77

**PCI to Lesion B**
Distal LAD FFR = 0.78

**PCI to Lesions A+B**
Distal LAD FFR = 0.85

Ihdayhid, et al. JACC Interventions 2017
What if only lesion A was stented?

Distal LAD \( \text{FFR}_{CT} = 0.84 \)

Ihdayhid et al, JACC Interven 2017
72 M with Typical chest pain; pMHx: dyslipidemia on Rosuvastatin 10mg
Family history of premature CAD (Father MI at age 50)
NCP LAD pS2 [25-49%], 5 other scattered segments [<25%; CAD RADS 2

Ahmadi, Nogaard, Leipsic, Narula et al. JACC Imaging 2018
SDM with the patient:

- Medical Therapy: Crestor increased 10 to 40 mg, added Ezetimibe 10 mg
- 6 mo. follow up: LDL 3.1 to 1.17mmol/L; symptomatic improvement.

Ahmadi, Nogaard, Leipsic, Narula et al. JACC Imaging 2018