Diagnostic management of patients with suspected stable CAD

Risk stratification

- PTP > 85%
- PTP 50-85%
- PTP 15-50%
- PTP < 15%

Patients with suspected stable CAD

Invasive Coronary Angiography

Stress imaging
- provided
- Patient suitability
- Local expertise

Exercise ECG Test

Coronary CTA
- provided
- Patient suitability
- Local expertise

FFR-CT

Investigate other causes

Ischemia

LV function

- LVEF < 50%
- LVEF ≥ 50%

Coronary CTA not available

modified from ESC guidelines on the management of stable CAD. Eur Heart J 2013
Rate of stress testing before PCI

44% of Medicare beneficiaries underwent stress testing in the 90 days before elective PCI

Lin GA, JAMA. 2008; 300: 1765-1773
Recommendations for the clinical value of intracoronary FFR

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFR to identify haemodynamically relevant coronary lesion(s) in stable patients when evidence of ischaemia is not available.</td>
<td>I</td>
<td>A</td>
<td>50,51,713</td>
</tr>
<tr>
<td>FFR-guided PCI in patients with multivessel disease.</td>
<td>IIa</td>
<td>B</td>
<td>54</td>
</tr>
</tbody>
</table>
Fractional Flow Reserve (FFR) for the Functional Assessment of Coronary Stenosis

Pijls NH et al. JACC 2012; 59: 1045–57
FFR measurement
intracoronary adenosine bolus

Dosages:
LCA: 600 µg
RCA: 150 µg

time-to-peak: 15"
Plateau: 8"
Total duration: 25"
FFR- vs Angio-guided PCI: persistence of 2-year outcome

Pijls NH and the FAME investigators, JACC 2010; 56:177-84
PCI vs OMT in stable CAD patients with FFR ≤ 0.80
FUncitional Testing Underlying REvascularization
The FUTURE trial

Patient with stable or stabilized angina
Multivx-disease (>50% stenosis) including LAD

Randomisation 1:1
(diabetes stratification)

FFR-guided

FFR on all target lesions

Only lesions with FFR≤0.80 are included in stratification

PCI + OMT
Surgery + OMT
OMT only

Angio-guided

All lesions with %S>50 are included in stratification

PCI + OMT
Surgery + OMT
OMT only

Rioful on behalf of FUTURE investigators, at AHA 2016
Results
- as analyzed by the DSMB committee -

Death from Any Cause (Data Safety Monitoring Board Analysis)

Over n = 836 first patients

All-cause deaths at 12 months(n=24):
- control : 7 (2%)
- FFR : 17 (4%)

Log Rank test, p=0.02

P=0.02

Rioful on behalf of FUTURE investigators, at AHA 2016
Results
- as halted by Sponsor and Steering committee -

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group (n=398)*</th>
<th>FFR Group (n=399)*</th>
<th>HR (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from any cause (%)</td>
<td>8 (1.8)</td>
<td>17 (3.9)</td>
<td>1.98 (0.85–4.60)</td>
<td>0.07</td>
</tr>
<tr>
<td>Cardiovascular death (%)</td>
<td>6 (1.3)</td>
<td>12 (2.7)</td>
<td>1.88 (0.70-5.01)</td>
<td>0.16</td>
</tr>
<tr>
<td>MACE(%)</td>
<td>58 (13.2)</td>
<td>65 (15.1)</td>
<td>1.09 (0.76-1.56)</td>
<td>0.63</td>
</tr>
<tr>
<td>Myocardial infarction (%)</td>
<td>24 (5.3)</td>
<td>29 (6.5)</td>
<td>1.23 (0.71-2.11)</td>
<td>0.46</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>4 (0.9)</td>
<td>2 (0.4)</td>
<td>0.48 (0.09-2.62)</td>
<td>0.40</td>
</tr>
<tr>
<td>Repeat revascularization (%)</td>
<td>33 (7.6)</td>
<td>32 (7.6)</td>
<td>0.97 (0.60-1.58)</td>
<td>0.91</td>
</tr>
<tr>
<td>EQ-5D – visual analogue scale</td>
<td>71±18</td>
<td>70±17</td>
<td></td>
<td>0.51</td>
</tr>
</tbody>
</table>

*only for patients having reached the one-year endpoint

Rioful on behalf of FUTURE investigators, at AHA 2016
Anatomic vs Functional testing for CAD

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

Patients with Event (%) vs Months since Randomization

Douglas PS on behalf of PROMISE investigators, NEJM 2015
Fractional Flow Reserve derived from Computed Tomography (FFR-CT)
FFR-CT in diffusely calcified coronary arteries

Leber WA, Herz 2016 (in press)
<table>
<thead>
<tr>
<th>Revascularisation strategy</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete anatomic revascularisation</td>
<td>Treatment of all coronary segments &gt; 1.5 mm with a ≥50% DS irrespective of their ability to produce ischemia.</td>
</tr>
<tr>
<td>Myocardial-specific functionally adequate revascularization</td>
<td>Treatment of all coronary segments &gt; 1.5 mm with a ≥50% DS supplying viable ischemic myocardium.</td>
</tr>
<tr>
<td>Lesion-specific revascularization</td>
<td>Treatment of all coronary segments &gt; 1.5 mm with a FFR&lt;0.80.</td>
</tr>
<tr>
<td>Incomplete revascularisation</td>
<td>Inability or unsuitability to treat all coronary segments with significant disease (either ≥50% DS or FFR&lt;0.80) supplying viable myocardium.</td>
</tr>
</tbody>
</table>
Performance of non-invasive diagnostic methods used to make diagnosis of CAD

<table>
<thead>
<tr>
<th>Method</th>
<th>Diagnosis of CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (%)</td>
</tr>
<tr>
<td>Exercise ECG a, 91, 94, 95</td>
<td>45–50</td>
</tr>
<tr>
<td>Exercise stress echocardiography 96</td>
<td>80–85</td>
</tr>
<tr>
<td>Exercise stress SPECT 96-99</td>
<td>73–92</td>
</tr>
<tr>
<td>Dobutamine stress echocardiography 96</td>
<td>79–83</td>
</tr>
<tr>
<td>Dobutamine stress MRI b, 100</td>
<td>79–88</td>
</tr>
<tr>
<td>Vasodilator stress echocardiography 96</td>
<td>72–79</td>
</tr>
<tr>
<td>Vasodilator stress SPECT 96, 99</td>
<td>90–91</td>
</tr>
<tr>
<td>Vasodilator stress MRI b, 98, 100-102</td>
<td>67–94</td>
</tr>
<tr>
<td>Coronary CTA c, 103-105</td>
<td>95–99</td>
</tr>
<tr>
<td>Vasodilator stress PET 97, 99, 106</td>
<td>81–97</td>
</tr>
</tbody>
</table>
ECG stress testing

Basal  Stress  Recovery
ST/HR Hysteresis

Normal

Indicative of Myocardial Ischemia

adapted from Okin PM et al. Circulation 1989;80:533–41
ST/HR hysteresis

### ST/HR Hysteresis and CPET

<table>
<thead>
<tr>
<th>Indicator</th>
<th>AUC</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST/HR hysteresis</td>
<td>0.82</td>
<td>0.699 to 0.913</td>
<td>0.001</td>
</tr>
<tr>
<td>ST-max</td>
<td>0.68</td>
<td>0.542 to 0.798</td>
<td>NS</td>
</tr>
<tr>
<td>( \text{VO}_2 / \text{Work } b-b^1 ) slope</td>
<td>0.63</td>
<td>0.481 to 0.747</td>
<td>NS</td>
</tr>
<tr>
<td>( \text{VO}_2 / \text{Work } (aa^1- bb^1) )</td>
<td>0.61</td>
<td>0.474 to 0.740</td>
<td>NS</td>
</tr>
</tbody>
</table>
Left ventricular hypertrophy

\[ \sigma = \frac{Pr^2}{2h} \]
ST/HR Hysteresis in patients with LVH

*all significance values are compared with the “neutral test” 0.5 AUC value.

Conclusions

• In pts with stable CAD (and with NSTE-ACS aside from culprit lesions) a thorough assessment of functional relevance of both myocardium and coronary severity is mandatory in most cases.

• FFR has a robust scientific evidence supporting its clinical relevance, although recently...

• FFR-CT seems promising, but clinical translation of its relevance is needed.

• Good old exercise testing should not be abandoned in the current era of resource containment, as the adjunctive analysis of ST/HR hysteresis increases its diagnostic accuracy.