MULTIVESSEL DISEASE, CORONARY REVASCULARIZATION DECISION - HEMODYNAMIC ASSESSMENT

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Multivessel coronary artery disease, defined as significant stenosis in two or more major coronary arteries.

The diagnosis and treatment of multivessel disease have evolved in the PCI era from solely a visual estimation of ischemic risk to a functional evaluation during angiography.
LIMITATIONS OF CORONARY ANGIOGRAPHY

- Interpretation is highly subjective
- Cannot accurately predict physiologic significance, especially for intermediate lesions (40-70%)
- Identification of normal and diseased segments is complicated by diffuse disease
- Artifacts of contrast streaming
- Image foreshortening
- Overlapping vessels
FRACTIONAL FLOW RESERVE (FFR) = \( \frac{P_d}{P_a} \)

The resistance to flow through a stenosis results in energy loss.

Energy loss produces pressure loss distal to the stenosis and thus a pressure gradient across the narrowed segment.
FRACTIONAL FLOW RESERVE (FFR) = Pd/Pa

- Normal value 1
- An FFR value 0.6 means the maximum myocardial flow across the stenosis is only 60% of what it should be without stenosis
- An FFR value <0.75 is associated with inducible ischemia (specificity 100%)
  Positive assessment indicates a significant functional stenosis, suggesting the need for coronary revascularization to improve blood flow and reduce the risk of adverse cardiac events.
- An FFR value >0.80 indicates absence of inducible ischemia (sensitivity 90%)
  Negative assessment indicates a non-significant functional stenosis, implying that revascularization may not be necessary, and medical management or observation may be appropriate.
FFR İS MEASURED DURING A MAXİMALLY İNDUCED HYPEREREMİA

- Epicardial and resistance arteries have to be vasodilated
- Epicardial vessels are dilated using a bolus of 100-200mcg of intracoronary nitroglycerine at least 30 seconds before the first measurement
- Hyperemia is induced in the resistance vessels using adenosine (IC or IV) or papaverine (IC)
# Hyperemic Agents for FFR

<table>
<thead>
<tr>
<th></th>
<th>Adenosine</th>
<th>Adenosine</th>
<th>Papaverine</th>
<th>NTP</th>
<th>Regadenoson</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Route</strong></td>
<td>IV</td>
<td>IC</td>
<td>IC</td>
<td>IC</td>
<td>IV</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>140 mcg/kg/min</td>
<td>200 mcg LCA, 100 mcg RCA</td>
<td>15 mcg LCA, 10 mcg RCA</td>
<td>50-100 mcg</td>
<td>0.4 mg</td>
</tr>
<tr>
<td><strong>Half Life</strong></td>
<td>1-2 min</td>
<td>30-60 sec</td>
<td>2 min</td>
<td>1-2 min</td>
<td>2-4 min (up to 30 min)</td>
</tr>
<tr>
<td><strong>Time to Max Hyperemia</strong></td>
<td>&lt; 1-2 min</td>
<td>5-10 sec</td>
<td>20-60 sec</td>
<td>10-20 sec</td>
<td>1-4 min</td>
</tr>
<tr>
<td><strong>Advantage</strong></td>
<td>GOLD STANDARD</td>
<td>Short action</td>
<td>Short action</td>
<td>Short action</td>
<td>IV bolus</td>
</tr>
<tr>
<td><strong>Disadvantage</strong></td>
<td>↓BP, chest burning</td>
<td>AV Block, ↓BP</td>
<td>Torsades, ↓BP</td>
<td>↓BP</td>
<td>↑HR, ?redose, long action</td>
</tr>
</tbody>
</table>
FFR TECHNIQUE - CATHETERS

- Diagnostic catheters cannot be used to measure FFR:

  ✓ pressure measurement can be inaccurate
  ✓ the wire manipulation is met with friction due to smaller internal diameters compared to guide catheters

- The main advantage of guide catheters is that PCI is immediately possible if required

- Guide catheters with side holes should not be used:

  ✓ it can create a false gradient between the side holes and the tip of catheter creating a false positive FFR
  ✓ vasodilatory agent may be flushed into the aorta instead of the coronary arthery
FRACTIONAL FLOW RESERVE (FFR)
RELATION BETWEEN FFR AND Viable MYOCARDIUM

If a stenotic vessel supplies a larger viable myocardial mass, there will be a larger hyperemic flow during maximal vasodilation resulting in a greater gradient between Pd and Pa, and thus, a lower value of FFR.

*Haemodynamic significance of a lesion is dependent on its perfusion territory*
Rationale for Physiologic Assessment of Coronary Stenosis

1. Defining ischemia-causing stenosis

2. Change in clinical management

3. Improved outcomes
The purpose of this study was to investigate the appropriateness of stenting a functionally nonsignificant intermediate stenosis.

- Patients with single vessel stenosis and FFR > 0.75 who did not undergo PCI had excellent outcomes.
- The risk of cardiac death or MI related to the stenosis was <1% per year and was not reduced with PCI.
- In contrast, patients with single vessel stenosis and FFR < 0.75 are 5x more likely to experience cardiac death or MI within 5 years, despite undergoing revascularization.
FAME Study (Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention)

✓ 1005 patients (all with multivessel disease)
✓ At least 2 stenoses >50% in 2 or 3 major coronary artery disease, amenable for stenting
✓ Exclusion criteria: left main disease or previous bypass surgery, STEMI with CK>1000 U/L within last 5 days, extremely tortuous or calcified coronary arteries

Routine measurement of FFR in patients with MVD who are undergoing PCI with drug-eluting stents significantly reduces the rate of the composite end point of death, nonfatal myocardial infarction, and repeat revascularization at 1 year.
FAME 2 Trial (stable coronary artery disease)

• A total of 888 patients underwent randomization (447 patients in the PCI group and 441 in the medical-therapy group)

• All patients with stable coronary artery disease (*multivessel disease consisting of 26% and 22% of patients*)

FFR-guided PCI vs optimal medical therapy alone

Trial stopped prematurely due to a significantly lower rate of death, myocardial infarction, or urgent revascularization in the FFR-guided PCI group of the study at 2 years.
NON-HYPEREMIC PRESSURE RATIOS (NHPR)

Although FFR is the gold standard in invasive physiologic assessment, its clinical and economical benefits have been proven, it remains underutilized (~6% of patients undergoing PCI for intermediate lesions)

- Operator reluctance to delay procedures (especially in vessels with multiple lesions)
- Hospital costs (high price for single FFR-wire: 600-800 euro)
- Conceptual scepticism
- Side effects of hyperemic pharmacologic agents

NYPR were developed as an alternative to FFR
NON-HYPEREMIC PRESSURE RATIOS (NHPR)

The resting distal/aortic pressure over either the whole cardiac cycle or confined to diastole only

- iFR (average $P_d/P_a$ during the wave-free period)
- dPR (diastolic pressure ratio)
- DFR (diastolic hyperemia-free ratio)
- RFR (resting full-cycle ratio)
Instantaneous Wave-Free Ratio (iFR)

iFR - measures the ratio of the average distal coronary pressure to the average aortic pressure during a specific period of the cardiac cycle, known as the diastolic "wave-free period" (beginning 25% of the way into diastole and ending 5ms before the end of diastole). In this period microvascular resistance is naturally minimized without the need of hyperemia induced by the administration of a vasodilator.

\[ iFR = \frac{P_d\_{\text{wave free period}}}{P_a\_{\text{wave free period}}} \]

ISHEMIC THRESHOLD 0.89
Instantaneous Wave-Free Ratio (iFR)
✓ iFR offers a more convenient and cost-effective alternative to FFR

✓ iFR does not require the administration of a pharmacological vasodilator to induce hyperemia. It eliminates the hyperemia-induced discomfort for the patient

✓ iFR can be enhanced by iFR-pullback. It is especially useful in diffuse disease and serial lesions, which provides the possibility to display iFR changes over the course of the vessel to create a hemodynamic map (individual estimation of each stenosis)

✓ Angiography co-registration available
Pull back pressure recordings. (Left), diffuse disease. (Right), focal step up in distal vessel with no gradient across circumfex ostium
Two large multicenter studies (DEFINE-FLAIR and SWEDHEART) proved the non-inferiority of iFR towards FFR.
DEFINE-FLAIR STUDY

✓ Multicenter, international, randomized, blinded study
✓ Primary endpoint: 1-year risk for MACE (cardiovascular death, nonfatal myocardial infarction, unplanned revascularization)
✓ 2492 patients were included, 1242 in the iFR and 1250 in the FFR-group.

The 1-year analysis showed comparable results regarding the endpoints, confirming the non-inferiority of iFR towards FFR.

✓ The length of the procedure time was significantly shorter in the iFR-group (iFR 40.5 min, FFR: 45.0 min; P < 0.001)
✓ Less patients suffered from adverse effects like angina pectoris and dyspnea (3.1% vs 30.8%, P < 0.001)
✓ When compared to FFR, iFR was identified as more economically advantageous.
SWEDEHEART STUDY

- Multicenter, randomized, clinical study
- **Primary endpoint:** 1-year risk for MACE (cardiovascular death, nonfatal myocardial infarction, unplanned revascularization)
- 2037 patients, 1019 received iFR and 1018 received FFR.
- **Major inclusion criteria:** Patients with suspected stable angina pectoris or unstable angina pectoris/NSTEMI with a clinical indication for physiology-guided assessment of coronary lesions (30-80% stenosis grade)
- **Major exclusion criteria:**
  - Known terminal disease with a life expectancy <1 year
  - Unstable hemodynamics (Killip class III-IV)
  - Inability to tolerate adenosine
  - Previous CABG with patent graft to the interrogated vessel
  - Heavily calcified or tortuous vessel where inability to cross the lesion with a pressure wire was expected
The 1-year analysis of endpoints confirmed the non-inferiority of the iFR-method.

- Especially in uncertain cases, where iFR and FFR results differ, the data indicate that iFR provides more accurate results.
- iFR was superior to FFR regarding procedural discomfort.
SAFETY OF INTRACORONARY SENSOR-WIRE MEASUREMENTS

- **Transient Bradycardia**: 1.7%
- **Coronary Spasm**: 2%
- **Ventricular Fibrillation**: 0.2%
FFR initially adopted as a Class IA recommendation in the ESC/EACTS guidelines of 2014 on myocardial revascularization

Besides FFR, iFR adopted as a CLASS IA recommendation in the ESC/EACTS guidelines of 2018.
Diqqətinizə görə təşəkkürlər!