CORONARY PHYSIOLOGY IN THE CATHLAB:

FFR AND COLLATERAL FLOW

Educational Training Program ESC
European Heart House
April 24th - 26th 2014

Nico H. J. Pijls, MD, PhD
Catharina Hospital,
Eindhoven, The Netherlands
Experimental Basis of Determining Maximum Coronary, Myocardial, and Collateral Blood Flow by Pressure Measurements for Assessing Functional Stenosis Severity Before and After Percutaneous Transluminal Coronary Angioplasty

Nico H.J. Pijls, MD; Jacques A.M. van Son, MD; Richard L. Kirkeeide, PhD; Bernard De Bruyne, MD; and K. Lance Gould, MD

Introduction of FFR in Circulation: may 1993
Experimental Basis of Determining Maximum Coronary, Myocardial, and Collateral Blood Flow by Pressure Measurements for Assessing Functional Stenosis Severity Before and After Percutaneous Transluminal Coronary Angioplasty

Nico H.J. Pijls, MD; Jacques A.M. van Son, MD; Richard L. Kirkeeide, PhD; Bernard De Bruyne, MD; and K. Lance Gould, MD
Including collaterals in the model……..
\[ Q_{\text{myo}} = Q_{\text{cor.artery}} + Q_{\text{collateral}} \]

Quantitative assessment of the contribution of *coronary arterial* and *collateral flow* to total *myocardial flow* is possible by coronary pressure measurements, but not trivial.

*Pijls & De Bruyne:*  
*Circulation* 1993  
*Coronary Pressure,* sec edition, Kluwer 2000
I \[ \frac{P_a - P_v}{P_w - P_v} = 1 + \frac{R_c}{R} = \text{constant} \]

IIa \[ FFR_{cor} = \frac{P_d - P_w}{P_a - P_w} = 1 - \frac{\Delta P}{P_a - P_w} \]

IIia \[ FFR_{myo} = \frac{P_d - P_v}{P_a - P_v} = 1 - \frac{\Delta P}{P_a - P_v} \]

IVA \[ Q_c = (FFR_{myo} - FFR_{cor}) \cdot Q^N \]
I \[ \frac{P_a - P_v}{P_w - P_v} = 1 + \frac{R_c}{R} = \text{constant} \]

IIa \[ \text{FFR}_{\text{cor}} = \frac{P_d - P_w}{P_a - P_w} = 1 - \frac{\Delta P}{P_a - P_w} \]

IIIa \[ \text{FFR}_{\text{myo}} = \frac{P_d - P_v}{P_a - P_v} = 1 - \frac{\Delta P}{P_a - P_v} \]

IVa \[ Q_c = (\text{FFR}_{\text{myo}} - \text{FFR}_{\text{cor}}) \cdot Q^N \]
I \[ \frac{P_a - P_v}{P_w - P_v} = 1 + \frac{R_c}{R} = \text{constant} \]

IIa \[ FFR_{cor} = \frac{P_d - P_w}{P_a - P_w} = 1 - \frac{\Delta P}{P_a - P_w} \]

IIIa \[ FFR_{myo} = \frac{P_d - P_v}{P_a - P_v} = 1 - \frac{\Delta P}{P_a - P_v} \]

IVa \[ Q_c = (FFR_{myo} - FFR_{cor}) \cdot Q^N \]
BEFORE PTCA

START ADENOSINE

\[ FFR_{myo} = \frac{53 - 5}{101 - 5} = 0.50 \]

HYPEREMIA

(venous pressure not displayed: 5 mmHg)
BALLOON INFLATION

$P_a$  

(coronary wedge pressure, also called $P_w$)

$P_d$
17 vb5-PTCA - de Wit-Stek (8)
After PTCA

Start Adenosine

Hyperemia

\[ FFR_{myo} = \frac{94-5}{97-5} = 0.97 \]
<table>
<thead>
<tr>
<th></th>
<th>before</th>
<th>occlusion</th>
<th>after</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pa</td>
<td>90</td>
<td>101</td>
<td>98</td>
</tr>
<tr>
<td>Pd</td>
<td>42</td>
<td>-</td>
<td>82</td>
</tr>
<tr>
<td>Pv</td>
<td>2</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Pw</td>
<td>(14)</td>
<td>18</td>
<td>(15)</td>
</tr>
<tr>
<td></td>
<td>before PTCA</td>
<td>at occlusion</td>
<td>after PTCA</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
<td>--------------</td>
<td>------------</td>
</tr>
<tr>
<td>FFRmyo</td>
<td>0.50</td>
<td>0.18</td>
<td>0.97</td>
</tr>
<tr>
<td>FFRcor</td>
<td>0.39</td>
<td>-</td>
<td>0.96</td>
</tr>
<tr>
<td>Qc/Q^N</td>
<td>0.11</td>
<td>0.18</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Note: The values in this matrix are independent of pressure or other hemodynamic variables. Such a matrix completely describes the distribution of flow in that part of the coronary circulation related to the respective artery.
<table>
<thead>
<tr>
<th></th>
<th>before PTCA</th>
<th>at occlusion</th>
<th>after PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFRmyo</td>
<td>0.50</td>
<td>0.18</td>
<td>0.97</td>
</tr>
<tr>
<td>FFRcor</td>
<td>0.39</td>
<td></td>
<td>0.96</td>
</tr>
<tr>
<td>Qc/Q^N</td>
<td>0.11</td>
<td>0.18</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Note: the values in this matrix are independent of pressure or other hemodynamic variables. Such a matrix completely describes the distribution of flow in that part of the coronary circulation related to the respective artery.
Fractional collateral flow =

$$\text{FFR_{coll}} = \frac{P_d - P_w}{P_a - P_w}$$

(later also called $CFIp$ by Seiler et al)
To determine collateral flow by pressure measurement, temporary occlusion of the coronary artery is necessary!

(prerequisite to measure coronary wedge pressure)
During balloon occlusion of the coronary artery:

\[ FFR_{\text{coll}} = \frac{P_w - P_v}{P_a - P_v} \]

FFR_{\text{coll}} = 0.28 (also called CFIp)

Circulation 1993;87:1354-1367
Coronary Pressure, 2nd ed, 2000
FFR_{coll} : experimental validation in chronic dog studies
Experimental basis of FFR

**Horizontal axis:**
- $\text{FFR}_{\text{cor}}$ measured by true flow

**Vertical axis:**
- $\text{FFR}_{\text{myo}}$ and $\text{FFR}_{\text{coll}}$ measured by Hyperemic pressure ratio

Pijls et al, Circulation, 1993
Do we have to bother about $P_v$?

Yes, in case of studies to collateral function, we have to take into account $P_v$.

$$FFR_{coll} = \frac{P_w - P_v}{P_a - P_v}$$

$$\frac{75 - 5}{100 - 5} = 0.74$$
$$\frac{75}{100} = 0.75$$
$$\frac{20 - 5}{100 - 5} = 0.15$$
$$\frac{20}{100} = 0.20$$
$\frac{P_w - P_v}{P_a - P_v}$

Fractional collateral flow is independent of changes in blood pressure.

**FFR** \(_{collaterals}\) is independent of changes in blood pressure.
Reproducibility of $\text{FFR}_{\text{collaterals}}$
Pressure-Derived Parameters for Assessing Coronary Collateral Circulation

Reproducibility:

- 50 patients

recruitable collateral flow assessment at 2 consecutive balloon occlusions with an interval of 15 minutes, by:

\[ \frac{Q_c}{Q^n} = \frac{P_W - P_V}{P_a - P_V} \]

- first occlusion: \(0.21 \pm 0.10\)
- second occlusion: \(0.20 \pm 0.11\)

Coefficient of variation: \(2 \pm 4\%\)

Pijls et al, JACC 1995
Recruitable fractional collateral blood flow $\frac{Q_c}{Q^N}$ at the consecutive balloon inflation (mean $\pm$ SEM)
One of the reasons why an apparently severe stenosis might have a high FFR Value, is the presence of good collaterals............
“One identical stenosis, but......”

Poor collaterals: FFR = 0.50

Poor collaterals → low FFR
Good collaterals: FFR = 0.75

Diff. extent of collaterals

Good collaterals → higher FFR
FEATURES OF FFR

• *Normal value* = 1.0 for every patient and every artery
• FFR is *not influenced by changing hemodynamic conditions* (heart rate, blood pressure, contractility)
• FFR specifically relates the influence of the epicardial stenosis to myocardial perfusion area and blood flow
• **FFR accounts for collaterals**
• FFR has a *circumscribed threshold value* (~ 0.75 – 0.80) to indicate ischemia
• FFR is *easy to measure* (success rate 99 %) and extremely *reproducible*
• Pressure measurement has an *unequaled spatial resolution*
This also means that a rather mild stenosis in a collateral-giving artery, might have a lower than expected FFR, if the perfusion territory is enlarged due to extensive collaterals!
Disconnect between Anatomy and Physiology

During Maximal Hyperemia

FFR = 0.85

FFR = 0.73

50% Stenosis

Collaterals

Myocardium

Collateral-Supplied Myocardium

Vessel-Supplied Myocardium
resting

hyperemia       pull-back

moderate LAD-stenosis with large perfusion area → *low FFR, functionally highly significant*
FFR is more than just Pd/Pa at hyperemia……..

It is a complete description of coronary, myocardial, And collateral blood flow in terms of pressure

FFR is a beautiful physiological index describing the relation between

- epicardial stenosis severity
- coronary blood flow
- extent of perfusion territory
- and myocardial ischemia

• **FFR in fact incorporates a large part of coronary physiology**
Relation between $\text{FFR}_{\text{coll}}$ and angiographic grading?
\[
\frac{P_w - P_v}{P_a - P_v} = \frac{Q_c}{Q^N} (\%)
\]

\( \text{FFR}_{\text{coll}} \)

(or \( \text{CFI}_p \))

angiographic grading according to renthrop

from Pijls et al, JACC 1995; 25: 1522-8
Collateral Flow assessment by FFR and OUTCOME
Recruitable Collateral Flow & Clinical Outcome:

- n=120 patients, undergoing PTCA
- quantitation of recruitable collateral flow by coronary pressure measurements
  - group I: \( \frac{Q_c}{Q^n} \geq 0.25 \) or \( \frac{P_w}{P_a} \geq 0.30 \) : n=34
  - group II: \( \frac{Q_c}{Q^n} < 0.25 \) or \( \frac{P_w}{P_a} < 0.30 \) : n=85
- 2-year follow-up:
  - group I: 1 acute ischemic event (3%)
  - group II: 15 acute ischemic events (18%)

Pw/Pa at occlusion \( \geq 0.30 \) \( \rightarrow \) 5x smaller chance for myocardial infarction or death in the next 5 years

Pijls & De Bruyne, Coronary Pressure, sec edition, 2000: pg 348-349
Recruitable Collateral Flow & Clinical Outcome:

- n=120 patients, undergoing PTCA with single vessel disease.
- Quantitation of recruitable collateral flow by coronary pressure measurements.
- Group I: \( Q_c/Q^n \geq 0.25 \) or \( P_w/P_a \geq 0.30 : n=34 \)
- Group II: \( Q_c/Q^n < 0.25 \) or \( P_w/P_a < 0.30 : n=85 \)
- 2-year follow-up:
  - Group I: 1 acute ischemic event (3%)
  - Group II: 15 acute ischemic events (18%)

\( P_w/P_a \) at occlusion \( \geq 0.30 \) → 5x smaller chance for myocardial infarction or death in the next 5 years.

Pijls & De Bruyne, Coronary Pressure, sec edition, 2000: pg 348-349
FFR and Collateral Flow: CONCLUSIONS

- FFR_{coll} (also called CFI_p) can be easily obtained during PCI.
- Is reproducible and independent of blood pressure.
- Has relevant relation to outcome.
- Is suitable tool for studies to collateral blood flow.

**Disadvantages:**

- Only applicable during PCI, not at diagnostic angio because of necessity of P_w.
- For studies, P_v should be included.
- Careful calibration and equalization is mandatory.
EINDE
FEATURES OF FFR

• Normal value = 1.0 for every patient and every artery
• FFR is *not influenced by changing hemodynamic conditions* (heart rate, blood pressure, contractility)
• **FFR specifically relates the influence of the epicardial stenosis to myocardial perfusion area and blood flow**
• FFR accounts for collaterals
• FFR has a *circumspect threshold value* (~ 0.75 – 0.80) to indicate ischemia
• FFR is easy to measure (success rate 99 %) and extremely *reproducible*
• Pressure measurement has un *unequaled spatial resolution*
similar stenosis but different extent of perfusion area

4 mm$^2$ is too small

IVUS identical CSA
4 mm$^2$

4 mm$^2$ is sufficient

identical CSA, but different significance of stenosis
With permission of Dr Haitma Amin, Bahrain
FFR accounts for the extent of the perfusion area:

Anatomic stenosis severity by IVUS or QCA is identical but physiologic severity has decreased.

→ FFR accounts for these changes !!!
### Recruitable Collateral Blood Flow at Consecutive Inflations

<table>
<thead>
<tr>
<th></th>
<th># 1</th>
<th># 2</th>
<th># 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Q_c/Q^N$ (%)</td>
<td>21 ± 11</td>
<td>21 ± 12</td>
<td>22 ± 14</td>
</tr>
</tbody>
</table>
Pressure-Derived Parameters for Assessing Coronary Collateral Circulation

**Cut-off value for Protection against ischemia:**

- **Meier (n=57):**
  - *Circulation 1987*
  - $P_w = 30$ mm Hg
  - accuracy 92%
  - $\approx P_w/P_a = 0.31$

- **Pijls (n=120):**
  - *JACC 1995*
  - $Q_c/Q^n = 0.25$
  - accuracy 94%
  - $\approx P_w/P_a = 0.30$

- **Piek (n=106):**
  - *JACC 1997*
  - accuracy 84%
  - $\approx P_w/P_a = 0.30$
Pressure-Derived Parameters for Assessing Coronary Collateral Circulation

**Advantages:**

- quantitative assessment of coronary collateral blood flow
- easily applicable in the clinical catheterization laboratory
- independent of blood pressure and other hemodynamic variations
- excellent reproducibility
- relevant clinical implications: $P_w/P_a \geq 0.30$ indicates protection against acute ischemic events (relative risk 6 x lower than in other patients)
Pressure-Derived Parameters for Assessing Coronary Collateral Circulation

Limitations:

• Coronary wedge pressure ($P_w$) is always necessary
  ⇒ only applicable at PTCA

• Measurement of central venous pressure ($P_v$) is mandatory in case this pressure is expected to be elevated
Fractional collateral flow (also called CFI\(p\)) =

\[
\text{FFR} \text{ coll} = \frac{P_{w} - P_{v}}{P_{a} - P_{v}}
\]

Venous pressure not negligible anymore!
normal → increasing stenosis → total occlusion

**Maximum myocardial perfusion:**

100% → 70% → 25%

**FFR:**

1.0 → 0.7 → 0.25

**H-SRv:**

0 → ? → ∞ or negative

**Resting indexes**

1.0 unpredictable 0.25
Predictive value of the different parameters to predict ischemia:

- Chest pain during balloon inflation: 67%
- Visible collaterals on angiogram: 76%
- Coronary wedge pressure: 84%
- Calculated collateral blood flow ($\frac{Q_o}{Q^N}$): 95%
Recruitable collateral flow during balloon inflation:

\[ \frac{Q_c}{Q^N} = \frac{P_w - P_v}{P_a - P_v} \]

- \( Q_c \): recruitable collateral blood flow at balloon inflation
- \( Q^N \): normal maximum myocardial blood flow
- \( P_a \): mean aortic pressure at balloon inflation
- \( P_v \): mean right atrial pressure at balloon inflation
- \( P_w \): coronary wedge pressure at balloon inflation

Circulation 1993;87:1354-1367
Pressure-Derived Parameters for Assessing Coronary Collateral Circulation

History:

Schaper: pressure gradient / arterial blood pressure ratio as a function of time after gradual occlusion by ameroid constrictor in dogs

Meier, De Bruyne, Rutishauser, 1987/88: systematic investigations to the relation between coronary wedge pressure ($P_w$) and extent of the coronary collateral circulation