PRACTICAL SET-UP OF FFR

Educational Training Program ESC
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During Maximal Vasodilatation

\[ FFR_{\text{myo}} = \frac{P_d}{P_a} = 0.70 \]
\[ \text{FFR } myo = \frac{P_d}{P_a} \]

\( P_a \) = mean aortic pressure at maximum hyperemia

\( P_d \) = mean distal coronary pressure pressure at maximum hyperemia
**FFR = 0.6 means:**

“Due to this particular stenosis, maximum achievable blood flow to the myocardium supplied by this artery, is only 60 % of what it would be if this coronary artery were completely normal”

**If, after PCI, FFR increases to 0.9, this means:**

“Maximum achievable flow (and therefore maximum oxygen supply) has increased by 50% and is 90 % now of the value achievable if the artery were completely normal”
Application in catheterization laboratory

pressure wire + hyperemic stimulus = FFRmyo
0.014 sensor-tipped PTCA guidewire (St Jude Medical & Volcano)
MAXIMUM VASODILATORY STIMULI

!! Maximum hyperemia is paramount !!

• PAPAVERINE i.c.
• ADENOSINE i.c.
• ADENOSINE i.v.
• ATP i.c
• ATP i.v.
• regadenoson ?

Bernard De Bruyne

Lokien Van Nunen
Mr van Z.
77 years,
stable ang 2-3
posit ET
Fractional Flow Reserve in Clinical Practice

**Rest**

**Hyperemia**

FFR = $\frac{58}{112} = 0.52$
Catharina Hospital, Eindhoven, NL

1800 FFR cases per year
95 % = central venous adenosine by femoral sheath
Venous sheath into femoral vein
Adenosine for i.v. infusion

(standard bag 200 mg = 100 ml)

price: Euro 2,= per bag

prepared by hospital pharmacy

manufacturing protocol available at carias@cze.nl
Infusion pump for adenosine (140 µg/kg/min)
Infusion rate simply adjusted according to body weight ( ….kg → ……ml/min)
- no preparation in the lab
- no difficult calculations
- always the same dilution
- no risk of dosage error
- no loss of time

Some notes on your sheaths
MAXIMUM HYPEREMIA IS OF PARAMOUNT IMPORTANCE:

NOTE:

• sometimes, periodic fluctuations are present during i.v. adenosine induced steady state hyperemia

• this is related to the speed of metabolization of adenosine (patient-dependent) and the breathing pattern

• *always take the lowest value of FFR*

PRACTICAL PERFORMANCE OF FFR - MEASUREMENT
Note!

As in any intracoronary manipulation, before entering the coronary circulation, administer **200-300 µg NTG i.c.**
200 – 300 µg NTG i.c.
Unpacking of the Pressure Wire
Flush the Pressure Wire
Connecting the Pressure Wire to Analyzer
Calibrating Pressure Wire
Pressure Wire Calibrated: Ok
Pressure Wire introduced into Y-connector
Shaping of the tip of the PW
Introducing the PW into the Guiding Catheter
start with verification of equal signals when sensor is located at tip of the guiding catheter and equalize.
NOTE:

introducer needle in or out !?!

→ doesn’t matter as long as you realize what you are doing

1. Know your needle

2. Realize that some apparent “drift” at the end is not drift per se but can be caused by the presence of the introducer when doing the initial measurement and absence of the (removed) introducer at the end
Introducer effect  (mistake in live case in PCR 2010)

Introduction of a “thin needle” into the valve of the ‘y’ connector

Introduction of a “large needle” in the valve of the ‘y’ connector
advance pressure wire through stenosis and induce hyperemia → FFR
FFR LAD (i.v. adenosine) = 0.66 → need for stent
Make **pullback recording** for optimal information
Because sensor is 3 cm from tip, easily pull-back and push-up for exact spatial information.

If desirable, perform pull-back recording for exact location of pressure drop / stent deposition.
Pull-back & Advance recording for detailed spatial information about distribution of lesions along the complete artery
If you need to treat, disconnect pressure wire
disconnecting the pressure wire..........
to assess *collateral flow*: measurement of coronary wedge pressure during balloon inflation can be done

Fractional collateral flow = \( \frac{(P_d - P_w)}{(P_a - P_w)} \)
Stent has been placed: LAD after stenting
If you like to evaluate post-stent result, connect again
measurement of **FFR after stenting** to assess result

FFR = 0.94
NOTICE:

After stenting, in the majority of patients no resting conditions are obtained anymore and “semi-hyperemic” status persists, with a lot of inter-individual variation.

It often takes > 30 minutes to achieve “baseline” again.

As a consequence, “resting” Pd/Pa (and iFR) are often lower after stenting than before.

To evaluate improvement by stenting, you need to compare FFR after and before stenting (e.g. FFR from 0.6 to 0.9 means increase of maximum achievable myocardial flow by 50%)
At the end, when sensor is back at tip of guiding catheter, verify absence of drift.
Complete Integration of FFR Measurement in the Regular Environment of the Cathlab
True FFR Integration (St Jude Medical)

- Receiver connects directly to any hemodynamic recording system.
- Used directly in the cathlab with no additional instrumentation.
- Utilizes the standard blood pressure transducer ports without any extra cabling.
- Requires FFR software upgrade from cathlab manufacturers General Electric, Philips, etc.
- No calibration, ready in 1 second
Identical display on Analyzer or Quantien and GE cathlab recording system
GE catlab recording system: full integration of FFR
A few final issues:

- pressure pullback recording
- always necessary to induce hyperemia?
- regadenoson
Hyperaemie: sensor in PLRCA

FFR = \frac{70}{118} = 0.61
Dist. stenose
Mid in-stent restenose
Dist. stenose
Prox. stenose

Hyperemia: Pull back recording
FFR = 0.65
Dist. Stenosis after treatment

Prox. stenosis after treatment

Hyperaemie: sensor in PLRCA

FFR = 116/118 = 0.98
A few final issues:

- pressure pullback recording
- *always necessary to induce hyperemia?*
- regadenoson
A bunch of older and newer resting indexes: *Pd/Pa at rest, diastolic Pd/Pa, iFR, i-iFR, bSRv, ("FFR-light")*, which have in common that they all avoid hyperemia and only have a moderate accuracy (70% - 80%)
necessity of hyperemia

- If Pd/Pa at rest (or comparable indices, like iFR) is < 0.80, as a matter of fact FFR will also be < 0.80 and hyperemia in itself is not strictly mandatory to decide upon inducible ischemia.

- But without hyperemia, you cannot make a meaningful pull-back recording and you are loosing a lot of valuable information.

- And without hyperemia and FFR, you cannot judge how much a patient improved by stenting: you don’t know where you came from (“did FFR go from 0.78 to 0.91 or from 0.65 to 0.91?”) and no resting conditions exist after PCI (paradoxical deterioration of resting indexes).
A few final issues:

• pressure pullback recording
• necessity of hyperemia
• *regadenoson* → Lokien Van Nunen
Adenosine (central venous infusion) vs Regadenoson

Patient scheduled for diagnostic FFR/FFR-guided PCI (n=100)

Informed consent

First vessel scheduled for FFR-measurement (Study artery)

Start of procedure

Equilibration (resting conditions)

IV Adenosine measurement 1

Regadenoson measurement 1 *

IV Adenosine measurement 2

Regadenoson measurement 2 *
Adenosine (central venous infusion) vs Regadenoson for maximum hyperemia

- 100 arbitrary patients admitted for FFR measurement
- central venous line (femoral sheath) and peripheral line
- adenosine 140 µg/kg/min as central venous infusion vs single bolus of 400 µg regadenoson in central or peripheral vein
- adenosine #1, regadenoson #1, adenosine#2, regadenoson #2
- randomization with respect to regadenoson:

  central/central (N=25)
  peripheral/central (N=25)
  central/peripheral (N=25)
  peripheral/peripheral (N=25)
Adenosine (central venous infusion) vs Regadenoson for maximum hyperemia

ss hyp + "baseline" 10 min ss hyp + 0.5 "1½ baseline" 10 min

adeno #1 regadenoson #1 (centr or periph) adeno #2 regadenoson #2 (periph or central)
Adenosine (central venous infusion) vs Regadenoson (central venous single bolus injection 400 µg)

N=30
courtesy of Dr Lokien van Nunen
Adenosine (central venous infusion) vs Regadenoson (peripheral venous single bolus injection 400 µg)

\[ R^2 \text{ Linear } = 0.968 \]

N=30
courtesy of Dr Lokien van Nunen
Regadenoson
(central venous single bolus injection 400 µg vs peripheral single bolus 400 µg)

N=20
courtesy of Dr Lokien van Nunen
Results of first 47 Patients

• Maximum hyperemia achieved by regadenoson in ALL patients (difference compared to central venous adenosine 0.00 +/- 0.02).

• No difference between central and peripheral regadenoson.

• Hyperemic plateau reached ≤ 40 sec in all patients both for central and peripheral regadenoson.

• Duration of hyperemic plateau varied from 75 sec to 9 minutes (sufficient for pull-back recording in all patients).

• Zero complications or side-effects both for adenosine (94 runs) or (repeated) regadenoson (94 injections), except the well-known and innocent chest discomfort (graded 6/10 vs 5/10, respectively) and a few skipped beats in 2 patients (adeno) without necessity to interrupt administration.
Adenosine (Central Venous Infusion) *versus* Single Bolus Injection of Regadenoson For Maximum Hyperemia
Aims of this study:

• To investigate if the hyperemic effect of single bolus regadenoson injection is equal to the present gold standard i.e. central venous adenosine infusion

• To determine time intervals to onset of maximum hyperemia and the duration of steady state hyperemia if present

• To compare central venous vs peripheral venous administration of regadenoson

• To investigate side-effects as well as safety of repeated regadenoson injections, if desired
Conclusions (halfway this study)

• Regadenoson as a single bolus injection of 400 µg, is an excellent alternative for central venous adenosine infusion to induce maximum hyperemia.

• Rapid onset (~ 30 sec) and steady state long enough (at least 75 sec) to perform pressure pullback recording,

• In case multiple arteries need to be investigated, repeated injection can be performed and is safe.

• No noticeable side effects of regadenoson or adenosine, except the harmless chest discomfort.
Correct Classification of Ischemic Stenosis

FFR

resting Pd/Pa, iFR, bSVr (“FFR-light”)

angiography

100 % certainty (holy grail)

95 %

hyperemia

80 %

resting indexes

angio

70 %

the pyramid of diagnostic accuracy
FRACTIONAL FLOW RESERVE:
The index FFR (Fractional Flow Reserve) is based upon the two following principles:

- *It is not resting flow, but maximum achievable flow which determines the functional capacity (exercise tolerance) of a patient.*

- *At maximum vasodilation (corresponding with maximum hyperemia or with maximum exercise), blood flow to the myocardium is proportional to myocardial perfusion pressure (~hyperemic distal coronary pressure)*
FRACTIONAL FLOW RESERVE =

\[ \frac{\text{MAXIMUM FLOW IN THE PRESENCE OF A STENOSIS}}{\text{NORMAL MAXIMUM FLOW}} \]

\[ \approx \frac{\text{Distal coronary pressure at maximum hyperemia}}{\text{Aortic pressure}} \]
Maximum myocardial perfusion:

100% → 70% → 25%

FFR: 1.0 → 0.7 → 0.25

In other words: FFR is linearly related to maximum achievable blood flow
Angina Pectoris & Pos MIBI:
Typical chest pain; positive MIBI-Spect inferior wall
Hyperemic pull-back recording along the RCA
FFR: The Pressure Pull-back Curve

**Pressure pull-back curve at maximum hyperemia:**

- place sensor in distal coronary artery
- induce sustained maximum hyperemia by i.v. adenosine, or i.c. papaverine
- pull back the sensor slowly under fluoroscopy
- the individual contribution of every segment and spot to the extent of disease can be studied in this way

*Coronary pressure is unique in this respect and such detailed spatial information cannot be obtained by any other invasive or non-invasive method*