Hyperemia

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Maximal Hyperemia

- Maximal Vasodilation
- Maximal Possible Blood-Flow to the Myocardium

Jeremias A, TCT 2009
Importance of maximal hyperemia

- Pressure and Flow are proportional only at the point of maximal hyperemia.

- To detect the presence and extent of myocardial ischemia, maximal hyperemia is mandatory.

Jeremias A, TCT 2009
We are measuring coronary pressure to measure coronary flow. It is at the point of maximal hyperemia that FFR is proportional to blood flow. At this point further blood flow is impossible, thus:

$$100\% \text{ flow} = FFR \ 1.0$$

Jeremias A, TCT 2009
Flow-Pressure Relationship

**Significant Coronary Stenosis**

- With a stenosis, maximal blood flow is lower despite maximal stimulation of the microvasculature— in this case only reaching 70% compared to normal.
- The corresponding Pd/Pa pressure will therefore be proportional to the flow at this new point.
- 70% blood flow is proportional to FFR 0.70.

Jeremias A, TCT 2009
Flow-Pressure Relationship
Sub-maximal Hyperemia

- FFR not reflective of stenosis severity
- With sub-maximal hyperemia, flow ≠ pressure
- FFR is higher, thus underestimating stenosis severity
- Only at point of maximal hyperemia = true FFR

FFR = 0.7
70% Flow
Pa/Pd Pressure

Jeremias A, TCT 2009
Pharmacologic Hyperemic Stimuli

**Intravenous Adenosine Infusion**

- Current gold standard for FFR measurement
- Hyperemia mediated via A2 receptor on cell membrane on resistance vessels
- Exogenously administered adenosine causes profound microvascular dilation
- Hyperemia is independent of metabolic demand

Jeremias A, TCT 2009
Pharmacologic Hyperemic Stimuli

**Intravenous Adenosine Infusion**

- 140mcg/kg/min
- Administered through a central (femoral) vein
- Intracoronary nitrate
- Peak effect in 30~45secs with effect wearing off in same time frame after the infusion is stopped
- Produces “Steady state hyperemia”

Jeremias A, TCT 2009
Pharmacologic Hyperemic Stimuli

**Intravenous Adenosine Infusion**

- AV block is much less common than with ic adenosine

- Brochoconstriction
  - Main contraindication is significant asthma (or COPD)

- Often accompanied by an angina like sensation in the chest and throat which can be associated with dyspnea
  - Harmless and does not indicate myocardial ischemia
  - Warn and reassure patients
  - Encourage patients to breathe normally (avoid valsalva)
Pharmacologic Hyperemic Stimuli

**Intravenous Adenosine Infusion**

- **Advantages**
  - Steady state hyperemia: Pull back curve & CFR

- **Limitations**
  - Infusion in femoral vein
  - High cost d/t large dose of adenosine
  - Setup cumbersome and time consuming
Pharmacologic Hyperemic Stimuli
Intravenous Adenosine Infusion

** SNUH protocol

Dextrose 5%  80 mL  
+  
Adenosine  60mg/20 mL  

Mixed solution : 600ug/mL

** Infusion rate :

140ug * Bwt (kg) /min
= 140ug*Bwt (kg) *60 / hr
= 14* Bwt (kg) * 600ug/hr
= 14×Bwt (ml/hr ) with infusion pump
Pharmacologic Hyperemic Stimuli

**Intracoronary bolus adenosine**

- Peak effect <10sec after administration
- Short duration of action of <20secs
- Recent studies
  - 40ug in the RCA
  - 60ug in the LCA
- If FFR remains >0.80 → incremental dose escalation
  - 20~30ug increments
  - Maximum of 150ug if FFR remains 0.75~0.80
- Main side effect is transient AV block
  - RCA or dominant LCx
Pharmacologic Hyperemic Stimuli

**Intracoronary bolus adenosine**

- **Advantages**
  - Easy administration: no IV setup, no central vein
  - Rapid testing: no wait for max hyperemia

- **Limitations**
  - Too transient hyperemia: Pull back, CFR impossible
  - Dose escalation frequently necessary to achieve maximal hyperemia
IC bolus injection of adenosine in Korean

*46% of LCA lesions and 42% of RCA lesions showed additional decrease of FFR after IC bolus injection of high dose adenosine (LCA 80ug, RCA 40ug).

Practical considerations when using intracoronary bolus adenosine

- Administer a standard dose of **IC nitrate** to decrease the possibility of arterial spasm influencing the FFR
- Use a guide catheter without side holes and ensure coaxial engagement
- Ensure the analyzer is set to display beat to beat mean
- Ensure the interruption in recorded aortic pressure (Pa) is as short as possible after the IC injection
Intracoronary Continuous Adenosine Infusion
— A Novel and Effective Way of Inducing Maximal Hyperemia for Fractional Flow Reserve Measurement —

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Hyo-Soo Kim, MD, PhD; Myoung-Mook Lee, MD, PhD; Byung-Hee Oh, MD, PhD;
Young-Bae Park, MD, PhD; Yun-Shik Choi, MD, PhD; Seung-Jae Tahk, MD, PhD**

Background  Various methods are used to induce maximal hyperemia for physiologic studies, but the feasibility and efficacy of continuous intracoronary (IC) infusion of adenosine for measurement of fractional flow reserve (FFR) has not been well-defined.

Methods and Results  Patients with intermediate coronary artery stenosis were consecutively enrolled. In the phase I study, FFR was measured after 3 dosages of IC adenosine infusion (180, 240 and 300 g/min) in 30 patients. The phase II study was performed to compare the hyperemic efficacy of IC infusion (240 g/min) with IC bolus injection (40, 80 g) and intravenous (IV) infusion (140 g·kg⁻¹·min⁻¹) of adenosine in 20 patients. In the phase I study, no significant differences in FFR were observed with the 3 different doses of IC infusion (p=0.06). In the phase II study, FFR after an IC bolus injection (0.83±0.06) was significantly higher than with IV (0.79±0.07) or IC (0.78±0.09) infusion (p<0.01). However, no difference in FFR was observed for IC and IV infusions.

Conclusion  IC infusion of adenosine seems to be a safe and effective method of inducing maximal hyperemia for FFR measurement.  (Circ J 2005; 69: 908–912)

Key Words: Adenosine; Fractional flow reserve; Hyperemia
Fig 1. Continuous recording of proximal and distal pressures during the intracoronary continuous infusion of adenosine using 2 pressure wires. Fractional flow reserve was calculated by the ratio of the mean distal pressure to the mean proximal pressure in each beat.
FFR according to the different methods of adenosine administration

- IC bolus: 0.83 (P<0.01)
- IC 240: 0.78 (P=0.4)
- IV 140: 0.79
Comparison with IC bolus

* **IC bolus vs. Infusion** (n=48)

<table>
<thead>
<tr>
<th></th>
<th>FFR</th>
<th>P value</th>
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<tbody>
<tr>
<td>IC bolus</td>
<td>0.85 ± 0.07</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IC infusion</td>
<td>0.81 ± 0.08</td>
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* Borderline FFR (0.75 – 0.8) at IC bolus
  - N = 9
  - All < 0.75 during IC infusion
## Comparison with IV infusion

* Hemodynamic changes (Pa) during IC & IV infusion

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<tr>
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<th>IC infusion</th>
<th>IV infusion</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>∆BP (%)</td>
<td>- 4.1 ± 6.1</td>
<td>- 11.4 ± 12.5</td>
<td>0.03</td>
</tr>
<tr>
<td>∆Heart rate (%)</td>
<td>4.1 ± 9.1</td>
<td>6.3 ± 10.7</td>
<td>0.5</td>
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Possible “steady state hyperemia”

Pressure pullback & CFR measurement possible?
Adenosine Triphosphate (ATP)

- ATP has a short half-life in plasma and is rapidly degraded into ADP, AMP and adenosine (pro-drug)

- Yamada et al / Sondoa et al
  - 50ug of IC ATP = 10ug of IC papaverine without any significant hemodynamic or ECG changes

- De Bruyne et al.
  - ATP and adenosine equipotent with no difference in their times of onset or duration of effect
  - Increasing the IV infusion of ATP to greater than 140ug/kg/min induced a marked decline in BP in some pts.
Intracoronary papaverine

- IC papaverine induces maximal coronary vasodilation
- Longer duration of action than IC adenosine
  - Peak effect is at 10~30 sec
  - Duration of plateau is around 45~60 sec
- Recommended dosages
  - 12~16 ug in RCA
  - 16~20 ug in LCA
- IC papaverine should not be used in combination with Hexabrix as crystalization can occur
Intracoronary papaverine

- Transient QT prolongation and T-wave abnormalities
- Polymorphic VT/ VF
  - Rare & Fatal complication
  - Associated with hypokalemia
  - Avoid use with QT-prolonging drugs
Intracoronary papaverine

- **Advantages**
  - Easy administration: no IV setup required, no central vein access
  - Rapid testing: no wait for maximal hyperemia
  - Steady state hyperemia: Pull back curve & CFR

- **Limitations**
  - Wait 5min b/w measurements: Hyperemia resolves in that time
  - No more than 3 doses: limit risk for side effects
Case

- M/56
- Intermittent resting chest pain for 1mo
- Risk factor: smoking

Lab

- ECG: NSR
- Outside TMT: inadequate study
- Gated myocardial SPECT: negative
- Echocardiography
  - EF 60%, relaxation abnormality
IC bolus 40 μg
IC bolus 80 μg
IV 140ug/kg/min
IC 240ug/min
50
100

Pa mean (95)
Pd mean (67)
0.71 FFR

IV 140 μg/kg/min

Pa mean (88)
Pd mean (66)
0.75 FFR

Pa mean (78)
Pd mean (56)
0.72 FFR

54.69 CURSOR
Patients with borderline FFR with IC bolus adenosine (0.75~0.85)

Incremental dose of IC bolus or IV infusion (IC infusion?) of adenosine
Conclusions

- IV adenosine infusion is a safe, reliable and well tolerated method for the induction of maximal coronary hyperemia

- IC adenosine is an acceptable alternative but does not produce steady state maximal hyperemia

- IC papaverine is a good alternative in pts with a contraindication to adenosine
Thank you !!