How to Make Optimal Hyperemia?

: From Adenosine to Contrast

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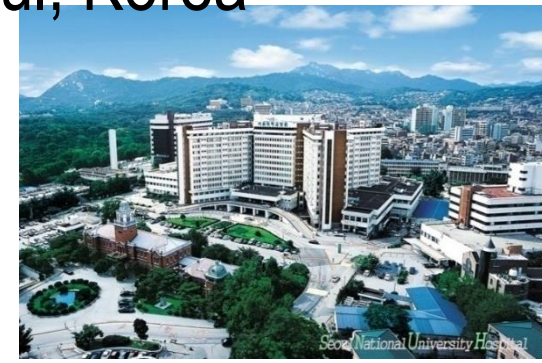


FFR and Microvascular resistance

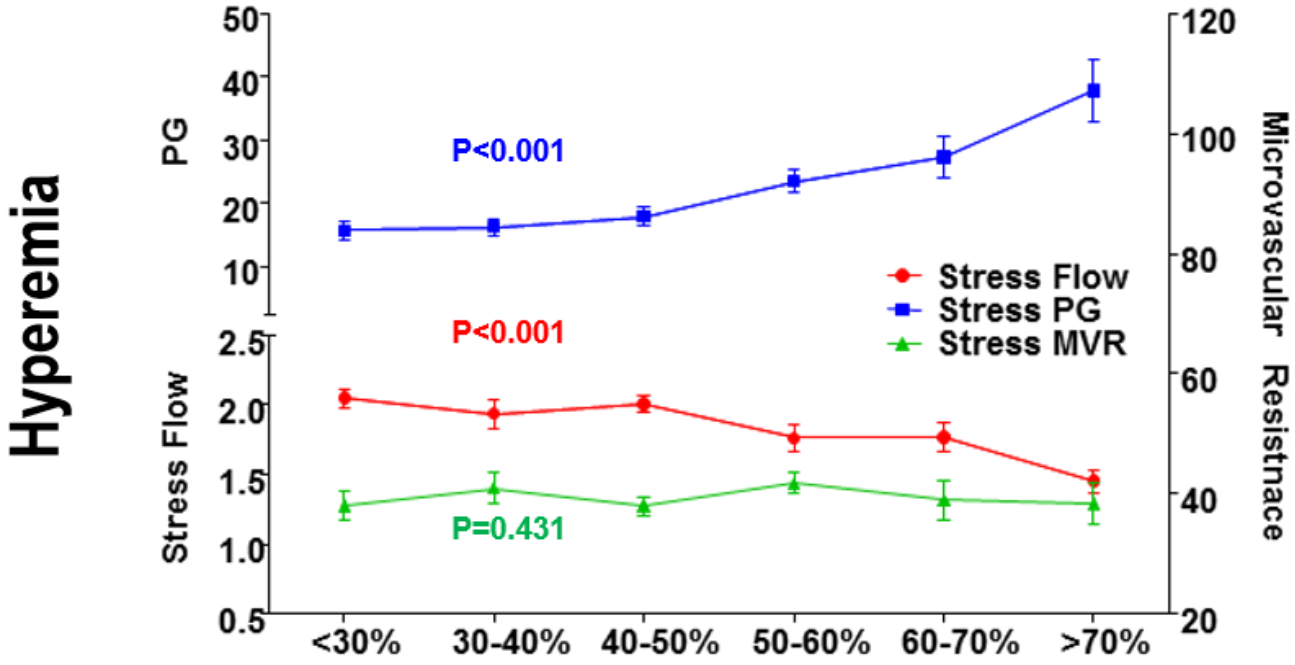
$$FFR = \frac{Q^{S}_{max}}{Q^{N}_{max}} = \frac{(Pd-Pv)/R}{(Pa-Pv)/R} = \frac{P_d}{P_a}$$

At constant Pa, determinants of Pd

- Epicardial stenosis
- Microvascular resistance

Maximal hyperemia is essential for FFR measurement!

Coronary Circulatory Response to Epicardial Stenosis



As stenosis severity increases

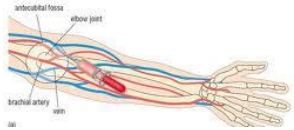
- Minimal and stable MV resistance during hyperemia
- Hyperemic flow ▼
- **Hyperemic pressure gradient ▲**

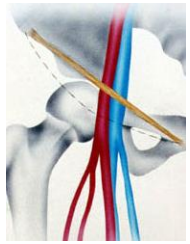
Lee JM, Koo BK, et al. Circulation 2017

Maximal hyperemia: Which and How?

Intravenous infusion

- **Adenosine, ATP** 140 μg/kg/min
- Dobutamine 20-40 μg/kg/min



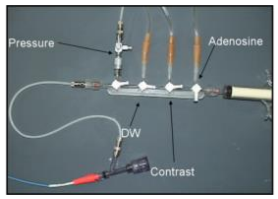


Intracoronary bolus

- Papaverine 10 - 20 mg
- **Adenosine, ATP** 20-720 μg
- Nitroprusside 0.3-0.9 μg/kg
- **Nicorandil** **2mg**

Intracoronary infusion

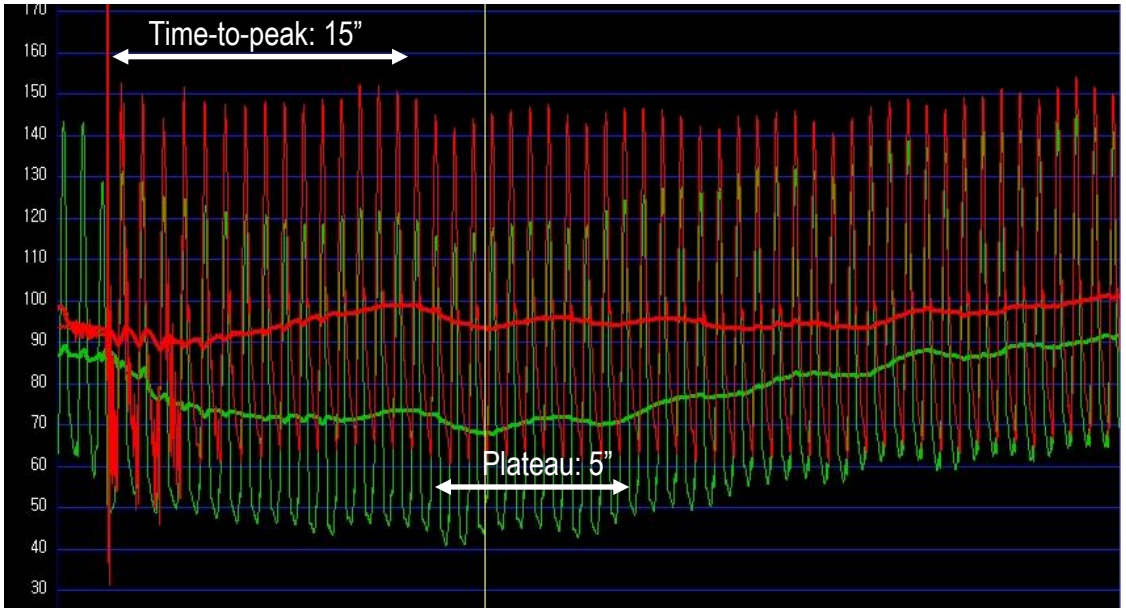
- Adenosine 240μg/min



Intravenous bolus

- **Regadenoson** 400μg

IC adenosine: the easiest, but not the best

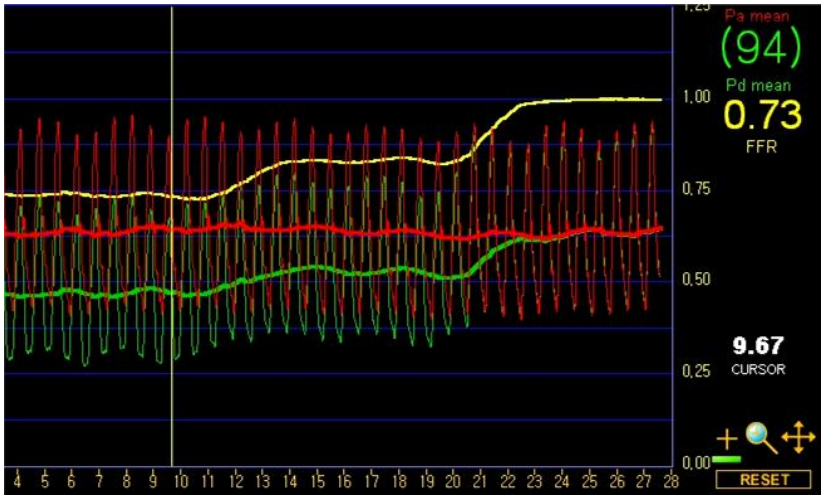


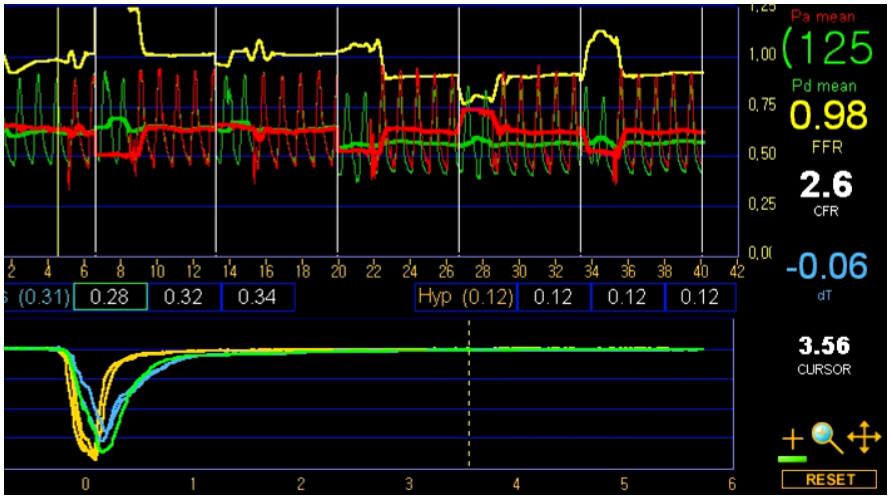
Quick, easy and inexpensive, BUT…..

- Short action time, not adequate for pressure pullback and IMR/CFR
- Less effective than IV infusion in some patients
- More frequent AV block than with IV infusion
- Difficult to use in patients with ostial disease and with a side hole guiding catheter

IV adenosine: “Gold standard”

- Very good safety profile
- One dose (140 μg/kg/min) is adequate for almost all patients
- Sustained hyperemia for pressure pullback and for CFR/IMR





False beliefs about “HYPEREMIA”

- Hyperemic agents are expensive.
- Hyperemia is inconvenient due to time consuming set-up.
- Sustained hyperemia always requires central vein access.
- FFR/IMR cannot be measured in patients with contraindications to adenosine such as AV block, severe asthma…..
- Hyperemia is not reliable nor reproducible.

It is not expensive and simple to use!

6mg ≈ 8 USD

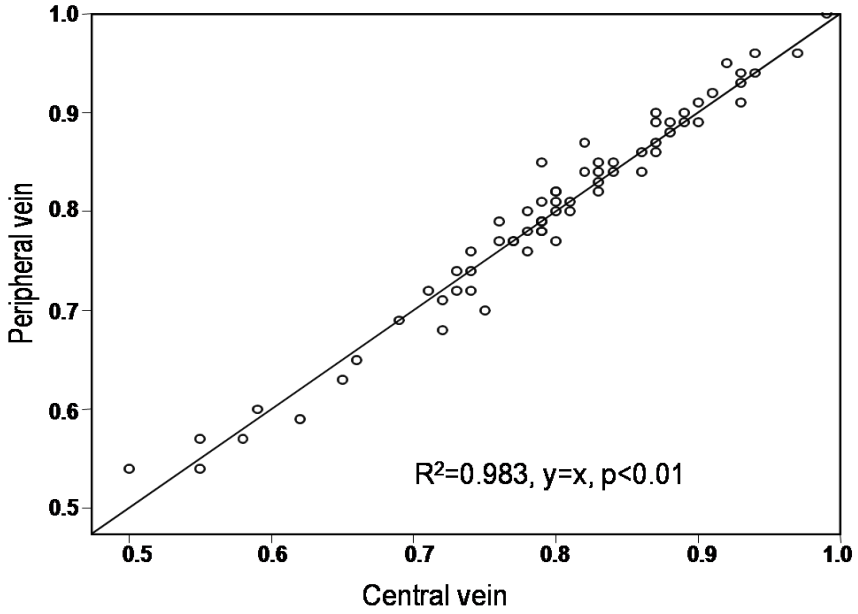
90mg ≈ 10 USD

IV adenosine can be prepared by the hospital pharmacy at a price of less than 5% of the commercial price….

Nico Pijls

Adenosine infusion via Forearm vein

(most commonly used venous access)



	Femoral vein	Forearm vein	P value
FFR	0.80±0.10	0.80±0.11	NS
FFR <0.8	27 (44%)	26 (42%)	NS
IMR	11.8±10.9	11.3±9.2	NS

Seo MK, Koo BK, et al. Circulation intervention, 2012

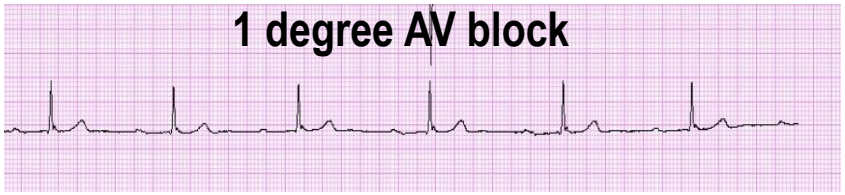
- Peripheral IV infusion can be the alternative to central IV infusion when the forearm is extended (uninterrupted venous return is guaranteed) and a large needle is used.

FFR cannot be measured in some patients ! ?

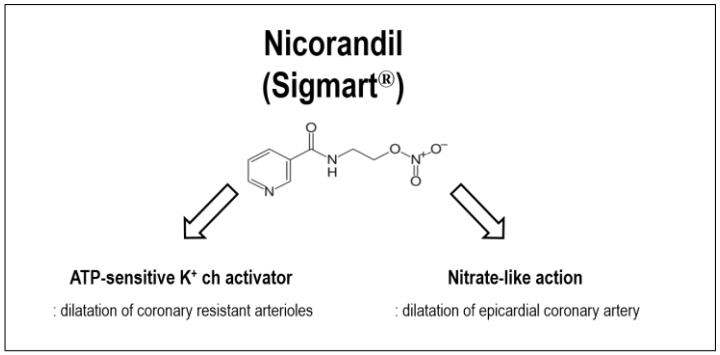
What to do with (relative) contraindications for adenosine?

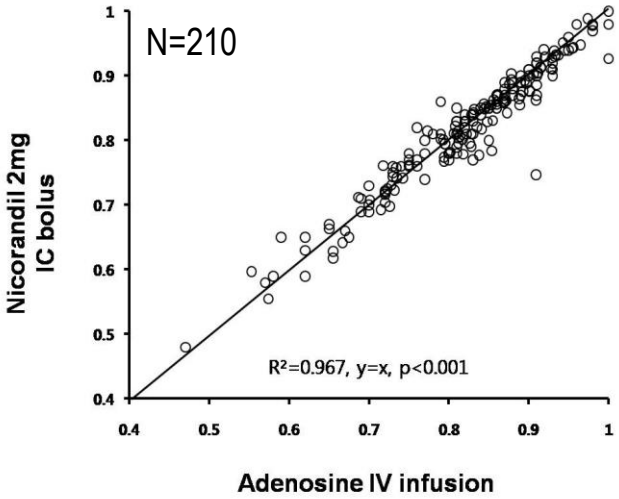
Severe symptomatic asthma

On levocetirizine, seretide diskus, ventolin, fluticasone, erdosteine…….



Nicorandil: a novel agent

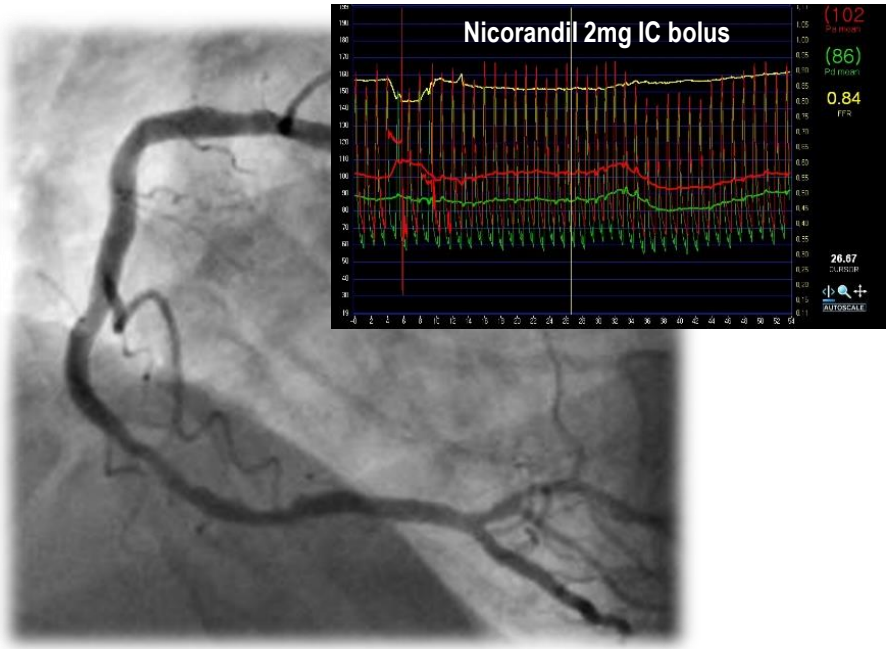




	Nicorandil bolus 2 mg	Adenosine IV infusion	P value
Fractional Flow Reserve	**0.82 ± 0.10**	**0.82 ± 0.10**	**0.33**
Time to max hyperemia, s	**18.3 ± 6.1**	**43.8 ± 16.0**	**<0.001**
Plateau time, s	**27.3 (IQR 17-33)**	**-**	
IMR	**17.2 ± 7.6**	**18.3 ± 8.7**	**0.29**

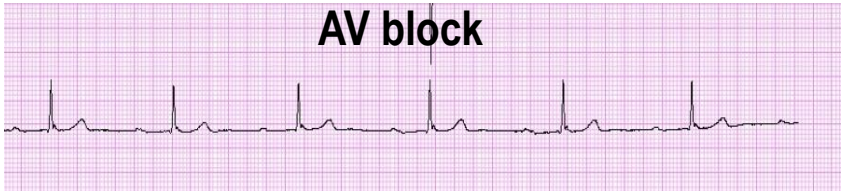
Jang HJ, Koo BK, et al. Eur Heart J 2013

What to do with (relative) contraindications for adenosine?



Severe symptomatic asthma

On levocetirizine, seretide diskus, ventolin, fluticasone, erdosteine…….



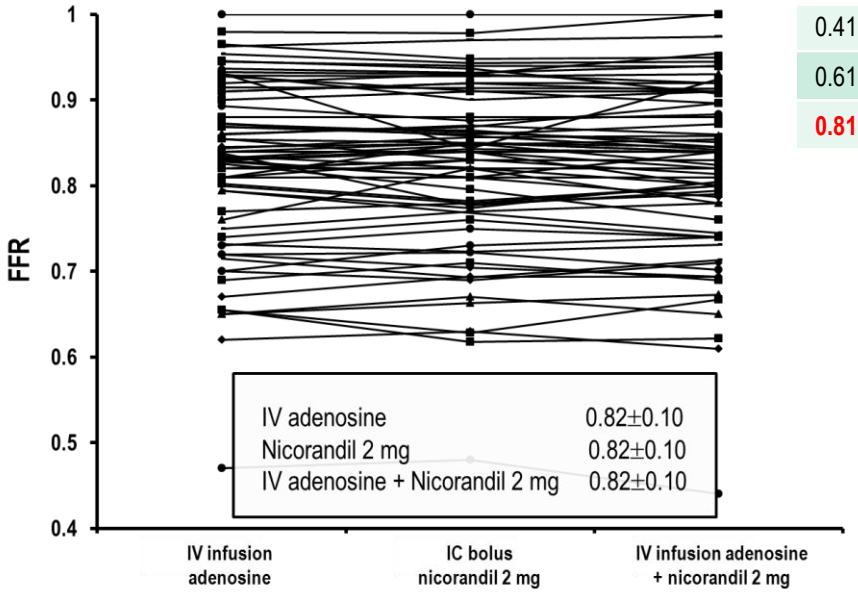
Hyperemia is not reliable nor reproducible! ?

Stability and reproducibility of FFR (n=389)

with different hyperemic drugs and different routes

	Kappa	P-value
Adenosine vs. Nicorandil	**0.80**	<0.001
ATP vs. Nicorandil	**0.84**	<0.001
Adenosine IV: Central vs. Peripheral	**0.82**	<0.001

Kappa	Interpretation
0.41 – 0.60	Moderate agreement
0.61 – 0.80	Substantial agreement
0.81 – 1.00	**Almost perfect agreement**



No change of FFR with different drugs acting on different receptors

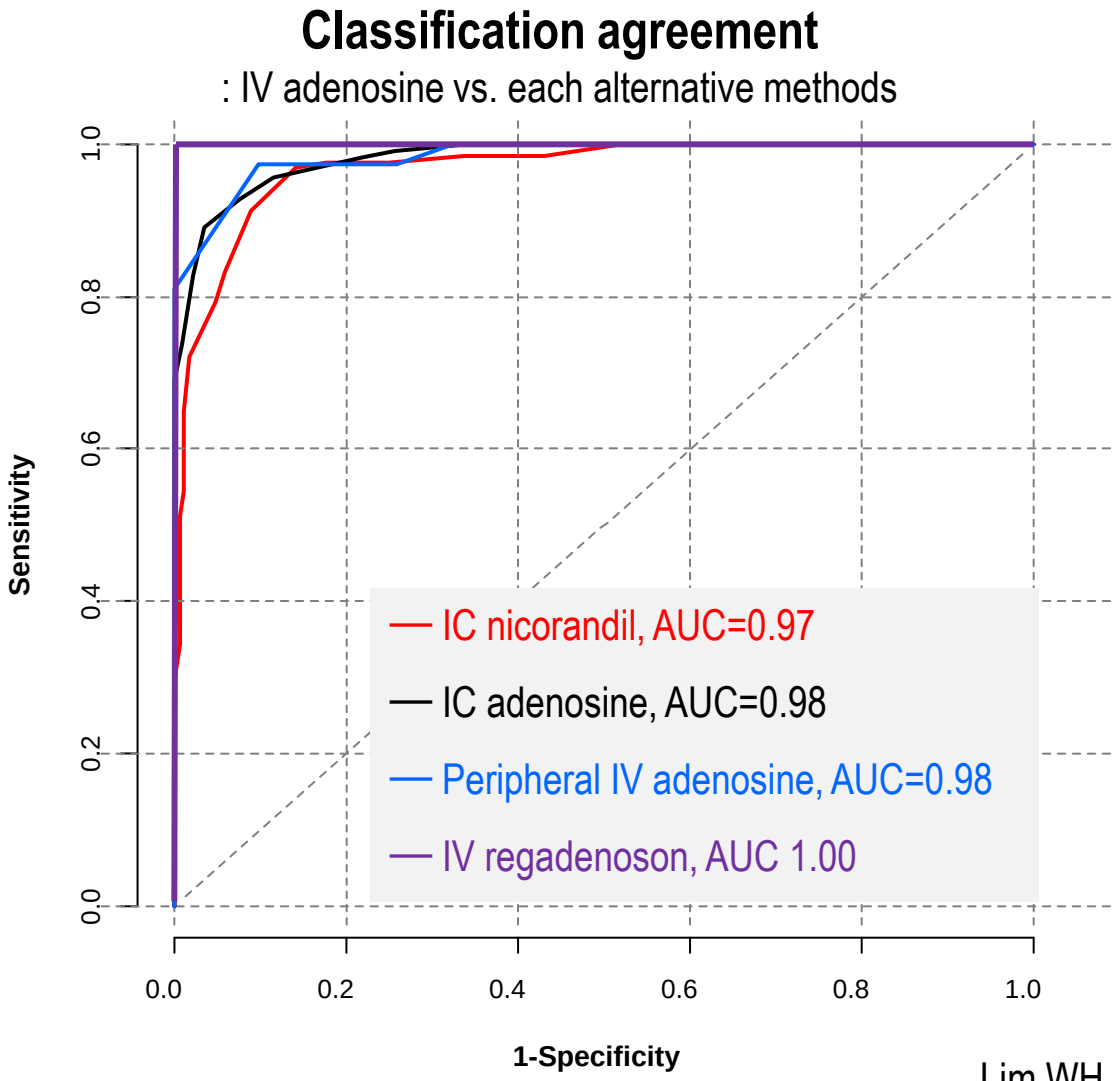
Lim WH, Koo BK, et al. CCI 2014

Jang HJ, Koo BK, et al. Eur Heart J 2013

Hyperemia is not reliable nor reproducible! ?

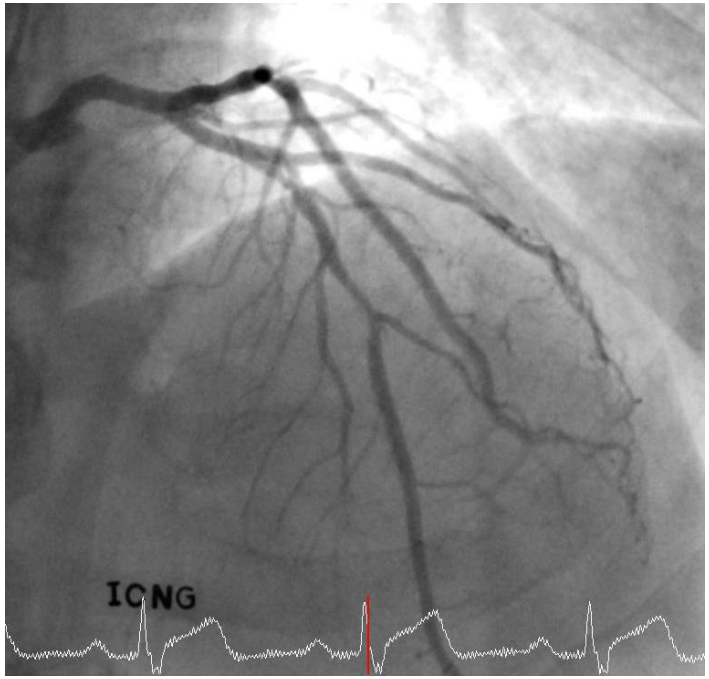
Stability and reproducibility of FFR

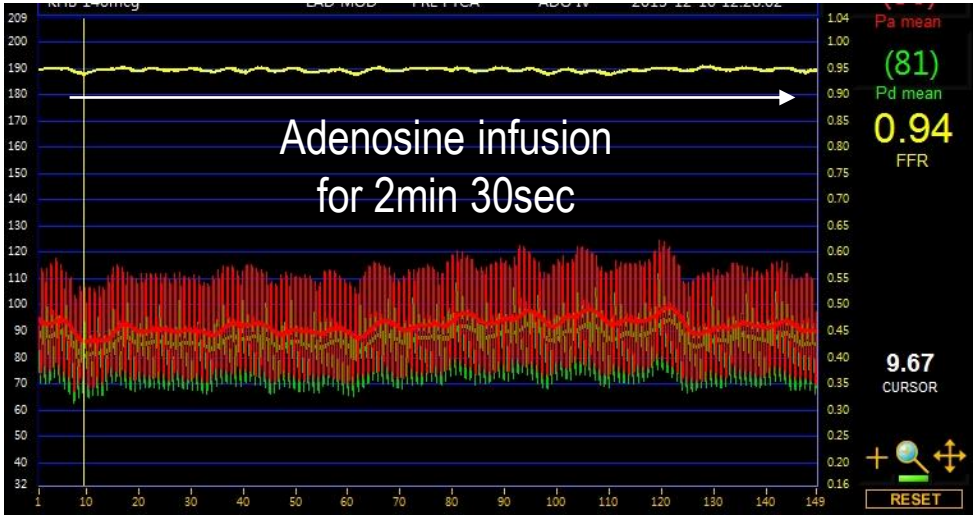
with different hyperemic drugs and different routes

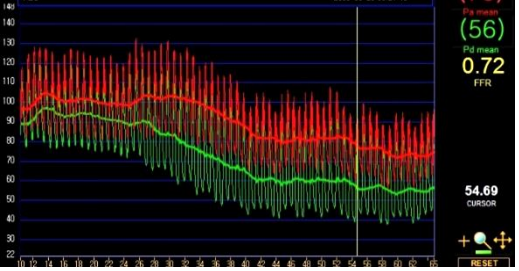


Lim WH, Koo BK, et al. CCI 2014

Is this hyperemia optimal?





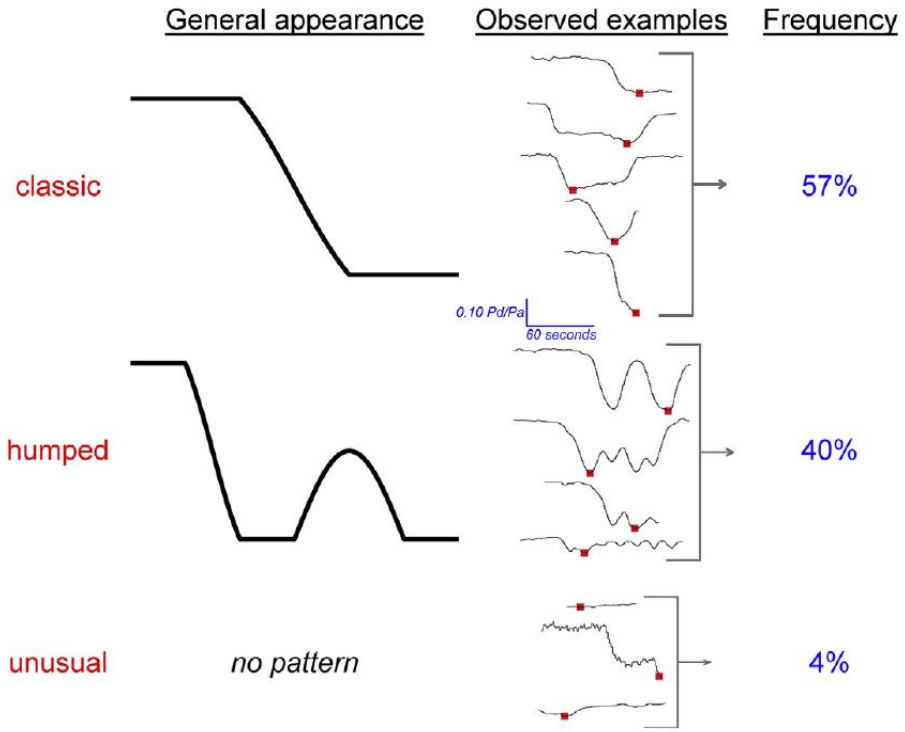


Hemodynamic changes with adenosine

	Femoral vein	Forearm vein	P value
Δ Blood pressure	-9.8±8.0 %	-9.6±6.3 %	0.86
Δ Heart rate	5.5±6.7 %	7.0±7.2 %	0.07
AV block	1 (1.6 %)	1 (1.6 %)	<0.0001

Seo MK, Koo BK, et al. Circ Cardiovasc Interv 2012

Patterns of pressure changes and Concept of "Smart Minimum"



"Smart minimum" FFR

- The lowest average of 5 consecutive cardiac cycles of sufficient quality within a run of 9 consecutive quality beats.
- Excellent repeatability: bias 0.001, SD 0.018

Johnson N, et al. JACC intervention 2015

Contrast FFR (cFFR)

Physiologic Basis for Assessing Critical Coronary Stenosis

Instantaneous Flow Response and Regional Distribution During Coronary Hyperemia as Measures of Coronary Flow Reserve

K. LANCE GOULD, MD
KIRK LIPSCOMB, MD
GLEN W. HAMILTON, MD

Seattle, Washington

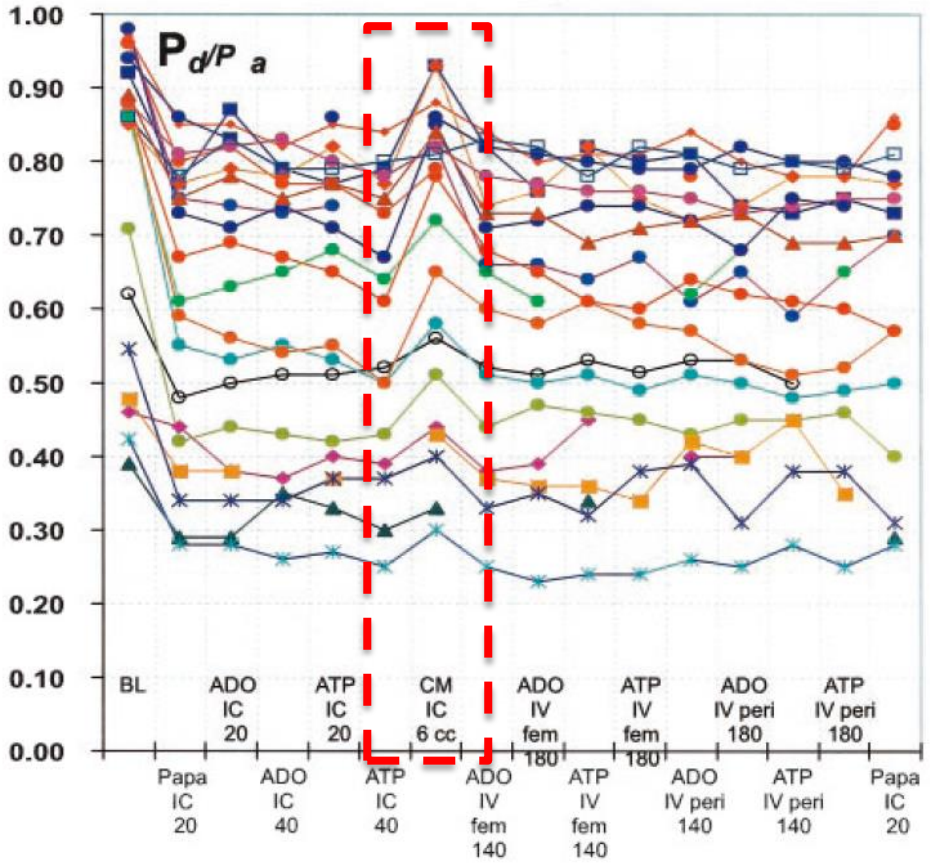
Quantitative hemodynamic assessment of coronary stenosis has not been previously reported. Resting coronary blood flow and its regional distribution are insensitive indexes for determining critical stenosis, but flow response to a hyperemic stimulus quantifies restrictions on maximal flow due to coronary arterial lesions. Coronary flow responses to temporary occlusion and to selective main coronary arterial injection of sodium diatrizoate (Hypaque-M 75 percent) were studied in 12 consecutive dogs with a surgically implanted electro-

Contrast FFR (cFFR)

Intracoronary and Intravenous Adenosine 5′-Triphosphate, Adenosine, Papaverine, and Contrast Medium to Assess Fractional Flow Reserve in Humans

Bernard De Bruyne, MD, PhD; Nico H.J. Pijls, MD, PhD; Emanuele Barbato, MD; Jozef Bartunek, MD, PhD; Jan-Willem Bech, MD; William Wijns, MD, PhD; Guy R. Heyndrickx, MD, PhD

Background—Inducing both maximal and steady-state coronary hyperemia is of clinical importance to take full advantage



2003 Circulation

Continuum of Vasodilator Stress From Rest to Contrast Medium to Adenosine Hyperemia for Fractional Flow Reserve Assessment

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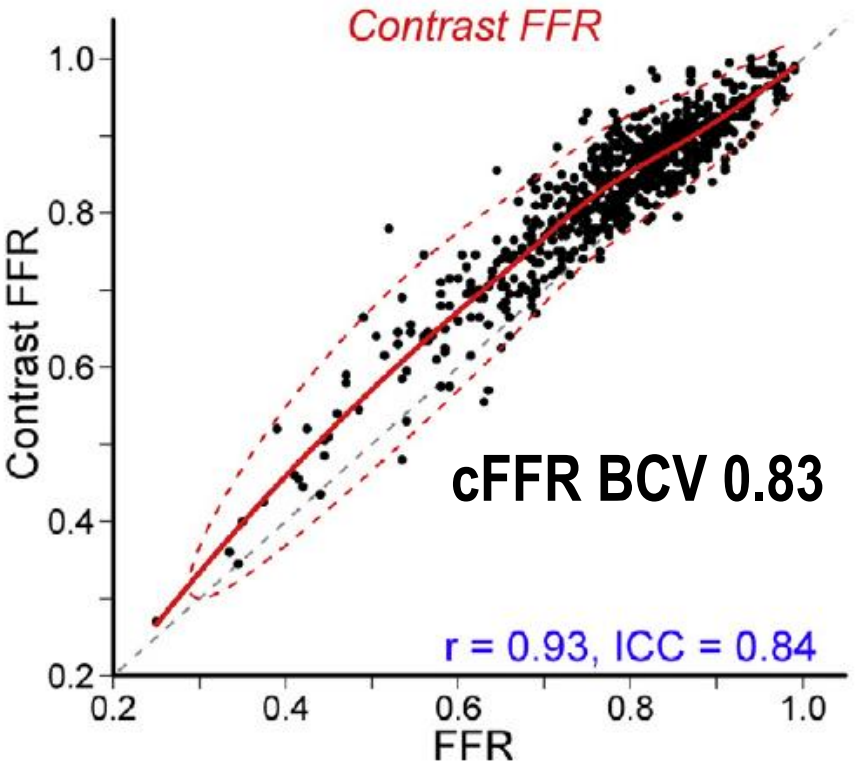

2016 JACC Intv

Optimal hyperemia for FFR

1. Optimal hyperemia is the key for accurate FFR measurement.

2. Hyperemia cannot be a barrier for FFR measurement.

2. IV infusion of adenosine is the gold standard for FFR/CFR/IMR measurement.

3. Other routes and drugs can be used when needed.

   - Adenosine: IC bolus, IC infusion
   - Sigmart, papaverine IC bolus
   - Regadenosone IV bolus
   - Contrast

4. When doubtful about optimal hyperemia,

   1) Check the infusion system and solution

   2) Increase the dose of hyperemic agent

   3) Use the different route of adminstration or different drug