

Practice and Application of FFR in the All-day Cath lab

Hyperemia

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FFR and Microvascular resistance

$$\text{FFR} = \frac{Q_{max}^S}{Q_{max}^N} = \frac{(P_d - P_v)/R}{(P_a - P_v)/R} = \frac{P_d}{P_a}$$

At constant P_a , determinants of P_d

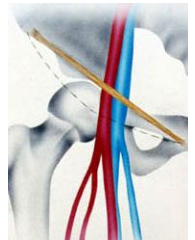
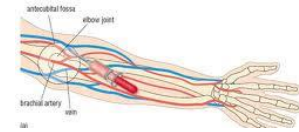
- Epicardial stenosis
- **Microvascular resistance**

Maximal hyperemia is essential for FFR measurement!

Maximal hyperemia: Which and How?

Intravenous infusion

- Adenosine, ATP 140 $\mu\text{g}/\text{kg}/\text{min}$
- Dobutamine 20-40 $\mu\text{g}/\text{kg}/\text{min}$



Intracoronary bolus

- Papaverine 10 - 20 mg
- Adenosine, ATP 20-720 μg
- Nitroprusside 0.3-0.9 $\mu\text{g}/\text{kg}$
- Nicorandil 2mg

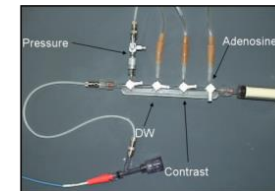


Intracoronary infusion

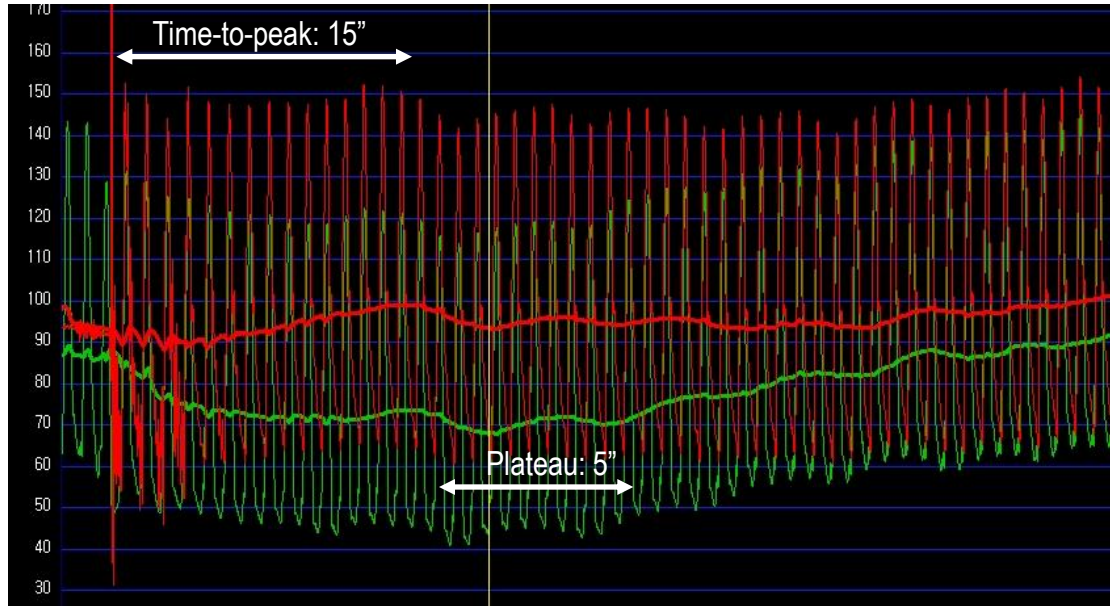
- Adenosine 240 $\mu\text{g}/\text{min}$

Intravenous bolus

- Regadenoson 400 μg



IC adenosine: the easiest, but not the best



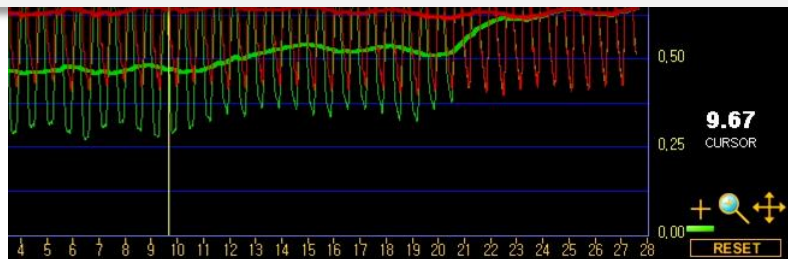
Quick, easy and inexpensive, BUT.....

- 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
- Inaccurate with side hole guiding catheter

IV adenosine: “Gold standard”

- Very good safety profile

It seems to be simple and straightforward, but why some people still believe that “HYPEREMIA” is a barrier?



Requires at least > 20 seconds

False beliefs about “HYPEREMIA”

- Hyperemia always requires large amount of adenosine which is expensive.
- Hyperemia is inconvenient due to time consuming set-up.
- Sustained hyperemia requires central vein access which is not risk-free.
- I don't use FFR as I prefer trans-radial intervention
- 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 expensive!



6mg \approx 8.0 USD

TABLE I. Dosage Table for IV Adenosine at 140 μ g/kg/min

Weight (lb)	Weight (kg)	Infusion (ml/hr)
99	45	378
110	50	420
121	55	462
132	60	504
143	65	546
154	70	588
165	75	630
176	80	672
187	85	714
198	90	756
209	95	798
220	100	840
231	105	882
243	110	924
254	115	966
265	120	1008

10min infusion
= 98mg \approx 130 USD

It is not expensive and simple to use!



6mg \approx 8 USD



90mg \approx 10 USD



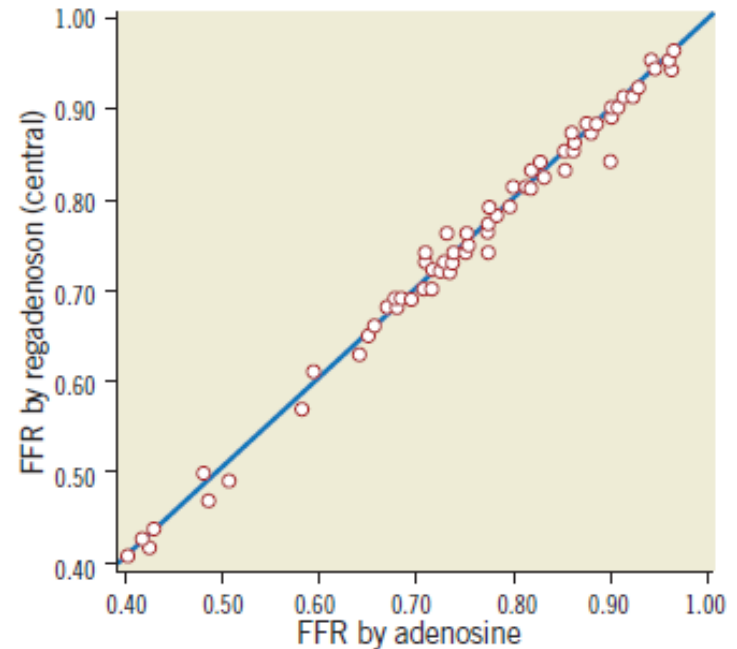
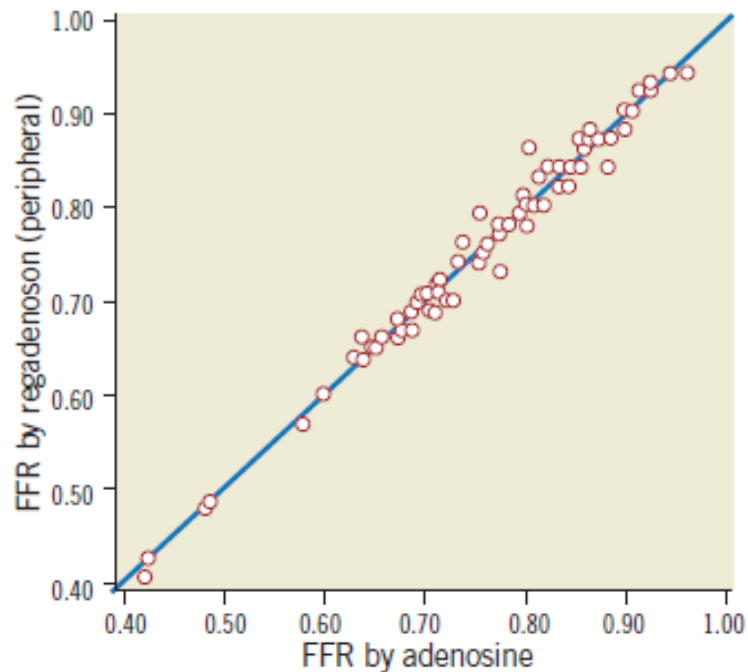
IV adenosine can be prepared by the hospital pharmacy at a price of less than 5% of the commercial price....

Nico Pijls

It will be more easier and simpler...

Regadenoson

- Selective A_{2A} – receptor antagonist
- Rapid onset and simple administration: IV bolus 400 μ g



Van Nunen, Pijls N, et al. Eurointervention 2014 in press

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Adenosine infusion via Antecubital vein

Clin Res Cardiol (2009) 98:717–723
DOI 10.1007/s00392-009-0056-7

ORIGINAL PAPER

Adenosine-induced maximal coronary hyperemia for myocardial fractional flow reserve measurements: comparison of administration by femoral venous versus antecubital venous access

Michael Lindstaedt · Waldemar Bojara ·

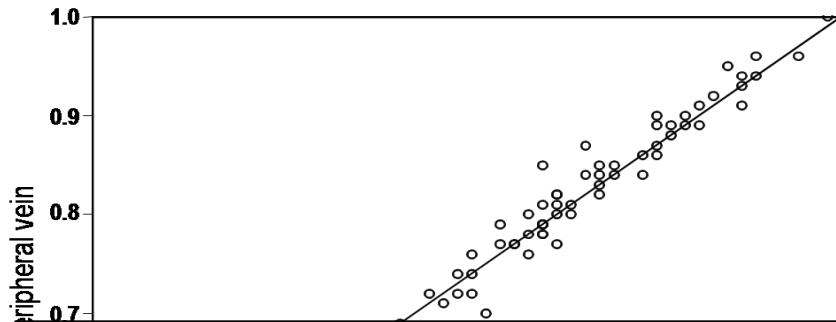
Table 2 Data on FFR measurement results in 50 patients with respect to different applications of the hyperemic stimulus

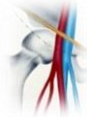

Adenosine application	FFR		Time to peak hyperemia (s)	
	Mean	STD	Mean	STD
Antecubital 140ug/kg/min	0.7504	0.11	61	27
Antecubital 170ug/kg/min	0.7440	0.11	52	23
Femoral 140ug/kg/min	0.7388	0.11	66	25

Lindstaedt et al. Clin Res Cardiol 2009

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

- Peripheral IV infusion can be an alternative to central IV infusion when the forearm is extended (uninterrupted venous return is guaranteed) and a large needle is used.
- When doubtful, higher dose can be helpful.

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Clinical scenario when adenosine is contraindicated...

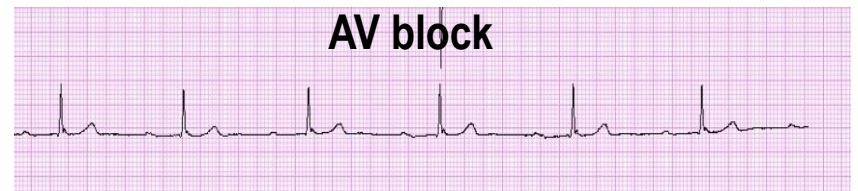


Severe symptomatic asthma

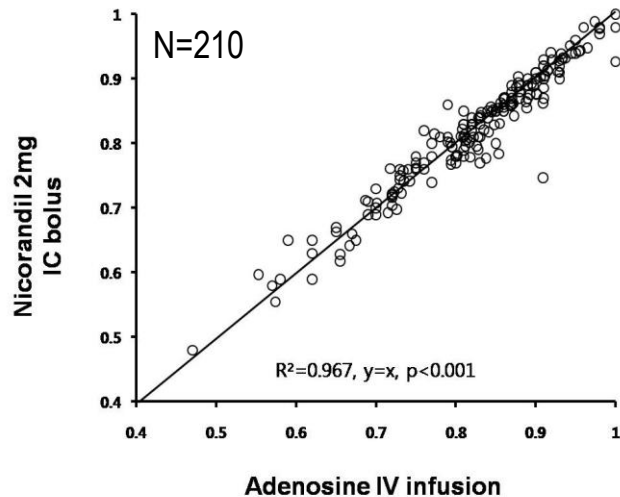
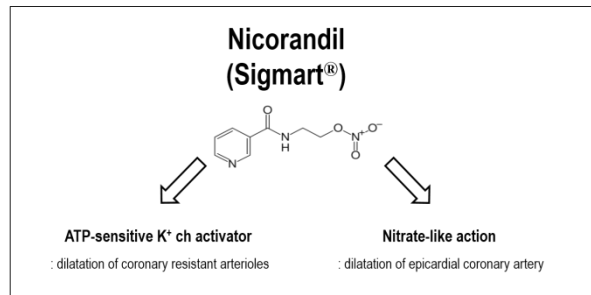
On levocetirizine, seretide diskus, ventolin, fluticasone, erdosteine.....



AV block



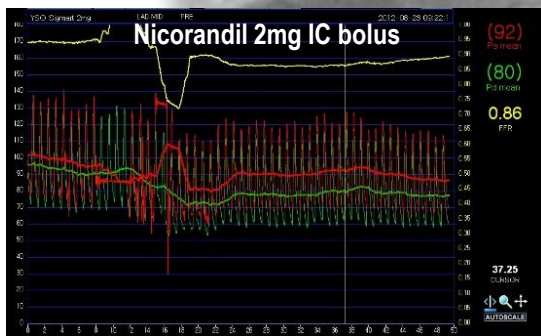
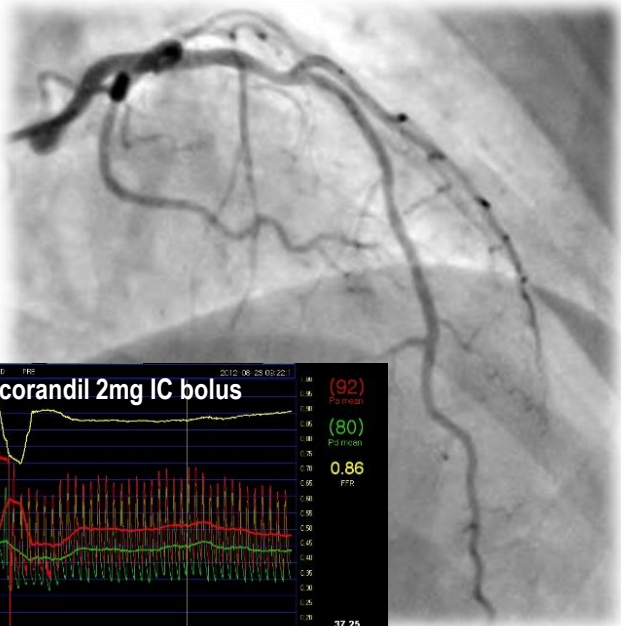
Nicorandil: a novel agent



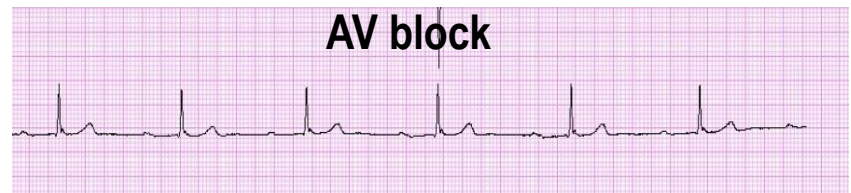
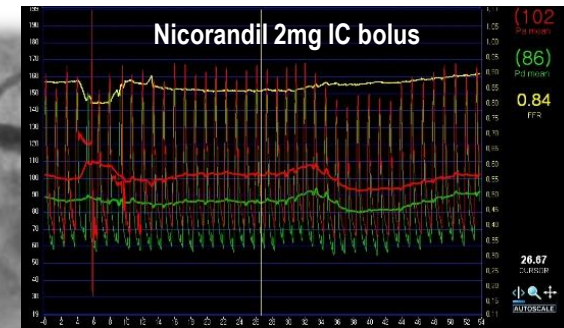
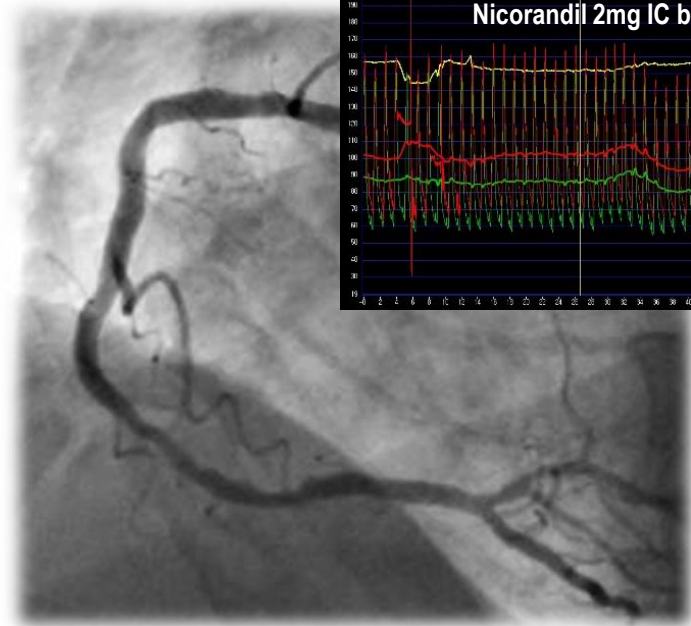
	Nicorandil bolus 2 mg	Adenosine IV infusion	P value
Fractional Flow Reserve	0.82 ± 0.10	0.82 ± 0.10	0.33
Time to max hyperemia, s	18.3 ± 6.1	43.8 ± 16.0	<0.001
Plateau time, s	27.3 (IQR 17-33)	-	
IMR	17.2 ± 7.6	18.3 ± 8.7	0.29

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

Clinical scenario when adenosine is contraindicated...



Severe symptomatic asthma
On levocetirizine, seretide diskus, ventolin, fluticasone, erdoستeine.....



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Is “HYPEREMIA” maximal, reliable, and reproducible?

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CLINICAL RESEARCH

Fractional Flow Reserve–Guided Revascularization

Practical Implications of a Diagnostic Gray Zone and Measurement Variability on Clinical Decisions

Ricardo Petraco, MD,* Savan Sen, MBBS,* Sukhinder Nijjer, MBChB*

REVIEWS

Fractional flow reserve as a surrogate for inducible myocardial ischaemia

Tim P. van de Hoef, Martijn Meuwissen, Javier Escaned, Justin F. Davies, Maria Siebes, Jos A. F. Spaan

Results Outside the [0.75 to 0.85] FFR range, measurement certainty of a single FFR result is >95%. However, closer to its cut-off, certainty falls to less than 80% within 0.77 to 0.83, reaching a nadir of 50% around 0.8. In clinical practice, that means that each time a single FFR value falls between 0.75 and 0.85, there is a chance that the FFR-derived revascularization recommendation will change if the

Adenosine and coronary vasodilatation

The assumption that the administration of adenosine in a standardized dose induces complete elimination of vascular tone in all patients is challenged by several well-known mechanisms that have an important role in daily clinical practice. First, α -adrenergic vasoconstriction

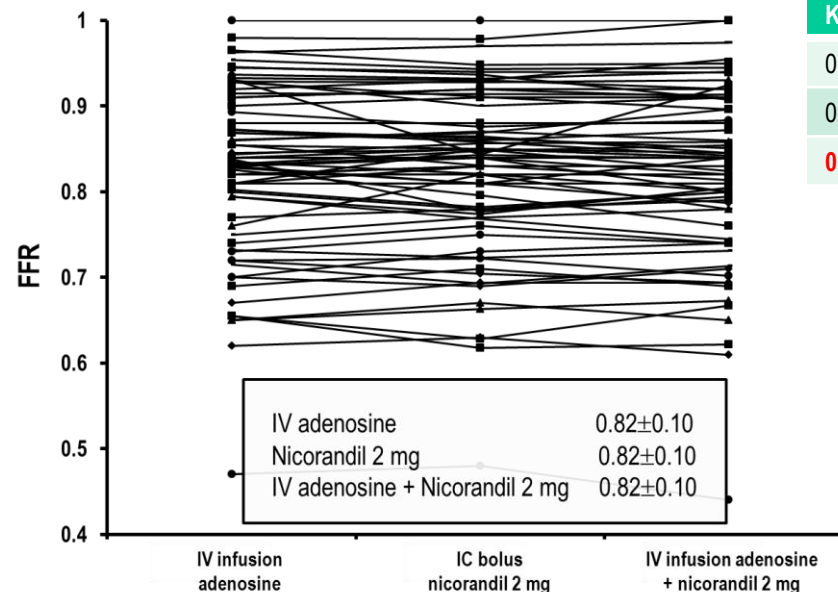
may occur primarily through activation of receptors of endothelin-1.⁹² Nevertheless, and contrary to common belief, adenosine could be intrinsically unable to induce true maximal vasodilatation of the coronary vascular bed and, therefore, to induce a true maximal hyperaemic state in the coronary circulation.⁹³ Consistent

with this theory, hyperaemic microvascular resistance during vasodilatation induced by a standardized dose of adenosine is highly variable between patients,⁶² and even between adjacent perfusion territories within the same patient.^{63,64} Ultimately, the extent of the hyperaemic

Stability and reproducibility of FFR (n=389)

with different hyperemic drugs, different routes and different time

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

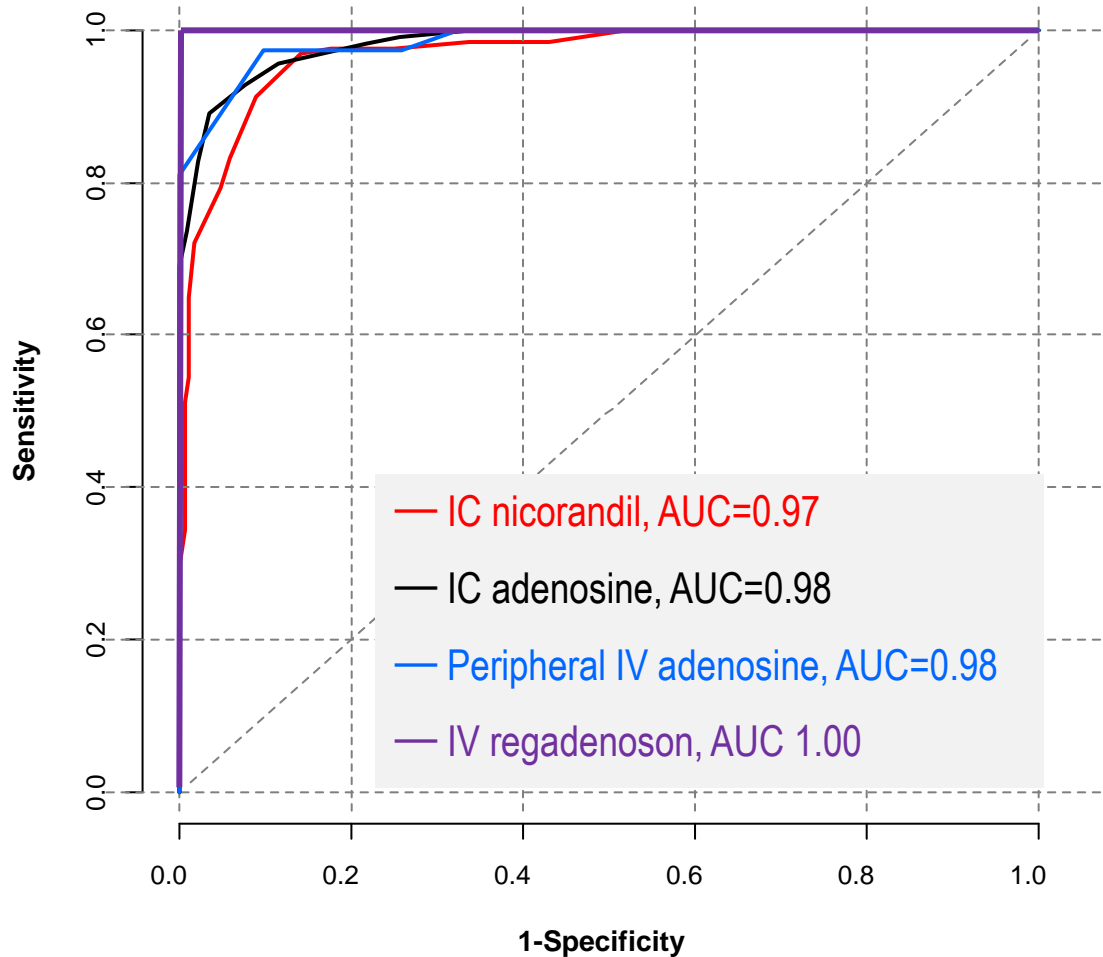
Lim WH, Koo BK, et al. CCI 2014 in press
Jang HJ, Koo BK, et al. Eur Heart J 2013

Stability and reproducibility of FFR

with different hyperemic drugs, different routes and different time

Classification agreement

: IV adenosine vs. each alternative methods



Maximal hyperemia for FFR

1. Maximal hyperemia is the key for accurate measurement of FFR.
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: IV infusion via large peripheral vein, IC bolus, IC infusion
 - Sigmart, papaverine IC bolus
 - Regadenosone IV bolus
4. When doubtful about maximal hyperemia,
 - 1) Check the infusion system and solution
 - 2) Increase the dose of hyperemic agent
 - 3) Use the different route of administration or different drug