Invasive Physiologic Assessment

: FFR, CFR, iFR and IMR

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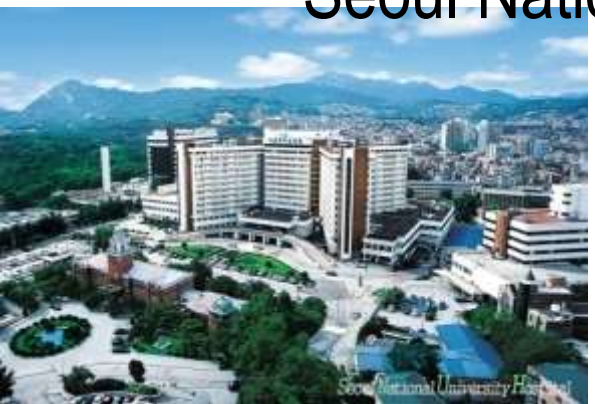
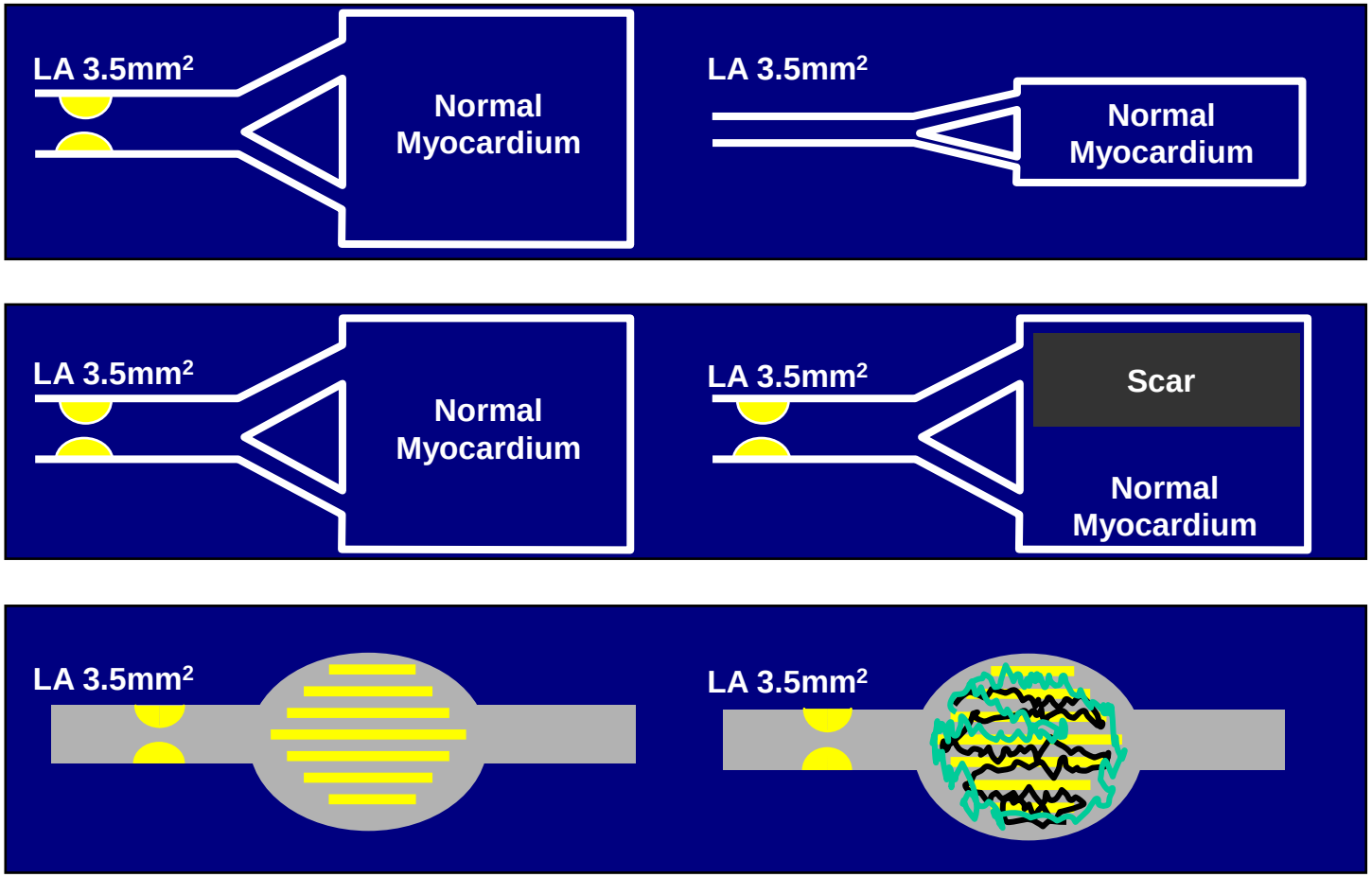


관혈적 생리학적 검사들

- **FFR**, Fractional Flow Reserve, 분획혈류 예비력
- **CFR**, Coronary Flow Reserve, 관상동맥 혈류예비력
- **iFR**, Instantaneous Flow Ratio, 동시 혈류비
- **IMR**, Index of Microcirculatory Resistance, 미세순환 저항지수

생리학적 검사 또는 기능적 검사의 의미

Same stenosis, same functional significance ?



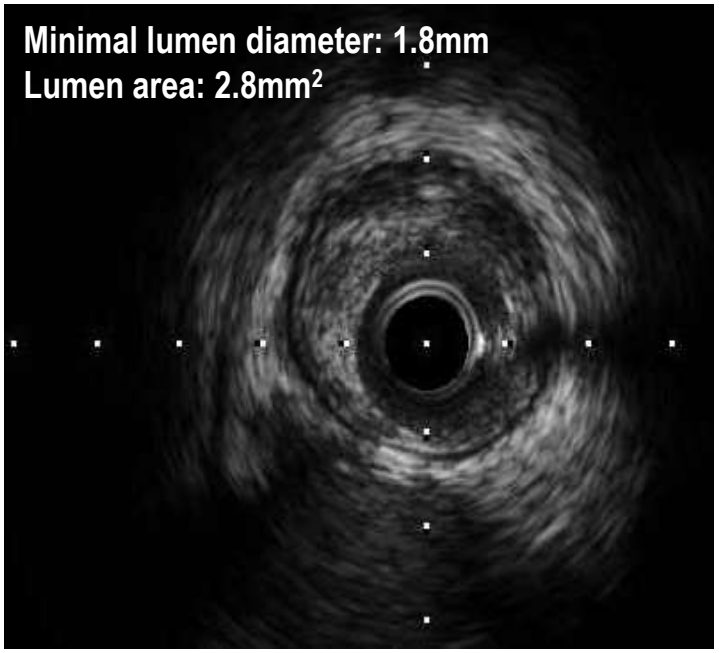
LA: Lumen cross sectional area

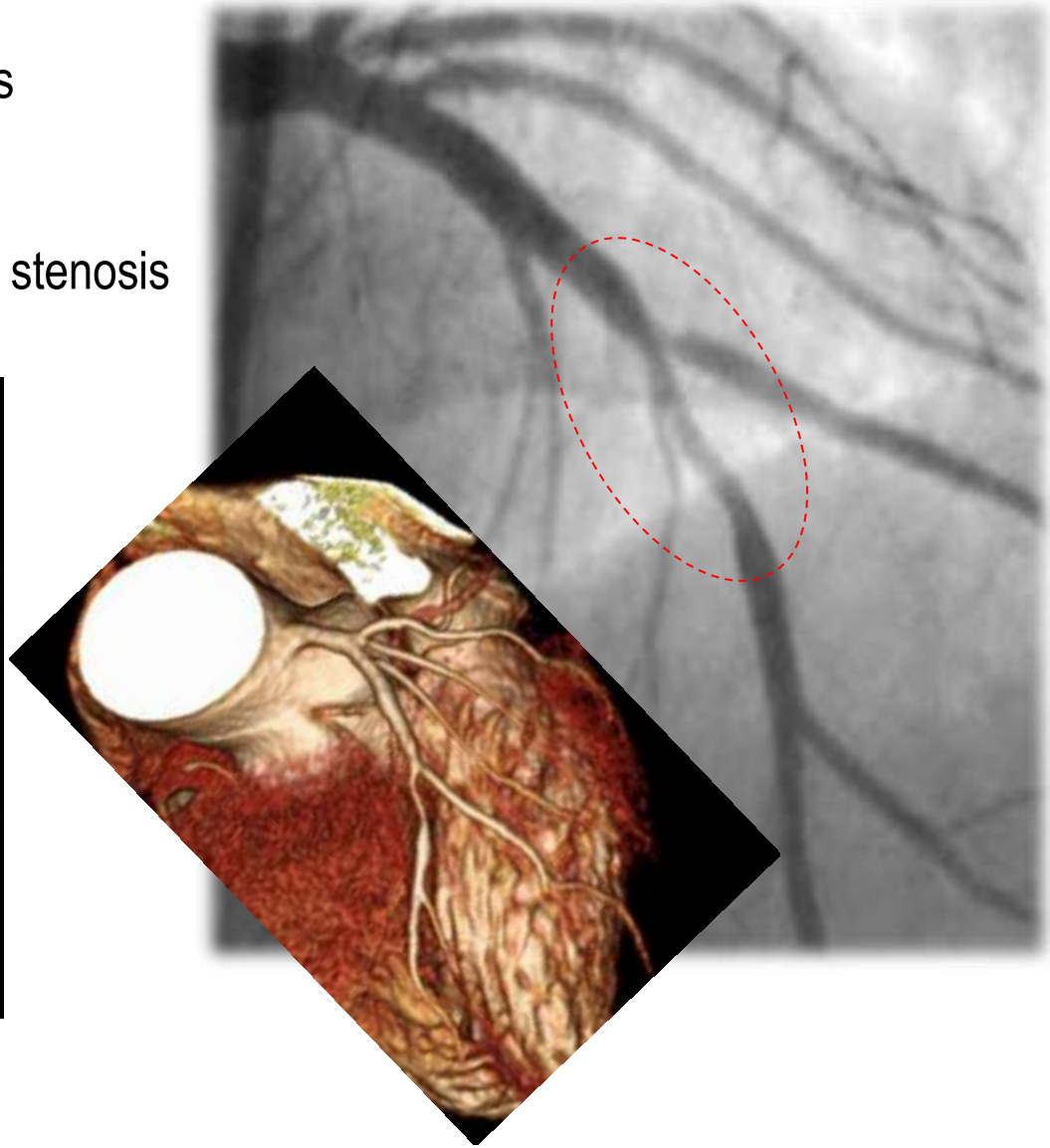
Is this lesion significant?

CT angiography: **significant** stenosis

Angiography: **significant** stenosis

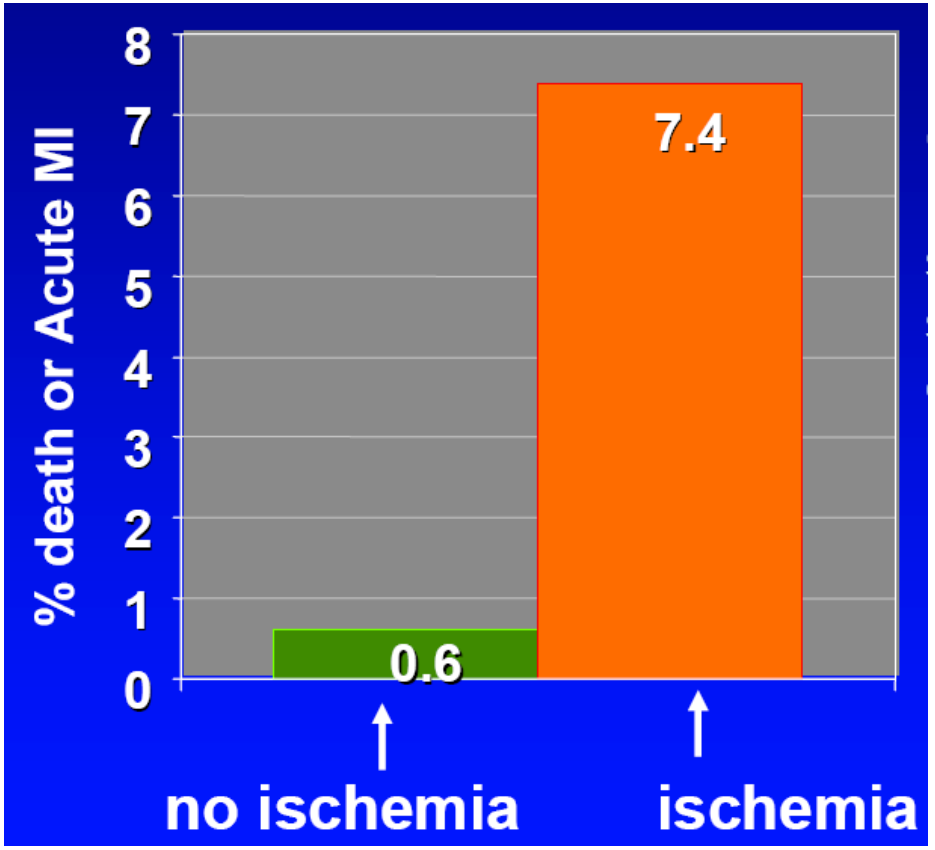
Intravascular ultrasound: **significant** stenosis





환자의 예후에 가장 중요한 것은?

The most important prognostic factor is **"Presence of Ischemia"!**



Iskander, et al. JACC 1998

FFR, Fractional Flow Reserve, 분획혈류예비력

- Since 2003

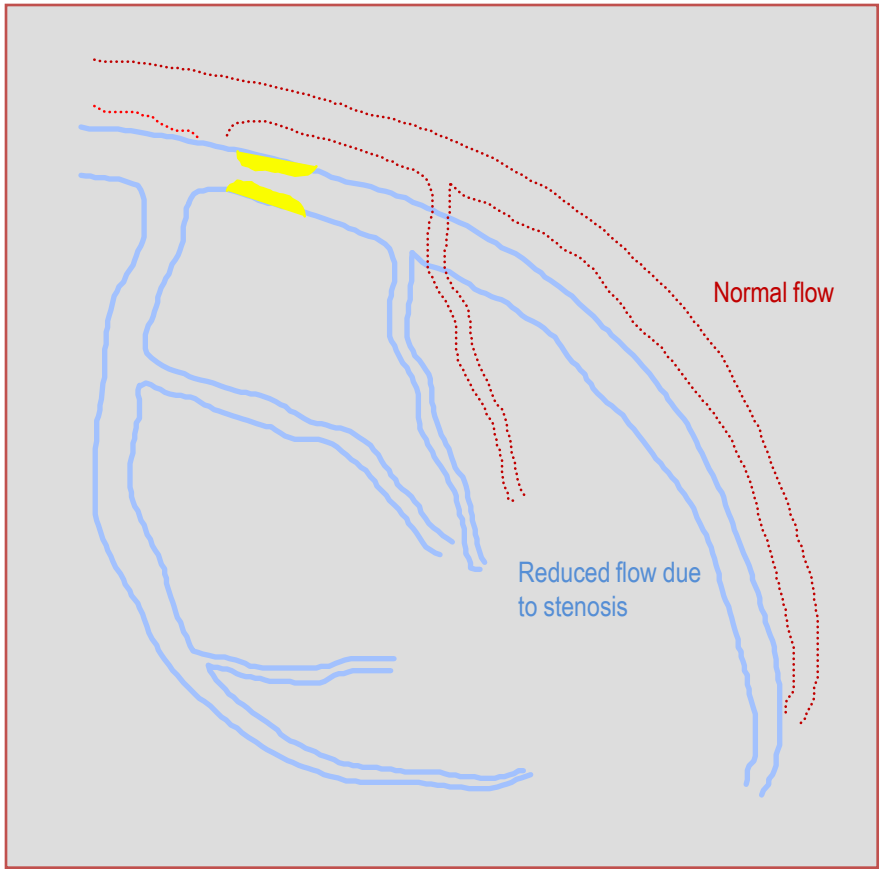
FFR, Fractional Flow Reserve, 분획혈류예비력

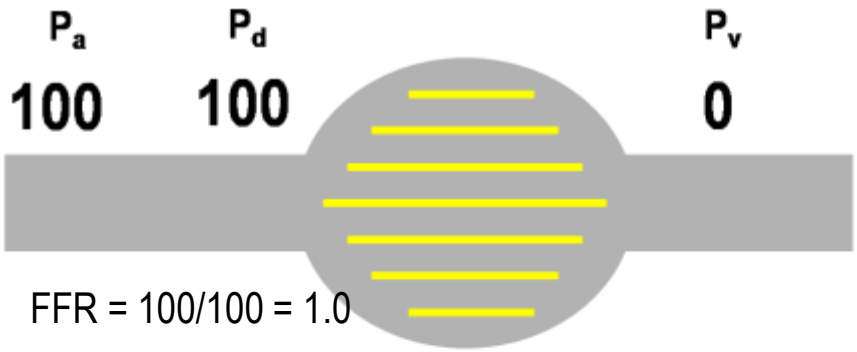
- Since 2003

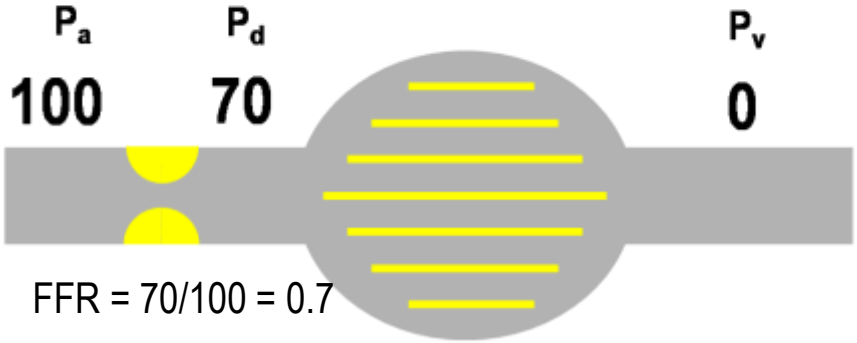
  : 정말 좋은데…. 표현할 방법이 없네…

Fractional Flow Reserve (FFR)

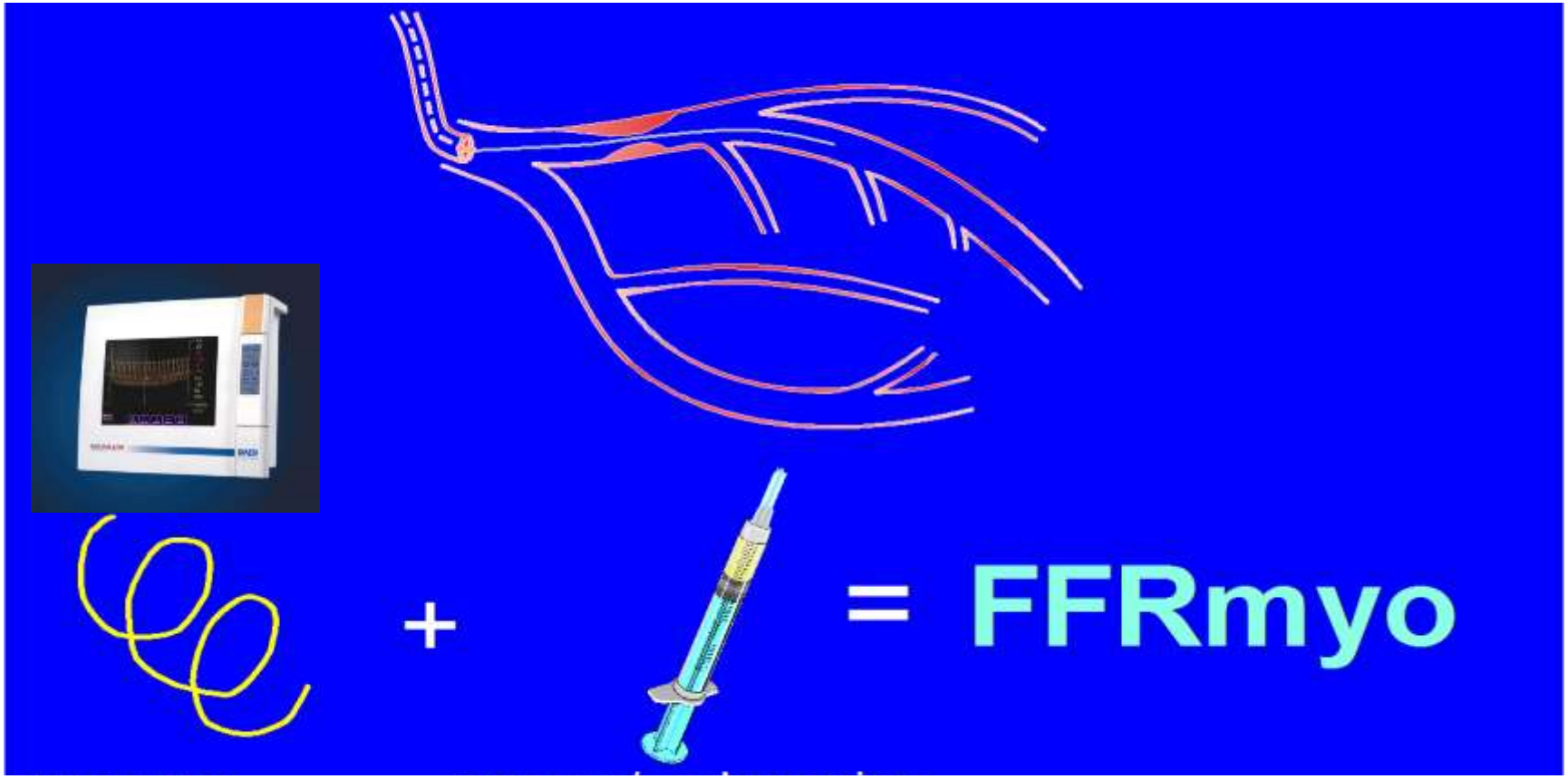
$$FFR = \frac{\text{Maximum flow in presence of stenosis}}{\text{Normal maximum flow}} = \frac{Q^{S}_{max}}{Q^{N}_{max}} = \frac{(Pd-Pv)/R}{(Pa-Pv)/R} = \frac{\text{Distal Pr } (P_d)}{\text{Proximal Pr } (P_a)}$$







Application in the cath lab



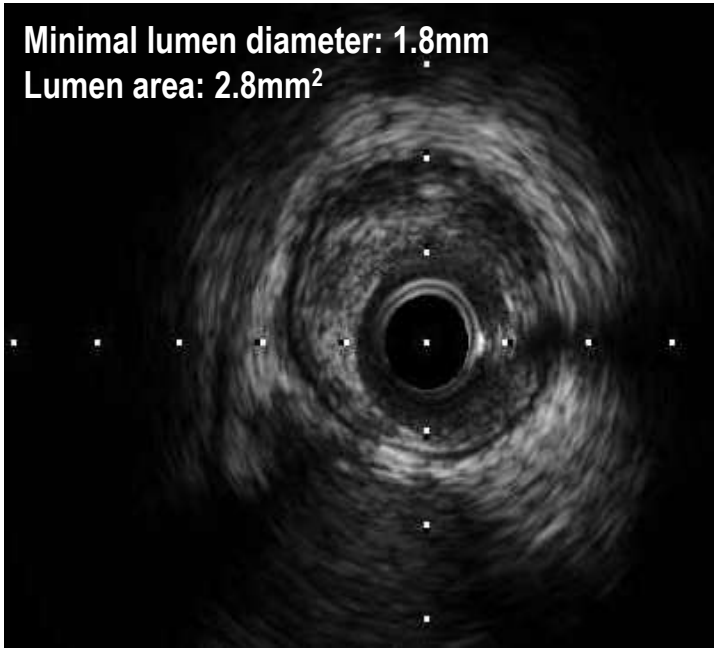
Pressure Wire **Adenosine**

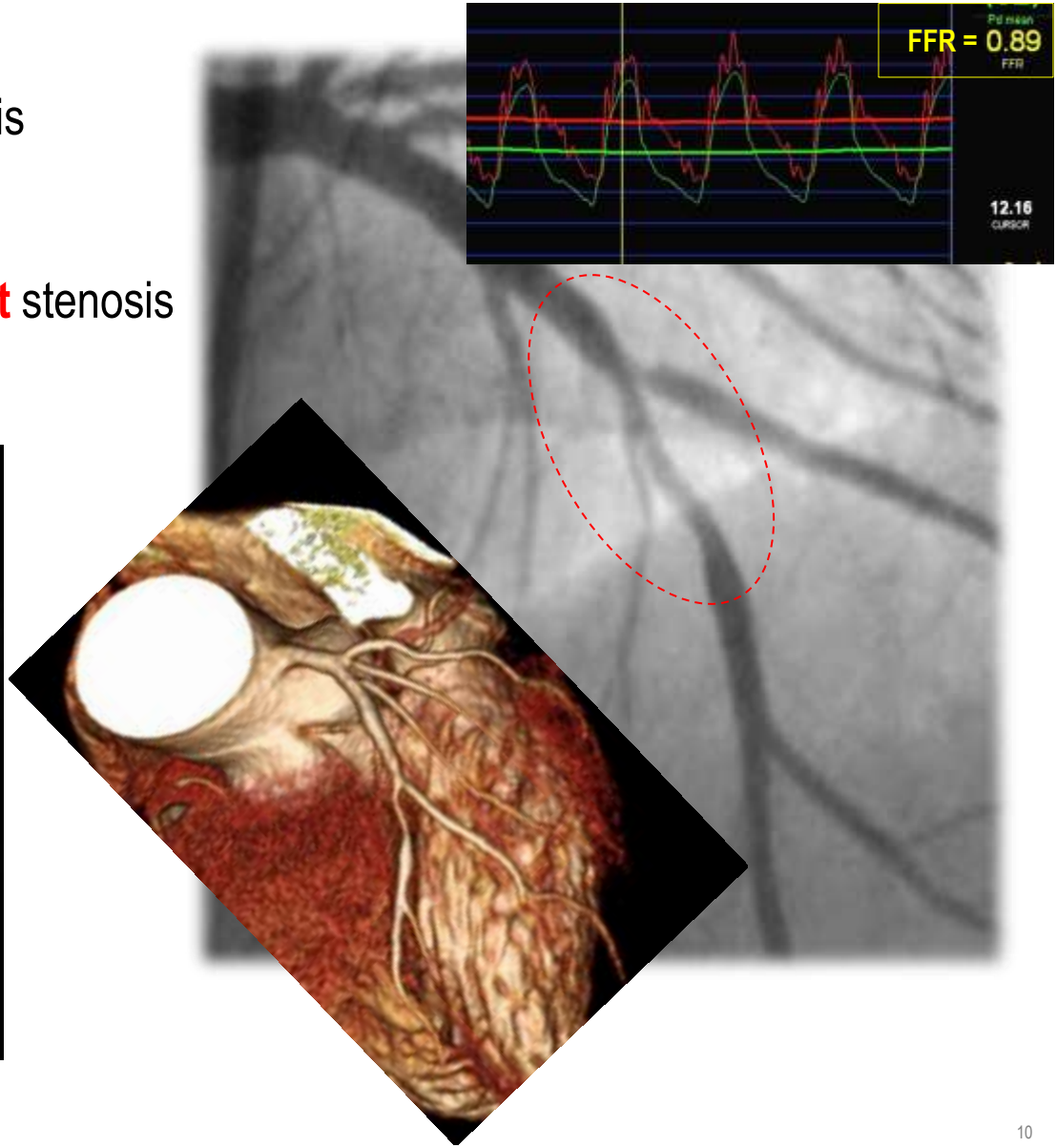
Is this lesion significant?

CT angiography: **significant** stenosis

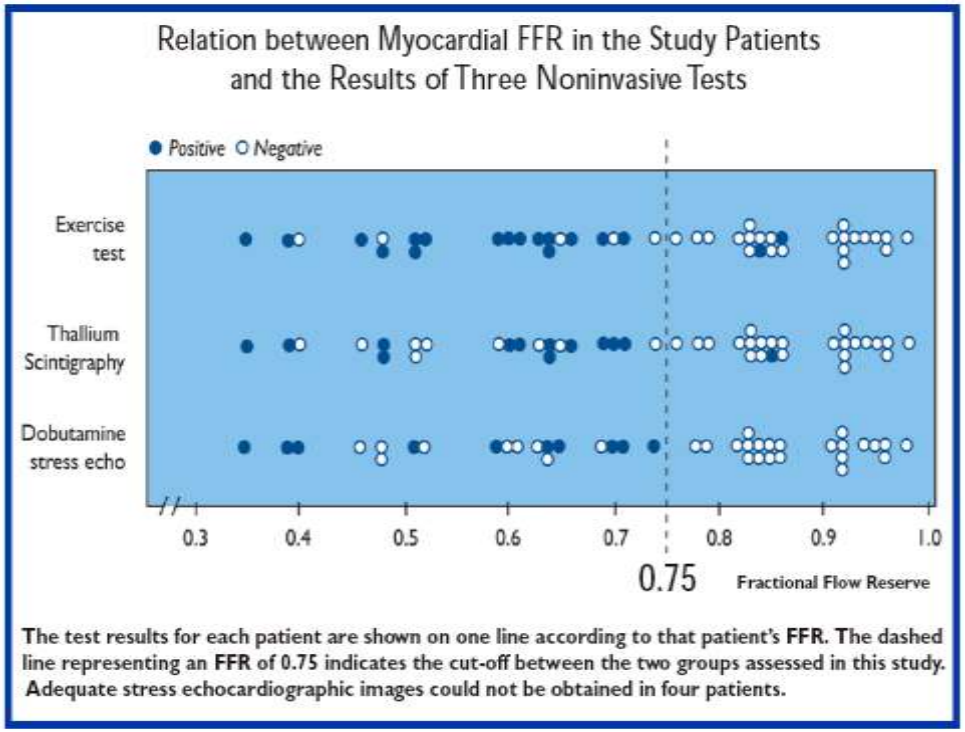
Angiography: **significant** stenosis

Intravascular ultrasound: **significant** stenosis





FFR criteria for “Presence of ischemia”

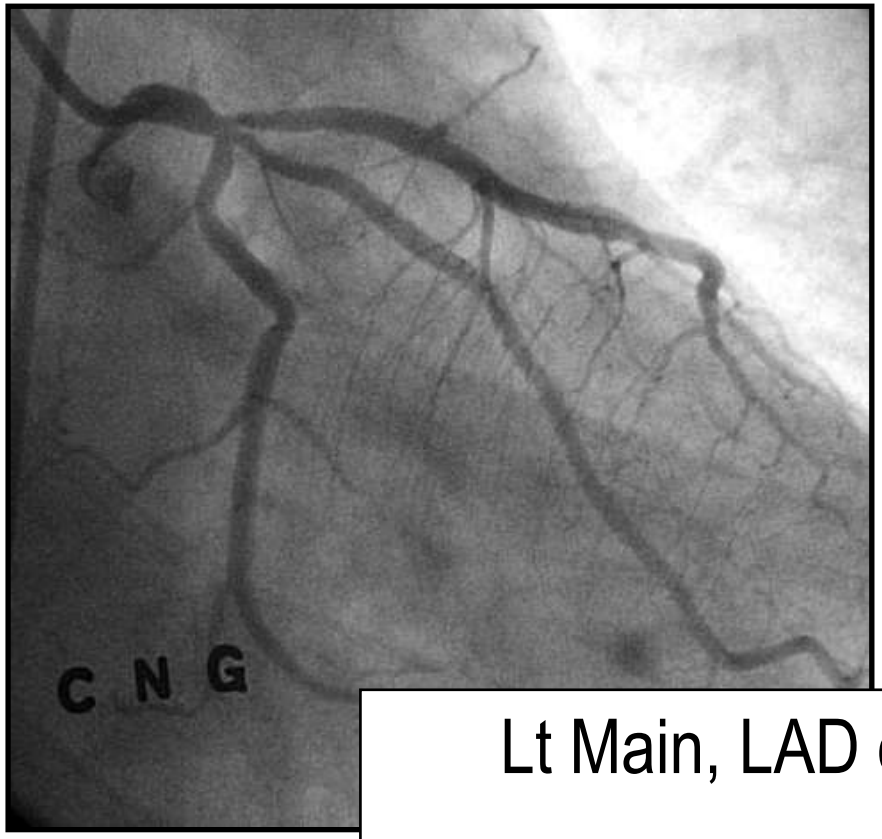


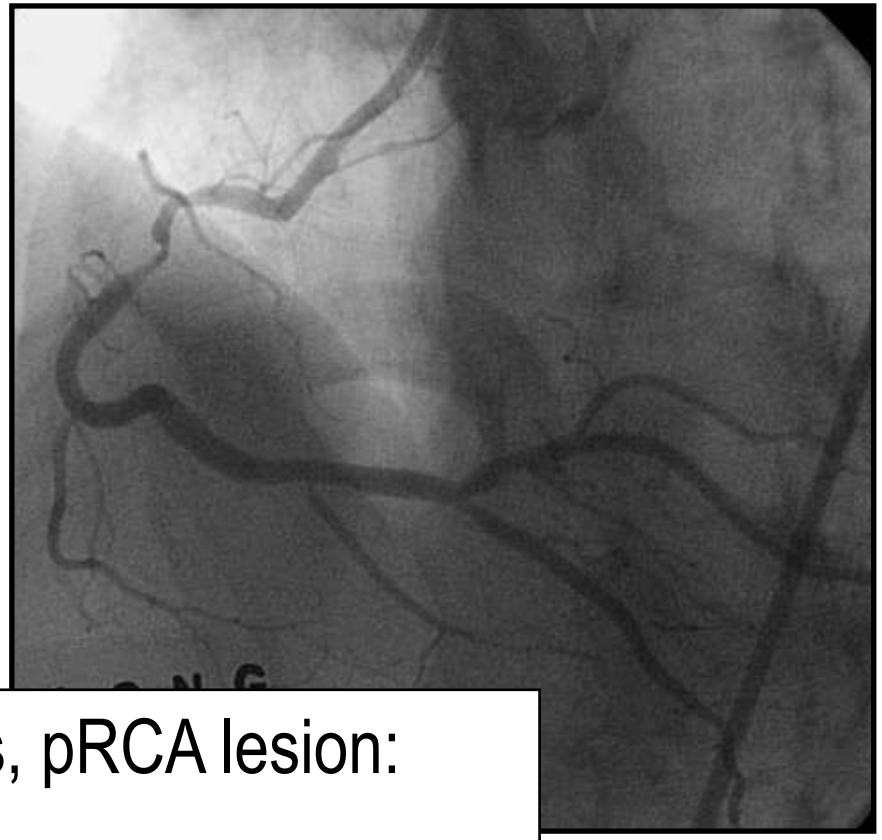
Overall results for FFRmyo	Percentage
Sensitivity	88 %
Specificity	100 %
Pos. Pred. Value	100 %
Neg. Pred. Value	88 %
Accuracy	93 %

Pijls NH et al. NEJM 1996

M/63 HT, Hyperlipidemia

Referred from other hospital after CAG for urgent CABG





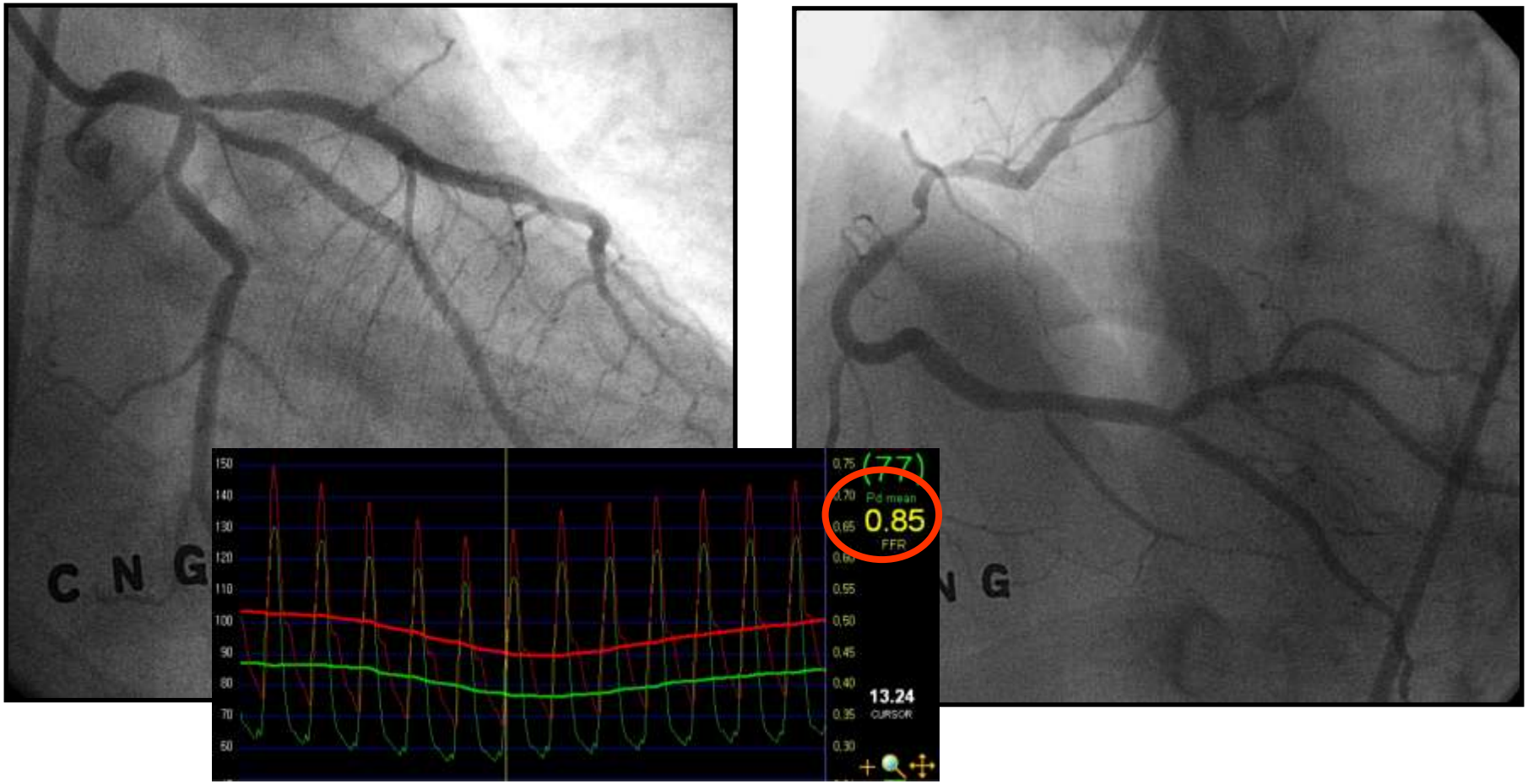
Lt Main, LAD os, pRCA lesion:

CABG? PCI?

M/63 HT, Hyperlipidemia

Recent onset resting and exertional chest pain

Referred from other hospital after CAG for urgent CABG



M/63 HT, Hyperlipidemia

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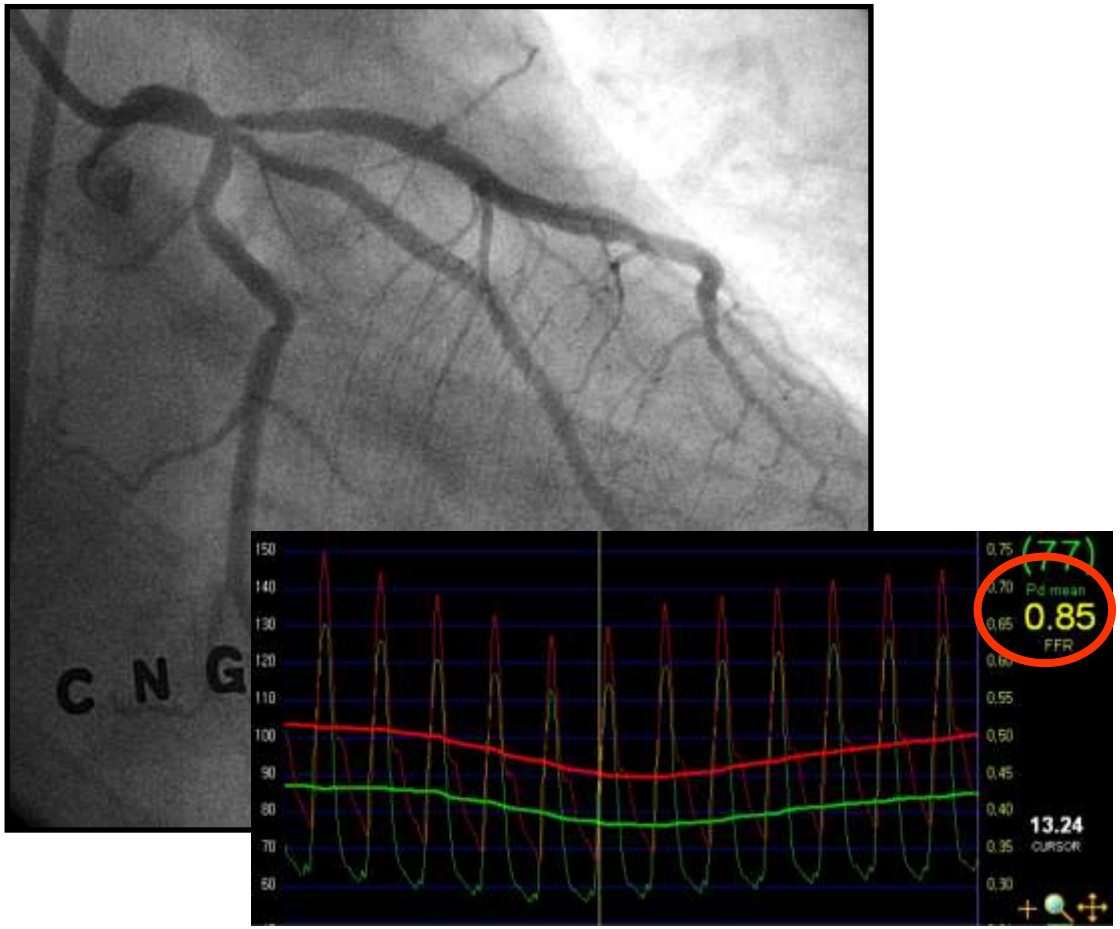
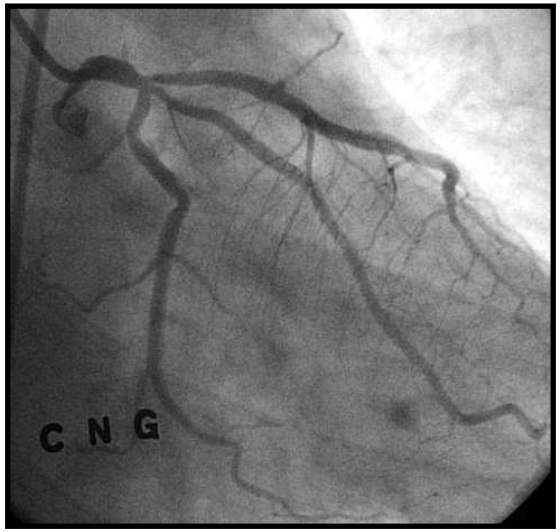
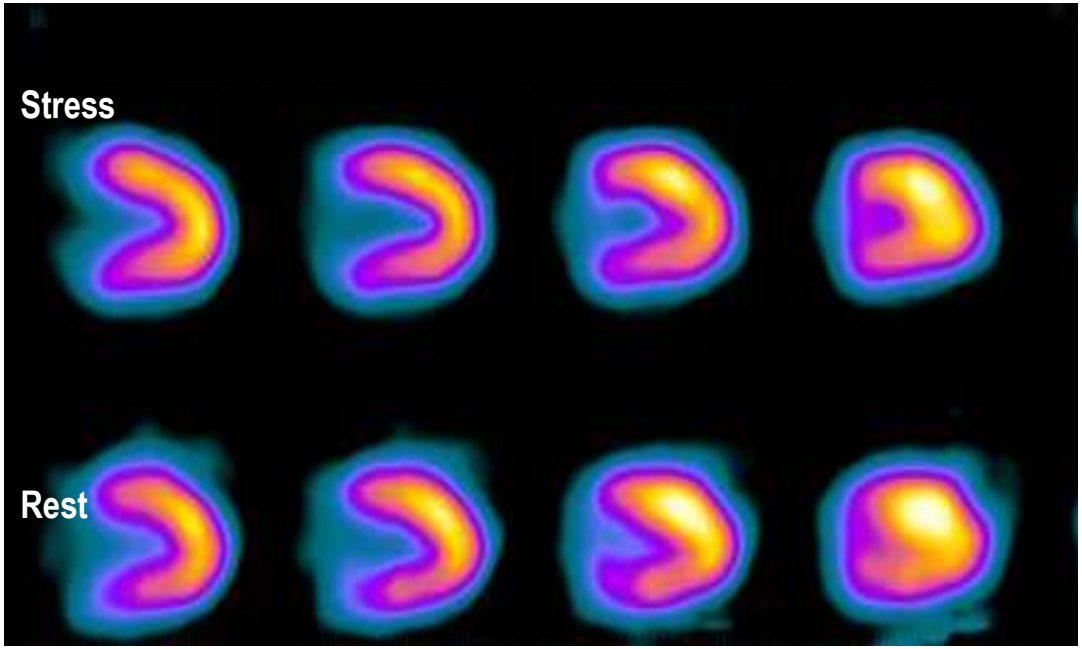


진짜 괜찮을까?

M/63 HT, Hyperlipidemia

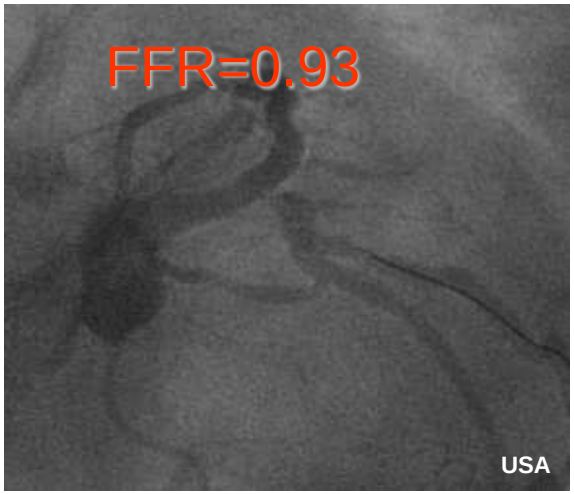


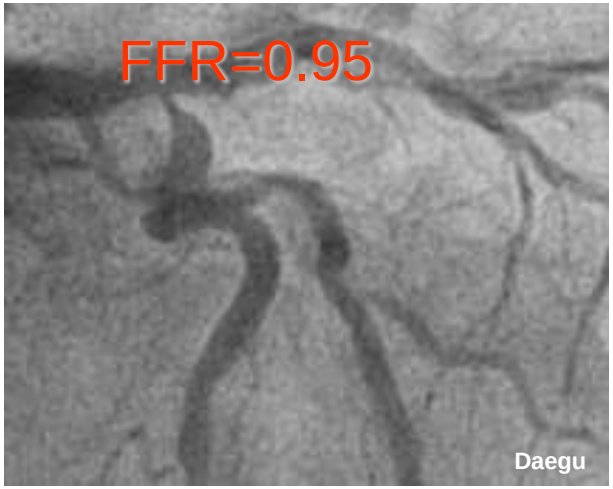
Myocardial SPECT 3yr after PCI



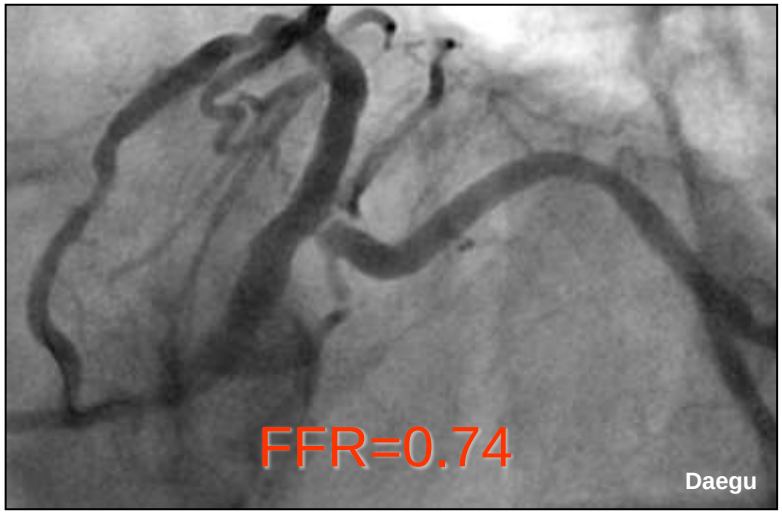
FFR 얼마?


FFR=0.67
Seoul


FFR=0.93
USA


FFR=0.95
Daegu

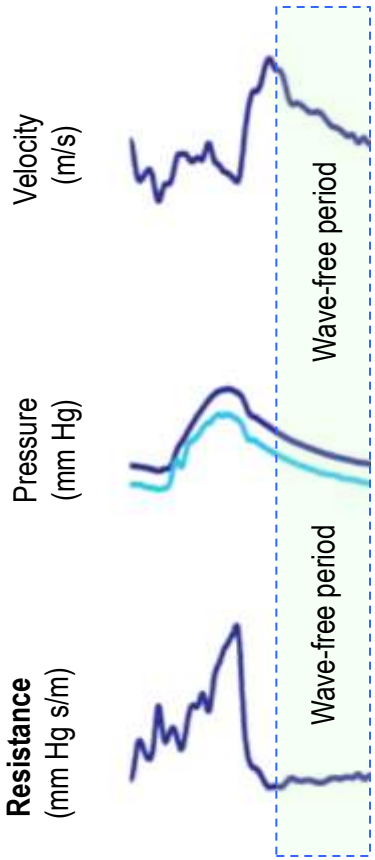

FFR=0.92
Italy

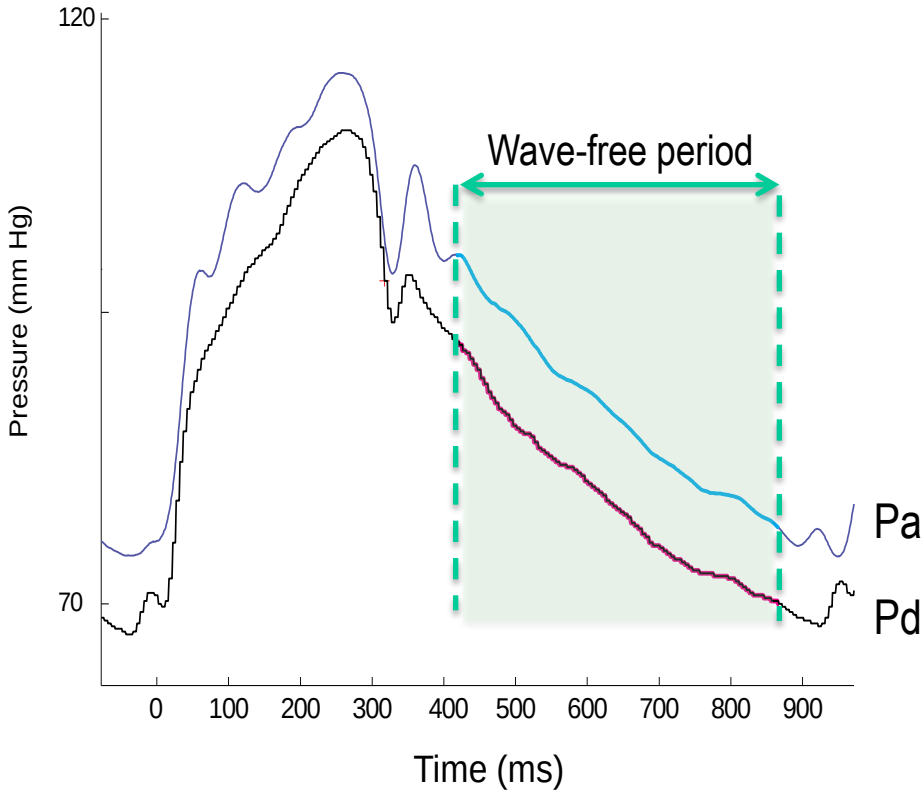

FFR=0.74
Daegu

근데 iFR은 뭐지? iFFR?

FFR without adenosine (hyperemia)

iFR = **i**nstantaneous wave-**F**ree **R**atio



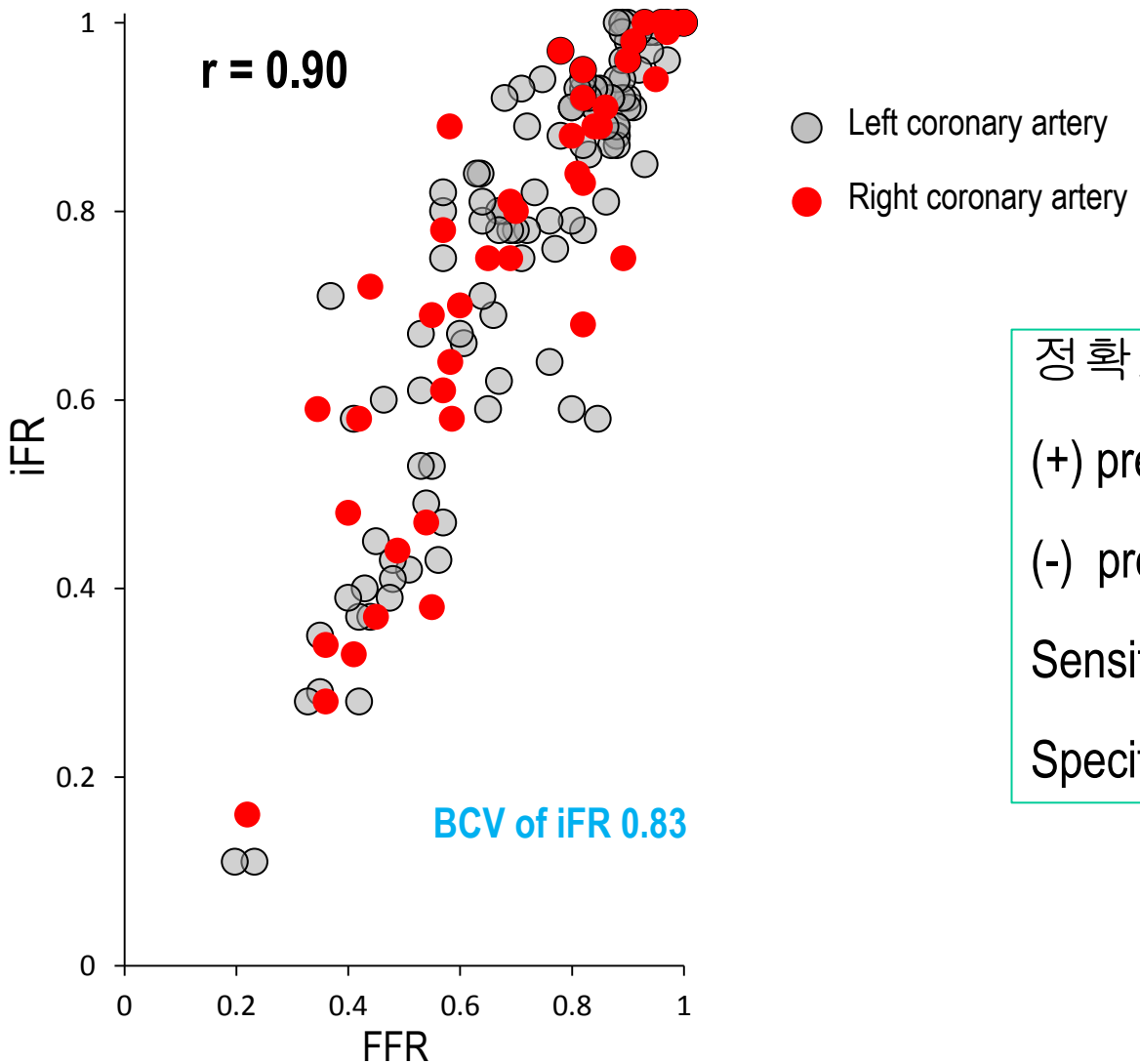


iFR: Pd/Pa ratio during the ***resting*** wave-free period

Courtesy of Justin E Davies

Diagnostic performance of iFR

ADVISE study (n=157)

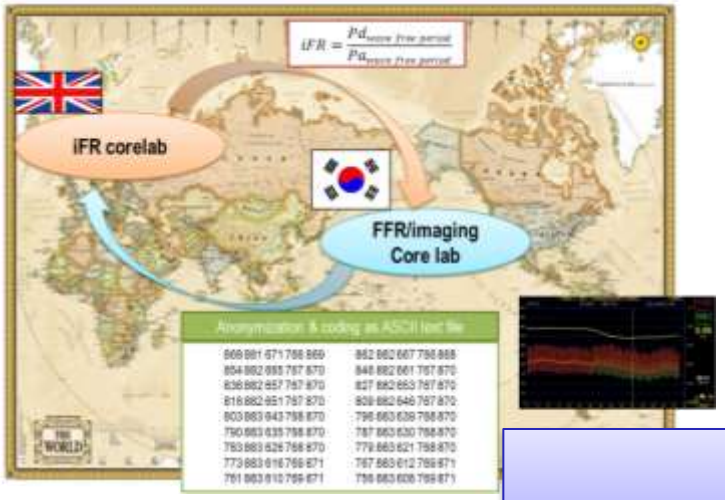


정확도	88%
(+) predictive value	91%
(-) predictive value	85%
Sensitivity	85%
Specificity	91%

Sen S, Escaned J, Davies JE et al. JACC *2012*

Diagnostic performance of a novel index, the instantaneous wave-free ratio (iFR), for the detection of functionally significant coronary artery stenosis

243 Lesions with FFRs by both IC bolus and IV infusion of adenosine



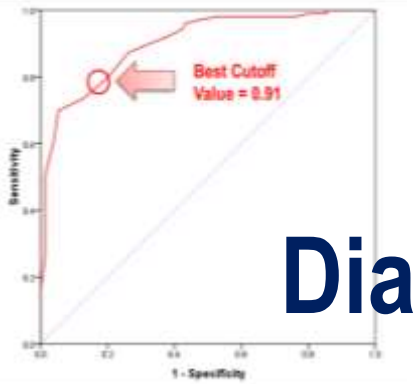
5 lesions excluded

- 3 inadequate data
- 1 frequent PVCs
- 1 AV-block

238 Lesions

Park JJ, Koo BK, et al. EuroPCR 2012

Best Cutoff Value of iFR



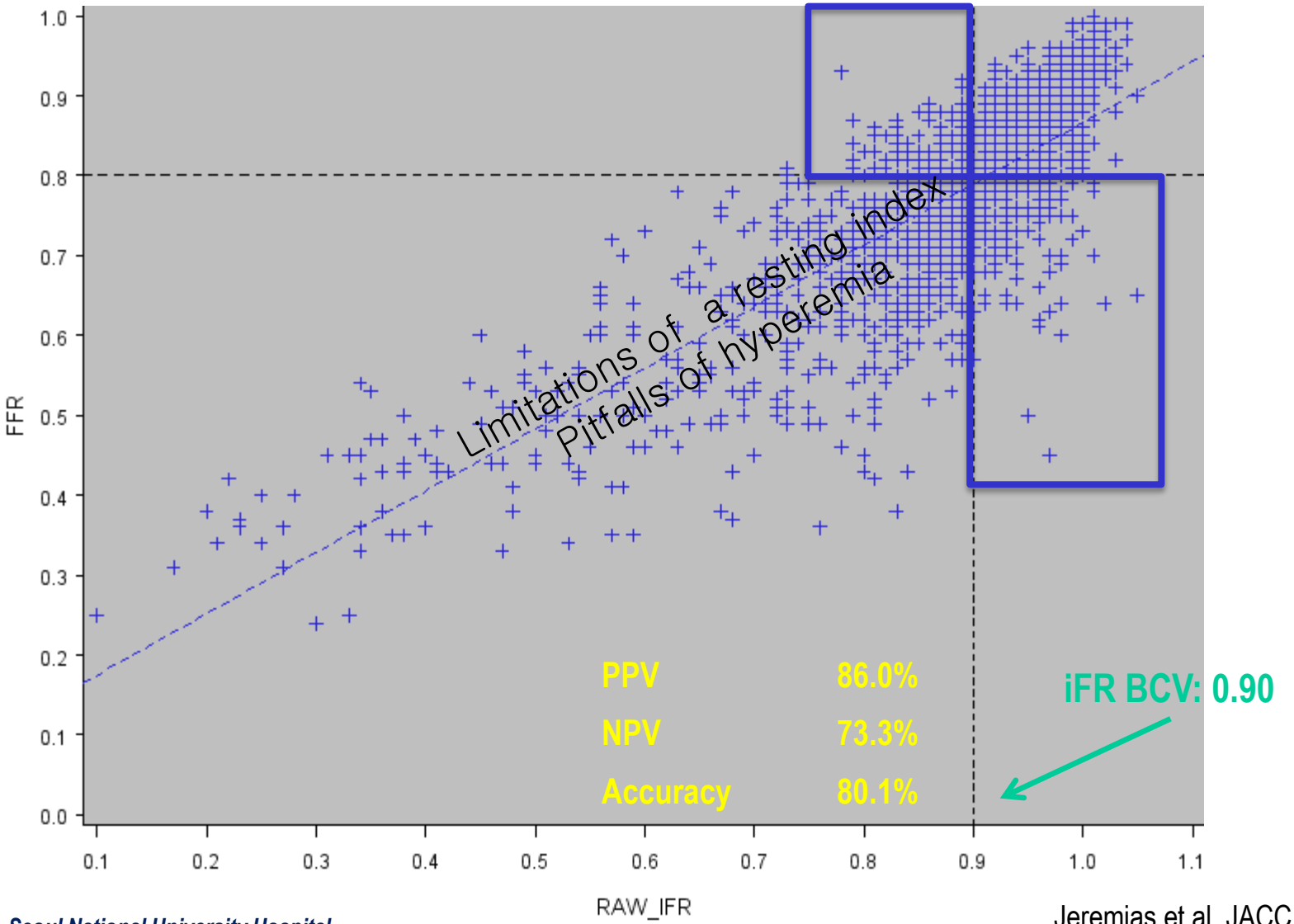
AUC = 0.89 (95% CI 0.85-0.93), P < 0.001

Diagnostic accuracy of iFR

	iFR < 0.91
Sensitivity	**0.81**
Specificity	**0.79**
Positive predictive value	**0.73 [0.64-0.81]**
Negative predictive value	**0.86 [0.79-0.91]**
Accuracy	**0.80**

Park JJ, Koo BK, et al. EuroPCR 2012

RESOLVE: FFR vs iFR (n=1539)

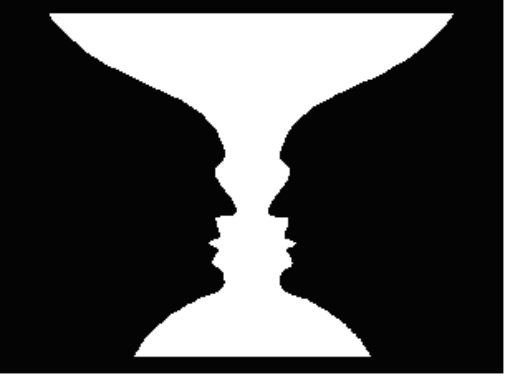


Jeremias et al. JACC 201

FFR, iFR만 알면 되지, 왠 CFR? 왠 IMR?

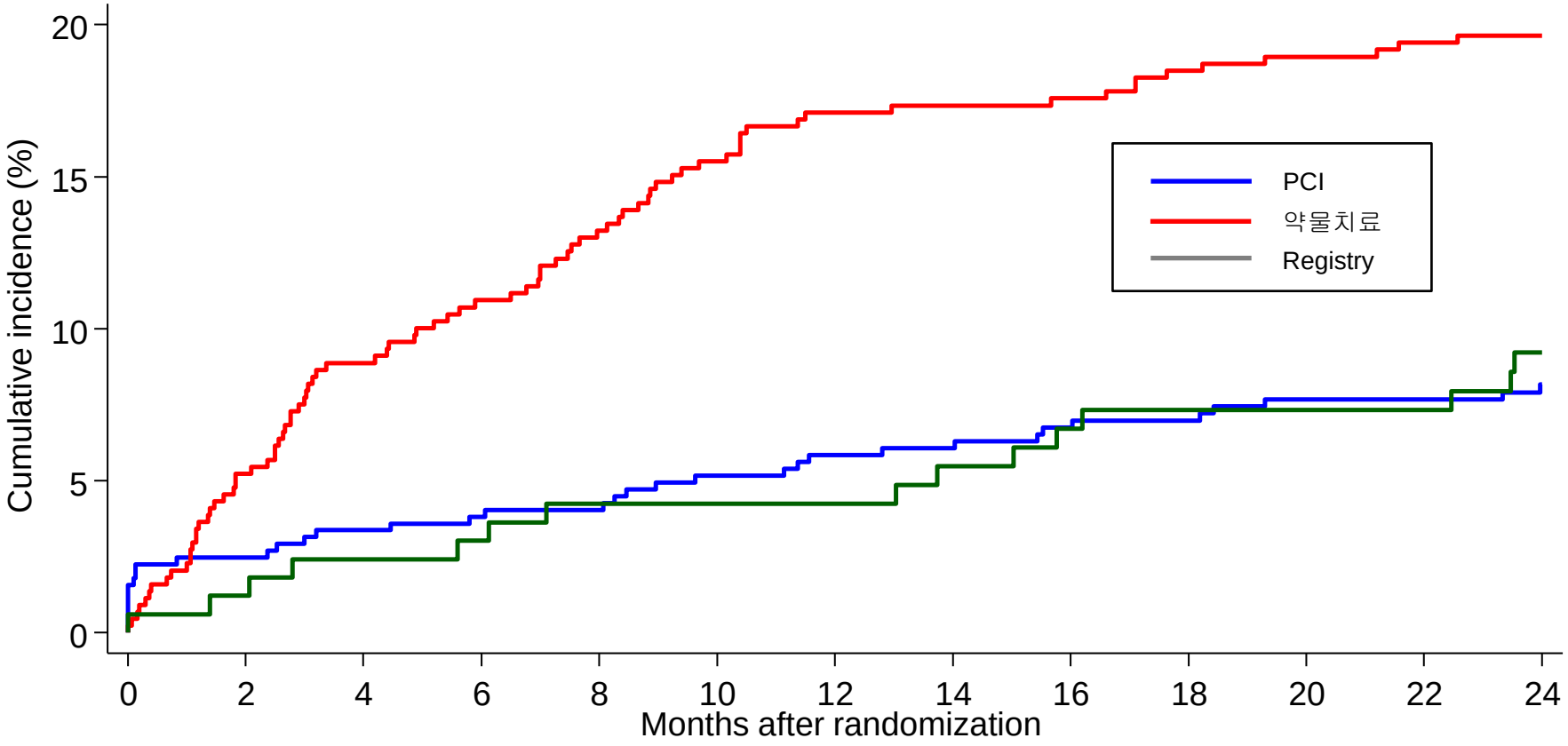
destin.egloos.com

괜찮은데 끝낼까요?

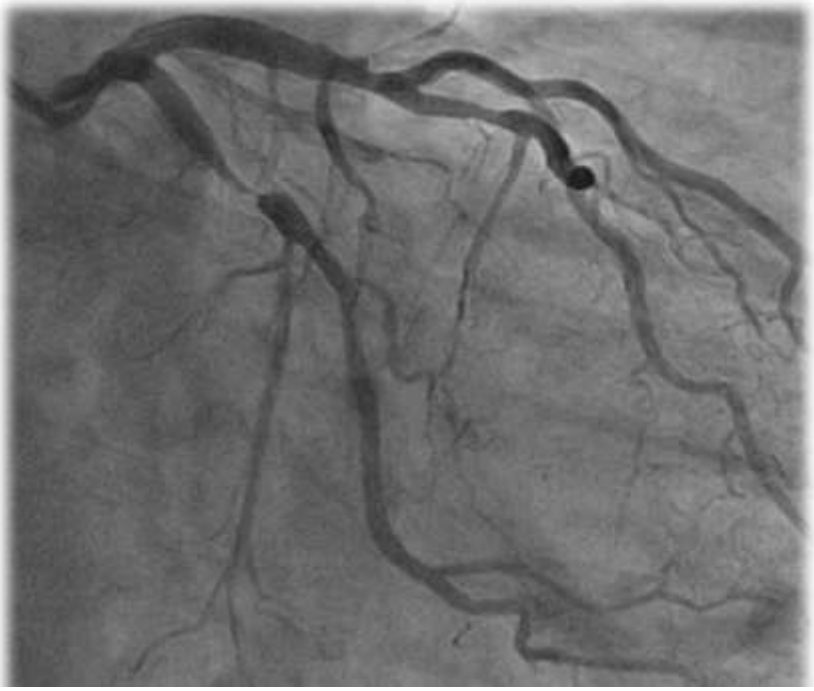


뭐가 보이나요?

FAME 2

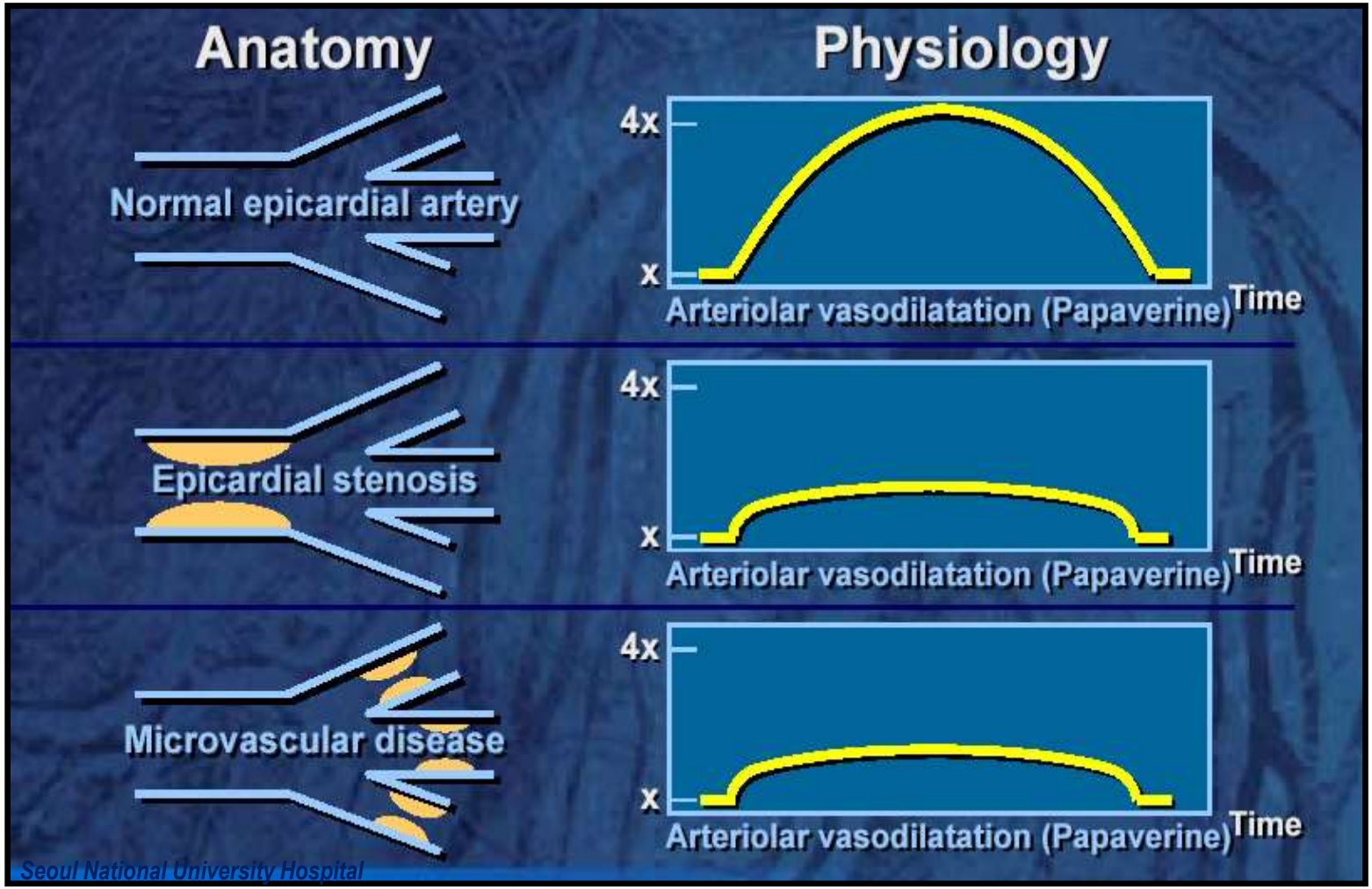


From “macro-” to “micro-circulation”

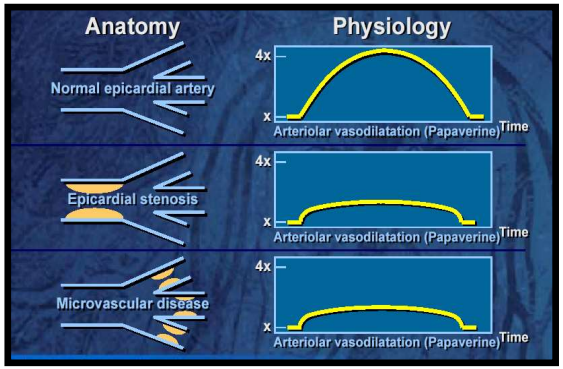


<5% of the total coronary tree

CFR, coronary flow reserve, 관상동맥 혈류예비력



CFR, coronary flow reserve, 관상동맥 혈류예비력

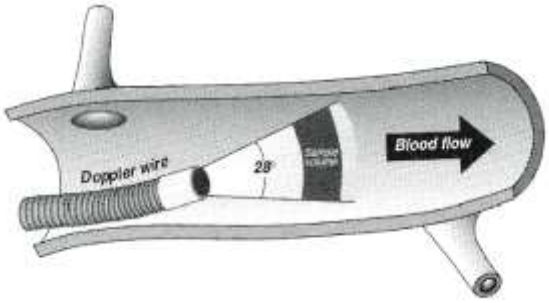


Coronary Flow Reserve

$$= \frac{\text{Hyperemic Flow}}{\text{Resting Flow}}$$

Coronary Flow Reserve (CFR)

- *The reservoir capacity of microvascular circulation according to demand.*
- *Ratio of maximal coronary blood flow at hyperemia and resting coronary blood flow*



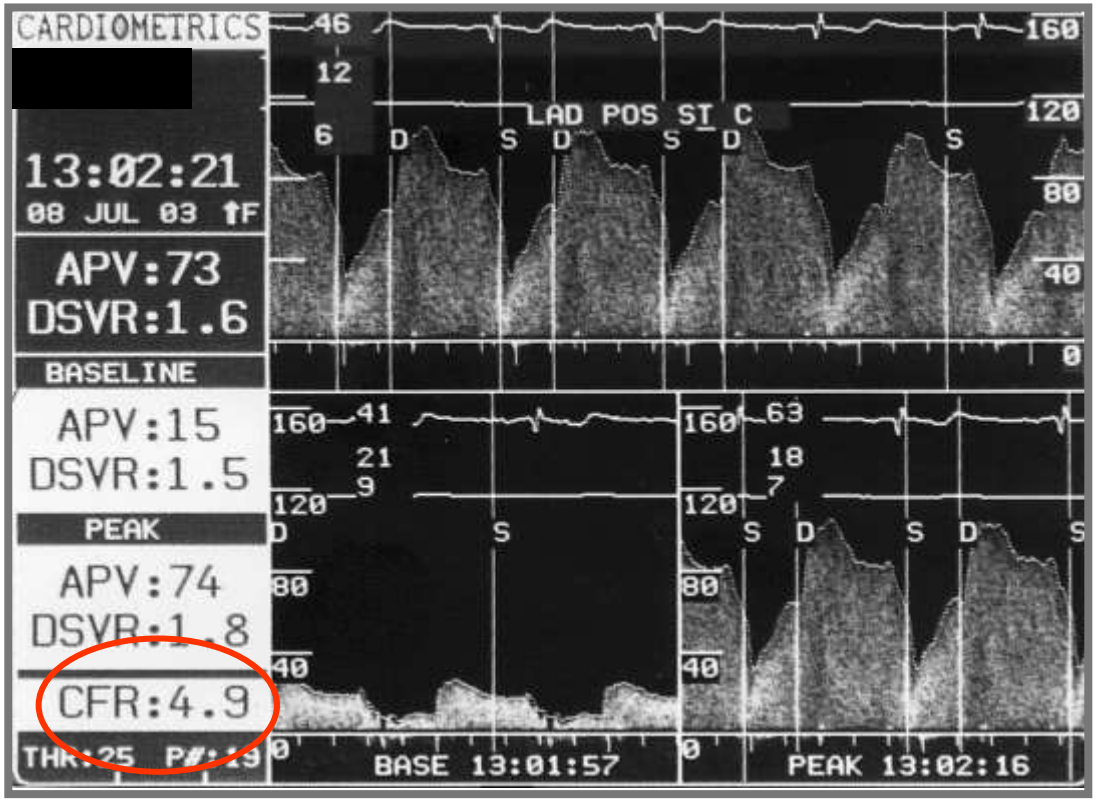
CFR Doppler

= hyperemic flow/resting flow

= [hAPV x CSA] / [bAPV x CSA]

= hAPV / bAPV

APV: averaged peak velocity
CSA: cross-sectional area

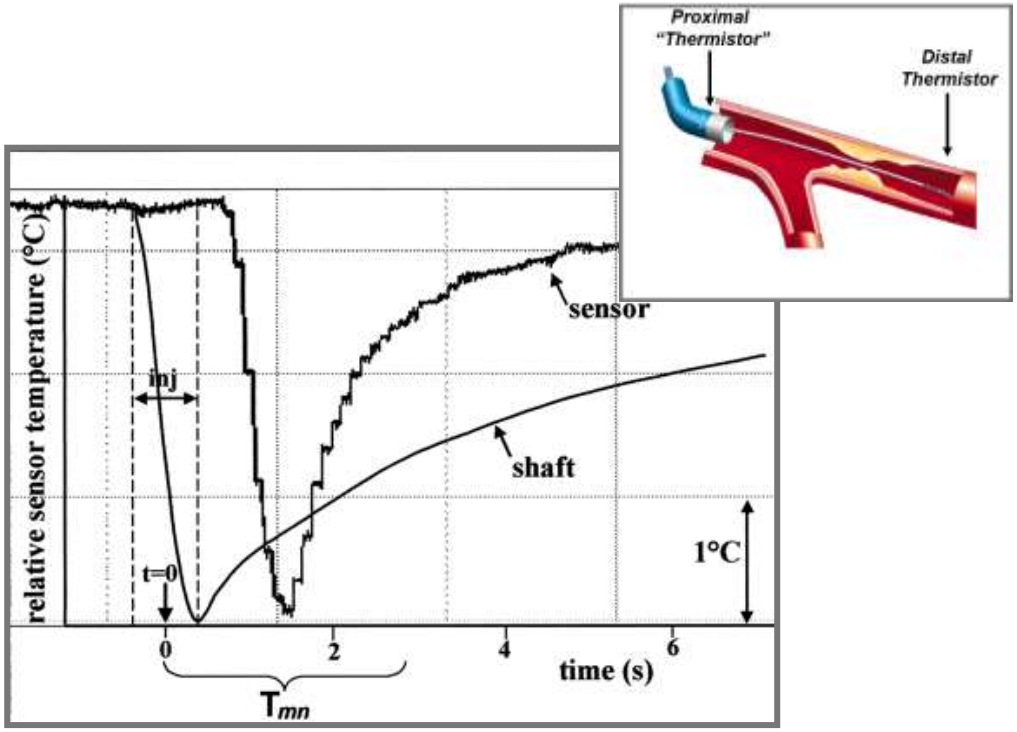


Thermodilution CFR

- Flow = the ratio of the volume and mean transit time (T_{mn}) of an injectate

- Assuming the epicardial volume remains unchanged, CFR can be calculated as follows.

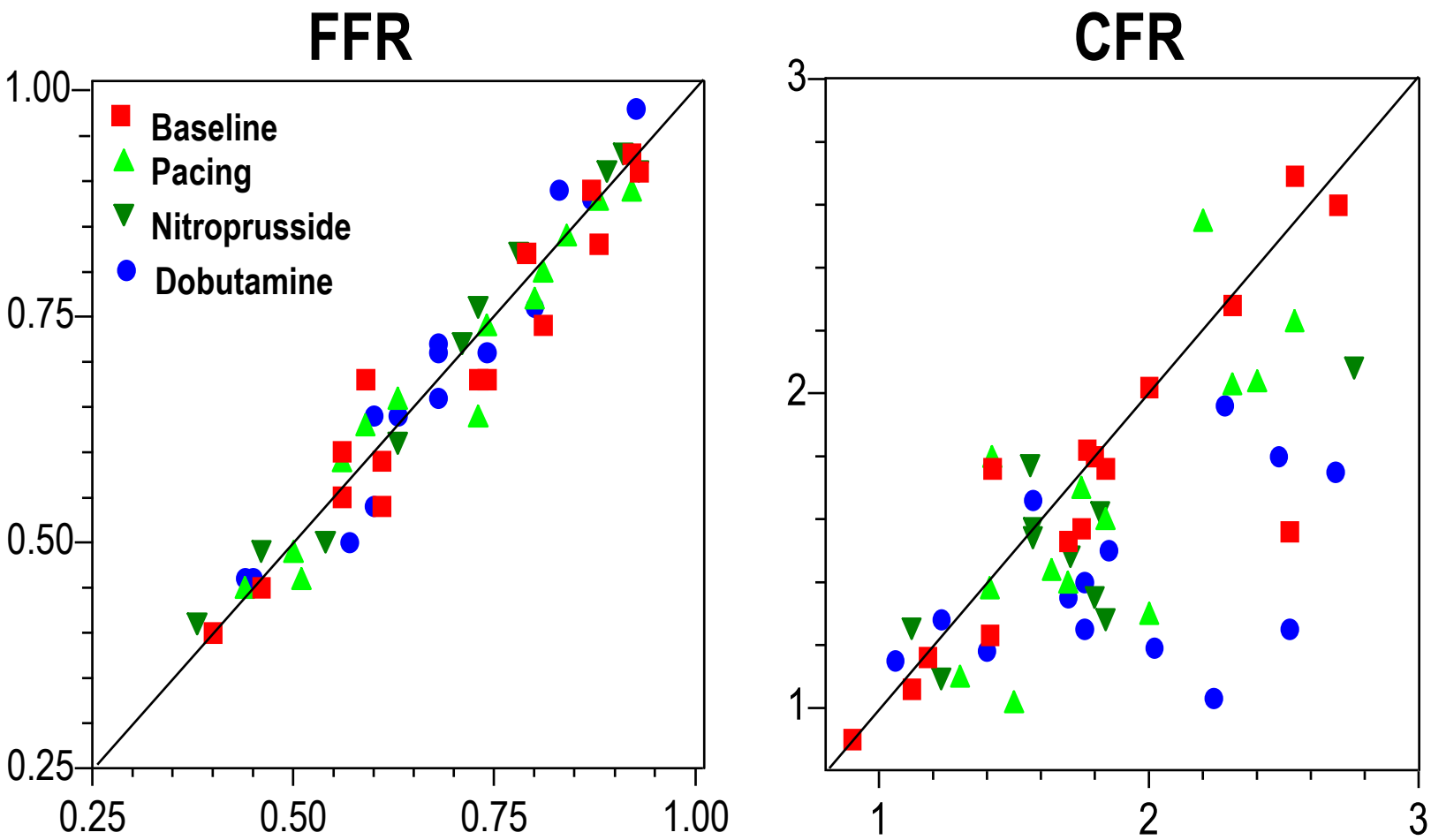
$$CFR = \frac{T_{mn} \text{ at rest}}{T_{mn} \text{ at hyperemia}}$$



Thermodilution방법으로 측정한 CFR

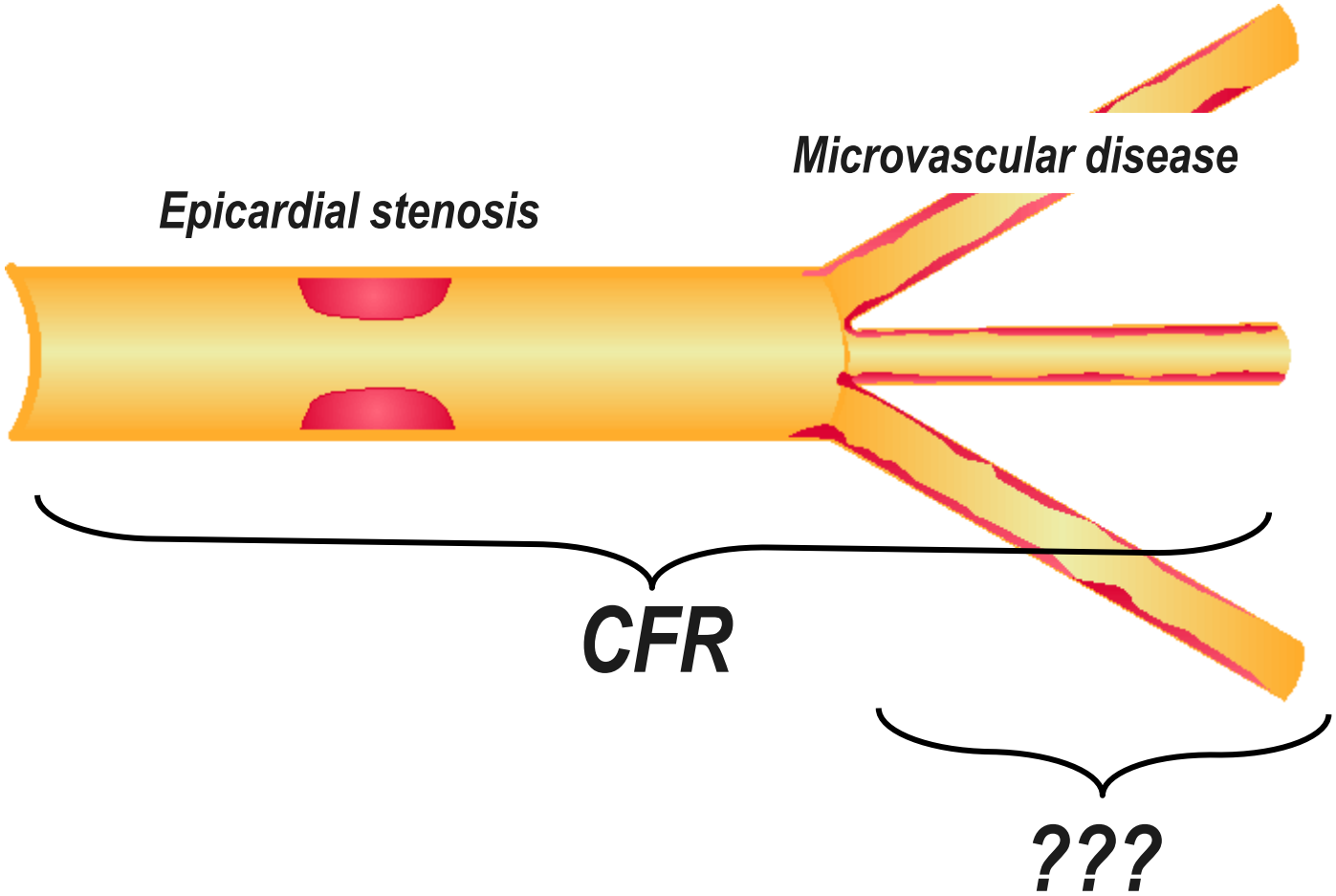
CFR은 왜 조영실에서 사라져버렸나?

Reproducibility of FFR and CFR



de Bruyne et al Circulation 1996

CFR은 왜 조영실에서 사라져버렸나?



Derivation of IMR

- *Resistance = Pressure / Flow*
- *Flow = $V/T_{mn} \cong 1/T_{mn}$*
- *IMR = Distal Pressure / $(1 / T_{mn})$*

= Distal Pressure x T_{mn}

at maximal hyperemia…

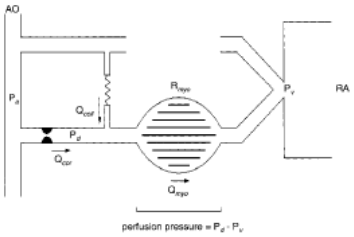


Figure 5. Schematic representing coronary circulation. AO, aorta; RA, right atrium.

myocardial flow, the following algorithm can be applied. In the mathematical derivation of that algorithm, standardized nomenclature will be used as in the initial study introducing the concept of FFR.[9]

Let us use the following terminology: Q_{myo}=myocardial blood flow, Q_{cor}=coronary artery blood flow (equal to F), and Q_c=collateral blood flow, all measured at maximum vasodilation. The "normal" values of these indexes at maximal vasodilation are indicated by the superscript N: Q^N_{myo}, Q^N_{cor}, Q^N_c. Equation 1, in this terminology, states that

(1a) $$Q_{cor} \approx 1/T_{mn},$$

which has also been validated both experimentally and clinically.[11–13]

R_{myo} is myocardial resistance at maximum vasodilation.

Myocardial flow equals the sum of coronary artery flow and collateral flow, so:

$$Q_{myo} = Q_{cor} + Q_c$$

Furthermore, it is assumed that $Q^N_c = 0$ and that $Q^N_{myo} = Q^N_{cor}$.

FFR_{myo} and FFR_{cor} are defined as follows[9]: $FFR_{myo} = Q_{myo}/Q^N_{myo}$ and $FFR_{cor} = Q_{cor}/Q^N_{cor}$.

The different pressures are defined as follows: P_a=aortic pressure, P_d=distal coronary pressure at maximum vasodilation, P_w=coronary wedge pressure, and P_v=central venous pressure, all at maximum dilation.

It has been demonstrated that FFR_{cor} and FFR_{myo} can be expressed in terms of pressures as follows[9]:

(4) $$FFR_{cor} = \frac{P_d - P_w}{P_a - P_w}$$

and

(5) $$FFR_{myo} = \frac{P_d - P_v}{P_a - P_v}$$

TMR equals:

$$R_{myo} = \frac{P_d - P_v}{Q_{myo}}$$

By multiplying the numerator and denominator by Q_{cor}, this can be rewritten as:

$$R_{myo} = \frac{P_d - P_v}{Q_{myo}} = \frac{P_d - P_v}{Q_{cor}} \cdot \frac{Q_{cor}}{Q_{myo}}$$

$$R_{myo} = (P_d - P_v) \cdot T_{mn} \cdot \left(\frac{Q_{cor}}{Q_{myo}}\right)$$

$$= (P_d - P_v) \cdot T_{mn} \cdot \frac{Q_{cor}}{Q^N_{cor}} \cdot \frac{Q^N_{cor}}{Q_{myo}}$$

Because $Q^N_{cor} = Q^N_{myo}$, we obtain

$$R_{myo} = (P_d - P_v) \cdot T_{mn} \cdot \frac{Q_{cor}}{Q^N_{cor}} \cdot \frac{Q^N_{cor}}{Q_{myo}}$$

$$= (P_d - P_v) \cdot T_{mn} \cdot \frac{FFR_{cor}}{FFR_{myo}}$$

Therefore,

(6a) $$IMR = (P_d - P_w) \cdot T_{mn} \cdot \frac{FFR_{cor}}{FFR_{myo}}$$

or in case P_v is close to zero,

(6b) $$IMR = P_d \cdot T_{mn} \cdot \frac{FFR_{cor}}{FFR_{myo}}$$

Note that if there are no collaterals, as in the case of a normal artery, $FFR_{cor} = FFR_{myo}$ and Equation 6b equals Equation 3, as should be the case.

Equation 6a can be rewritten in terms of measured pressures by substitution of Equations 4 and 5 as follows:

$$IMR \approx (P_d - P_v) \cdot T_{mn} \cdot \left(\frac{P_d - P_w}{P_a - P_w}\right) \div \left(\frac{P_d - P_v}{P_a - P_v}\right)$$

$$= (P_d - P_v) \cdot T_{mn} \cdot \left(\frac{P_d - P_w}{P_a - P_w}\right) \cdot \left(\frac{P_a - P_v}{P_d - P_v}\right)$$

$$= (P_a - P_v) \cdot T_{mn} \cdot \left(\frac{P_d - P_w}{P_a - P_w}\right)$$

And by neglecting P_v, we obtain

(7a) $$IMR \approx P_a \cdot T_{mn} \cdot \left(\frac{P_d - P_w}{P_a - P_w}\right)$$

or expressed in a different way,

(7b) $$IMR \approx P_a \cdot T_{mn} \cdot FFR_{cor}$$

In summary, Equation 7a constitutes the general form of IMR, universally applicable in both the presence and absence of a significant stenosis. If studies are performed in patients without significant epicardial disease, the simpler Equation 3 can be used for IMR. In addition, when Doppler-derived indexes of microvascular resistance are used,[4–7] they should be corrected in a similar way as in Equation 6b by multiplying them by (FFR_{cor}/FFR_{myo}).

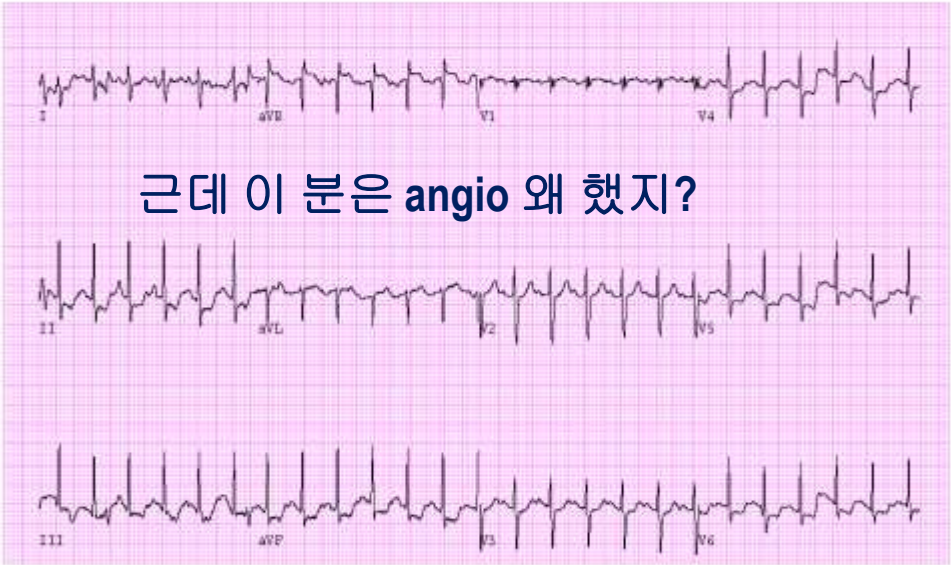
Finally, it is clear that overestimation of microvascular resistance when collateral flow is neglected increases with increasing stenosis severity and with increasing recruitable collateral flow. This percentage overestimation can be defined as

$$\left(\frac{IMR_{neglect}}{IMR}\right) - 1 \cdot 100\%$$

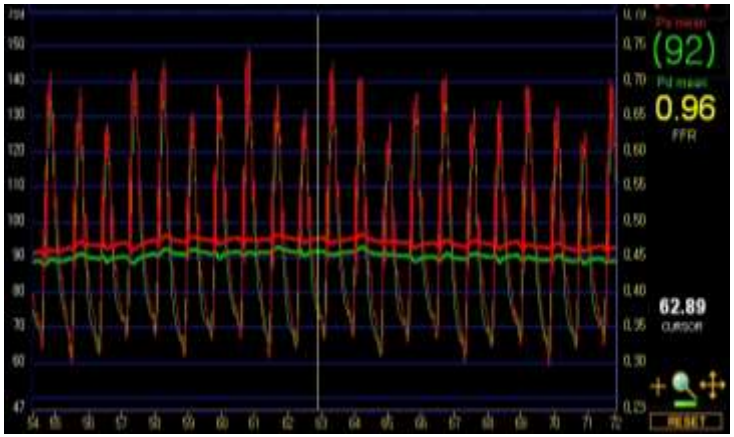
(8) $$= \left(\frac{P_d \cdot T_{mn}}{P_a \cdot T_{mn}[(P_d - P_w)/(P_a - P_w)]}\right) - 1 \cdot 100\%$$

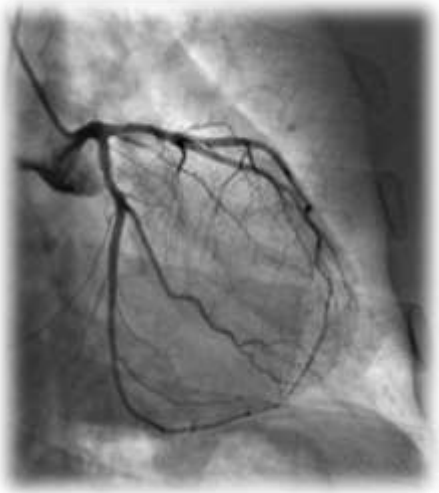
$$= \left(\frac{P_d}{P_a} \cdot \left(\frac{P_a - P_w}{P_d - P_w}\right) - 1\right) \cdot 100\%$$

괜찮은데 끝낼까요?



FFR한번 재 볼까? →괜찮은데요...

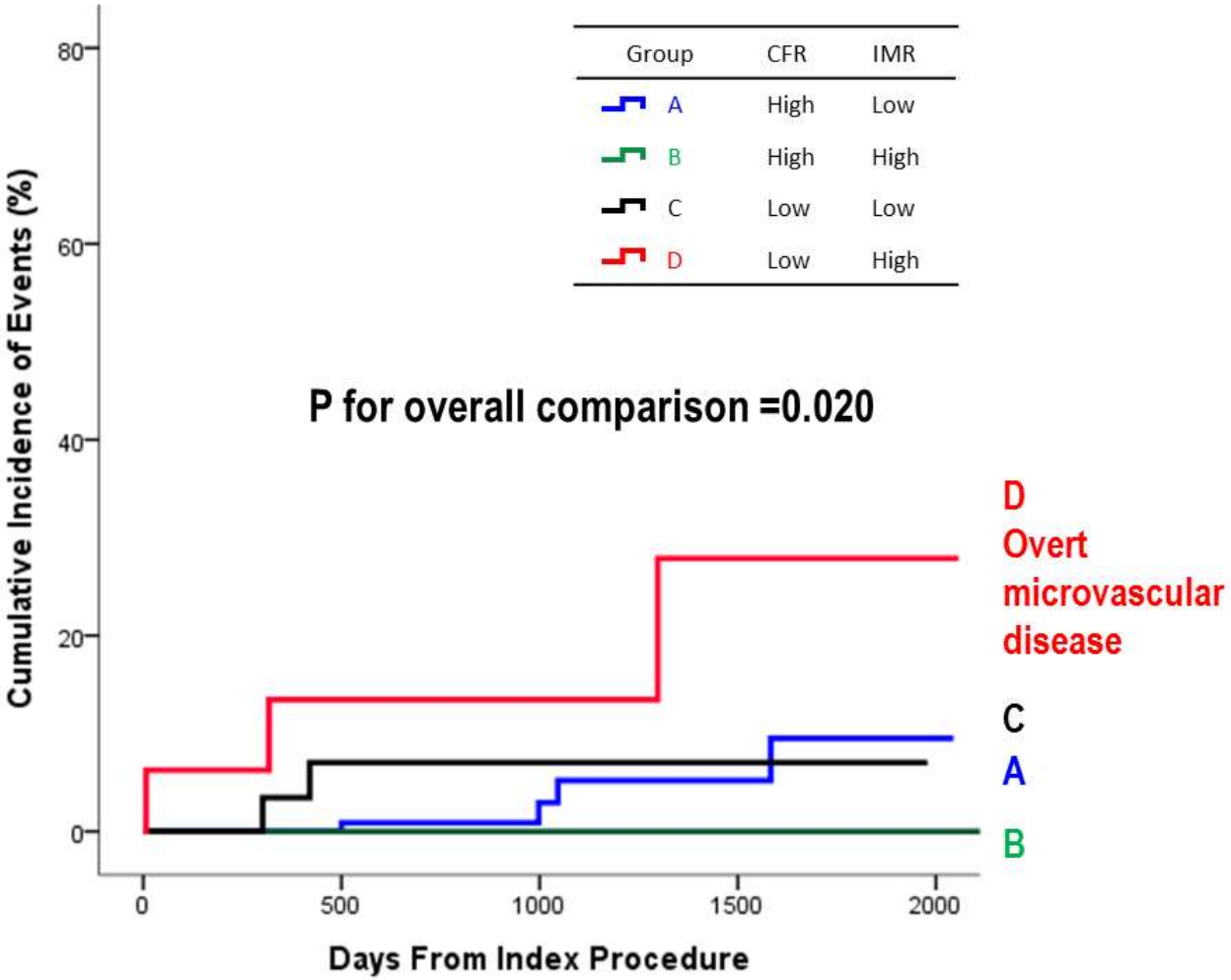




Microvascular disease

IMR = Pd x Tmn = 93 x 0.42 = 39

FFR높은데 왜 CFR과 IMR 을 재야하나?



관혈적 생리학적 검사들

- **FFR**, Fractional Flow Reserve, 분획혈류 예비력
- **CFR**, Coronary Flow Reserve, 관상동맥 혈류예비력
- **iFR**, Instantaneous Flow Ratio, 동시 혈류비
- **IMR**, Index of Microcirculatory Resistance, 미세순환 저항지수

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