

Physiology Matters

Seung Hun Lee

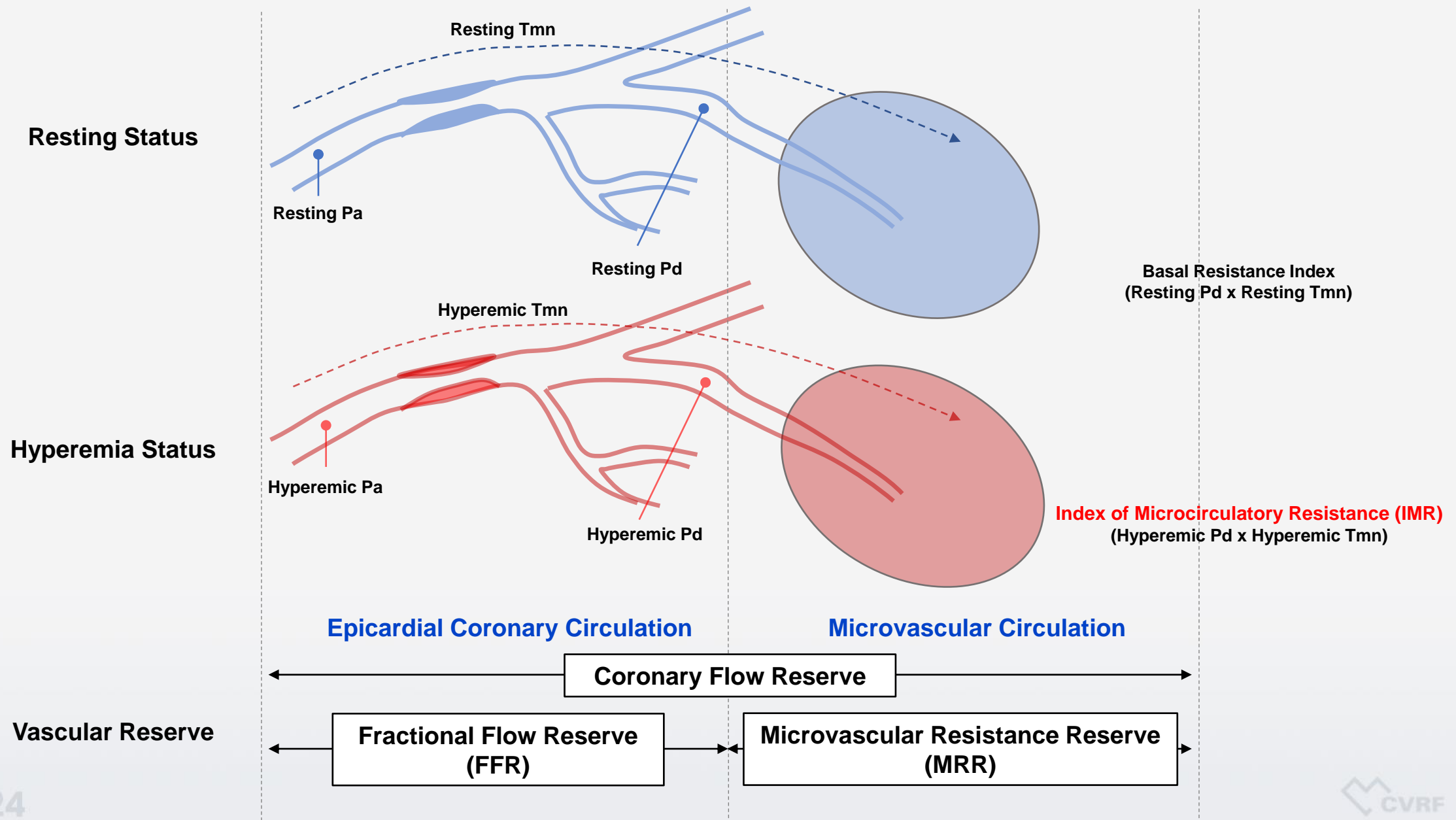
**Chonnam National University Hospital
South Korea**

Disclosure

Relationships with commercial interests:

- **Grants/Research Support: Abbott Korea, Abbott Vascular, Korean Cardiac Research Foundation**
- **Speakers Bureau/Honoraria: Abbott Vascular, Boston Scientific, Medtronic, MicroPort**
- **Consulting Fees: Dotter**
- **Other: None**

Overview of Invasive Coronary Physiology Index



Make Our Decision Simple with FFR

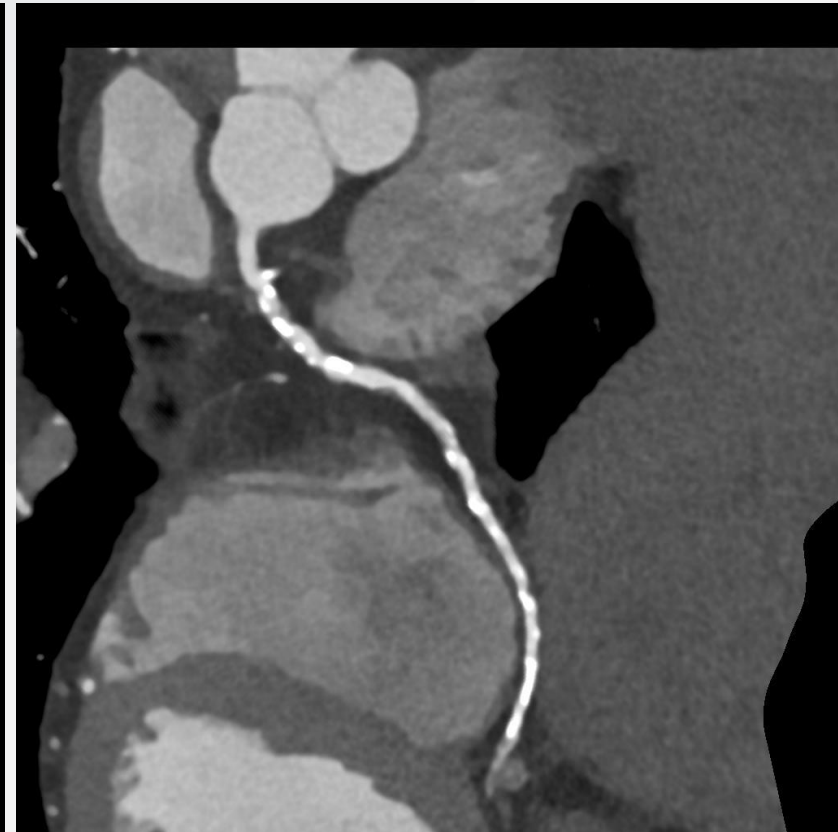
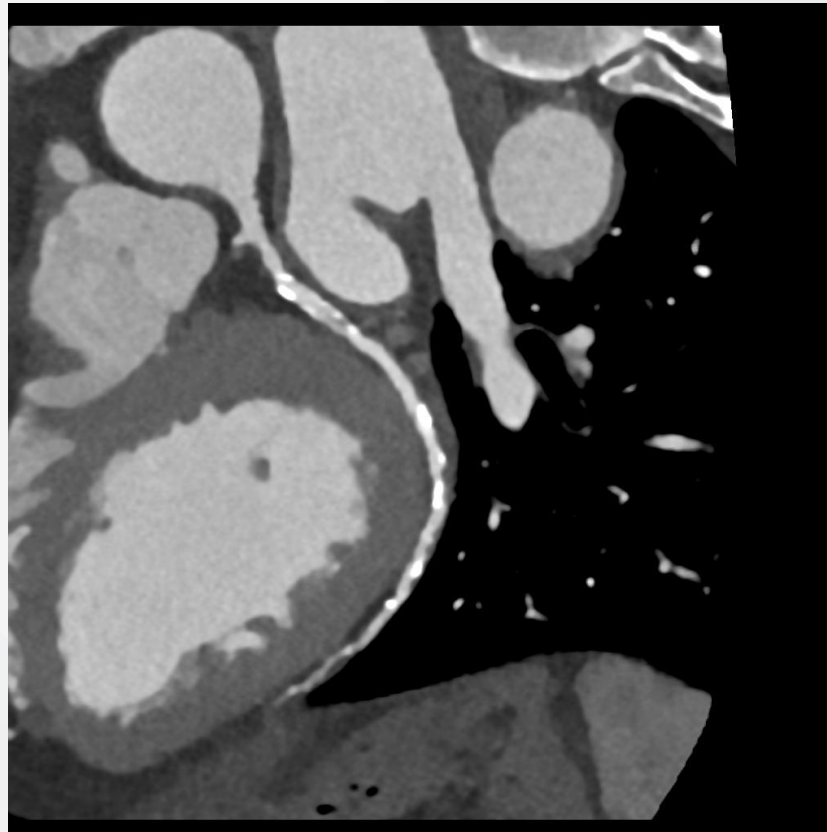
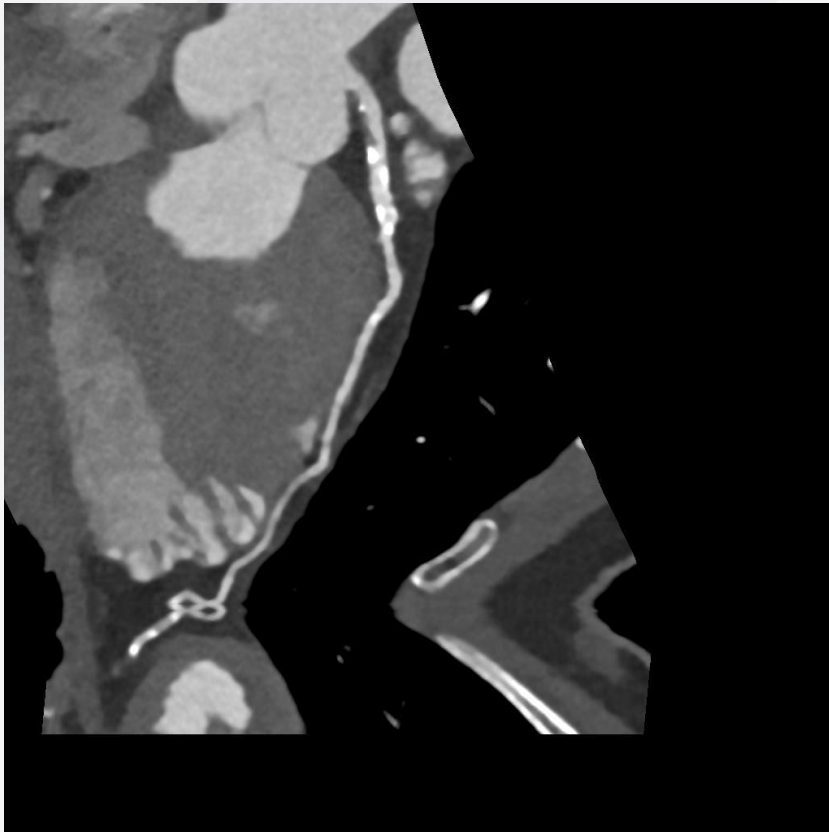
62/M, Stable IHD, CCS II

CCTA: 3VD, EchoCG: EF=74%, No RWMA → CABG vs. PCI?

LAD

LCX

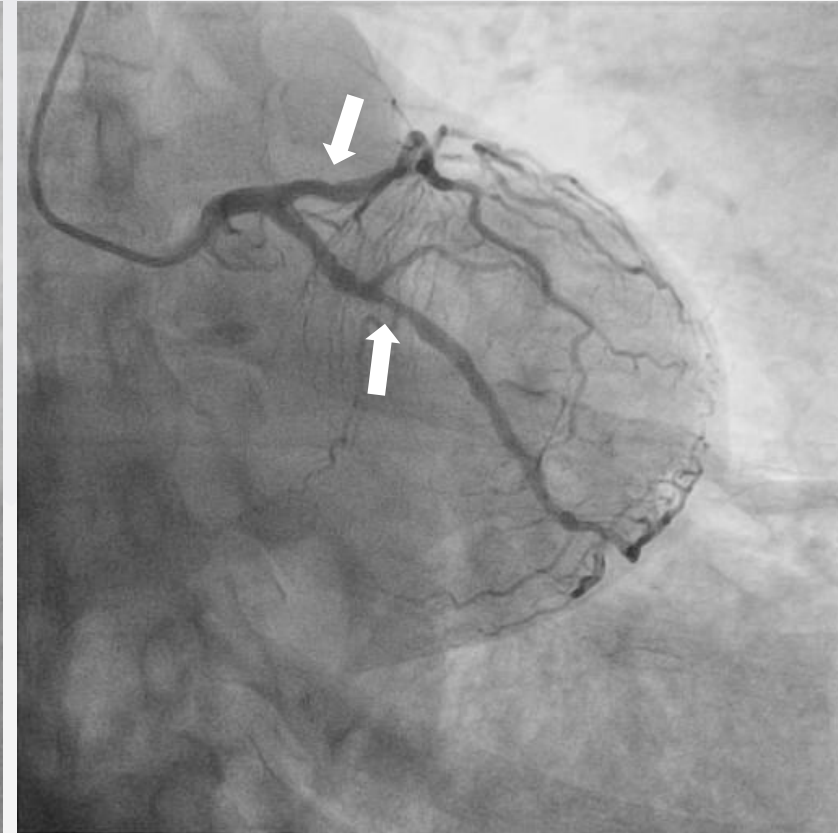
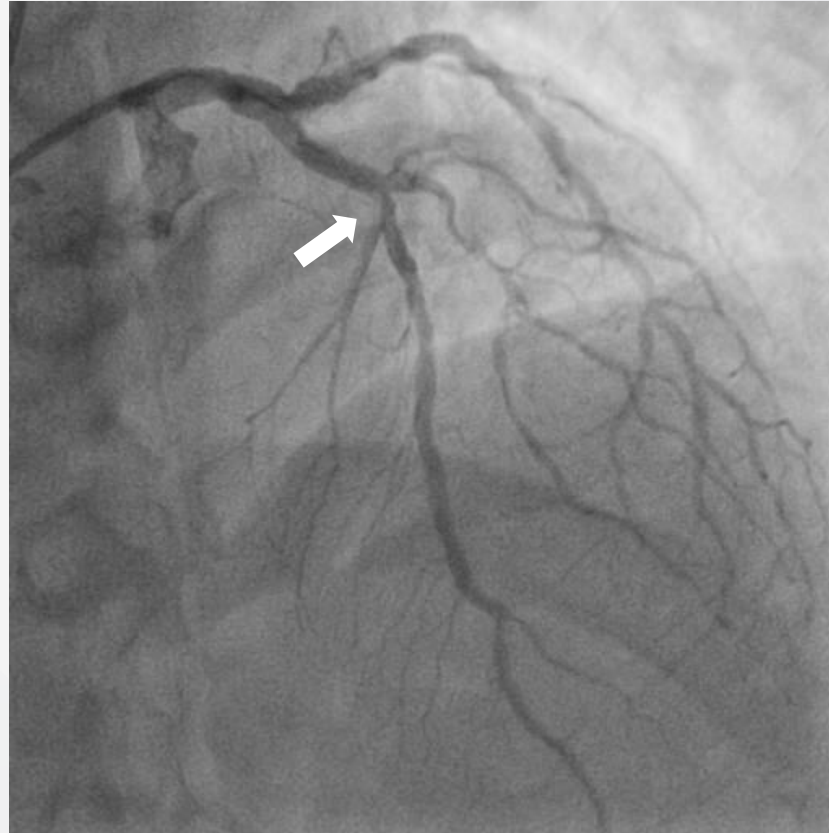
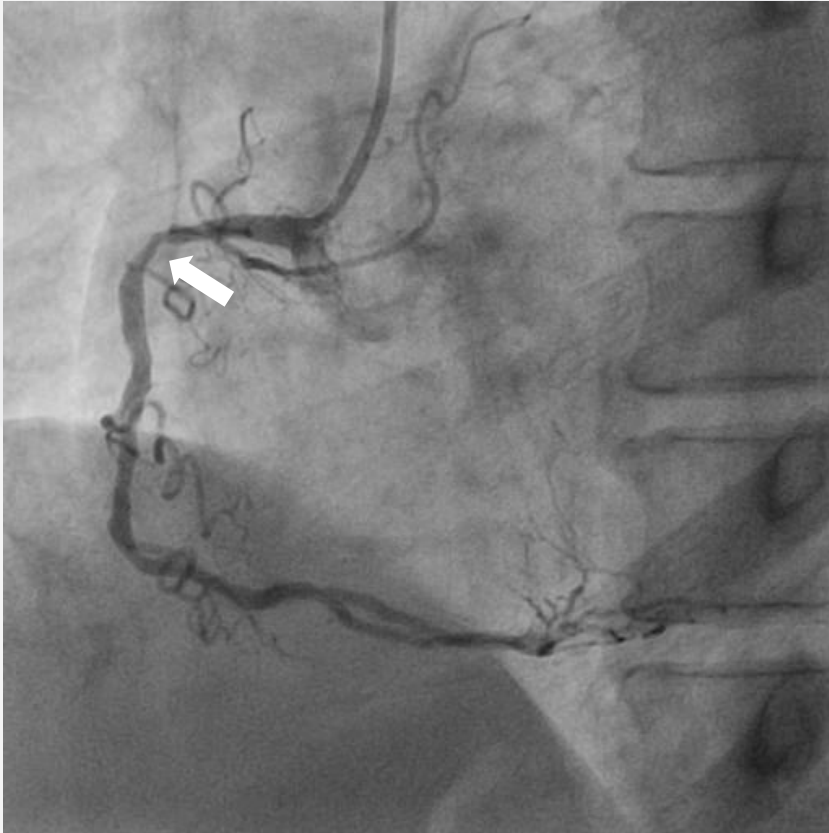
RCA



Make Our Decision Simple with FFR

62/M, Stable IHD, CCS II

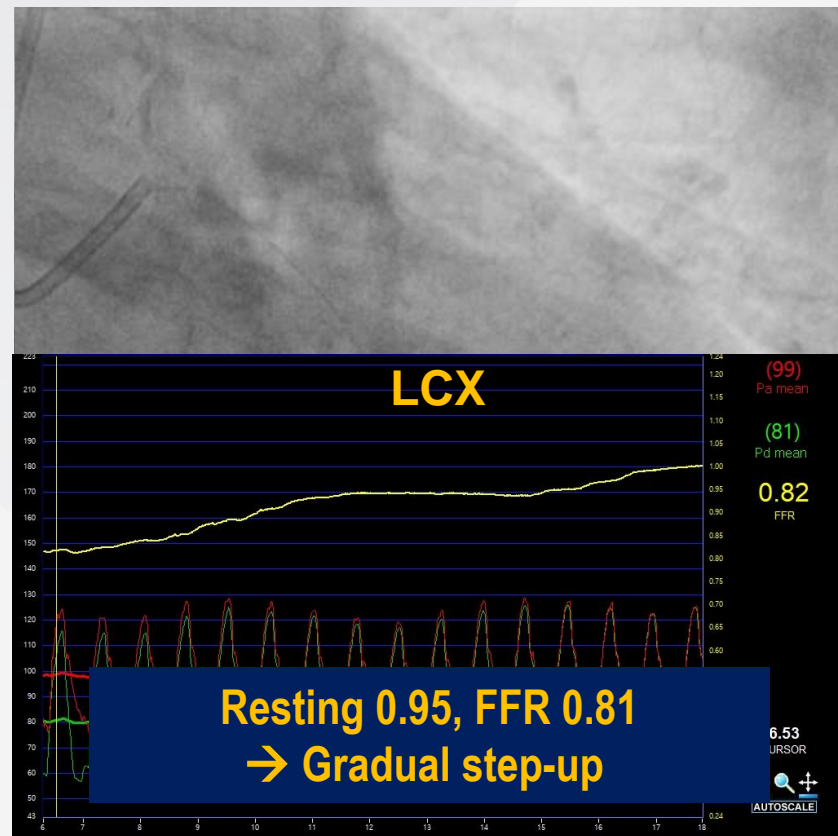
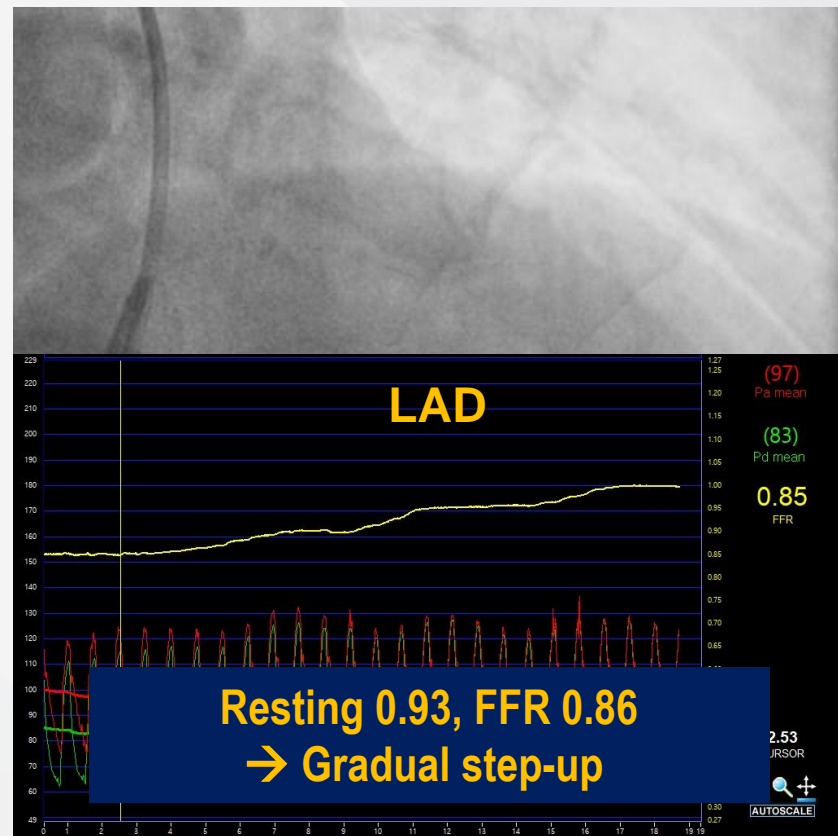
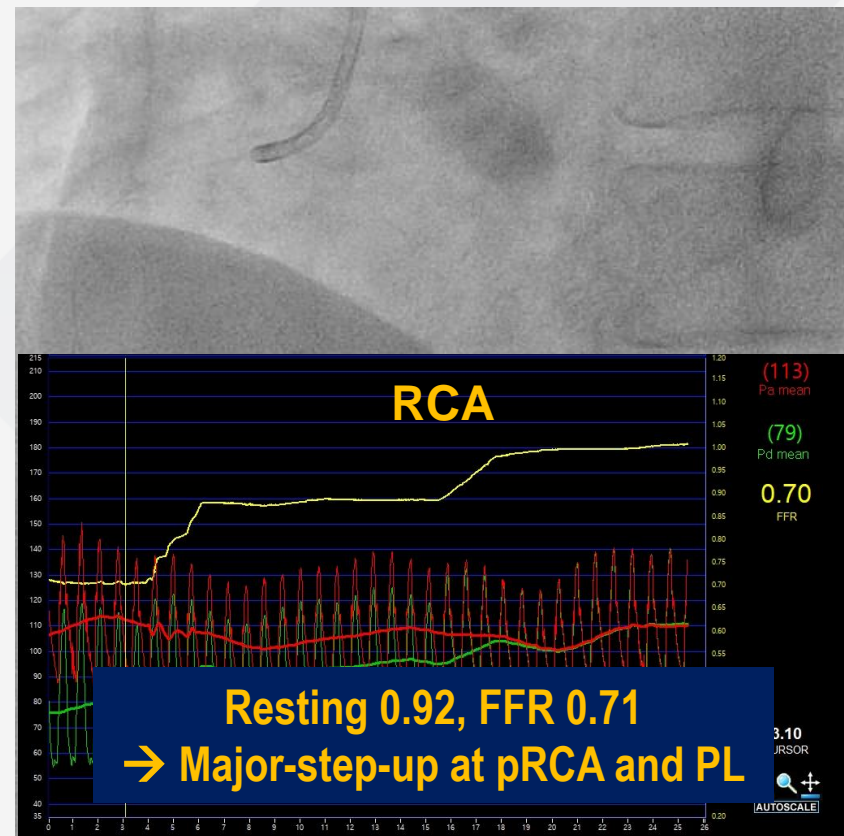
CCTA: 3VD, EchoCG: EF=74%, No RWMA → CABG vs. PCI?



Make Our Decision Simple with FFR

62/M, Stable IHD, CCS II

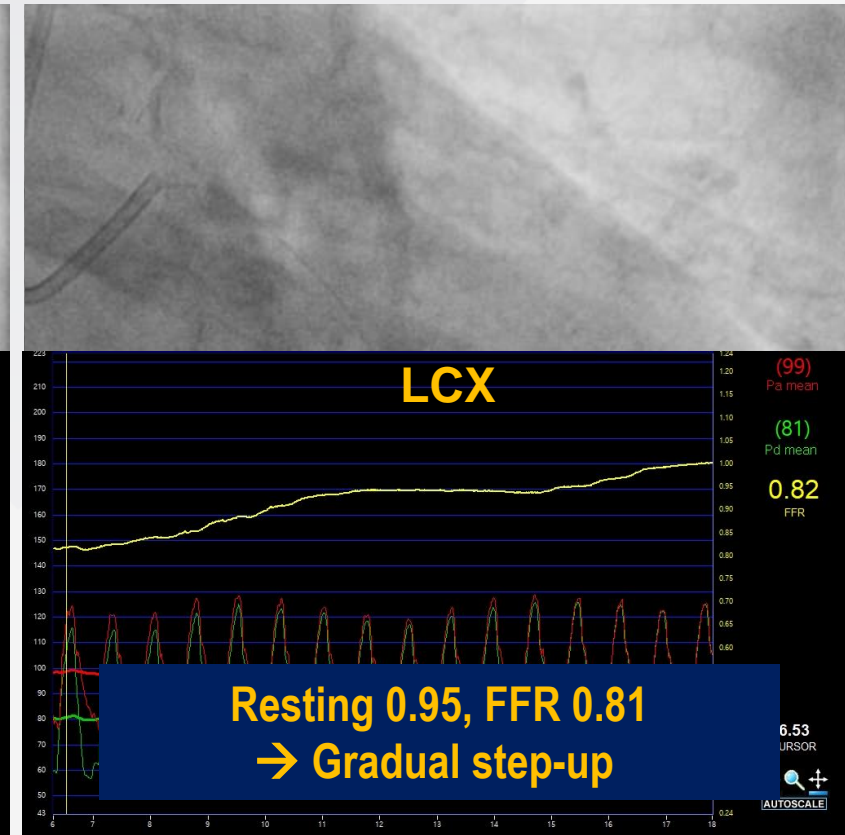
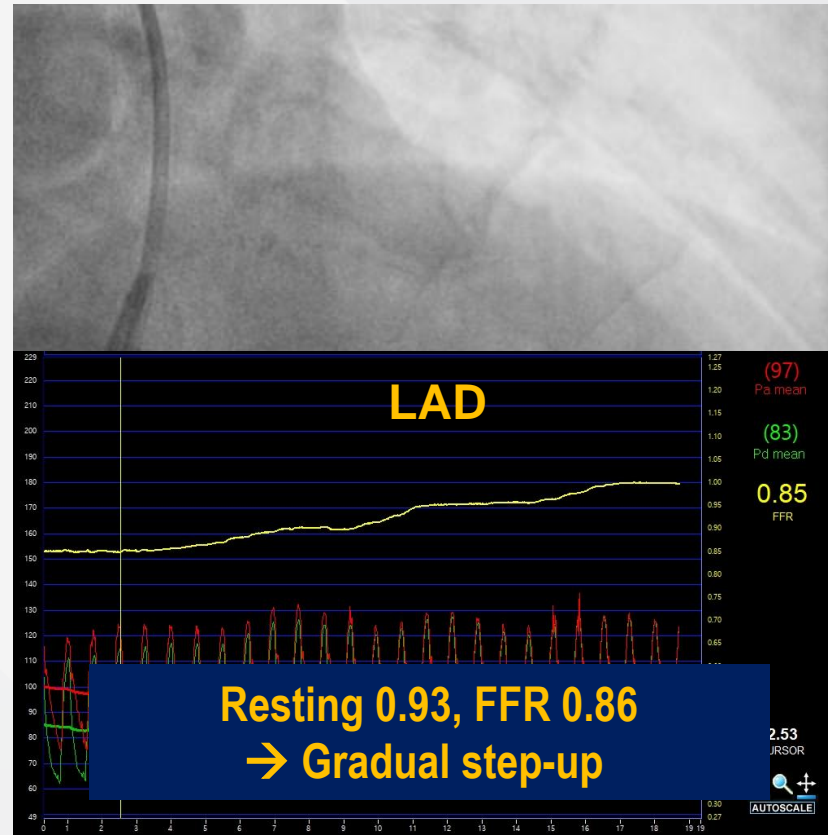
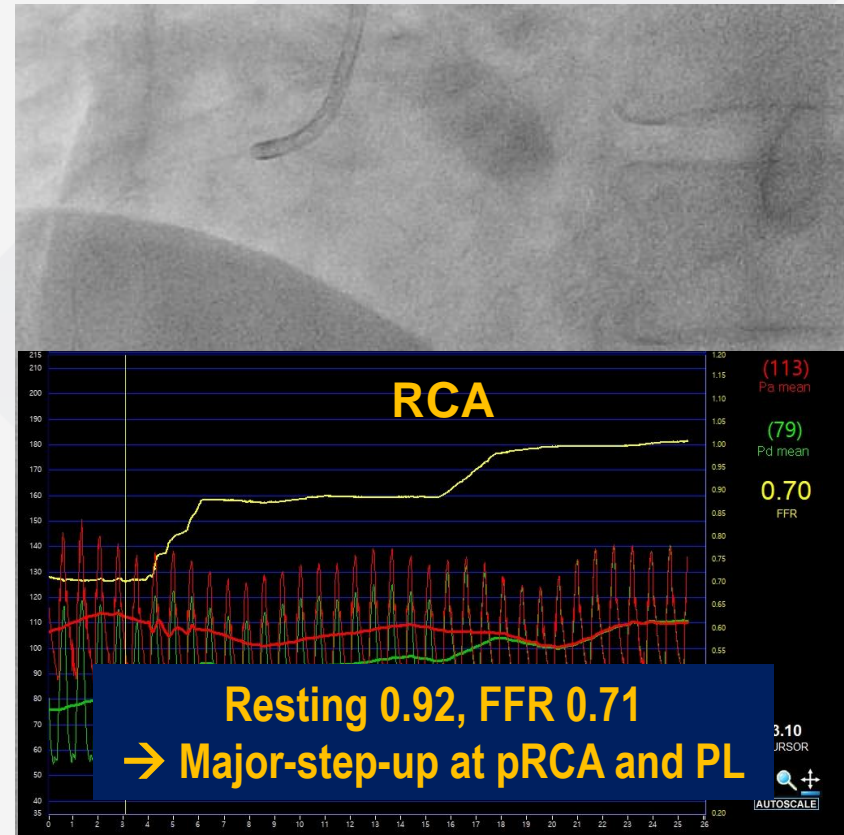
CCTA: 3VD, EchoCG: EF=74%, No RWMA → CABG vs. PCI?



Make Our Decision Simple with FFR

62/M, Stable IHD, CCS II

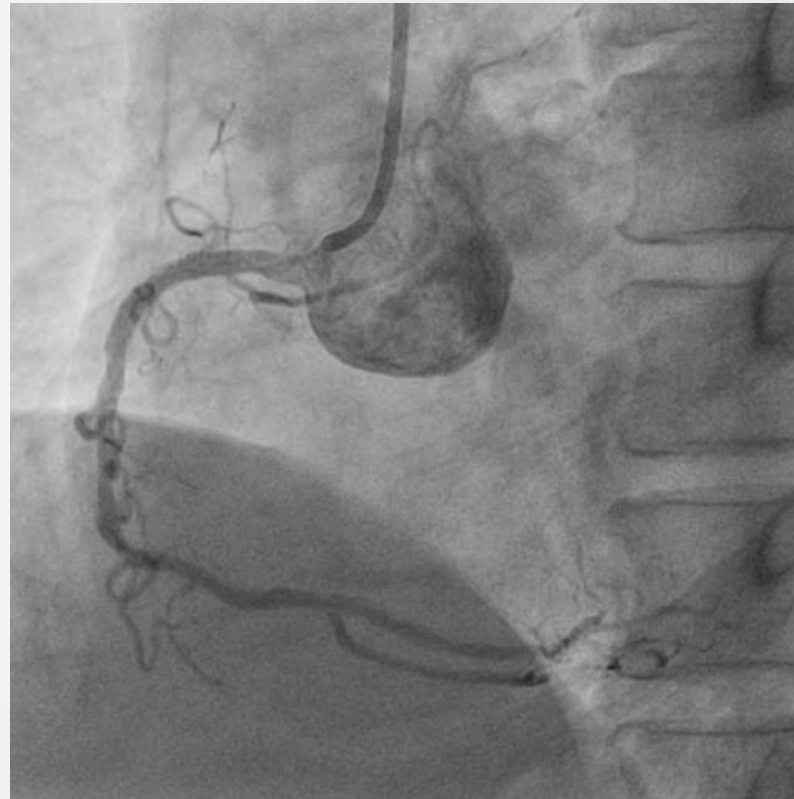
CAG with Physiologic Study : 1VD, Functionally → PCI



Make Our Decision Simple with FFR

62/M, Stable IHD, CCS II

CAG with Physiologic Study : 1VD, Functionally → PCI

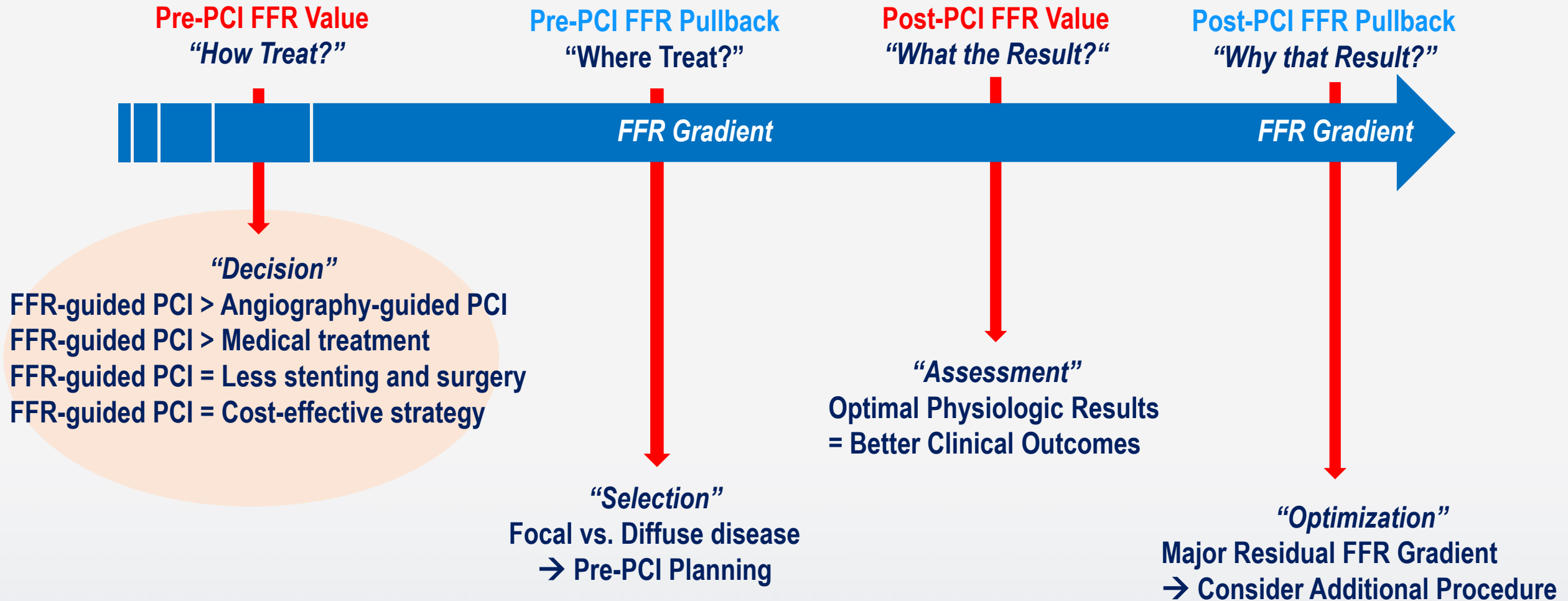


3.0x23mm Xience Sierra at pRCA
2.5x20mm DCB at PL

Post-PCI FFR for RCA



Summary of FFR for Clinical Practice



Current Status of Coronary Physiology to Guide PCI

2018 ESC Guideline for Myocardial Revascularization

Recommendations	Class ^a	Level ^b
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis. ^{15,17,18,39}	I	A

2021 ACC/AHA/SCAI Coronary Revascularization Guideline

COR	LOE	RECOMMENDATIONS
1	A	1. In patients with angina or an anginal equivalent, undocumented ischemia, and angiographically intermediate stenoses, the use of fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) is recommended to guide the decision to proceed with PCI (1-6).
3: No benefit	B-R	2. In stable patients with angiographically intermediate stenoses and FFR >0.80 or iFR >0.89, PCI should not be performed (7-10).

Both guidelines have recommended the FFR-guided decision making as Class IA.

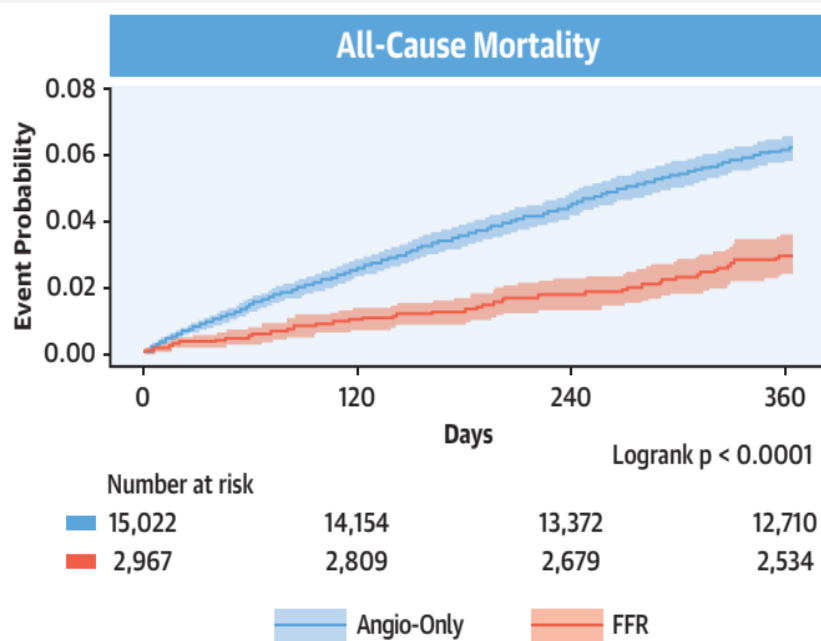
What about real-world data and adoption rate?

FFR-guided PCI improve patient survival in nationwide cohort studies

All-Cause Mortality

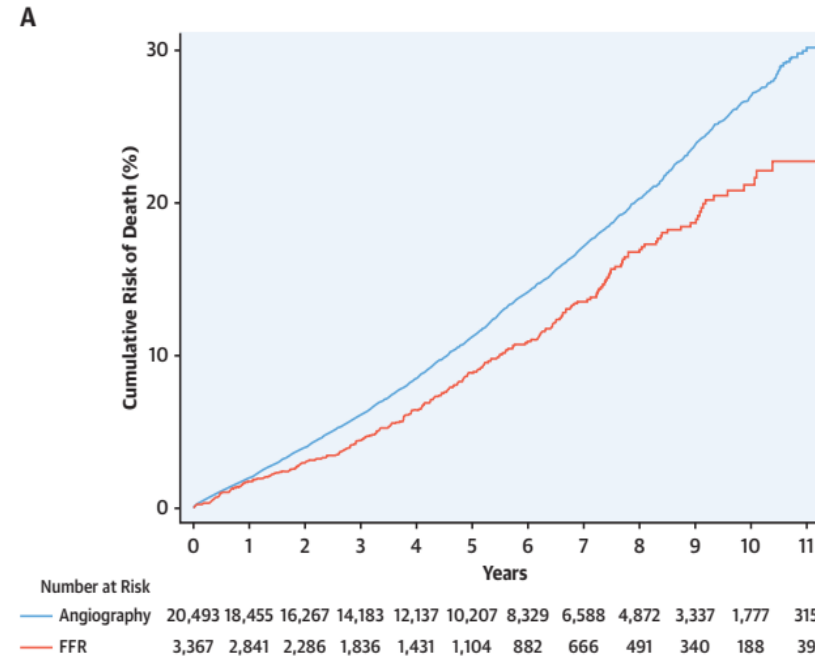
FFR-Guided PCI versus Angiography-Only PCI

USA



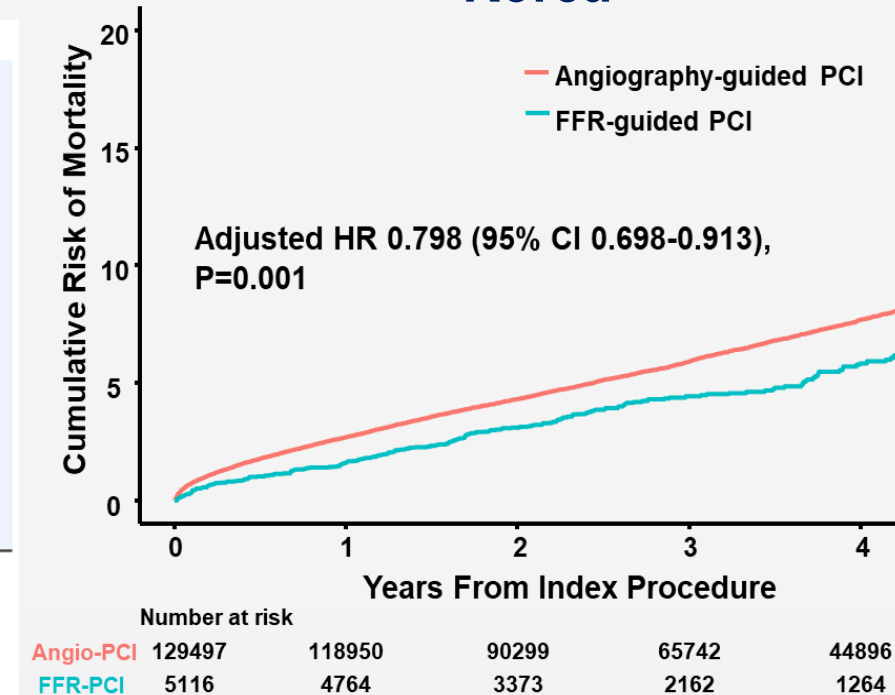
Veterans Affairs registry 2009-2017
(Stable IHD N=17,989, 1 Year)

Europe (Sweden)



SCAAR registry 2005-2016
(Stable IHD N=23,860, Median 4.7 Years)

Korea

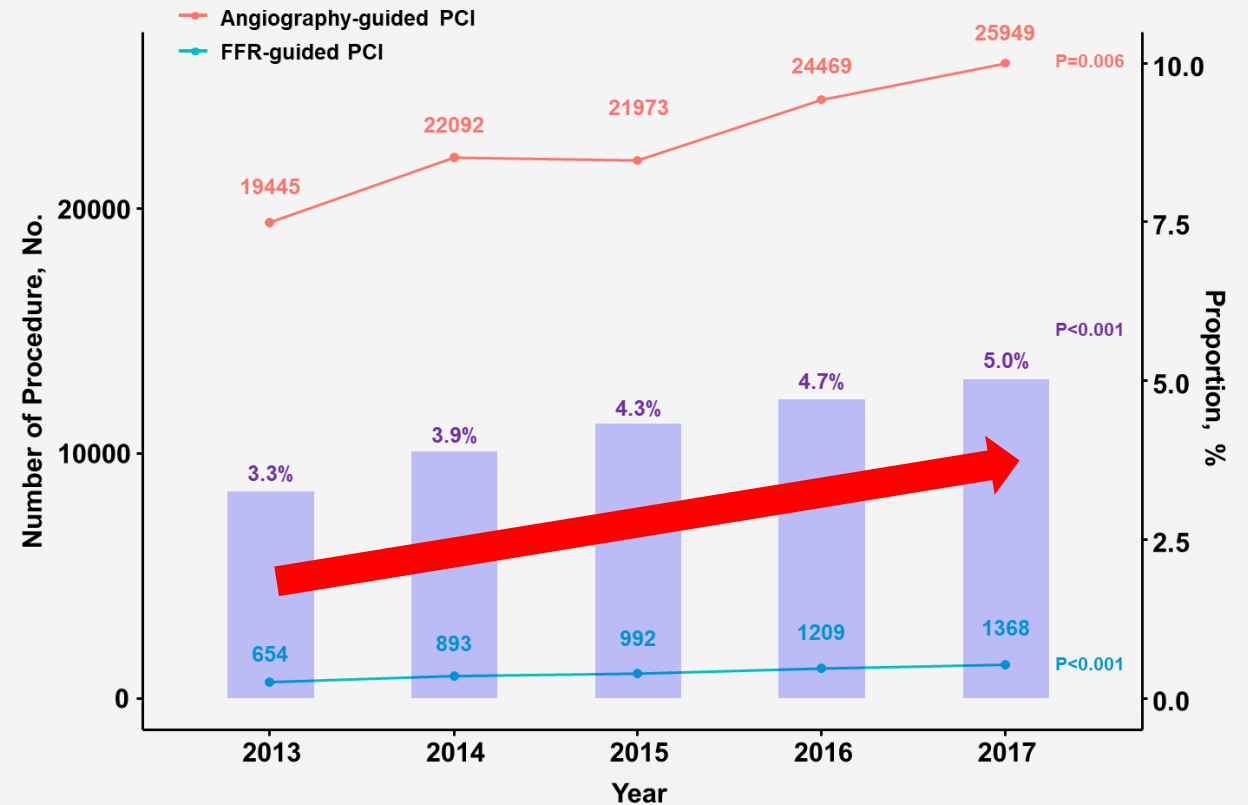
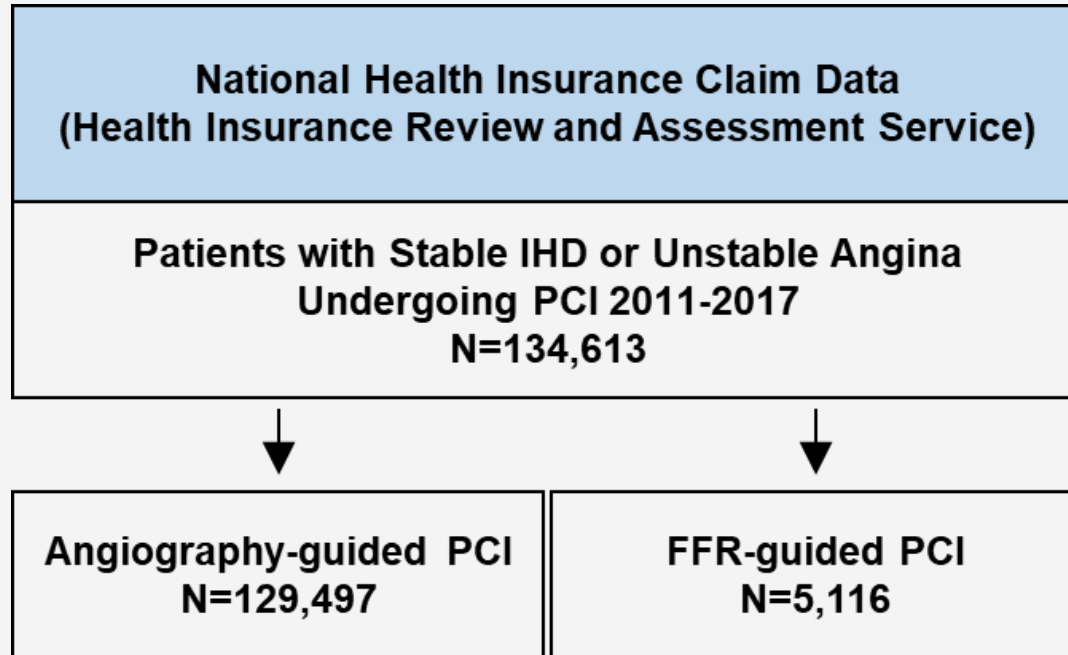


Korean NHIS-HIRA 2013-2018
(Total N=134,613, 4 Years)

Real-world Data of FFR-guided PCI in Korea

Health Insurance Review and Assessment Service Data

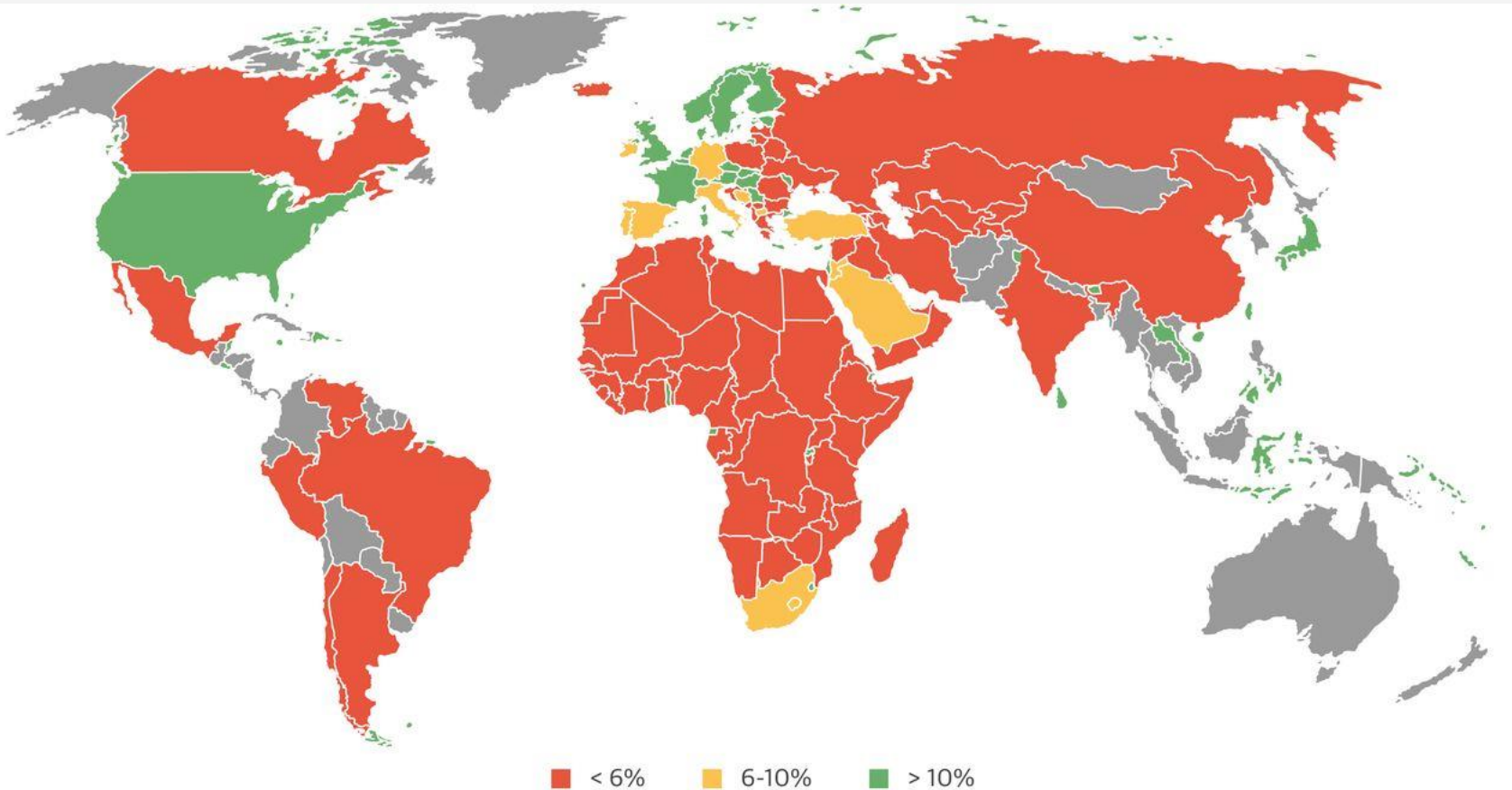
134,613 Patients with Stable and Unstable Angina (2011~2017)



Although the **annual number** and **proportion of FFR-guided PCI** significantly increased, **only 3.8% were FFR-guided PCI** in Korea.

Low Adoption Rate of FFR in Contemporary Practice

*Experts emphasized the role of FFR.
Guidelines endorsed Class IA.
RWDs showed reductions in mortality.*



Multifactorial reasons for limited adoption rates.

Whether FFR can reduce

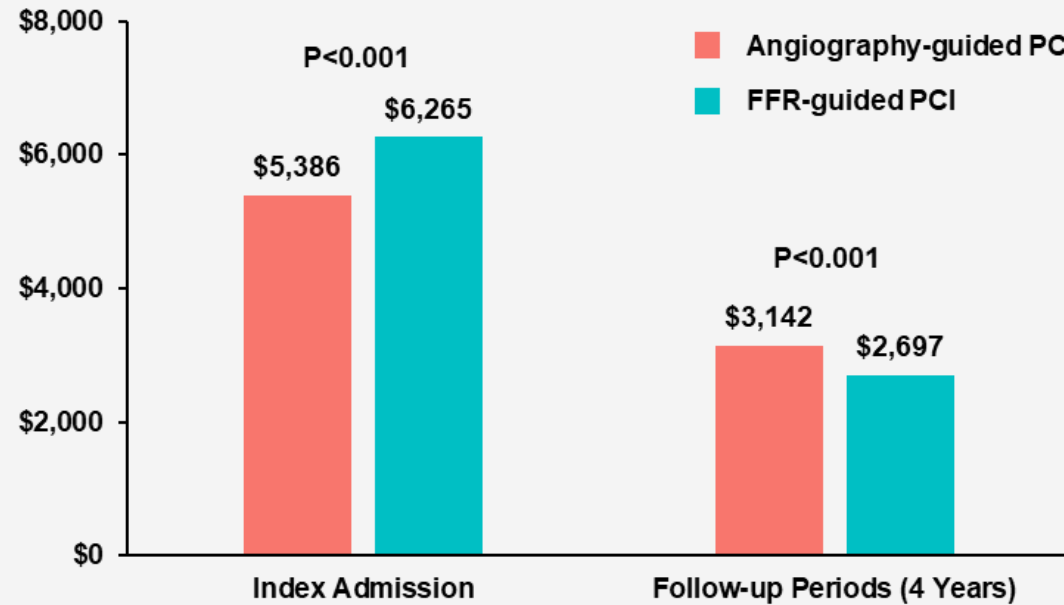
- 1. Cost-Effectiveness**
2. Additional procedural time
3. Knowledge Barrier
4. Physician attitude remains questionable...

Real-world Data of FFR-guided PCI in Korea

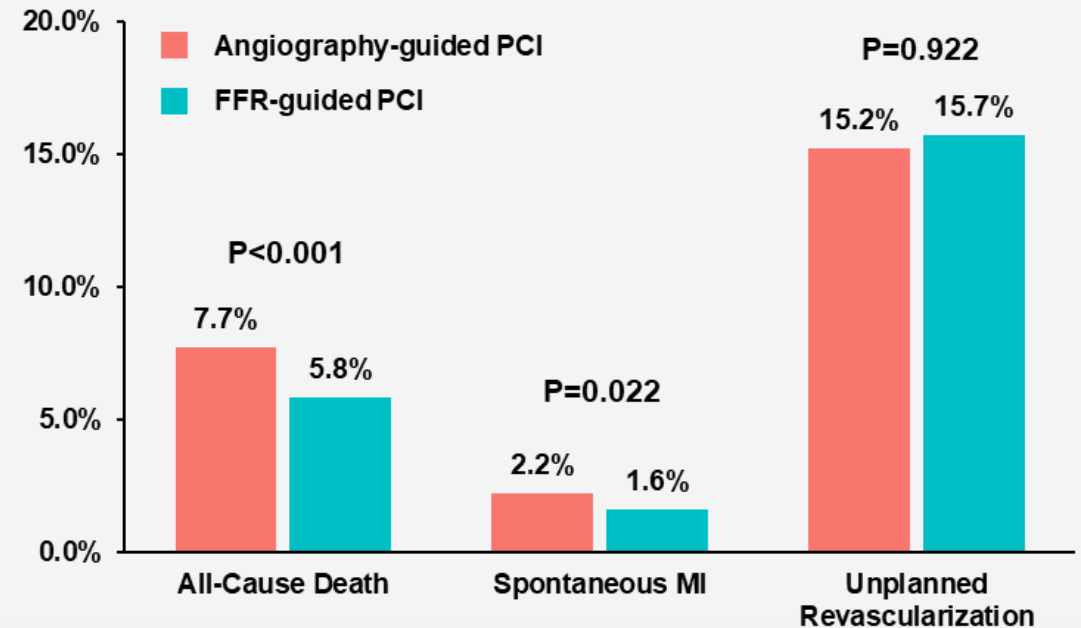
Health Insurance Review and Assessment Service Data

134,613 Patients with Stable and Unstable Angina (2011~2017)

Medical Costs



Adverse Clinical Events



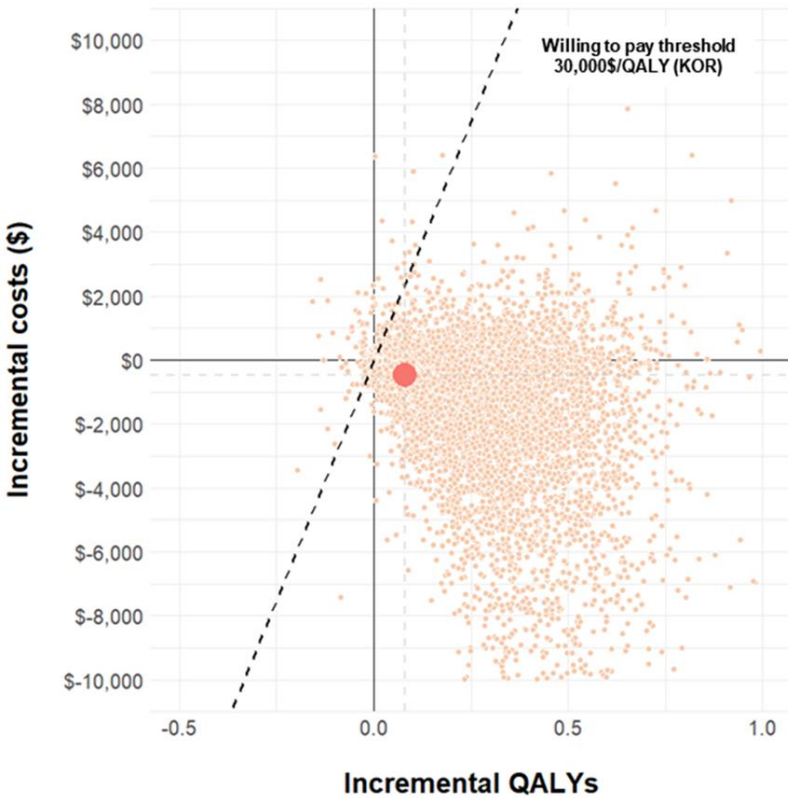
- FFR-guided PCI showed significantly lower risk of **all-cause death** or **spontaneous MI** at 4 years.
- Although FFR group showed higher medical cost during index admission, **cumulative medical cost after index admission was significantly lower in the FFR group.**

Cost-Effectiveness Analysis of FFR from Nationwide Data

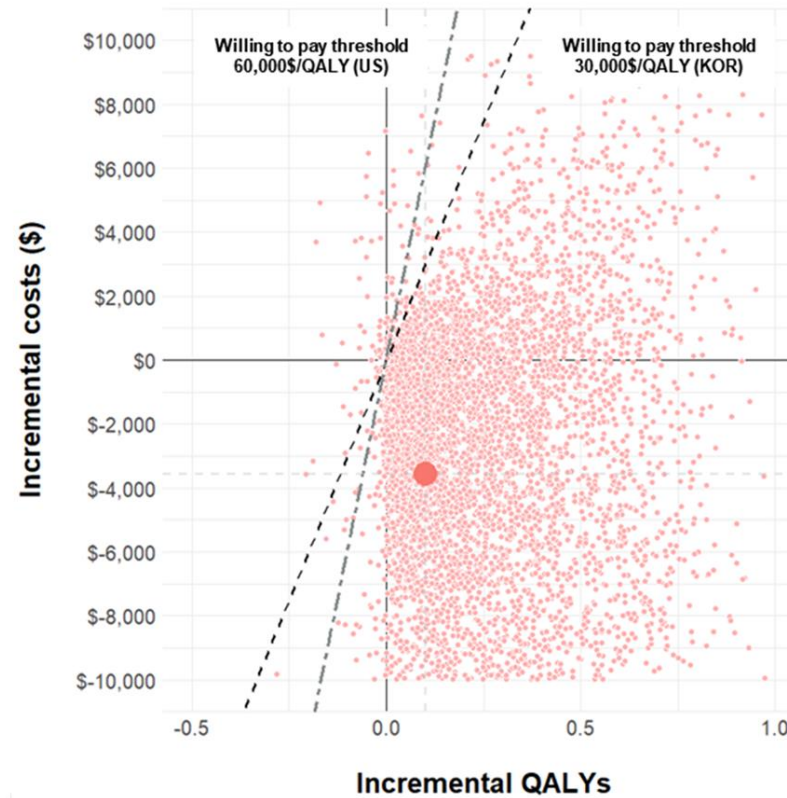
Model-Based: Probabilistic Sensitivity Analysis (PSA)

Bootstrap Technique with 25,000 Replications

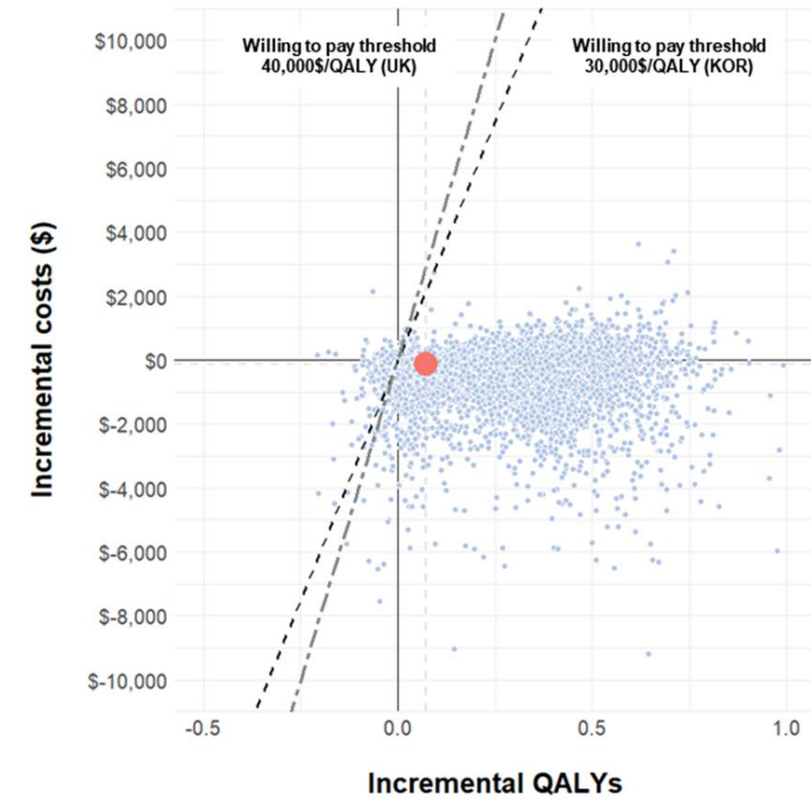
Korea



US



UK



Given the GDP per capita in each country, cost-effectiveness for FFR-based PCI were **93.5%, 92.3% and 90.8%** for Korea, US and UK in PSA analysis, respectively.

FFR-guided vs. Angio-guided PCI for Non-IRA Lesions

FLOWER-MI Trial

Prospective, Multi-center, Open-Label Randomized Trial
1171 MV-STEMI Patients from 41 French Centers

**Primary Endpoint: all-cause death,
nonfatal MI (+ preprocedural MI), revascularization**

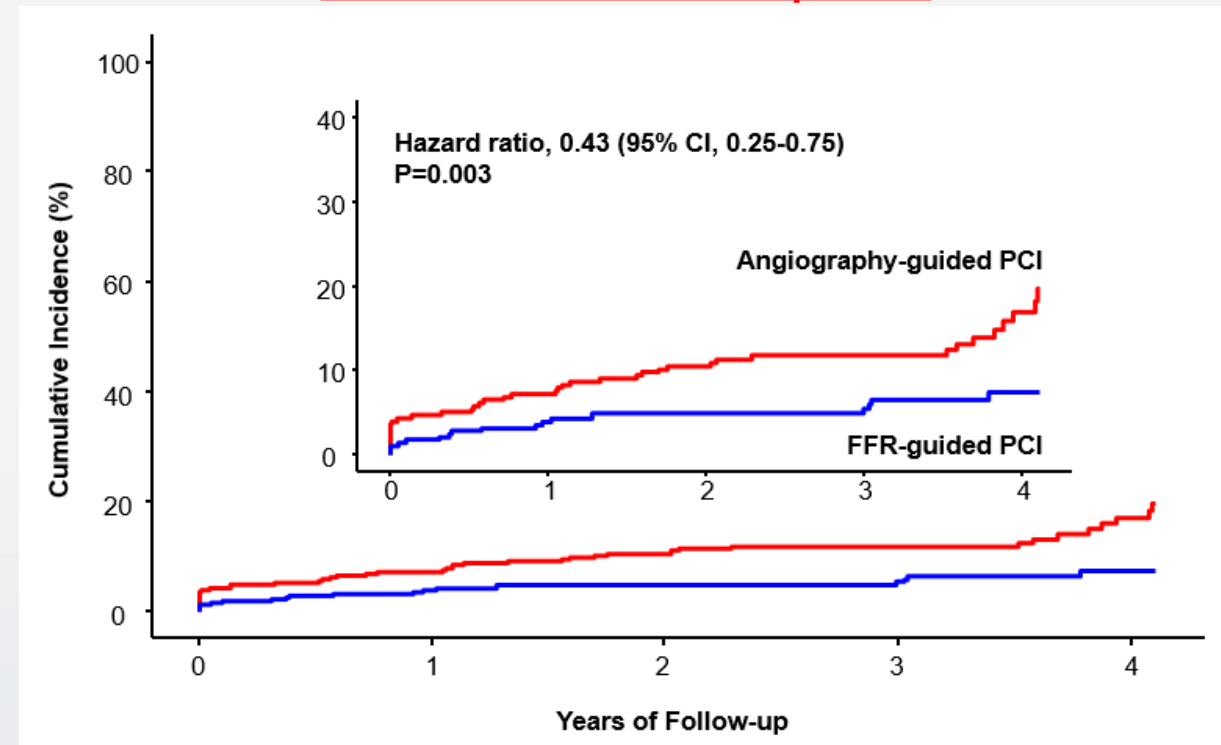
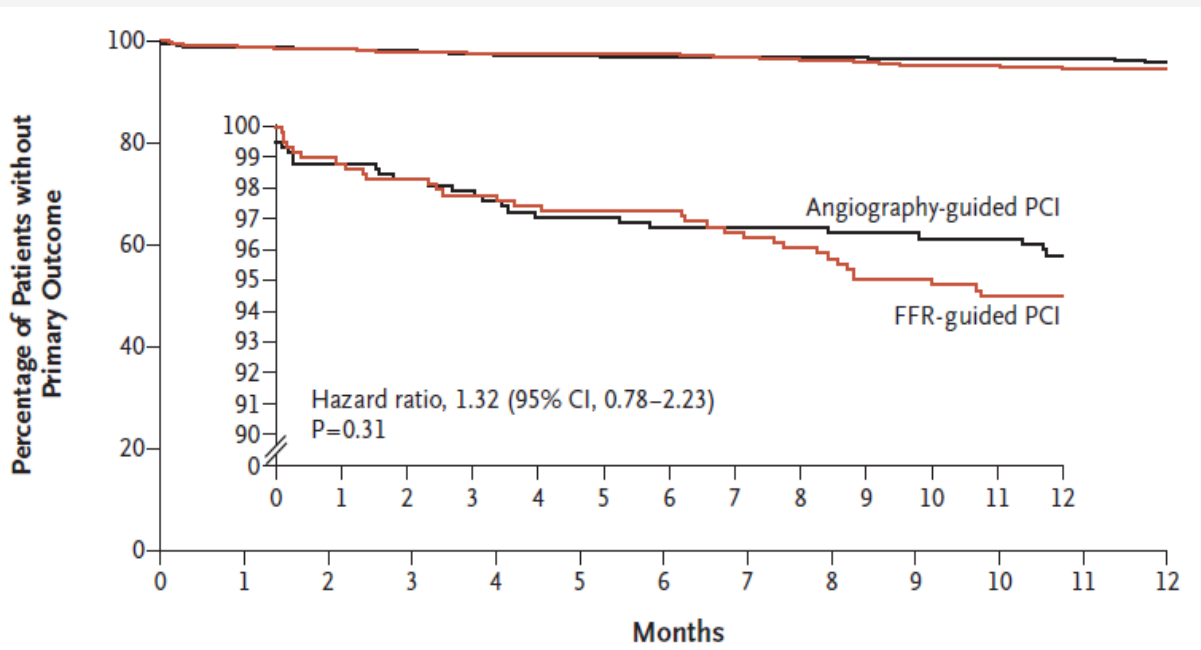
**FFR 5.5% vs. Angiography 4.2% at 1 Year
96.2% staged PCI**

FRAME-AMI Trial

Prospective, Multi-center, Open-Label Randomized Trial
562 MV-AMI Patients from 14 Korean Centers

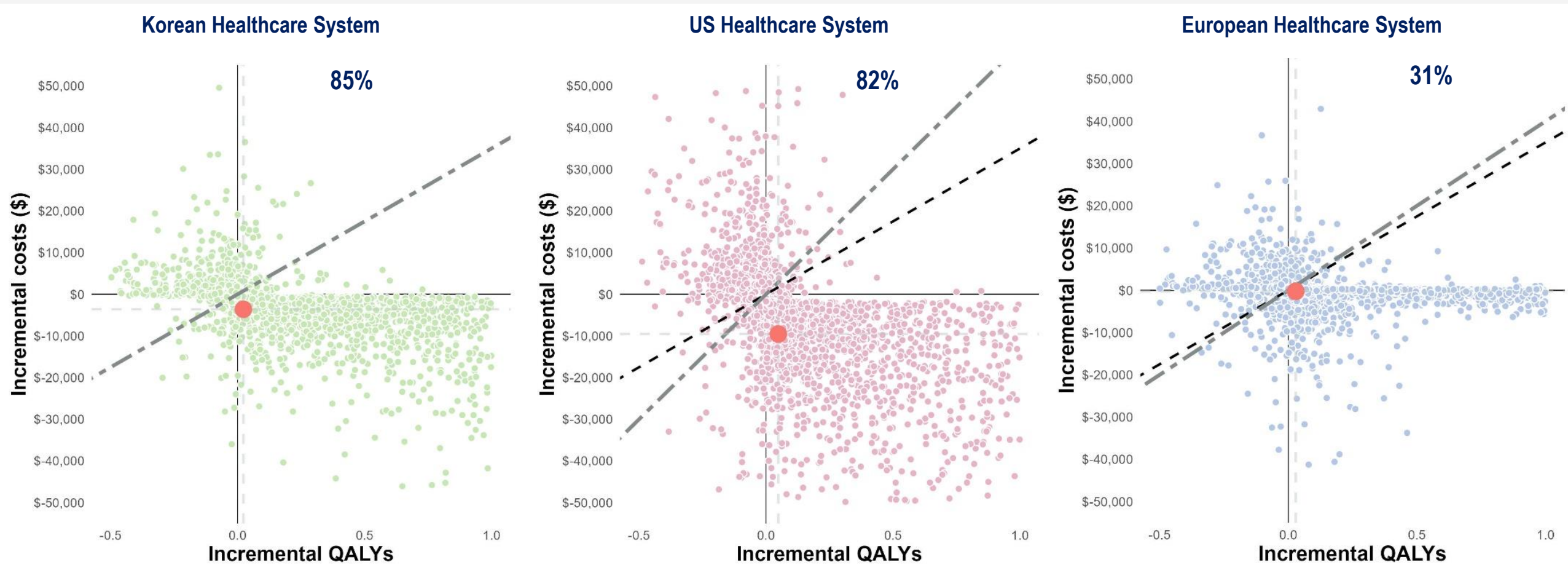
**Primary Endpoint: all-cause death,
nonfatal MI (+ preprocedural MI), revascularization**

**FFR 7.4% vs. Angiography 19.7% at 3.5 Years
60.0% immediate non-culprit PCI**



Cost-Effectiveness Analysis of FFR-guided PCI in AMI and MVD

Cost-Effectiveness of FFR-Guided PCI in 3 Different Healthcare Systems Probabilistic Sensitivity Analysis (PSA)



FFR-guided PCI was a **more cost-effective** across Korea, USA, and Europe.

Summary #1

- **FFR-guided PCI continuously showed clinical benefit and cost-effectiveness among patients with stable ischemic heart disease.**
- **FFR-guided PCI for Non-IRA lesions in AMI patients has been tested compared with angiography-guided PCI, and two RCTs (FLOWER-MI and FRAME-AMI) showed inconclusive results.**
- **CEA of FFR-guided PCI in the FRAME-AMI study showed that the FFR-guided strategy was a more cost-effective approach for AMI patients with MVD.**

Coronary Microvascular Dysfunction (CMD)

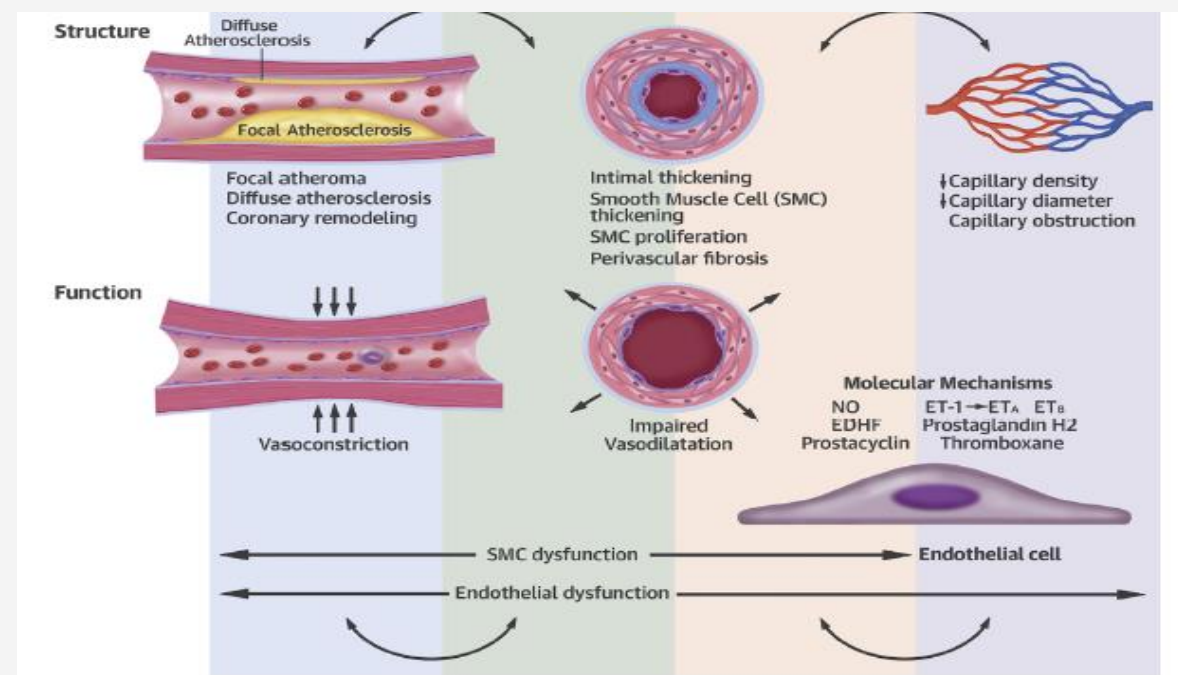
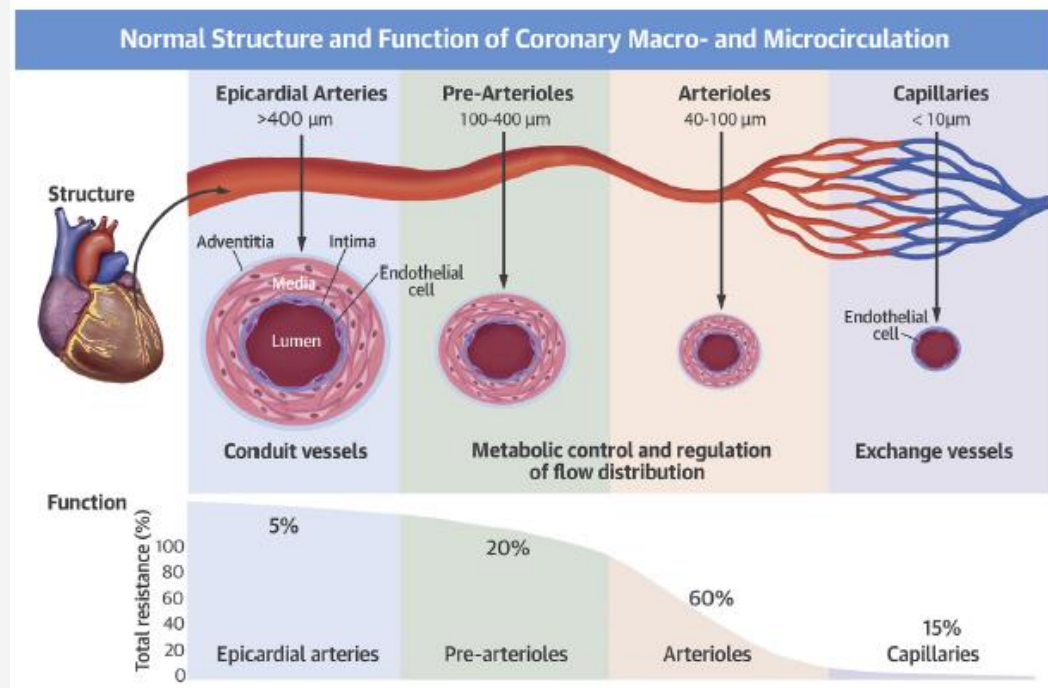
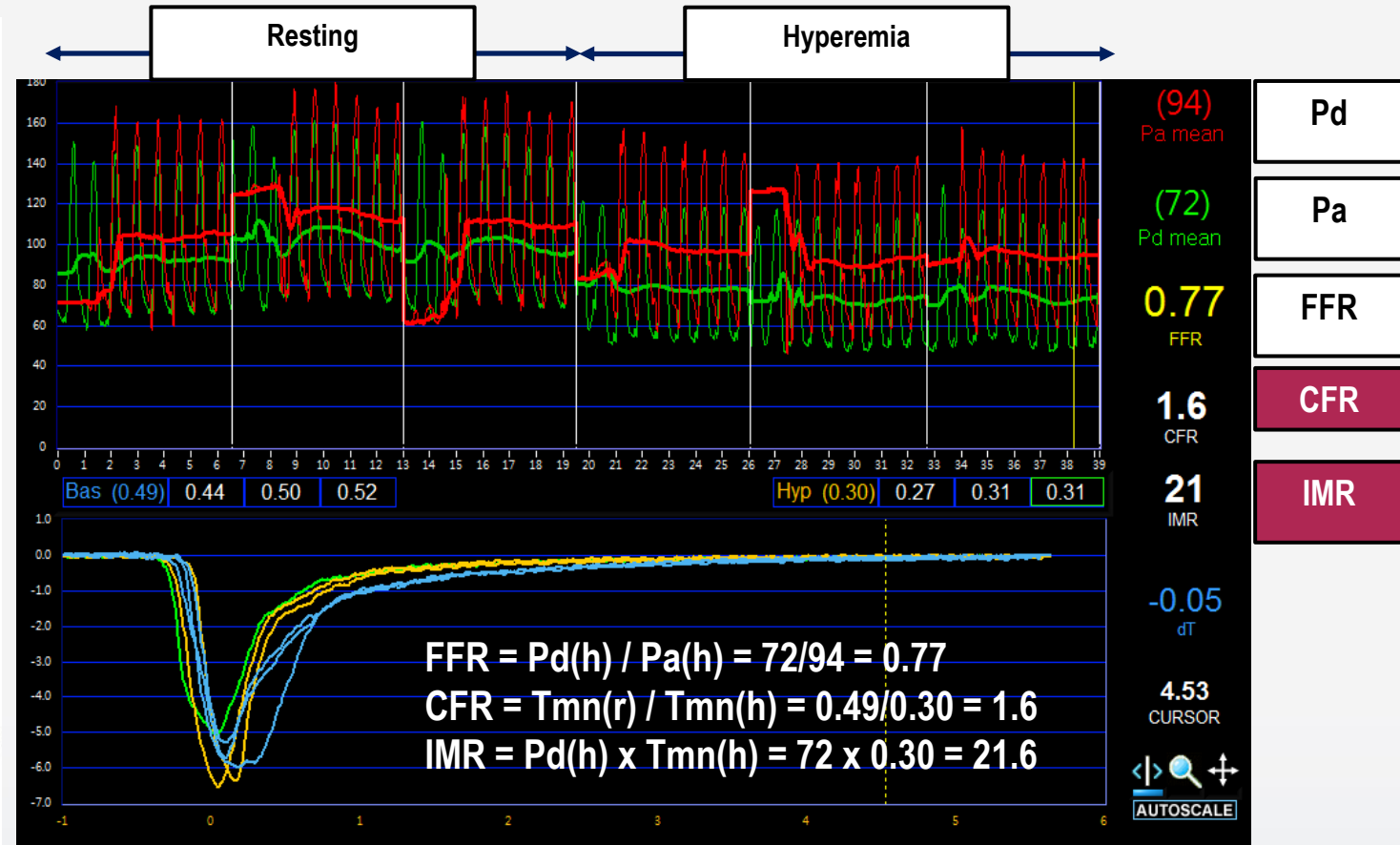
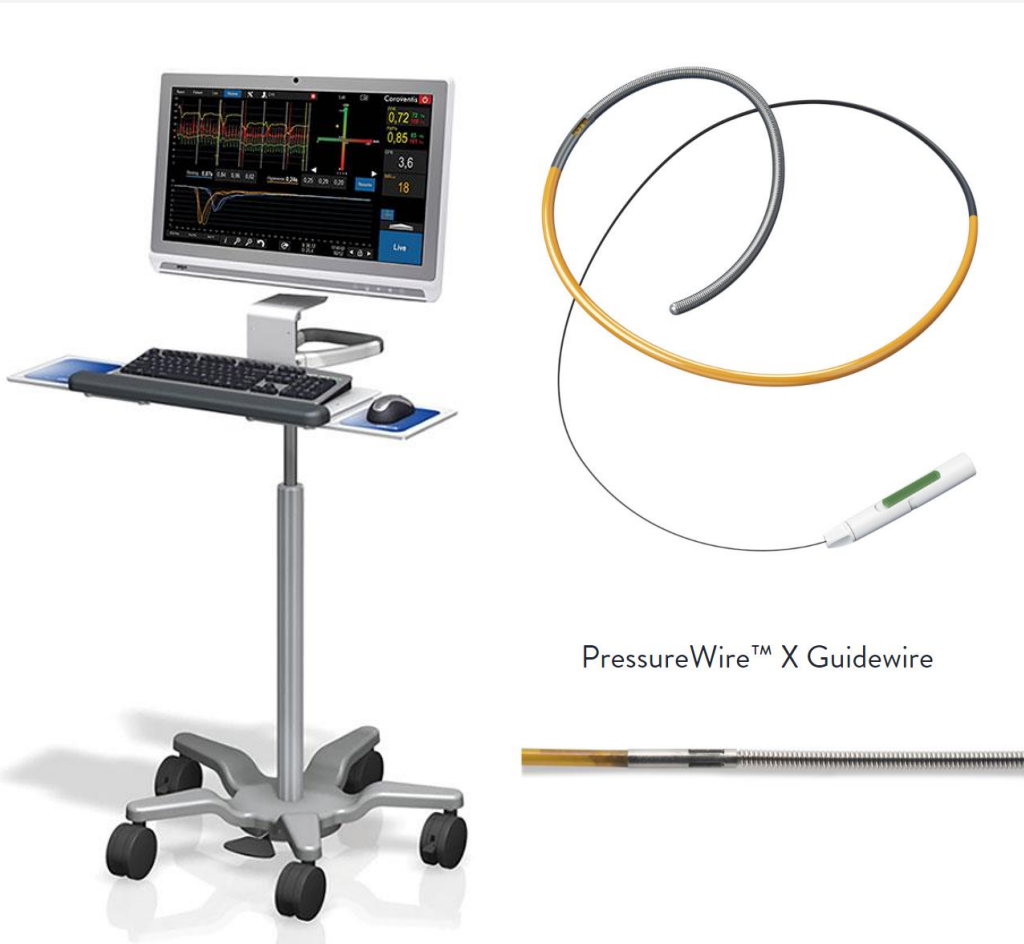


TABLE 1 Strengths and Limitations of Select Diagnostic Techniques for the Evaluation of CMD

	Accuracy	Reproducibility	Diagnostic Threshold	Prognostic Validation	Availability	Cost
Noninvasive*						
PET	++++	++++	CFR <2	+++	++	\$\$\$
CMR	+++	+++	MPRI <2	++	++	\$\$\$
Doppler echocardiography	++	+++	CFVR <2	+++	++++	\$
Invasive*						
CFR	++++	++++	<2.3	+++	++++	\$\$\$\$
IMR	++++	+++	>25 U	++	++	\$\$\$\$

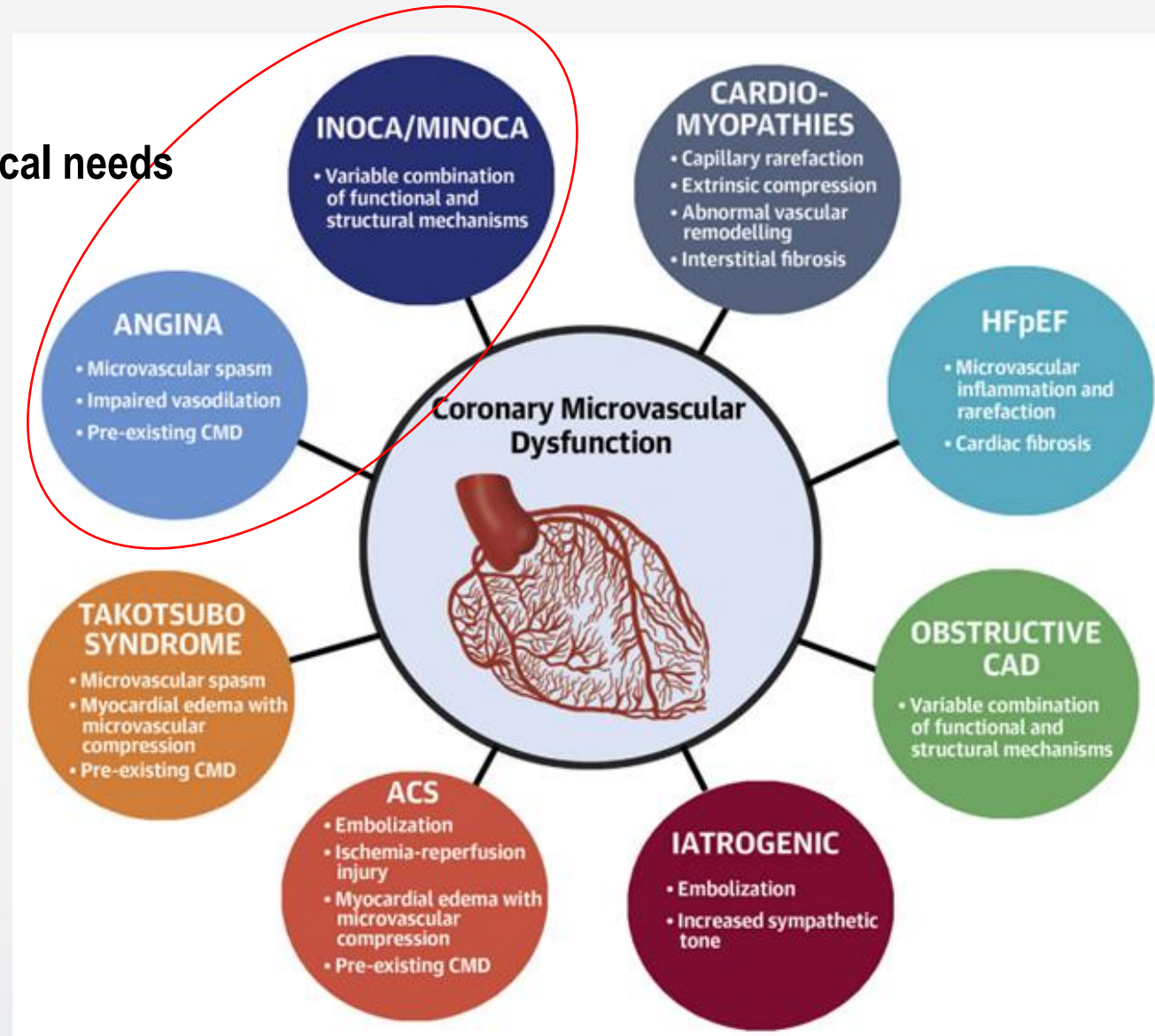
Physiological Indexes for Assessment of CMD

RADI analyzer → Coroflow



Role of CMD Across Different Cardiovascular Disease

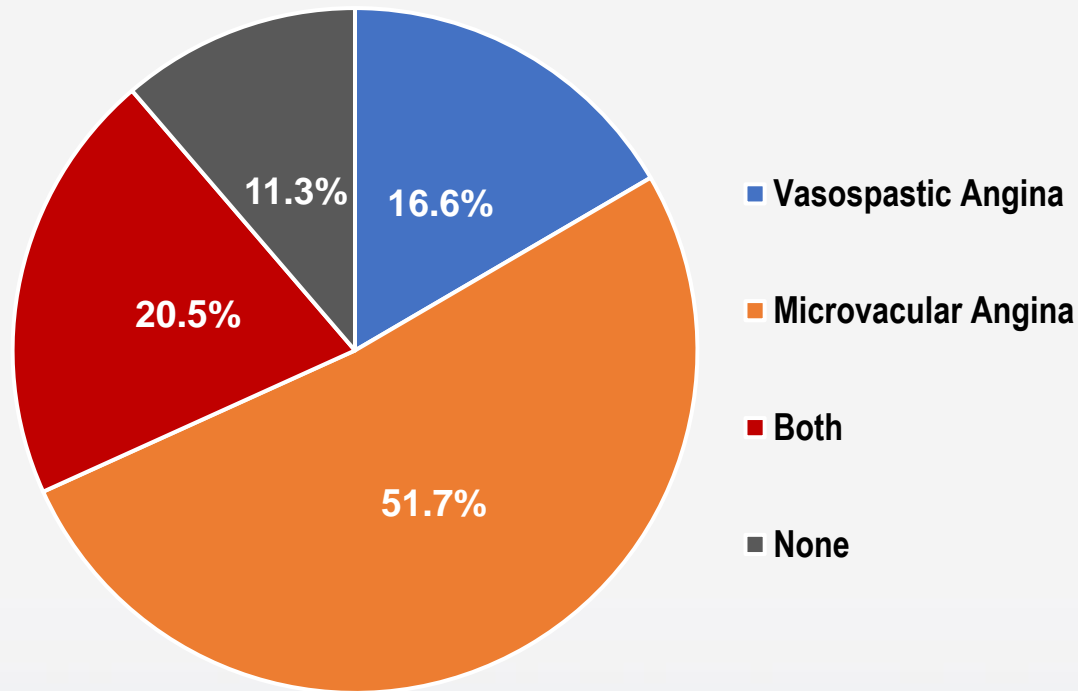
Clinical needs



Why do we have to look beyond epicardial coronary arteries?

- Prevalence of non-epicardial coronary disease -

151 Stable Patients with $<50\%$ stenosis and/or $FFR > 0.80$,
Ach challenge test and FFR/CFR/IMR measurement



Definition

Significant vasoconstriction ($\geq 90\%$),
chest pain (+), and ECG change

Any of $IMR \geq 25U$, $CFR < 2.0$, or microvascular spasm
to Ach (chest pain and ECG change, but no
epicardial vasoconstriction)

Substantial Proportion of Patients with No Obstructive Stenosis
shows Abnormal Vasomotor / Microvascular Function

Angina Symptom, Positive Non-invasive Tests, But, No Obstructive Epicardial Disease

Ischemia with Non-Obstructive Coronary Arteries “INOCA”

Presence of symptoms suggestive of myocardial ischemia

ANGINA

Objective Documentation of Ischemia
(by non-invasive test or invasive test)

ISCHEMIA

Absence of Obstructive CAD (< 50% DS on CAG or FFR>0.80)

NO CAD

Why do we have to look beyond epicardial coronary arteries?

- Prognosis of INOCA -

Major Adverse Cardiovascular Events (MACE)

¹CIAO-ISCHEMIA (2021): About 2% at 1 year

²Meta-Analysis of 54 Studies (2018) : 1.32 / 100 person-year

MACE or Chest Pain Hospitalization

¹CIAO-ISCHEMIA (2021): About 4% at 1 year

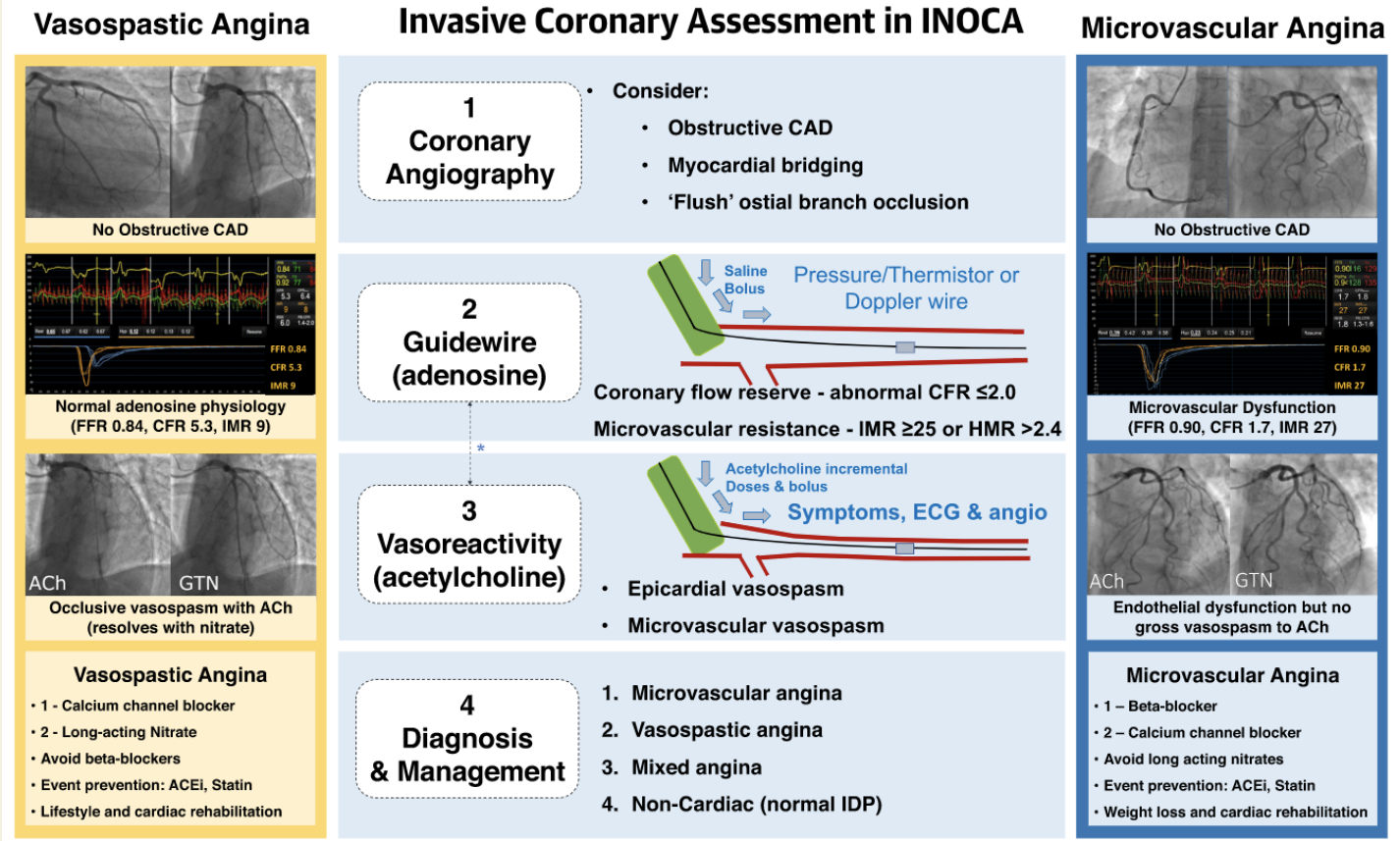
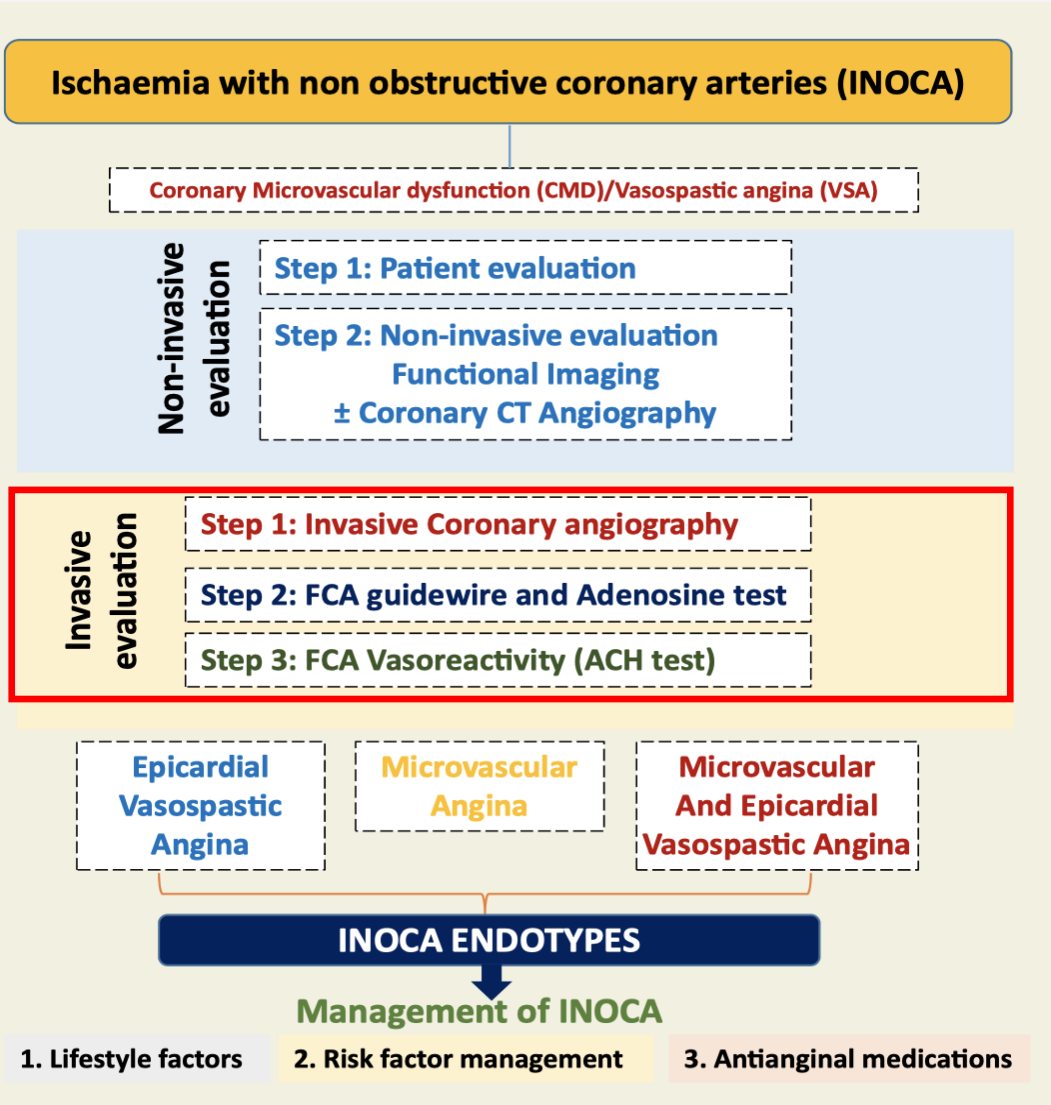
³WISE Study (2006) : 20% over 5 years

INOCA is not Benign.

INOCA was associated with MACE and high economic burden due to hospitalization.

How to Diagnose INOCA?

Expert Consensus on INCOA



What do the Guidelines say on Evaluation of CMD?

2019 ESC Guideline for Chronic Coronary Syndrome (CCS)

2023 American Guideline for Chronic Coronary Disease (CCD)

Investigations in patients with suspected coronary microvascular angina

Recommendations	Class ^a	Level ^b
Guidewire-based CFR and/or microcirculatory resistance measurements should be considered in patients with persistent symptoms, but coronary arteries that are either angiographically normal or have moderate stenoses with preserved iwFR/FFR. ^{412,413}	Ia	B
Intracoronary acetylcholine with ECG monitoring may be considered during angiography, if coronary arteries are either angiographically normal or have moderate stenoses with preserved iwFR/FFR, to assess microvascular vasospasm. ^{412,438–440}	IIb	B
Transthoracic Doppler of the LAD, CMR, and PET may be considered for non-invasive assessment of CFR. ^{430–432,441}	IIb	B

CFR = coronary flow reserve; CMR = cardiac magnetic resonance; ECG = electrocardiogram; FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; LAD = left anterior descending; PET = positron emission tomography.

^aClass of recommendation.

^bLevel of evidence.

© ESC 2019

Recommendation for INOCA

Referenced studies that support the recommendation are summarized in the [Online Data Supplement](#).

COR	LOE	RECOMMENDATION
2a	B-R	1. In symptomatic patients with nonobstructive CAD, a strategy of stratified medical therapy* guided by invasive coronary physiologic testing can be useful for improving angina severity and QOL. ^{1,2}

Class Ia, LOE B

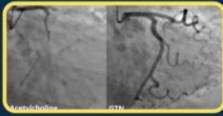


- Non-invasive << Invasive methods
- When? for stratified medical therapy
- Why? Improving angina severity and QOL

How to Manage INOCA?

CorMiCa Trial

A randomized, controlled, blinded trial of medical therapy vs standard care in INOCA

Stratified Therapy Used in the CorMiCa Trial

	Microvascular Angina <ul style="list-style-type: none">• Guideline directed therapy – e.g. Betablocker & Lifestyle
	Vasospastic Angina <ul style="list-style-type: none">• Guideline directed therapy – e.g. CCB & Lifestyle
	Non-Cardiac (Normal Function) <ul style="list-style-type: none">• Cease antianginal therapy +/- non-cardiac Ix

Management of CMD is not different from epicardial disease

- Symptomatic Control with Angina medication
- Secondary Prevention of Co-morbidity
- Patient education and lifestyle modification

Main Results:



**Sustained Benefits:
Improved Angina and
Quality of Life**

Summary #2

- **INOCA** is prevalent and has significant worse prognosis. Along with vasospastic angina, **coronary microvascular disease (CMD)** is one of the major component of INOCA.
- Current Expert Consensus and Guideline recommends **comprehensive physiologic assessment** for classifying the endotypes.
- **Stratified treatment for INOCA** may work well in terms of **improvement in angina symptoms**, but we need further studies for improving the patients' outcomes
- The **Coroflow** system provides full physiology data of entire coronary vasculature for making clear diagnosis.

Thank You For Your Attention

Seung Hun Lee, MD, PhD
Clinical Assistant Professor

Division of Cardiology, Department of Internal Medicine
Chonnam National University Hospital, Gwangju, Republic of Korea

If you have any question, don't hesitate to e-mail me.
lsh8602@naver.com ; gfmaniac@gmail.com

Stable IHD with Intermediate Stenosis

Case #1. Stable Angina

69/M, Chest pain(+), TMT(+)

CCTA: 1VD, EchoCG: EF=58.5%



Intermediate stenosis at p-mLAD

Case #2. r/o Silent Ischemia

66/M, Chest pain(-)

CCTA: 1VD, EchoCG: EF=71.4%



Intermediate stenosis at p-mLAD

Case #3. Stable Angina

75/M, Chest pain(+), TMT: Equivocal

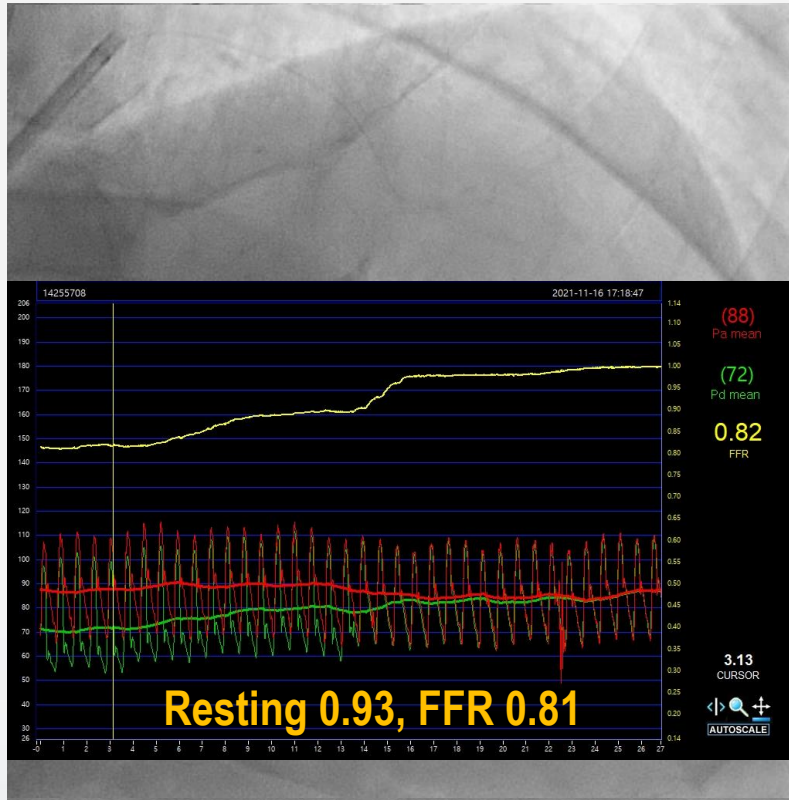
CCTA: 1VD, EchoCG: EF=69.3%



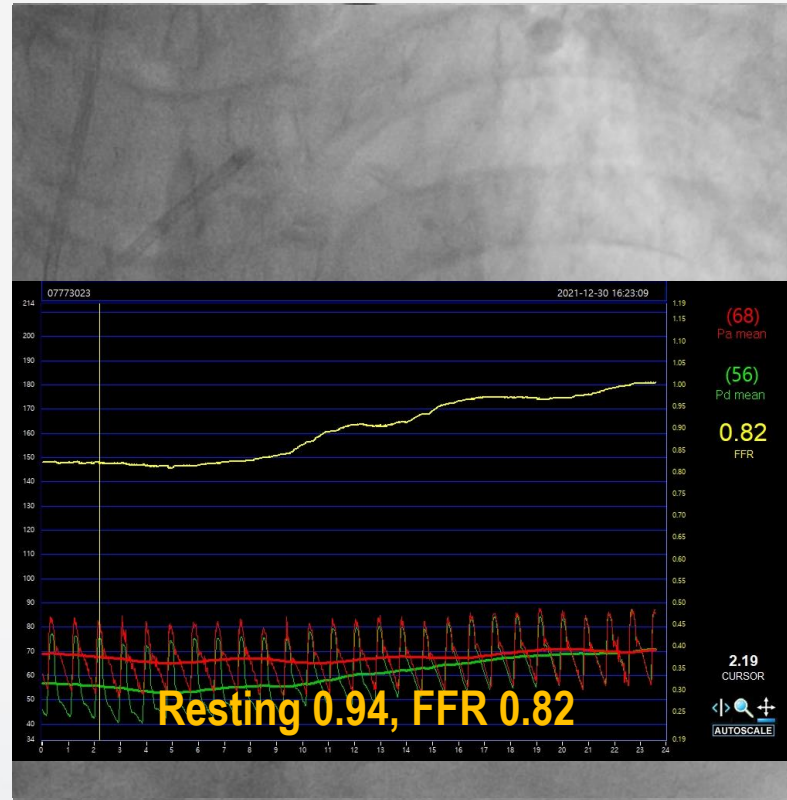
Intermediate stenosis at mLAD

Stable IHD with Intermediate Stenosis

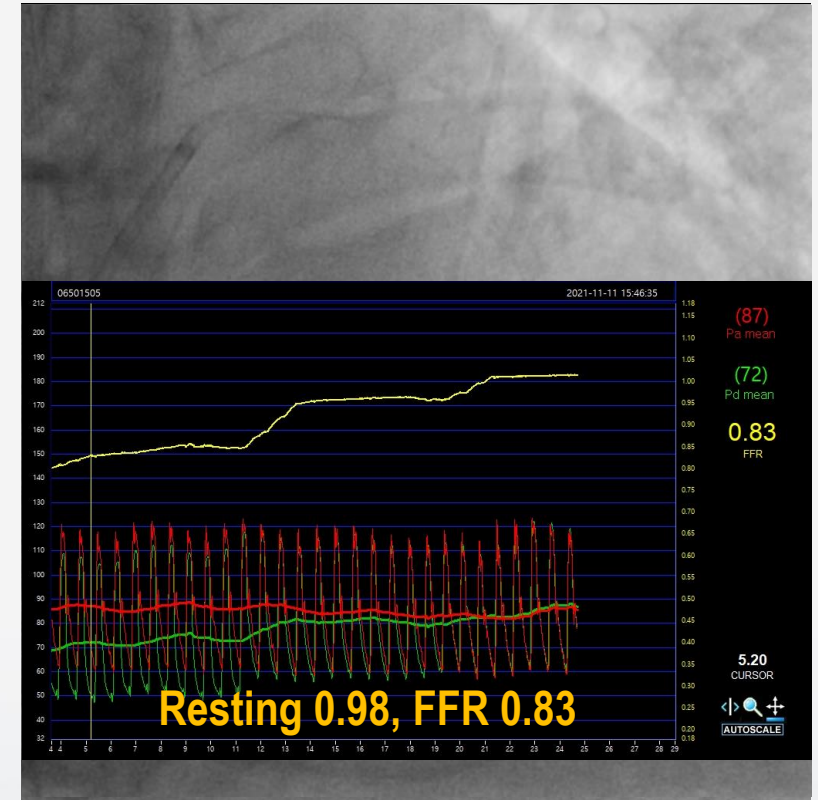
Case #1. Stable Angina
69/M, Chest pain(+), TMT(+)
CCTA: 1VD, EchoCG: EF=58.5%



Case #2. r/o Silent Ischemia
66/M, Chest pain(-)
CCTA: 1VD, EchoCG: EF=71.4%



Case #3. Stable Angina
75/M, Chest pain(+), TMT: Equivocal
CCTA: 1VD, EchoCG: EF=69.3%



Deferred stenting
→ No Event for 4 years

Deferred stenting
→ No Event for 4 years

Deferred stenting
→ No Event for 3 years