MINOCA Physiology Work-up
- Brief reviews and cases -

Joo Myung Lee, MD, MPH, PhD

Heart Vascular Stroke Institute,
Samsung Medical Center, Seoul, Republic of Korea

Disclosures

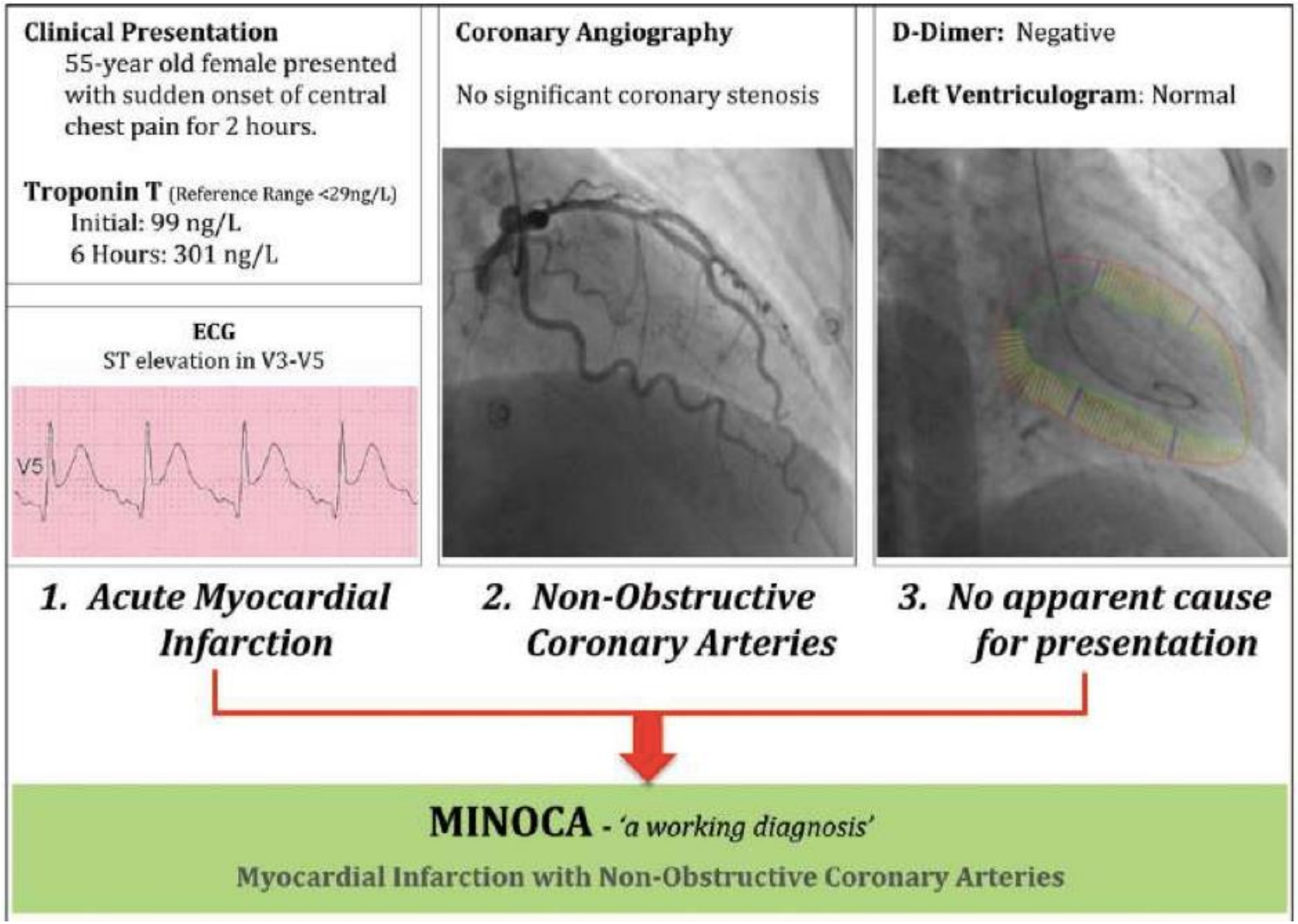
Relationships with commercial interests:

- Grants/Research Support: Abbott Vascular, Boston Scientific, Philips Volcano, Terumo Corporation, Donga-ST, Zoll Medical, and Yuhan Pharmaceutical
- Speakers Bureau/Honoraria: Abbott Vascular, Boston Scientific
- Consulting Fees: Genoss
- Other: None

Definition of MINOCA

The diagnosis of MINOCA is made immediately upon coronary angiography in a patient presenting with features consistent with an AMI, as detailed by the following criteria:
(1) Universal AMI criteria[8]
(2) Non-obstructive coronary arteries on angiography, defined as no coronary artery stenosis ≥50% in any potential IRA
(3) No clinically overt specific cause for the acute presentation

MINOCA is a working diagnosis with multiple causes



Prevalence of MINOCA

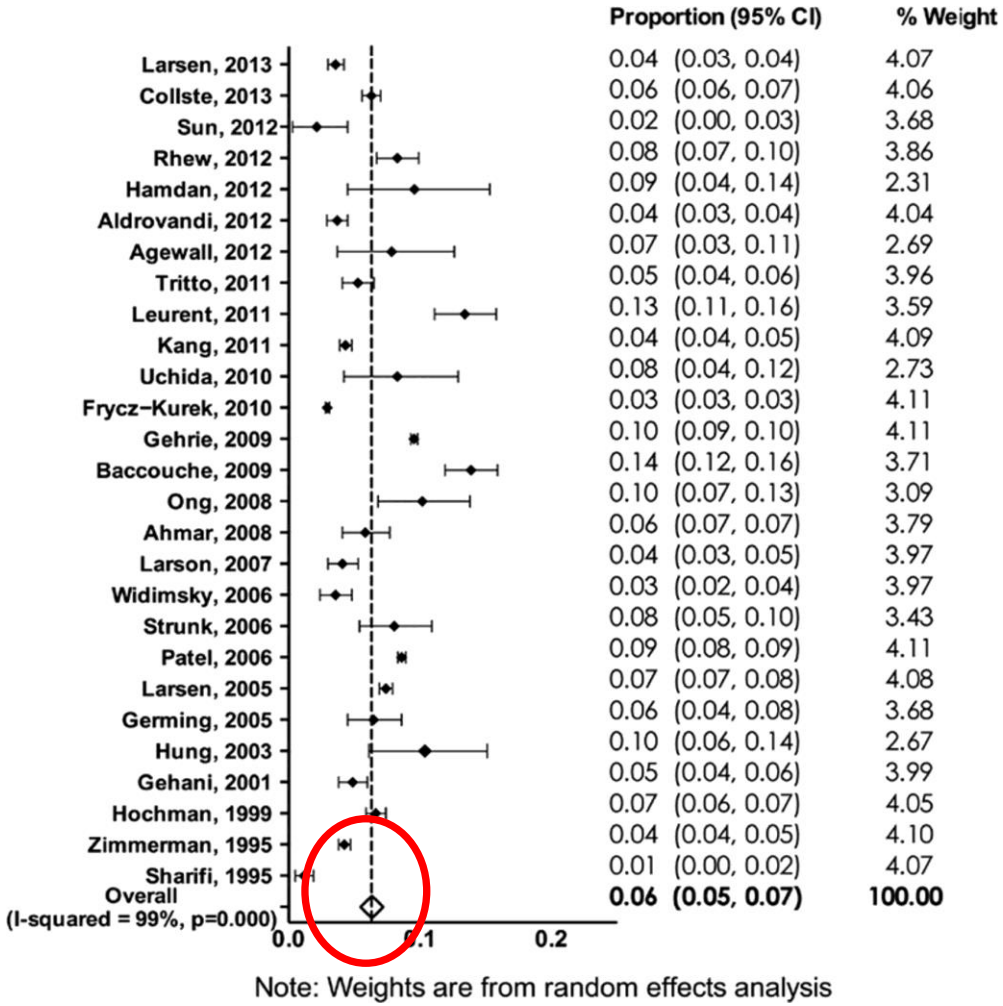
In 1939 earlier report, 8% AMI showed minimal or normal coronary artery

MYOCARDIAL INFARCTION WITHOUT SIGNIFICANT LESIONS OF CORONARY ARTERIES

HARRY GROSS, M.D.
AND
WILLIAM H. STERNBERG, M.D.
NEW YORK

The occurrence of major myocardial damage with a minimum or even absence of coronary disease is not rare. S. A. Levine [5] cited 11 of his own cases studied at autopsy in which major myocardial lesions were accompanied by corresponding disease of the coronary arteries. In a study of 100 cases of myocardial infarction Lisa and Ring [6] found 8 in which the lesions in the vessels were minimal or the vessels were normal. Barnes and Ball,[7] Brown,[8] Davenport [9] and others observed

In Meta-analysis (N=176,502), prevalence of MINOCA was 6% (range 1-14%)



Note: Weights are from random effects analysis

Arch Intern Med 1939;64:249-67
Circulation. 2015;131(10):861-70

Prognosis of MINOCA

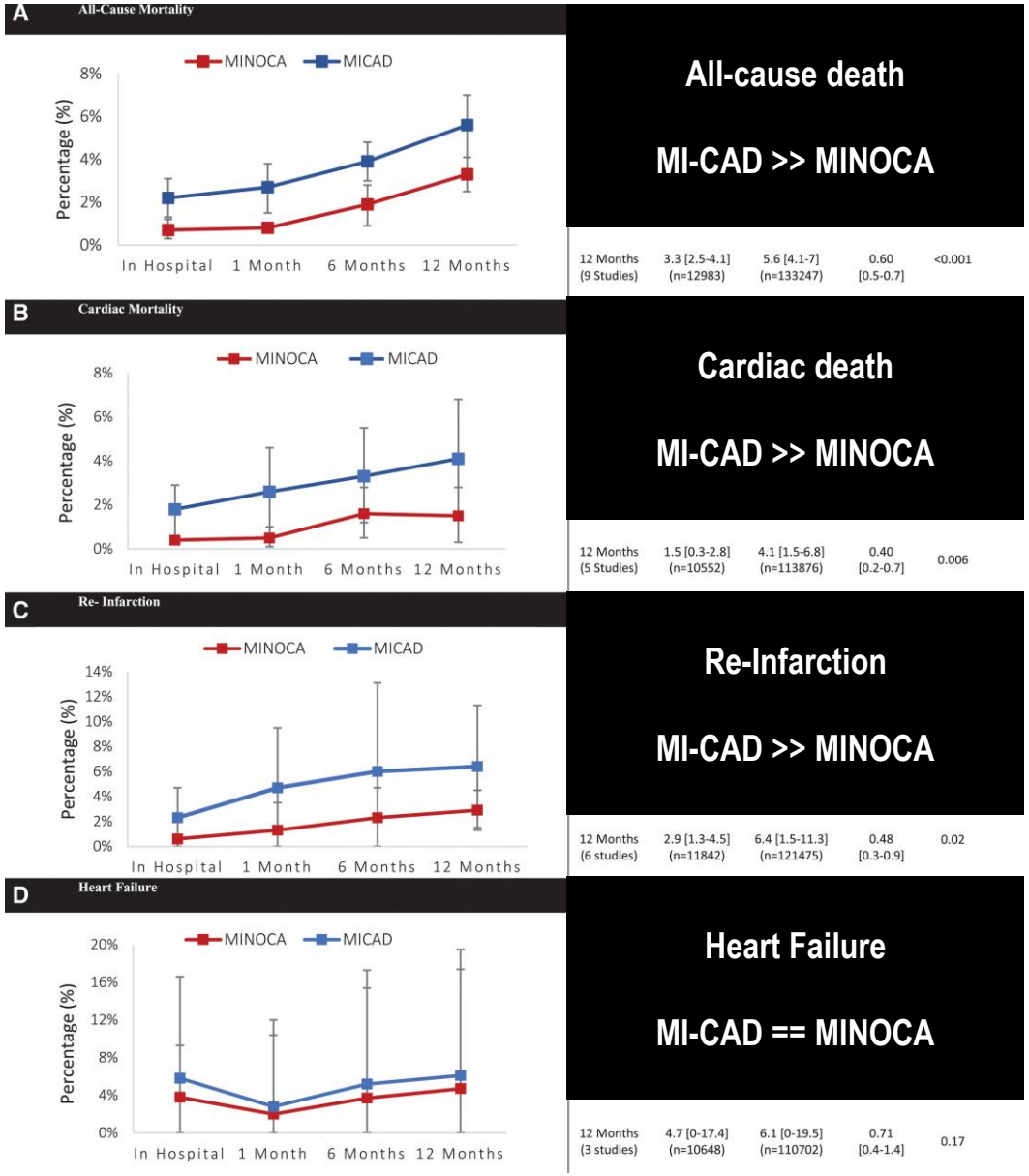
All-Cause Mortality
In-hospital mortality – 5 studies (N=9564)
12-month mortality – 4 studies (N=1924)

All-Cause Mortality	Comparative Studies: MI-CAD % (95% CI)	Comparative Studies: MINOCA % (95% CI)	OR (95% CI) *P* Value	All MINOCA Studies
In-hospital	3.2% (1.8%, 4.6%)	1.1% (-0.1%, 2.2%)	0.37 (0.2–0.67) *P*=0.001	0.9% (0.5%, 1.3%)
12-month	6.7% (4.3%, 9.0%)	3.5% (2.2%, 4.7%)	0.59 (0.41–0.83) *P*=0.003	4.7% (2.6%, 6.9%)

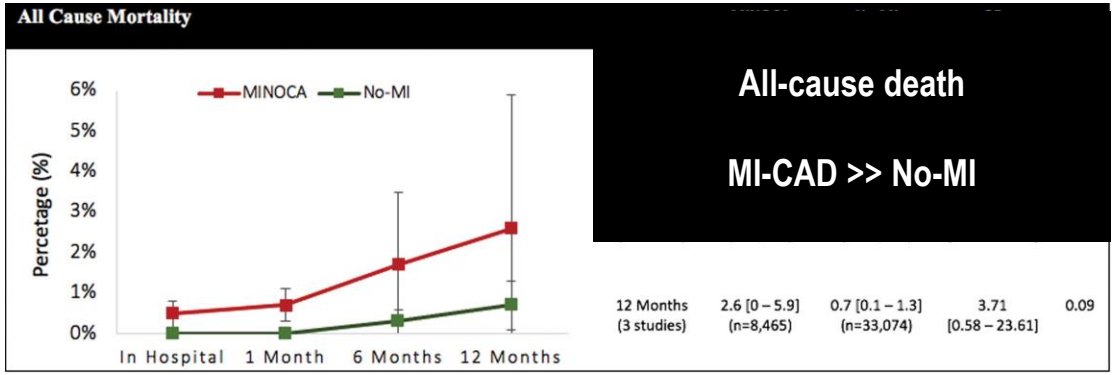
In this meta-analysis, all-cause mortality of MINOCA was lower than MI-CAD

Circulation. 2015;131(10):861-70

Prognosis of MINOCA



Collaborative Meta-analysis of 23 studies
55,369 MINOCA, 485382 MI-CAD, 33074 No-MI



Comparative Prognosis
All-cause mortality
MI-CAD >> MINOCA >> No-MI

Generally, MINOCA showed better clinical outcome than MI-CAD for Death or Re-MI.

SAMSUNG MEDICAL CENTER

Circ Cardiovasc Qual Outcomes. 2021 Nov;14(11):e007880.

Potential Underlying Causes of MINOCA

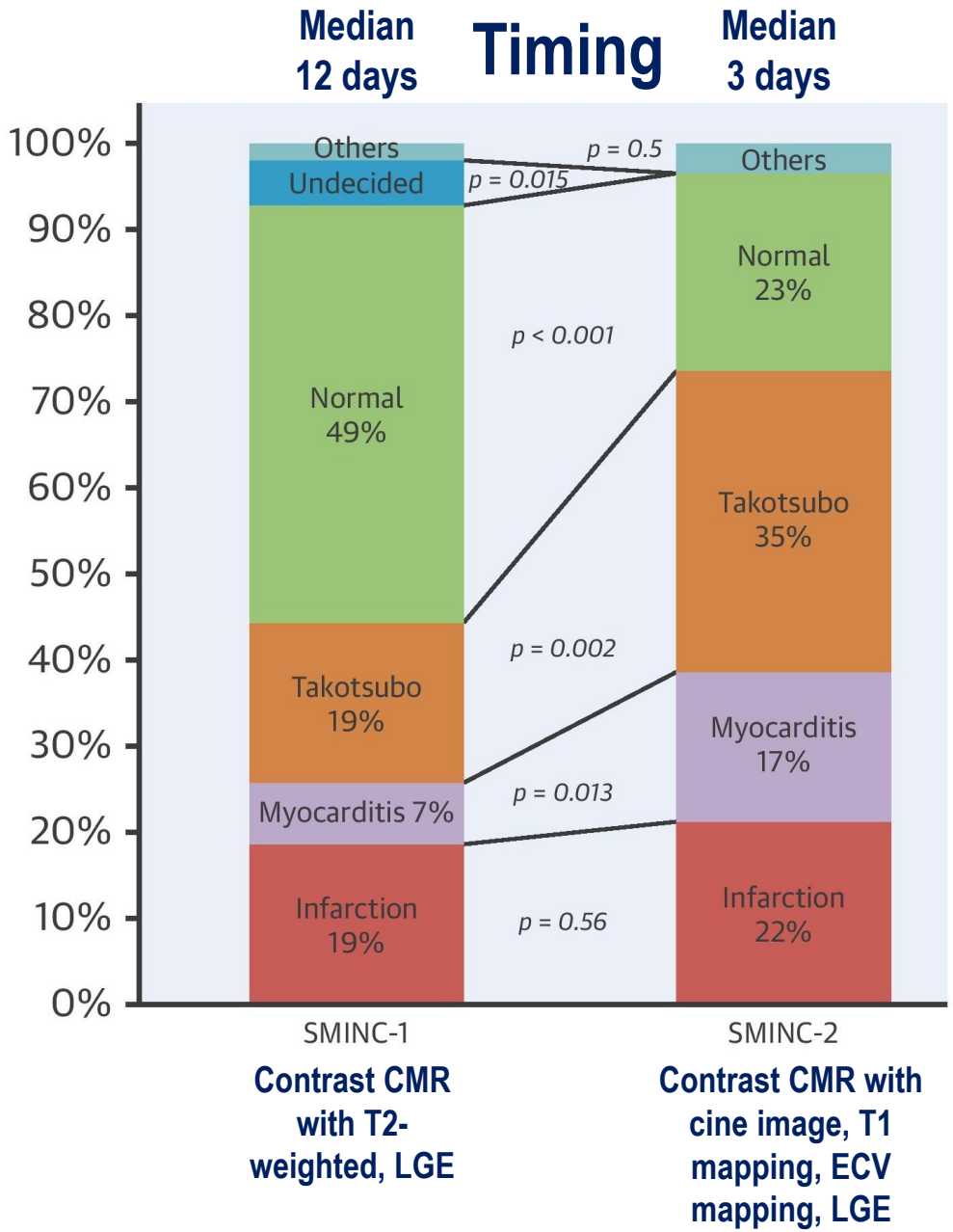
• Plaque erosion • Spontaneous dissection	→ Intravascular Imaging (preferred OCT)
• Vasospasm	→ Ergonovine/Acetylcholine provocation test
• Thromboemolism	→ TEE / CT / MRI (embolic source work up)
• Microvascular dysfunction	→ Invasive physiologic assessment (CFR/IMR/MRR)
• Supply/demand mismatch	→ General medical condition work up
• Myocarditis	→ Echo / MRI / Endomyocardial biopsy

Potential Underlying Causes of MINOCA
- Guideline recommendations -

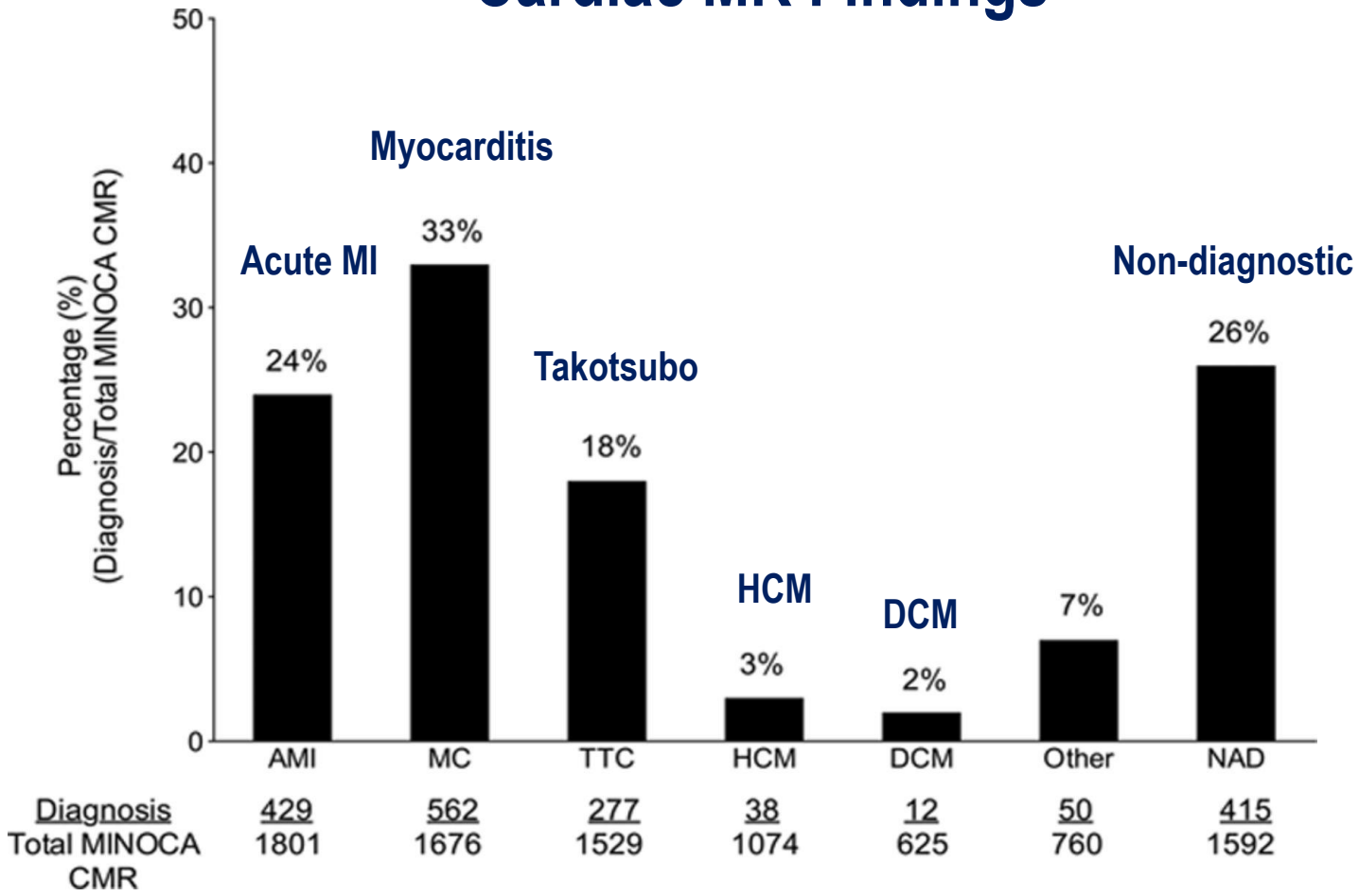
SUSPECTED DIAGNOSIS AND FURTHER DIAGNOSTIC TESTS

	Non-invasive	Invasive
Myocarditis	**TTE Echo** (pericardial effusion) **CMR** (myocarditis[2], pericarditis)	**Endomyocardial biopsy** (myocarditis)
Coronary (epicardial/ microvascular)	**TTE Echo** (Regional wall motion abnormalities, embolic source) **CMR** (small infarction) **TOE/Bubble Contrast Echo** (Patent foramen ovale, atrial septal defect	**IVUS/OCT** (plaque disruption/dissection) **Ergonovine/Ach test** [I] (spasm) **Pressure/Doppler wire** (microvascular dysfunction)
Myocardial disease	**TTE Echo** **CMR** (Takotsubo, others)	
Pulmonary Embolism	**D-dimer** (Pulmonary embolism) **CT scan** (Pulmonary embolism) **Thrombophilia screen**	
Oxygen supply/ demand imbalance- Type 2 MI	**Blood tests, Extracardiac investigation**	

Role of Cardiac MR



Cardiac MR Findings



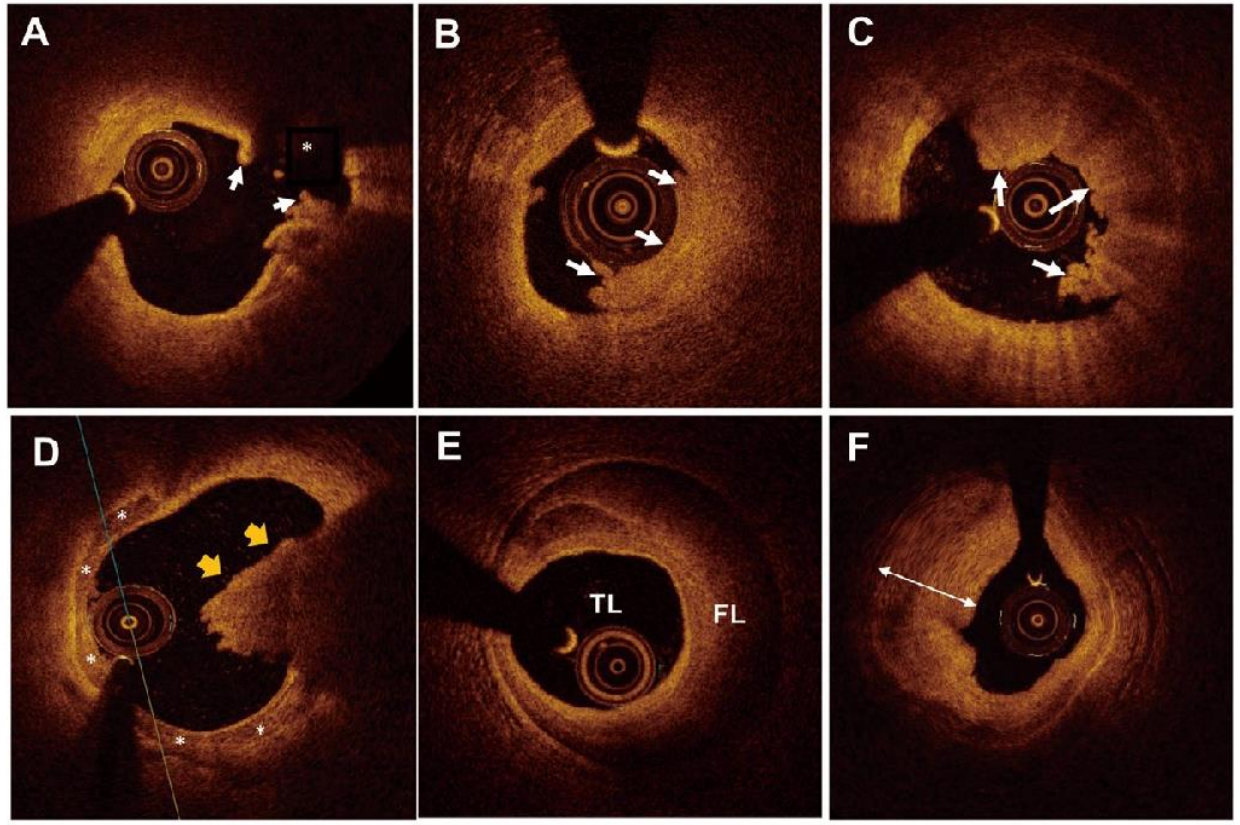
CMR is useful tool to further clarify the underlying cause of MINOCA

J Am Coll Cardiol Img 2021;14:1774–1783
Circulation. 2015;131(10):861-70

Role of Intravascular Imaging

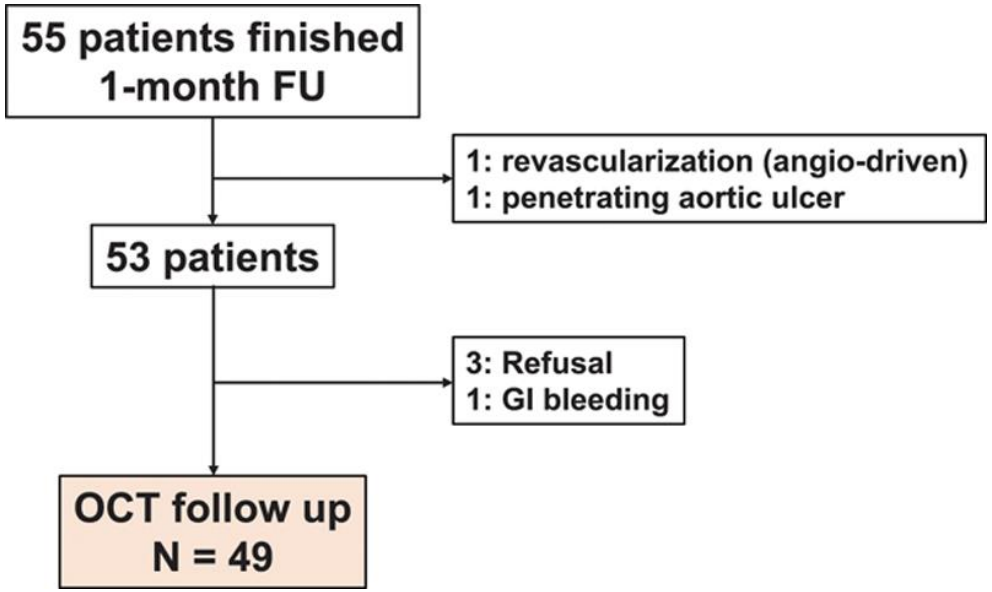
OCT/IVUS can detect hidden plaque rupture, erosion, thrombus
OCT can also provide further therapeutic decision in plaque erosion

Plaque Erosion Images (from Pf. Kubo T.)



OCT-based Plaque Erosion and no Stenting (EROSION STUDY)

53 Patients with plaque erosion by OCT
Conservative treatment without stenting

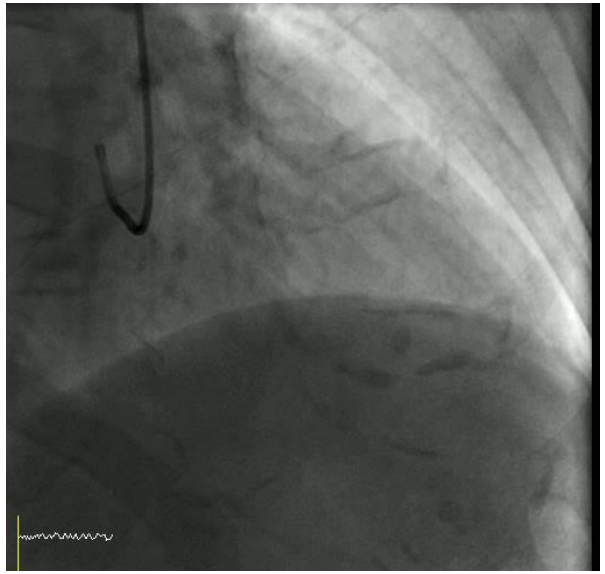


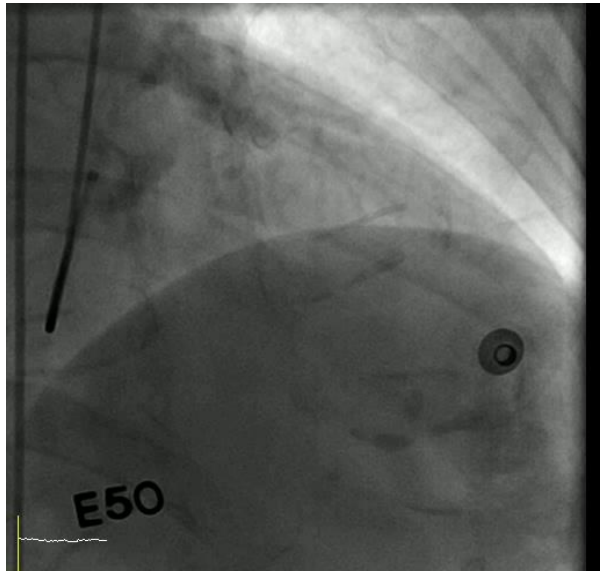
92.5% of patients were free of MACE

Kubo T et al. Circ J. 2018 Jan 25;82(2):302-308.
Xing L. et al. Circ Cardiovasc Interv. 2017;10:e005860.

Role of Provocation test

F/75, STEMI





Prospective registry of 80 Patients with MINOCA
Acetylcholine provocation: LCA (20-200ug), RCA (20-50ug), 2-3min
Ergonovine: LCA (8-64ug), RCA (8-40ug), 2-3min

Diagnostic Criteria	≥90% epicardial spasm	Reproduction of Sx	Ischemic ECG change
Epicardial Spasm	O	O	O
Microvascular Spasm	X	O	O

Provocation test was positive in 46.2%.
Among these patients, epicardial spasm 64.9%, microvascular spasm 35.1%.
No procedural complication

Table 2 Clinical outcomes of overall population and according to invasive provocative test response

	Total population ($n = 80$)	Positive functional test ($n = 37$)	Negative functional test ($n = 43$)	*P*-value
Death from any causes, *n* (%)	14 (19.7)	12 (32.4)	2 (4.7)	0.002
Cardiac death, *n* (%)	7 (9.4)	7 (18.9)	0 (0)	0.005
Recurrence of acute coronary syndrome, *n* (%)	13 (17.5)	10 (27.0)	3 (7.0)	0.015
Seattle Angina Score (*n*), median (range)	100.0 (33.0–100.0)	88.0 (33.0–100.0)	100.0 (44.0–100.0)	0.001
Median follow-up time (months), median (range)	36.0 (12.0–60.0)	24.0 (12.0–60.0)	36.0 (12.0–60.0)	0.49

Eur Heart J. 2018 Jan 7;39(2):91-98.

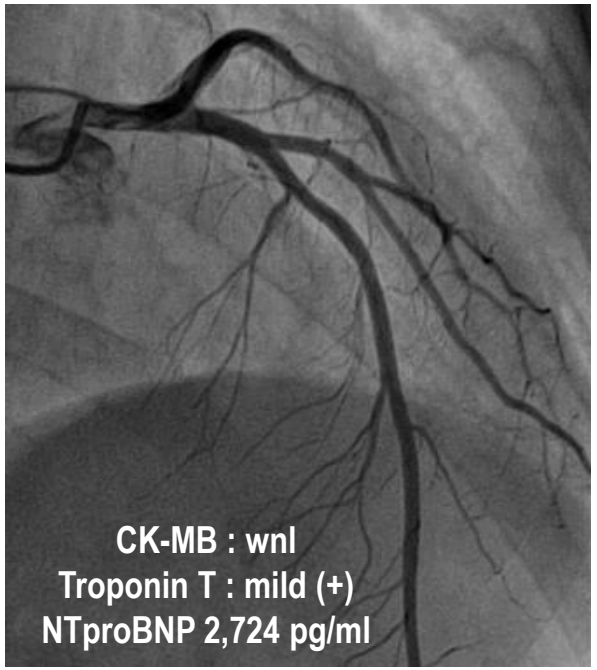
Role of Microcirculatory Dysfunction in MINOCA

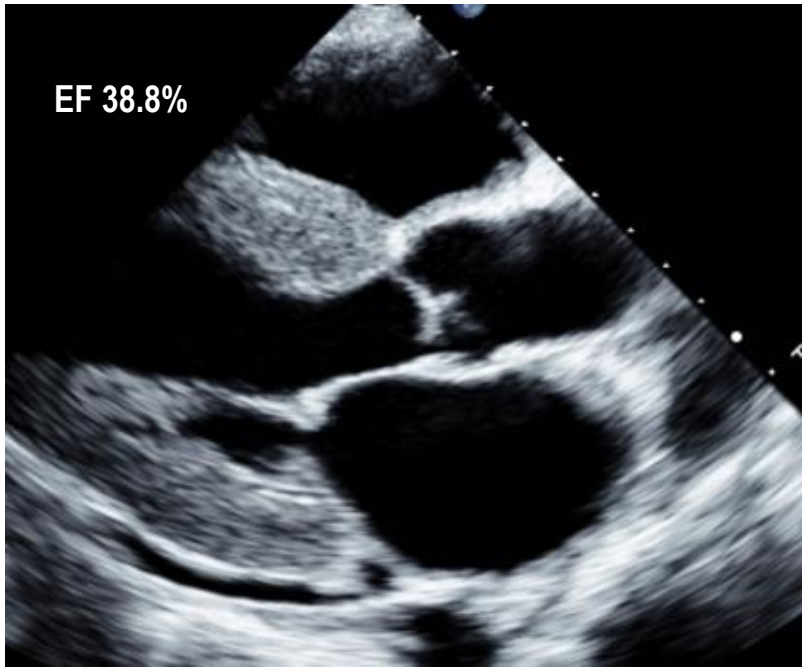
In working diagnosis of MINOCA,

CMD can be rare cause of cardiac enzyme elevation and chest pain

CMD is a syndrome originated from heterogeneous causes

F/57, Recent chest pain and dyspnea on exertion





Consultation to HF Specialist and Endomyocardial Biopsy

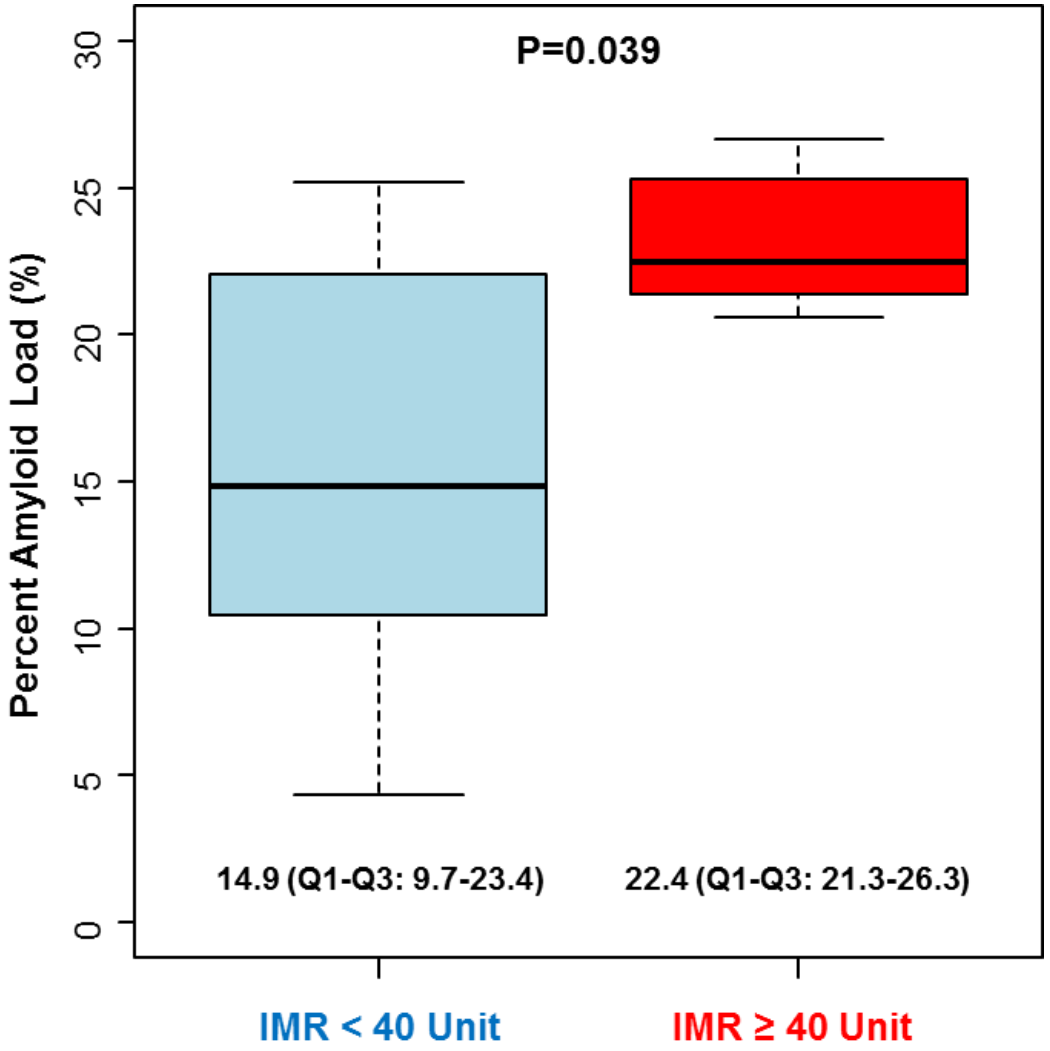
Final Diagnosis : ATTR cardiac amyloidosis

SAMSUNG MEDICAL CENTER

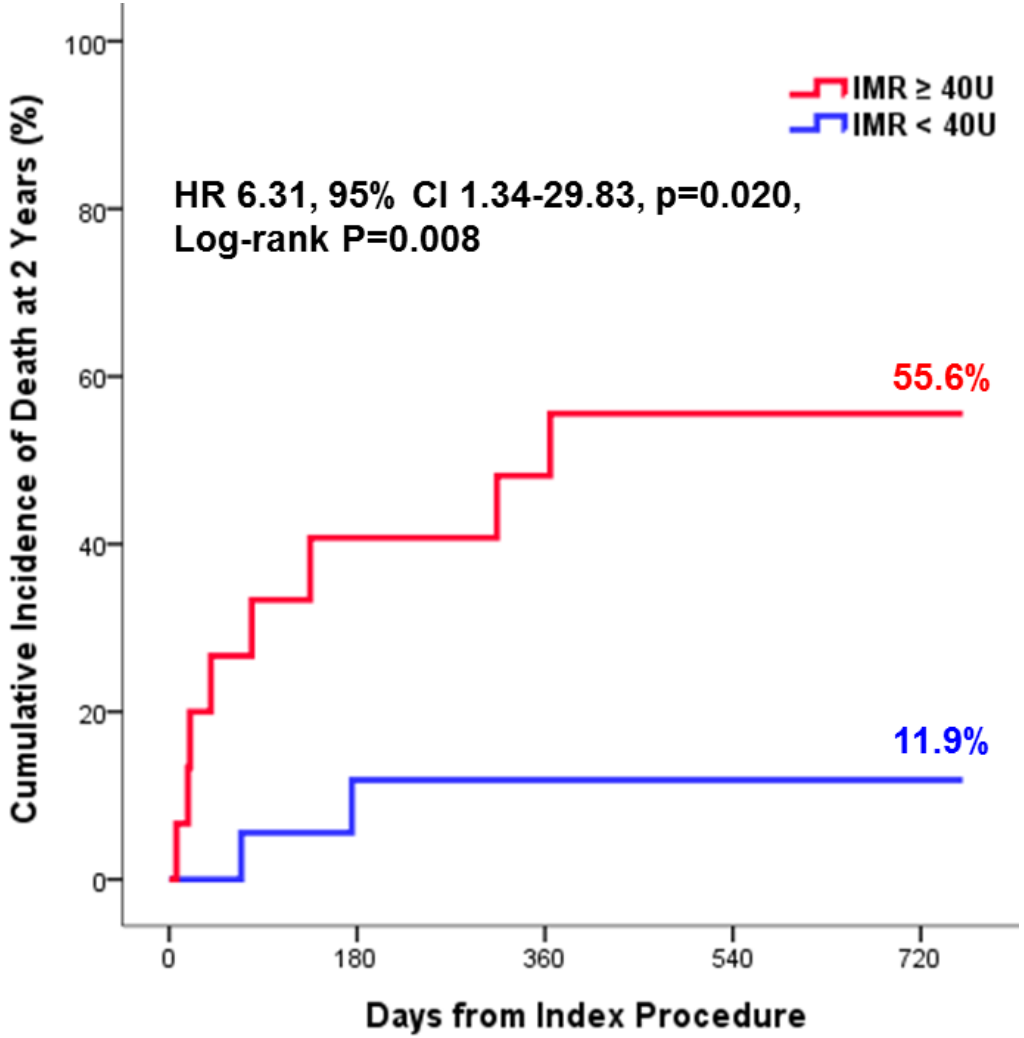
Cardiac Amyloidosis registry, NCT02798705, J Am Coll Cardiol. 2020 Feb 11;75(5):560-561

Coronary Physiology and Cardiac Amyloidosis

IMR as Marker of Pathologic Severity



IMR as Prognostic Indicator (Mortality)

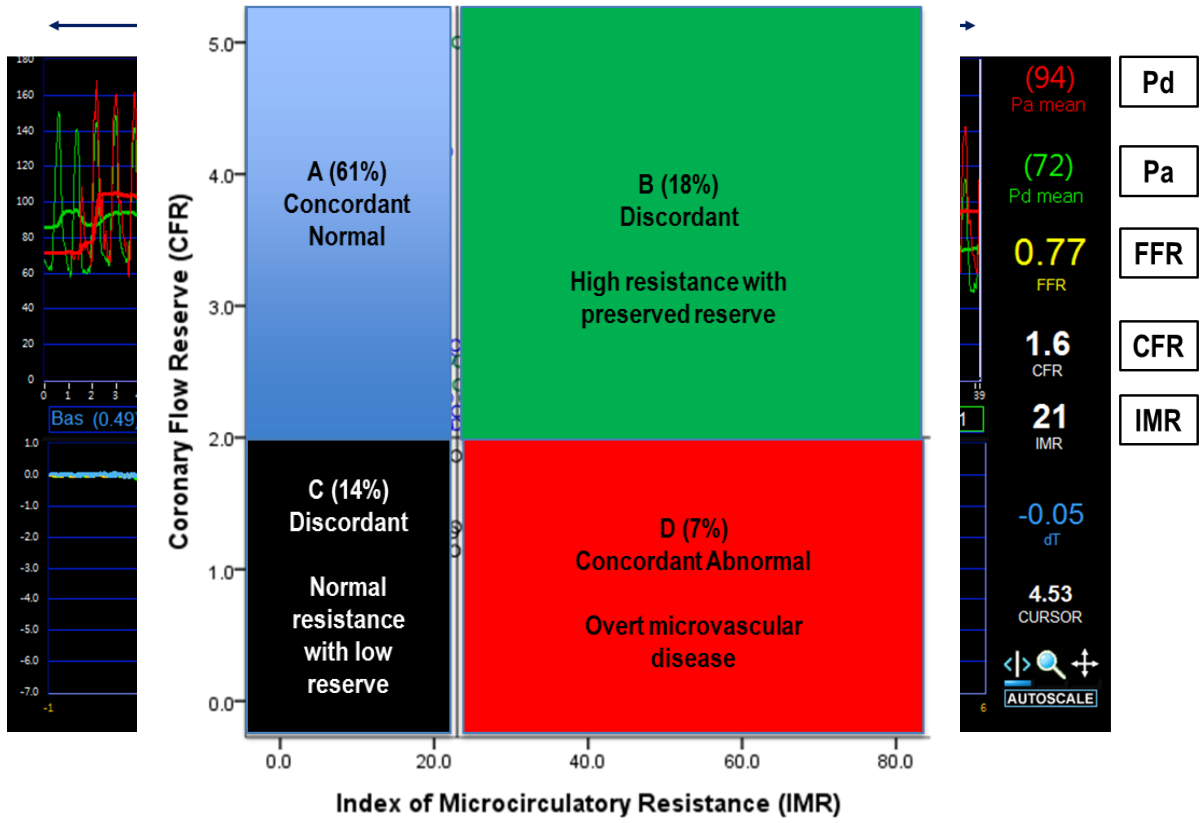


Choi KH… Lee JM/Jeon ES, J Am Coll Cardiol. 2020 Feb 11;75(5):560-561.

Residual Microcirculatory Dysfunction after CTO PCI
- How to define CMD? -

230 Stable IHD Patients with FFR>0.80, Stratified by CFR (≤2.0) and IMR(≥23U) measurement

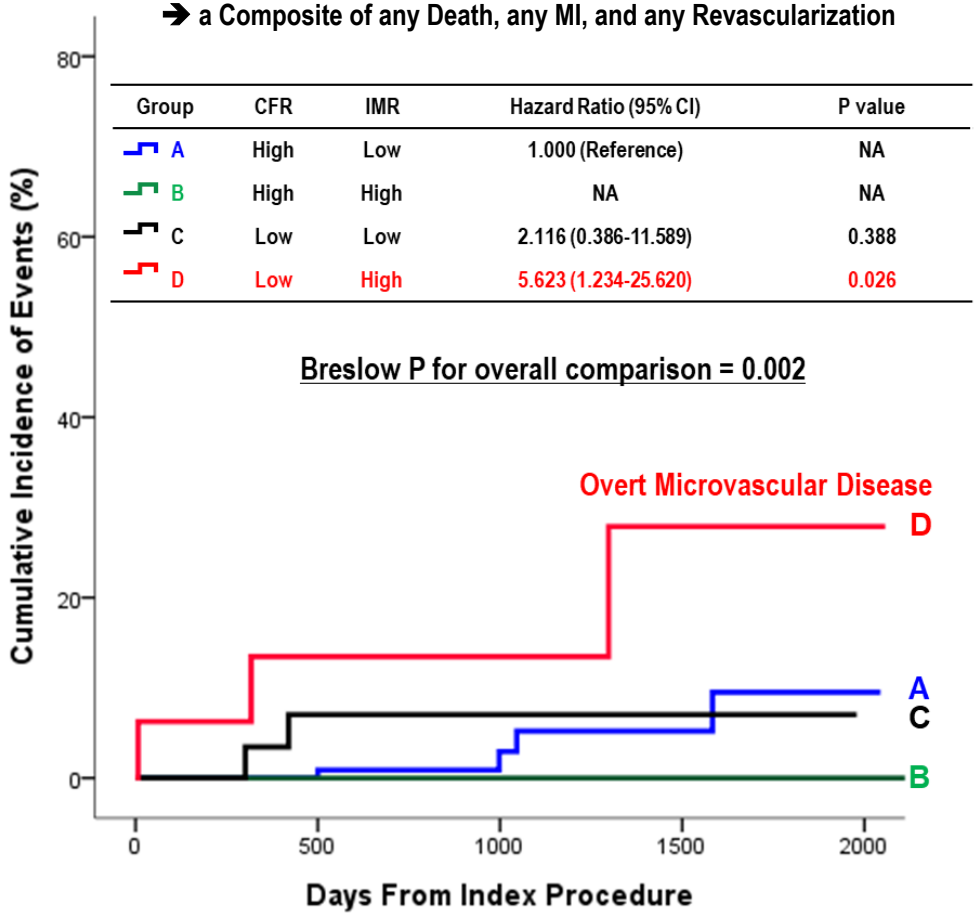
Definition of CMD by 2 x 2 Classification using CFR and IMR



POCO, Patient-oriented Composite Outcomes
➔ a Composite of any Death, any MI, and any Revascularization

Group	CFR	IMR	Hazard Ratio (95% CI)	P value
A	High	Low	1.000 (Reference)	NA
B	High	High	NA	NA
C	Low	Low	2.116 (0.386-11.589)	0.388
D	Low	High	5.623 (1.234-25.620)	0.026

Breslow P for overall comparison = 0.002



SAMSUNG MEDICAL CENTER

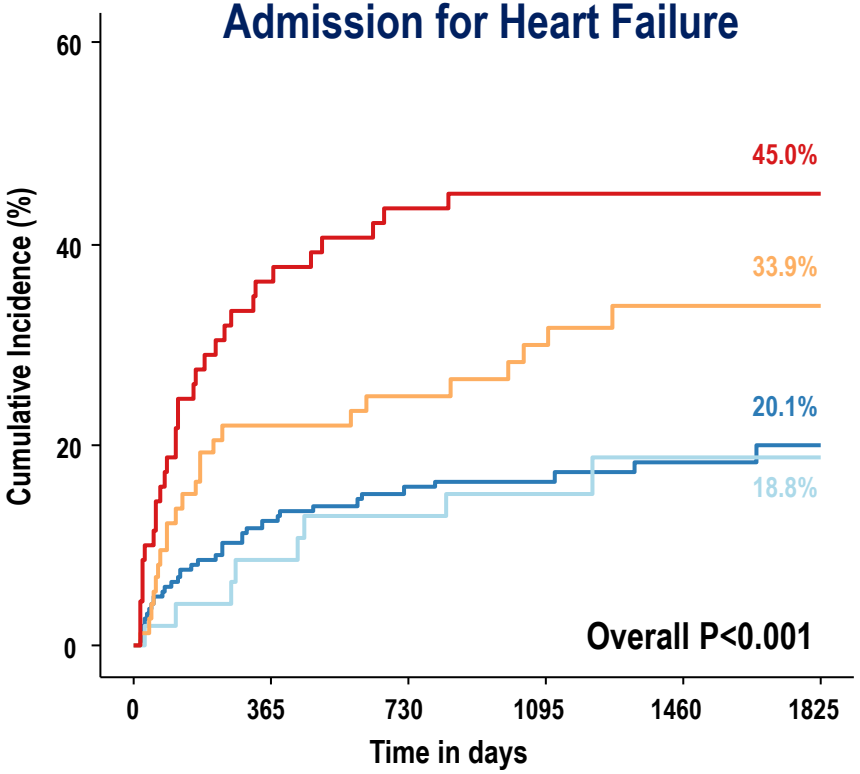
Lee JM….Koo BK, J Am Coll Cardiol. 2016 Mar 15;67(10):1158-1169.

Residual Microcirculatory Dysfunction after CTO PCI
- How to define CMD? -

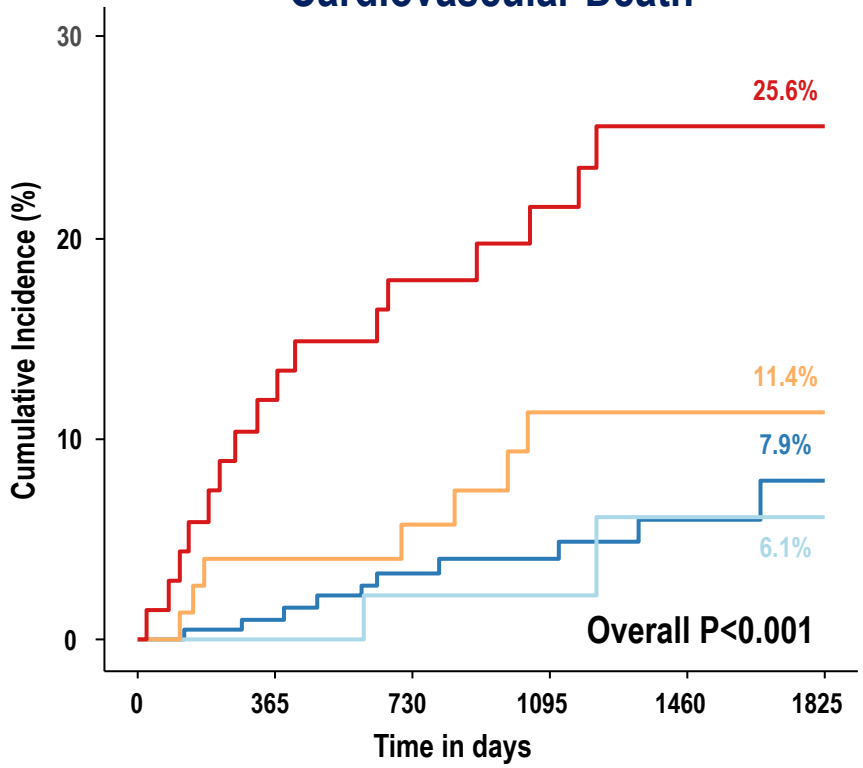
DIAST-CMD Registry (NCT05058833)

547 consecutive patients undergoing comprehensive coronary physiologic evaluation
Stable IHD 81.7%, ACS 8.6%, Ischemic CMP 9.7%, Median 3.3 Years of follow-up

Cardiovascular Death or Admission for Heart Failure



Cardiovascular Death



Measurement variability (CFR), Influence from epicardial stenosis (CFR and IMR),
Influence from subtended myocardial territory (IMR), Operator dependency (CFR and IMR)

Hong D,,,,, Lee JM et al. Circ Cardiovasc Interv. 2023 Mar;16(3):e012621

Residual Microcirculatory Dysfunction after CTO PCI
- New Index – Microvascular Resistance Reserve (MRR) -

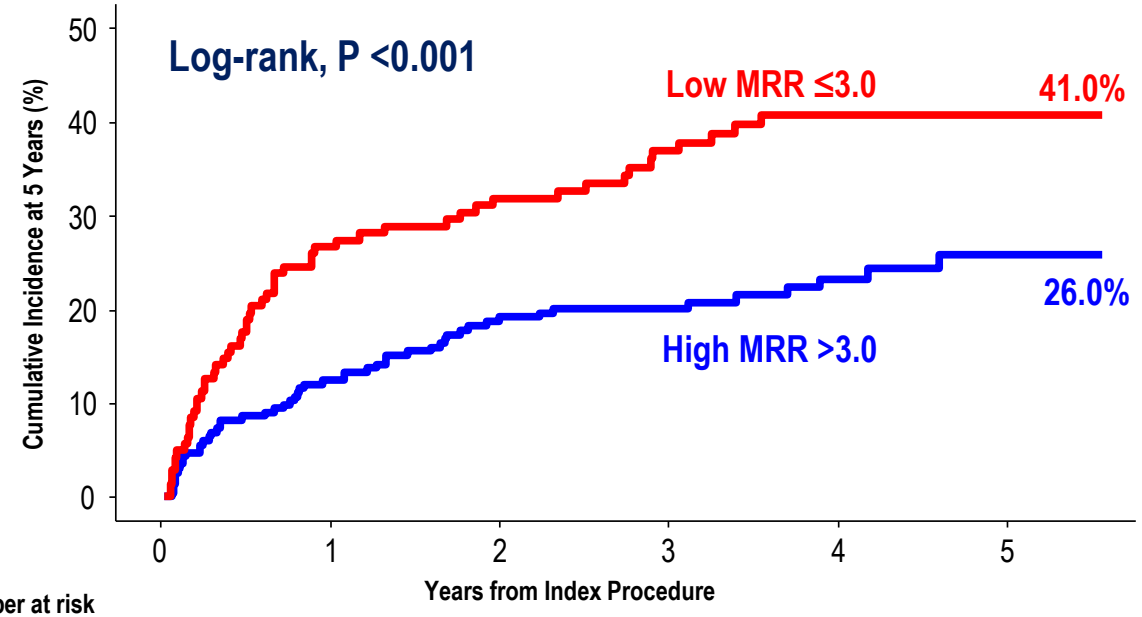
DIAST-CMD Registry (NCT05058833)

547 consecutive patients undergoing comprehensive coronary physiologic evaluation

MACE (a composite of CV death, MI, repeat revascularization, and admission for heart failure) during median 3.3 years

MRR = [CFR/FFR] × [resting Pa/hyperemic Pa].

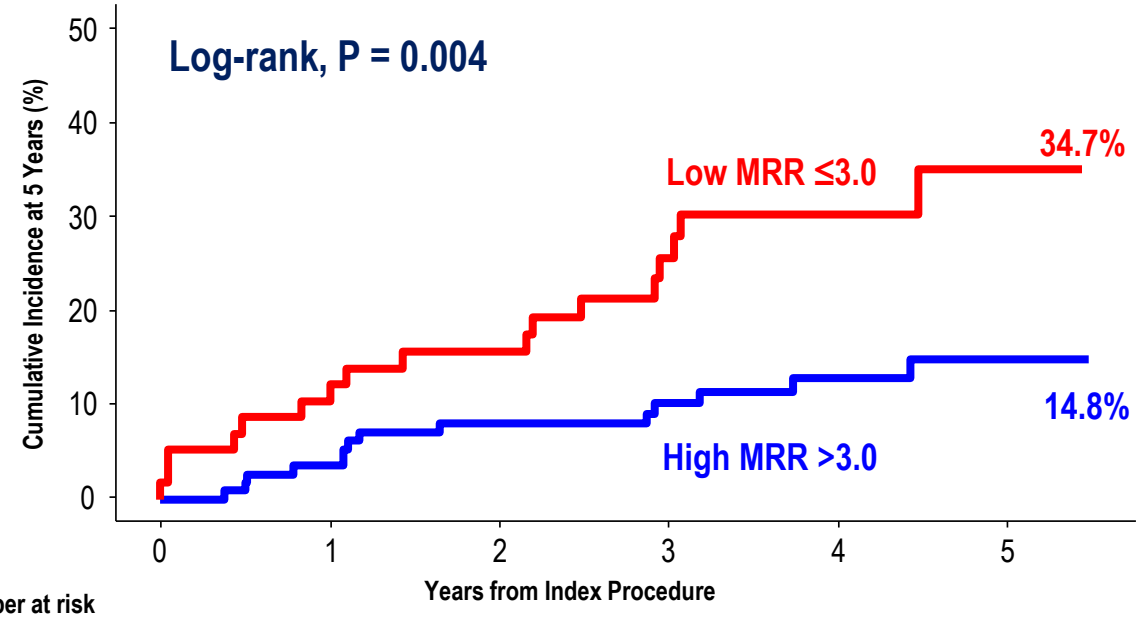
Insignificant epicardial disease (FFR >0.80)



Number at risk

High MRR >3.0	233	199	171	123	78	25
Low MRR ≤3.0	142	101	90	69	40	11

Significant epicardial disease (FFR ≤0.80)



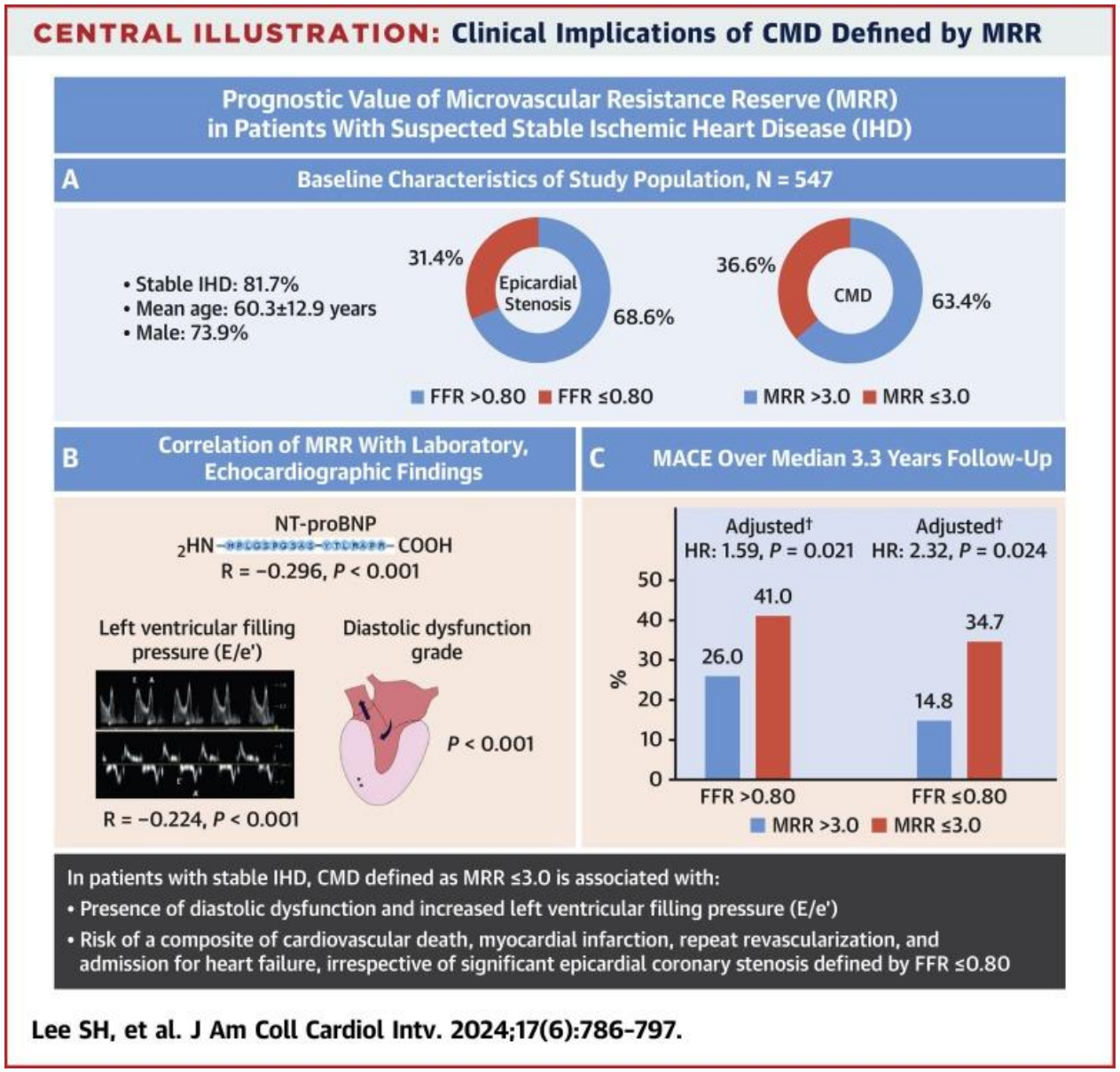
Number at risk

High MRR >3.0	114	109	102	81	56	22
Low MRR ≤3.0	58	52	46	33	25	9

SAMSUNG MEDICAL CENTER

Lee SH,,,,, Lee JM et al. JACC Cardiovasc Interv. 2024 Mar 25;17(6):786-797

Prognostic Impact of Microcirculatory Dysfunction, defined by MRR



DIAST-CMD Registry (NCT05058833)

- 547 consecutive patients undergoing comprehensive coronary physiologic evaluation
- Stable IHD 81.7%, ACS 8.6%, Ischemic CMP 9.7%
- MRR = [CFR/FFR] × [resting Pa/hyperemic Pa].
- Depressed MRR ≤ 3.0 was associated with NTproBNP ↑, E/E' ↑, diastolic dysfunction grades ↑.
- Depressed MRR ≤ 3.0 was associated with higher risk of MACE, regardless of FFR during median F/U of 3.3 years.

Lee SH,,,,, Lee JM et al. JACC Cardiovasc Interv. 2024 Mar 25;17(6):786-797

Summary

- Prevalence of MINOCA – 1 to 12% of STEMI patients
- MINOCA is working diagnosis and further clarification of underlying cause is crucial.
- Multimodality diagnostic work up including Cardiac MR, OCT/IVUS, provocation test, coronary physiologic assessment are needed.
- Coronary microcirculatory dysfunction (CMD) is rare cause of MINOCA. Only coronary physiologic assessment can reveal the hidden CMD.
- MRR is a simple and reliable diagnostic index to define CMD and also prognostic indicator, regardless of the presence of epicardial coronary stenosis.