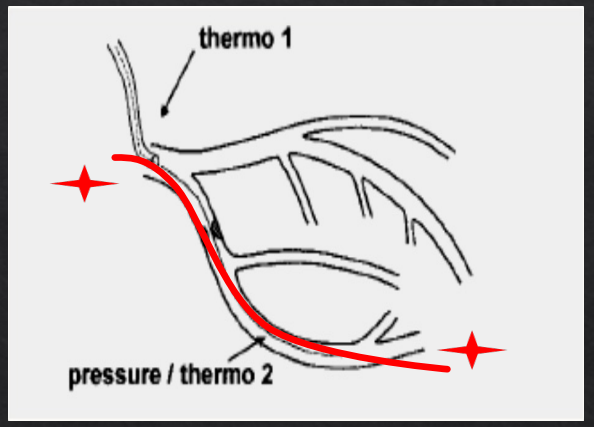
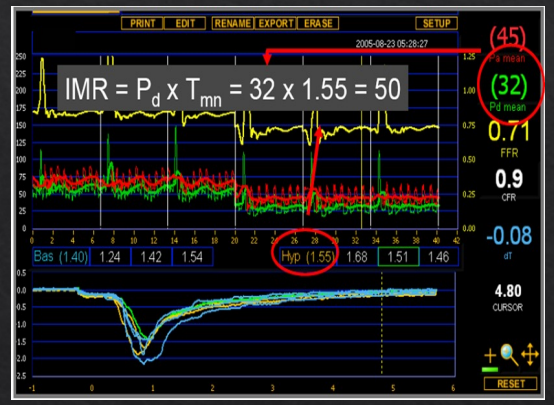
Le rôle de l'IMR dans les patients MINOCA ?





Georgios Sideris
HEGP Paris
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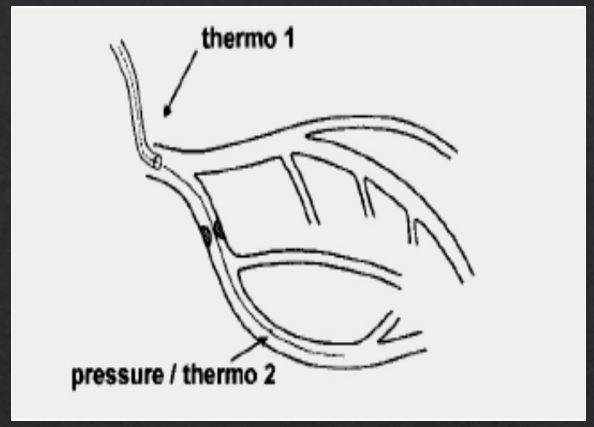
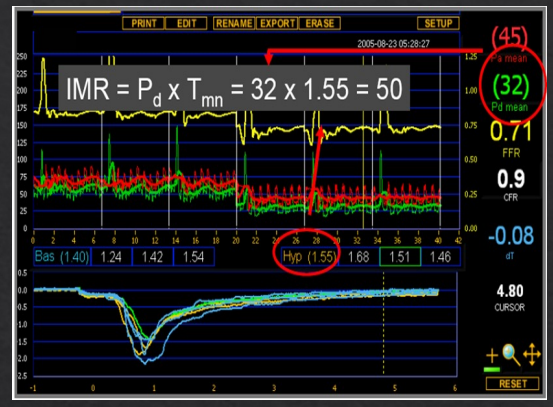
Université Paris Cité

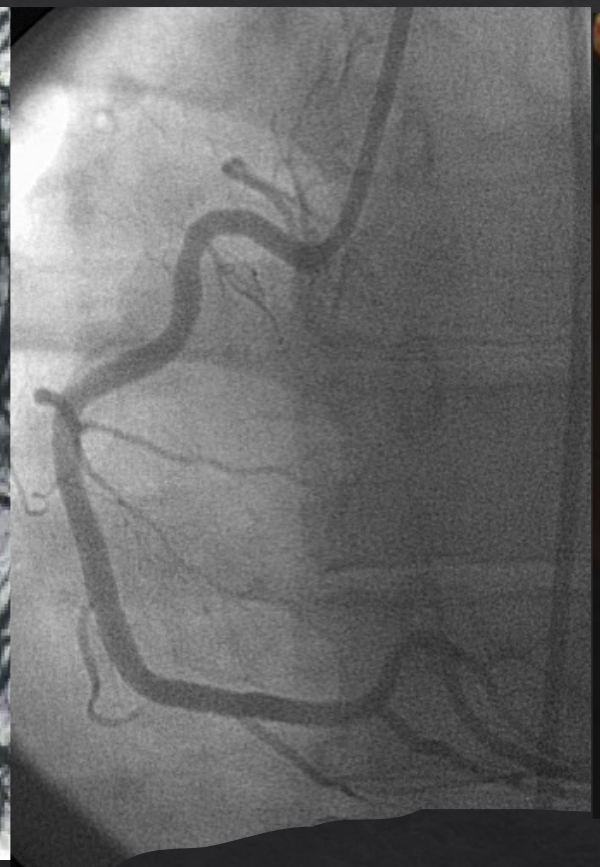
HÔPITAUX UNIVERSITAIRES PARIS OUEST
Hôpital européen Georges-Pompidou





☑ Je déclare les liens d'intérêt potentiel à suivants :

Consultant (board Abbott)

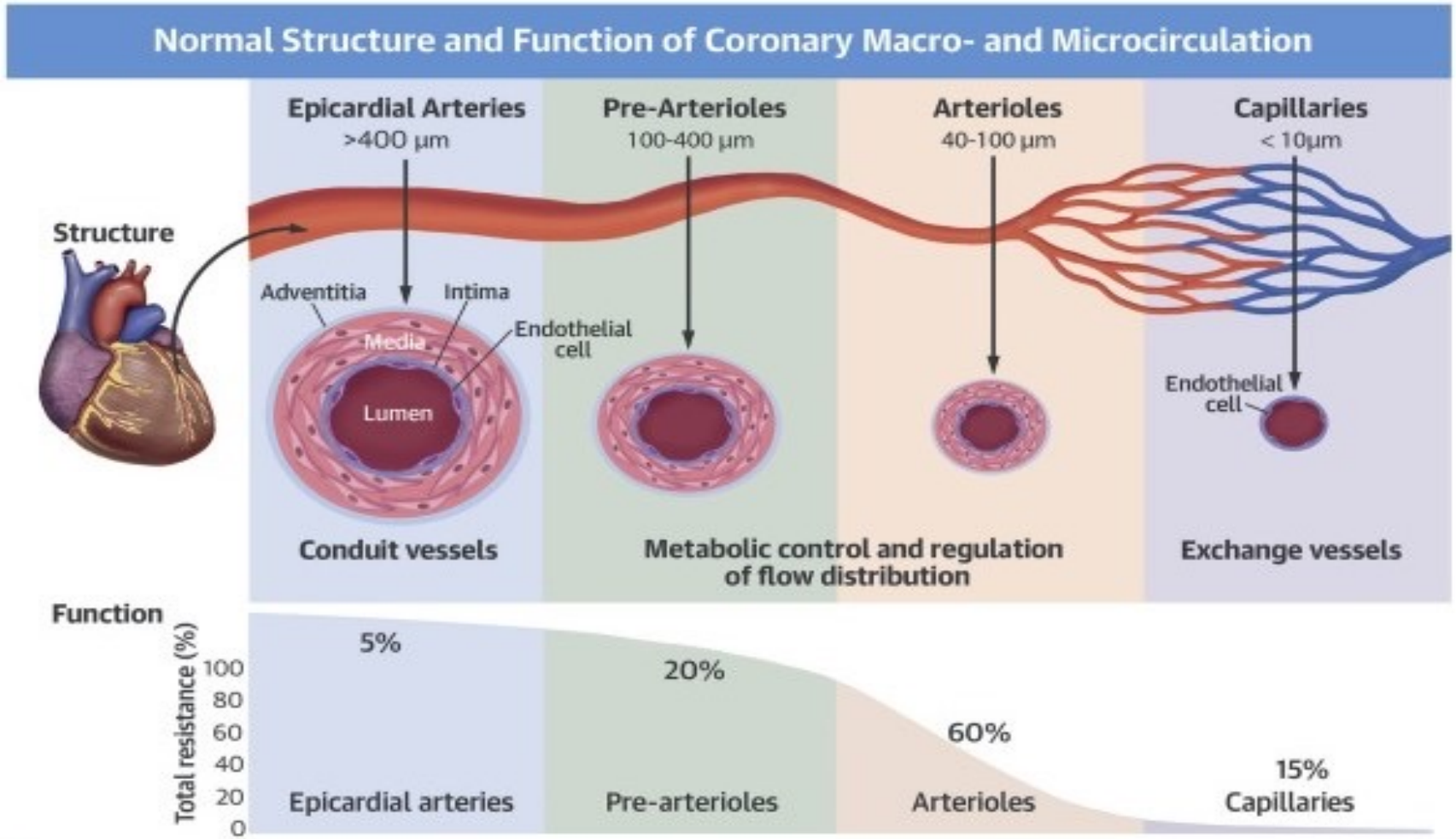


Microcirculation >90 % de la circulation coronaire

Réseau coronaire épicardique:

L' arbre qui cache la forêt …..

Artères épicardiques : seulement 5% des résistances totales



Taqueti, V.R. et al. J Am Coll Cardiol. 2018;72(21):2625–41.

Microvascular disease

How can we diagnose what we cannot see?

Microvascular disease, what little we know

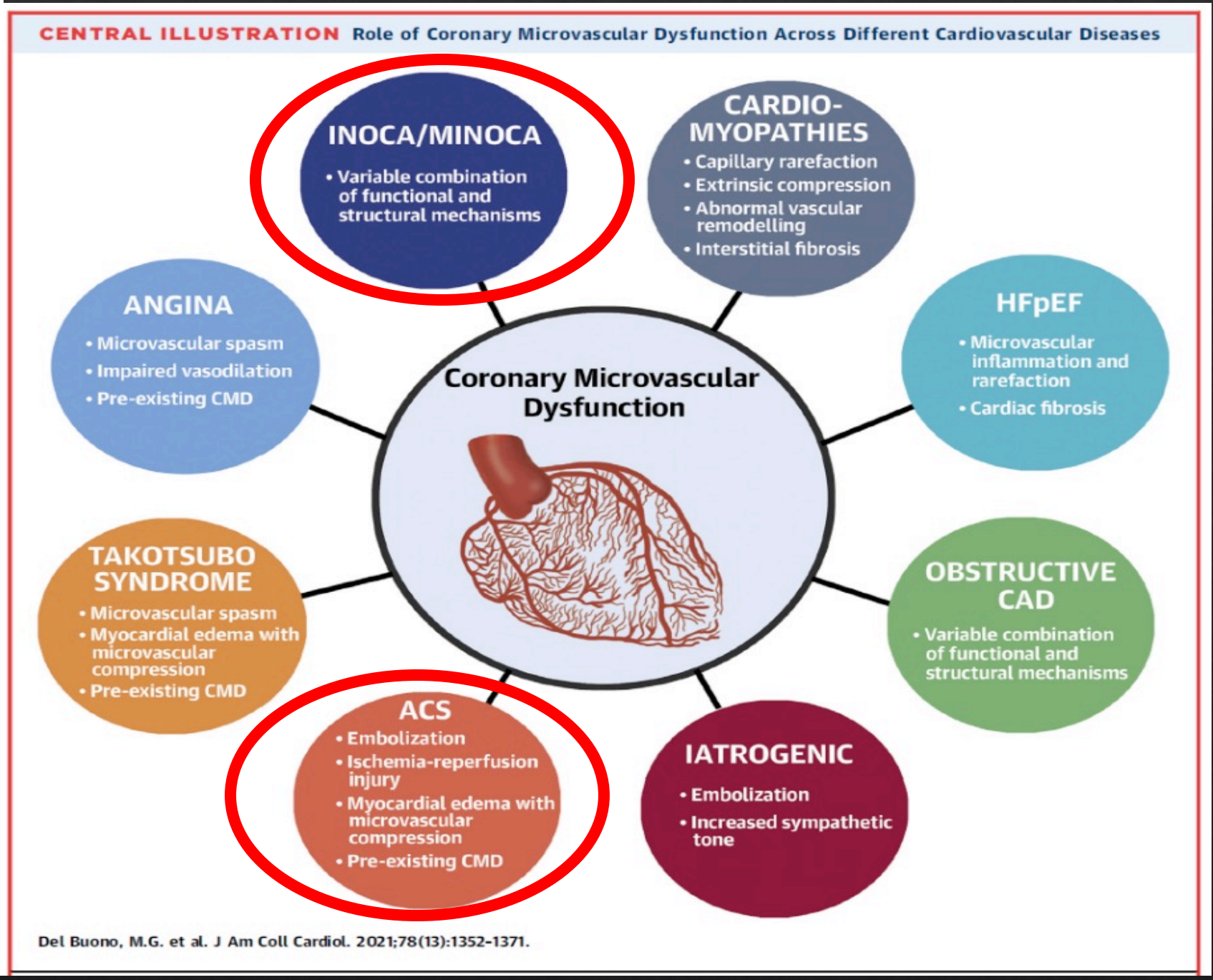
Yolande Appelman*, MD, PhD
Chair Thinktank Women & Health VU University Medical Center, Member of EAPCI-Women

Coronary Microvascular Dysfunction Across the Spectrum of Cardiovascular Diseases

JACC State-of-the-Art Review

Marco Giuseppe Del Buono, MD,[a] Rocco A. Montone, MD, PhD,[b] Massimiliano Camilli, MD,[a] Salvatore Carbone, PhD,[c,d] Jagat Narula, MD, PhD,[e] Carl J. Lavie, MD,[f] Giampaolo Niccoli, MD, PhD,[g] Filippo Crea, MD[a,b]

CENTRAL ILLUSTRATION Role of Coronary Microvascular Dysfunction Across Different Cardiovascular Diseases



Del Buono, M.G. et al. J Am Coll Cardiol. 2021;78(13):1352-1371.

Coronary Microvascular Dysfunction Across the Spectrum of Cardiovascular Diseases

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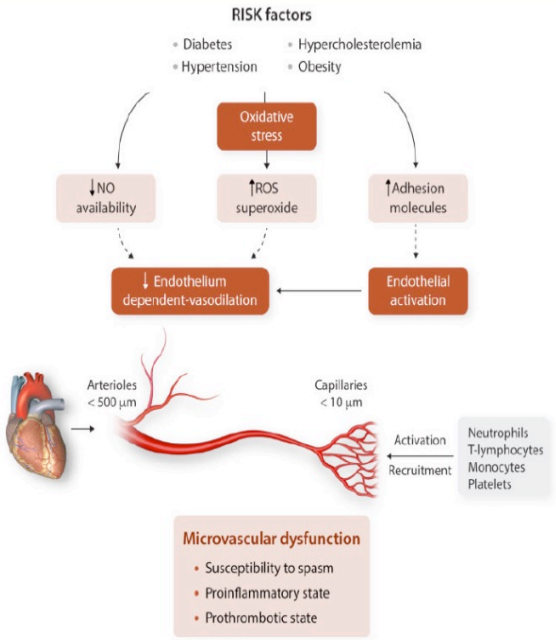
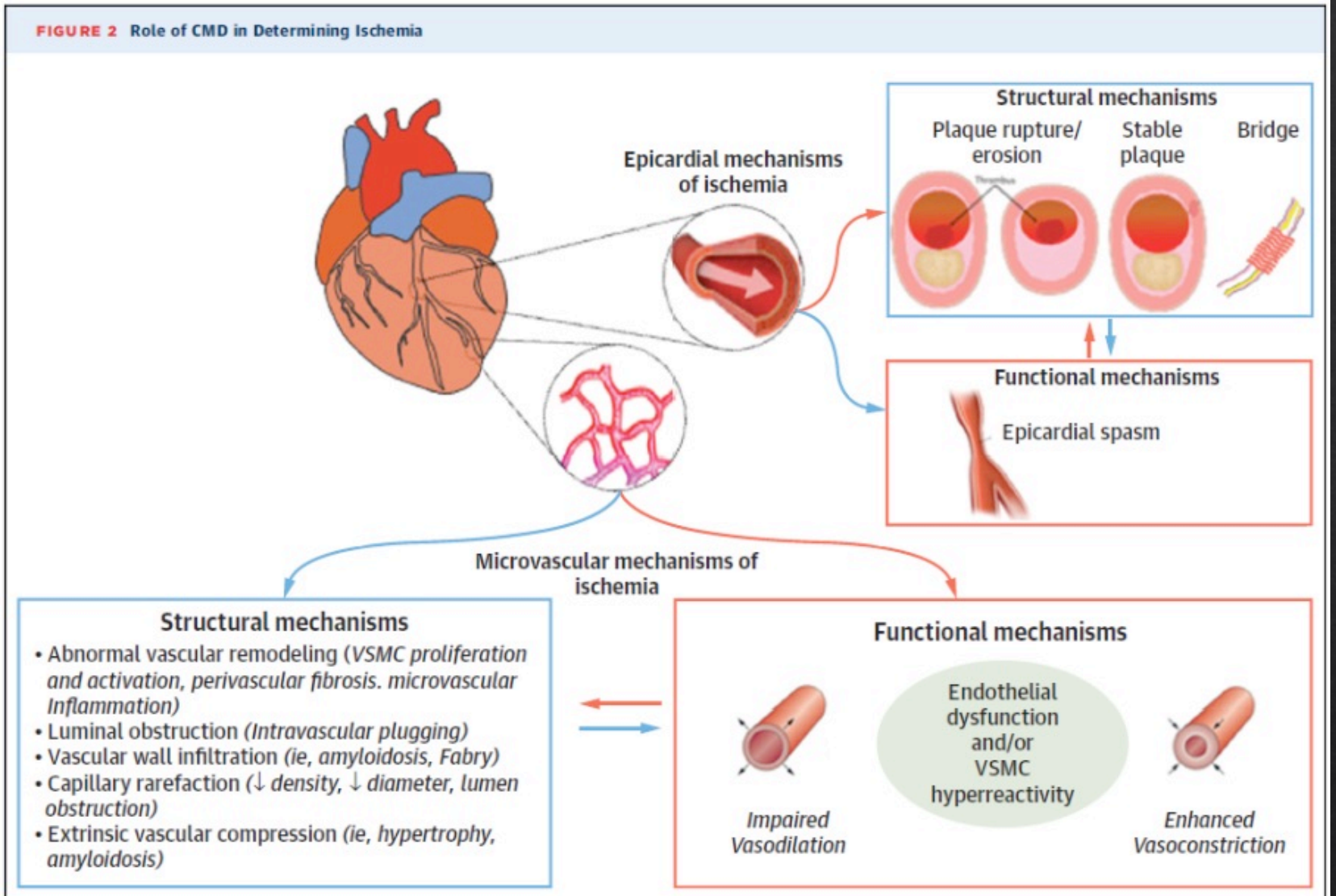


Figure 4 Microvascular response to risk factors. NO, nitric oxide; ROS, reactive oxygen species.

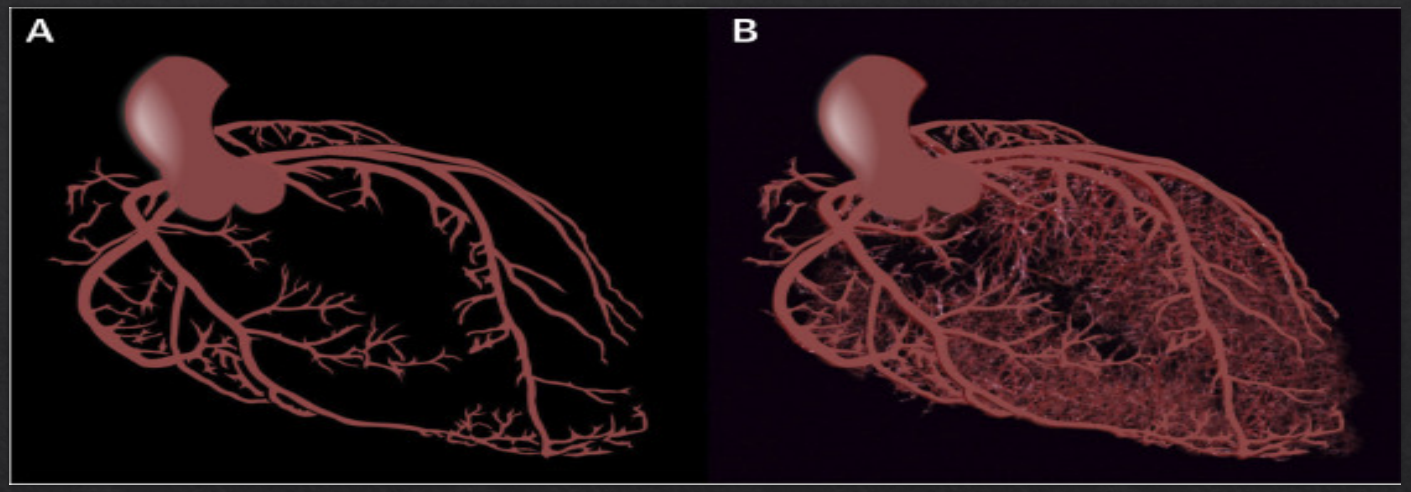
FDR ?

FIGURE 2 Role of CMD in Determining Ischemia



Ischemia may be cause by subtended by epicardial and/or microvascular structural and functional mechanisms. Epicardial causes determining ischemia include acute plaque disruption with lumen occlusion and epicardial coronary spasm, myocardial bridge, or progressive obstruction with vessel narrowing. CMD can result from an abnormal vasodilatory ability of the microvasculature, compressive external forces affecting the intramural microvessels, or microvascular spasm. CAD = coronary artery disease; VSMC = vascular smooth muscle cells.

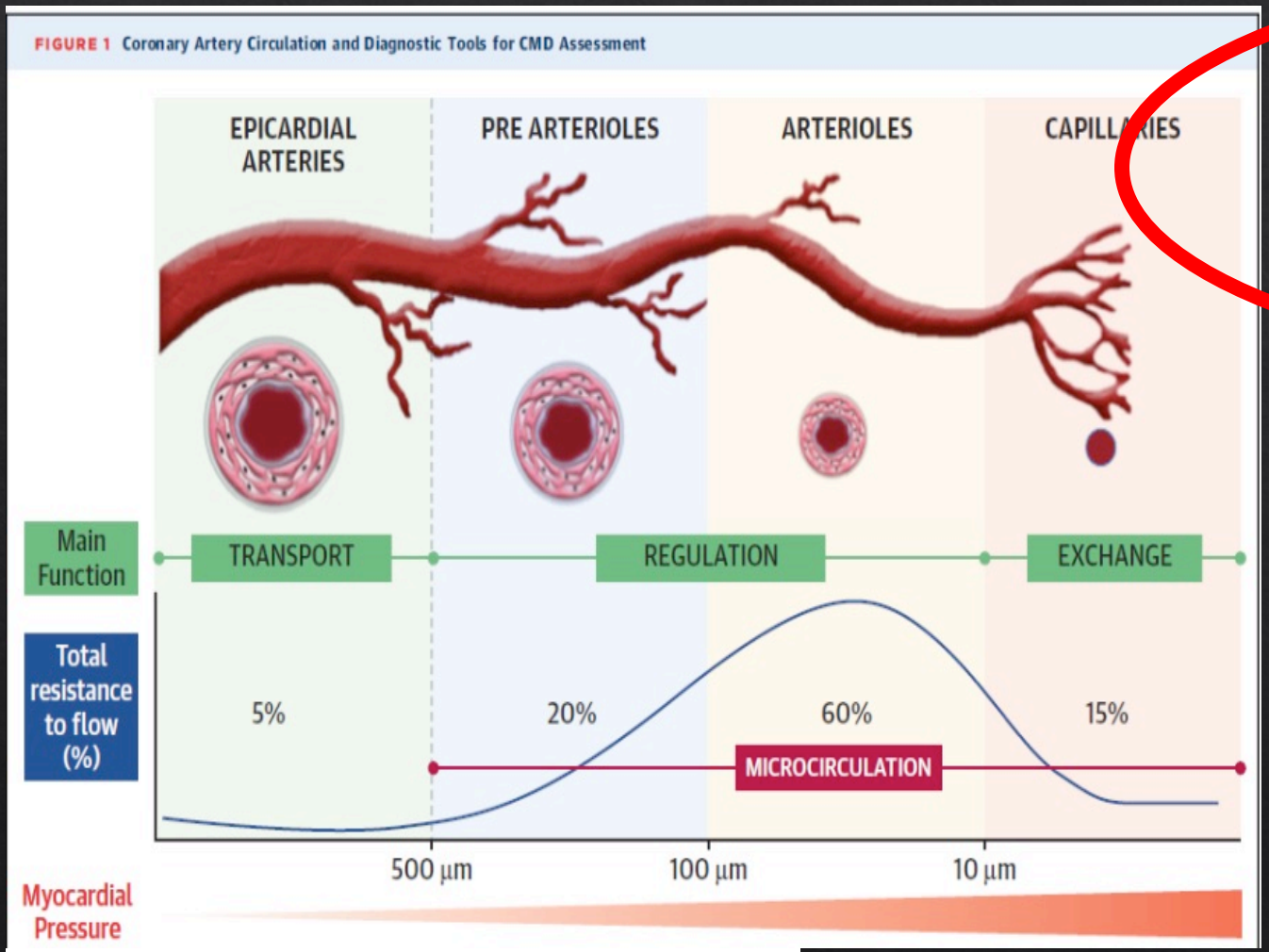
Exploration de la microcirculation coronaire en 2024



- Comment ?
- Pour quel patient ?
- Pourquoi ?

Exploration de la dysfonction microcirculatoire

Comment ?



Coronary Microvascular Dysfunction Across the Spectrum of Cardiovascular Diseases

JACC State-of-the-Art Review

Marco Giuseppe Del Buono, MD,[a] Rocco A. Montone, MD, PhD,[b] Massimiliano Camilli, MD,[a] Salvatore Carbone, PhD,[c,d] Jagat Narula, MD, PhD,[e] Carl J. Lavie, MD,[f] Giampaolo Niccoli, MD, PhD,[g] Filippo Crea, MD[a,b]

Invasive assessment of CMD

Assessment of both epicardial and microvascular compartments	Assessment of microvascular compartment
• CFR (with Doppler or thermodilution technique) Ratio between coronary blood flow at maximal hyperemia and under resting condition	• IMR (with thermodilution technique) Product of the distal coronary pressure and mean transit time of a saline bolus during maximal hyperemia
• Intracoronary Provocative Testing (Acetylcholine) Assessment of vasoconstriction disorders (epicardial or microvascular spasm)	• HMR (with dual Doppler and pressure wire technique) Pressure distal to a stenosis (or in the absence of a stenosis distal coronary pressure) divided by the distal average peak velocity during maximal hyperemia, during the whole cardiac cycle

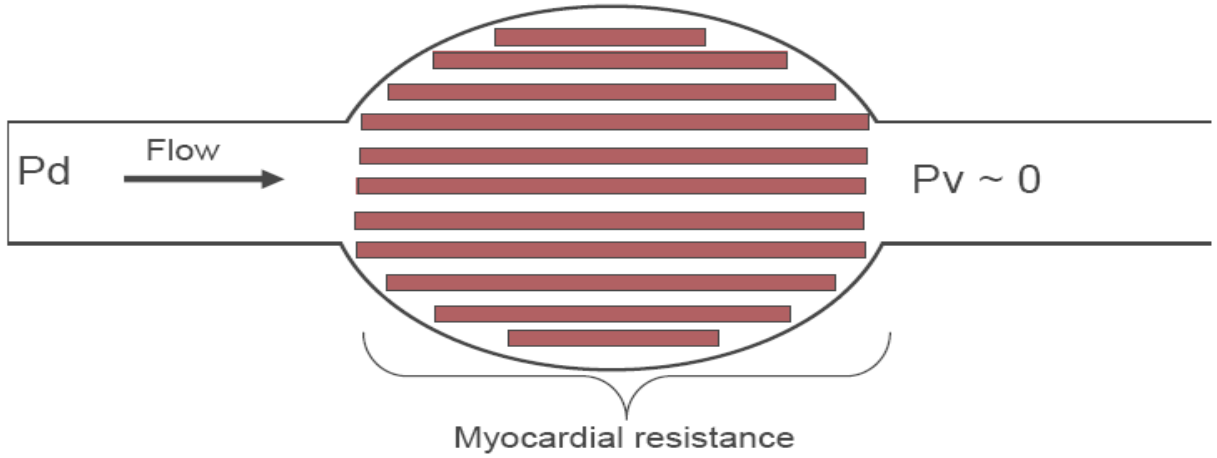
Noninvasive assessment of CMD

Assessment of both epicardial and microvascular compartments
• CFRV (with Doppler transthoracic echocardiography technique): Ratio between coronary blood flow at maximal hyperemia and under resting condition
• MPR (PET, CMR, CT-scan technique): Ratio between myocardial blood flow at peak stress and rest
• MPRI (CMR technique): Ratio of myocardial blood flow at hyperemia/rest for the whole myocardium and separately for the 16 segments

Comment ?

IMR= Pd x Tmn
at maximal hyperemia

Myocardial resistance = Δ Pressure / Flow (simplified)



Δ Pressure = Pd - Pv = Pd (assuming Pv = 0)

Flow ≅ 1 / T_{mn}

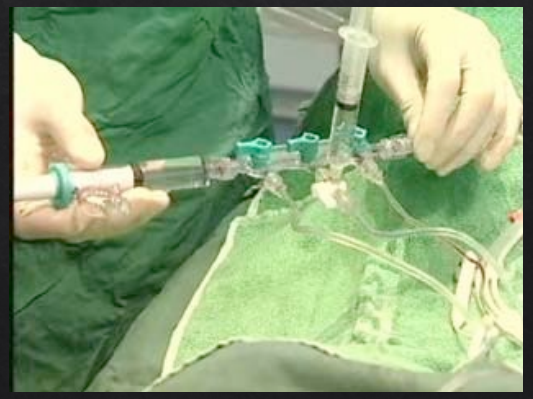
IMR = Pd / (1 / T_{mn})

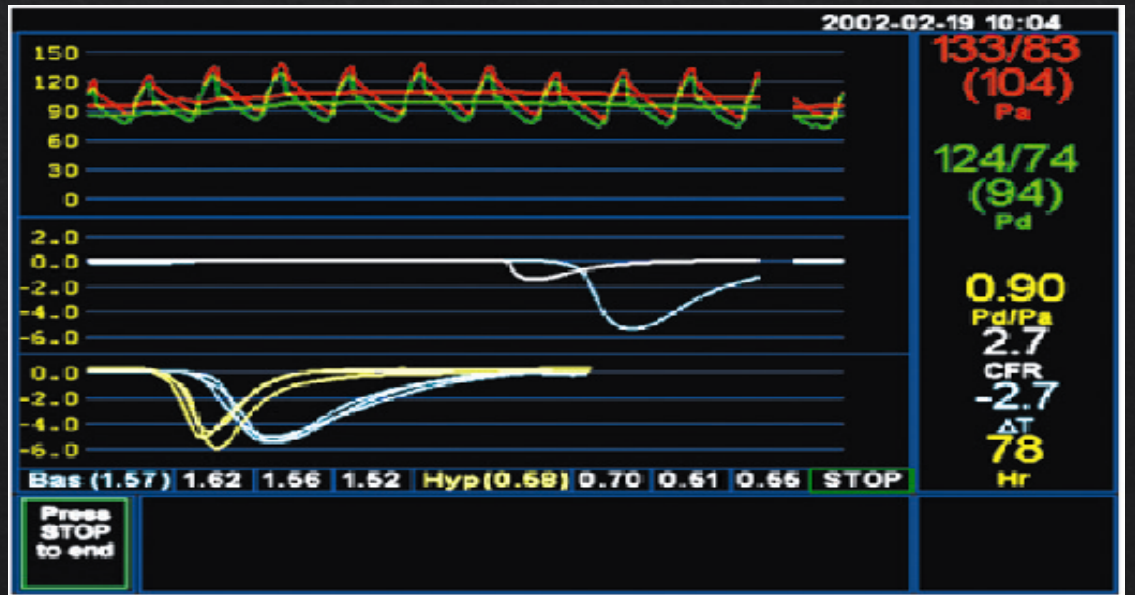
IMR = Pd x T_{mn} (at maximal hyperemia)

Comment ?

IMR-Procedure (3)

- **Maximal hyperaemia** will be induced using 140 µg/kg/min of intravenous adenosine via a central venous catheter preceded by a 2 ml intracoronary bolus of 200 µg nitrate.





IMR-Procedure (5)

Comment ?

- The **mean** aortic and **distal coronary pressures** will be recorded during **peak hyperaemia**. The IMR is defined as distal coronary pressure divided by flow during peak hyperaemia and calculated by dividing the mean distal coronary pressure by the inverse of the hyperaemic transit time,

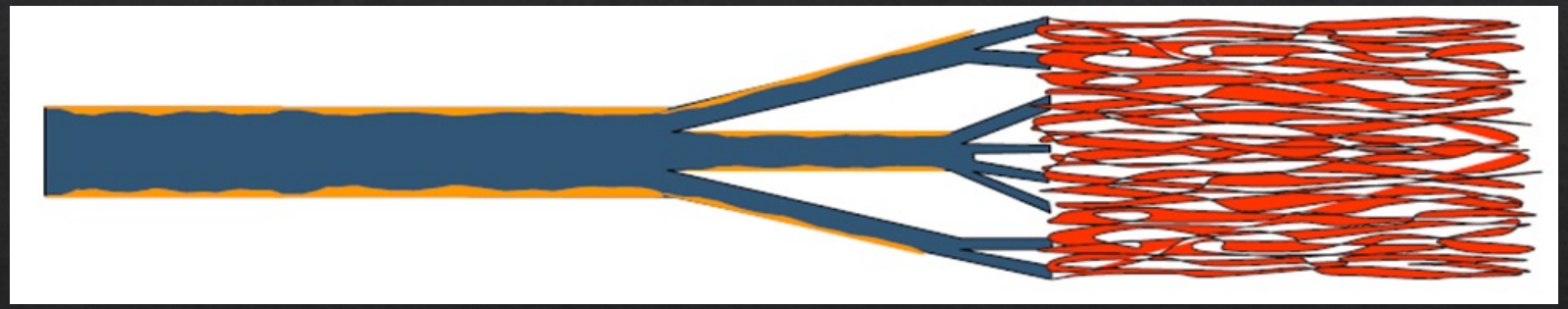
or, **more simply**, multiplying the **mean distal coronary pressure** by the **hyperaemic transit time** (mm Hg × s, or U) where s are seconds and U: units

IMR = Pd × TmnHyp,

Exploration invasive fonctionnalité coronaire

Comment ?

CFR : mean resting transit time/mean hyperaemic transit time
Vasodilatory capacity of epicardial and microvascular compartments



FFR : Pd / Pa
at maximal hyperaemia

IMR : Pd x mean transit time
at maximal hyperaemia
Microvascular resistance

RRR : RI / IMR
RI= resting Pd x mean resting transit time
Vasodilatory capacity of the microcirculation

ESC European Society of Cardiology
European Heart Journal (2020) 41, 3504–3520
doi:10.1093/eurheartj/ehaa503

SPECIAL ARTICLE
Ischaemic heart disease

An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary

Angor microvasculaire: Définition

Table 1 Diagnostic criteria for microvascular angina

Criteria	Evidence	Diagnostic parameters
1	Symptoms of myocardial ischaemia[a]	Effort or rest angina Exertional dyspnoea
2	Absence of obstructive CAD (<50% diameter reduction or FFR >0.80)	Coronary CTA Invasive coronary angiography
3	Objective evidence of myocardial ischaemia[b]	Presence of reversible defect, abnormality or flow reserve on a functional imaging test
4	Evidence of impaired coronary microvascular function	Impaired coronary flow reserve (cut-off <2.0), invasive or noninvasively determined Coronary microvascular spasm, defined as reproduction of symptoms, ischaemic ECG shifts but no epicardial spasm during acetylcholine testing Abnormal coronary microvascular resistance indices (e.g. IMR >25)

Review Article

Coronary microvascular dysfunction and myocardial infarction with non-obstructive coronary arteries: Where do we stand?

Abdul-Quddus Mohammed [a,†], Fuad A. Abdu [a,†], Lu Liu [a], Guoqing Yin [a], Redhwan M. Mareai [a], Ayman A. Mohammed [a], Yawei Xu [a], Wenliang Che [a,b,*]

European Journal of Internal Medicine 117 (2023) 8–20

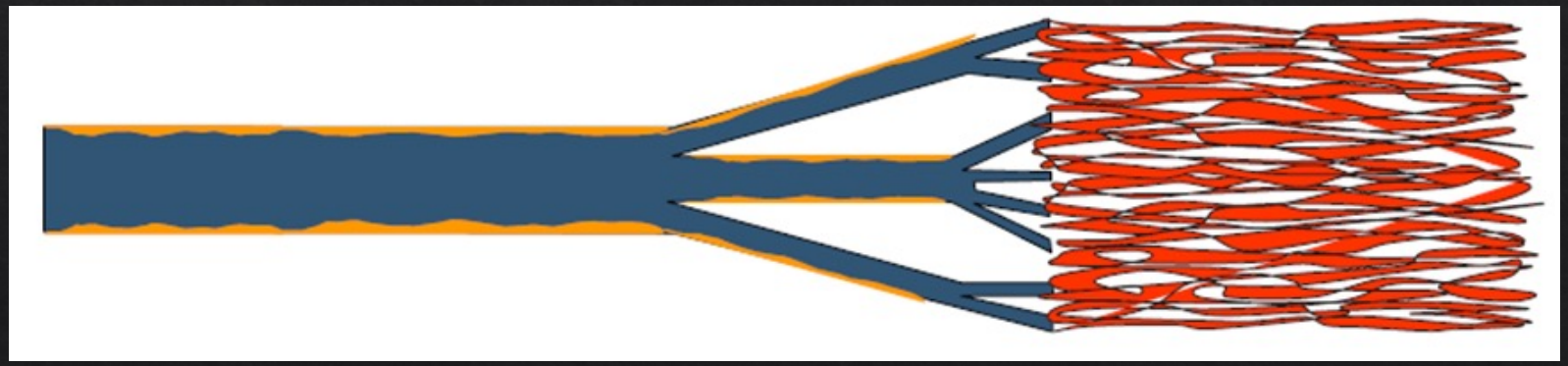
Angor microvasculaire: Phénotypes

Table 2
Methods to identify specific dysfunction, pathological mechanisms, and hemodynamic profile of CMD.

Specific dysfunction	Methods	
Impaired dilation (Functional) (Endothelial-independent dysfunction)	CFR (Doppler/ thermodilution), TDE, MPRI, MBF (by non-invasive techniques)	
Microvascular spams (Endothelial-dependent dysfunction)	Provocation spasm test (ACH/Erg)	
Structural remodeling	IMR, HMR, caIMR	
Pathological mechanisms	*Hemodynamic profile*	
	Adenosine test	Vasoreactivity (acetylcholine test)
Coronary microvascular dysfunction Structural remodeling	CFR<2.0 HMR>1.9 IMR>25	No or <90% diameter reduction No angina and EKG changes
Coronary microvascular dysfunction Microvascular spasm	CFR<2.0 HMR<1.9 IMR<25	No or <90% diameter reduction + Angina and EKG changes
Coronary microvascular dysfunction Structural remodeling and Microvascular spasm	CFR<2.0 HMR>1.9 IMR>25	No or <90% diameter reduction + Angina and EKG changes

CFR: coronary flow reserves; TDE: Transthoracic doppler echocardiography; MPRI: myocardial perfusion reserve index; MBF: myocardial blood flow; ACH: Acetylcholine; Erg: ergonovine; HMR: hyperemic microvascular resistance; IMR: index of microvascular resistance; caIMR: coronary angiography derived index of microvascular resistance; EKG: electrocardiography.

IMR: preuves cliniques ?



IMR preuves cliniques ?

ESC Working Group on Coronary Pathophysiology and Microcirculation position paper on 'coronary microvascular dysfunction in cardiovascular disease'

ESC European Society of Cardiology
Cardiovascular Research (2020) 116, 741–755
doi:10.1093/cvr/cvaa003

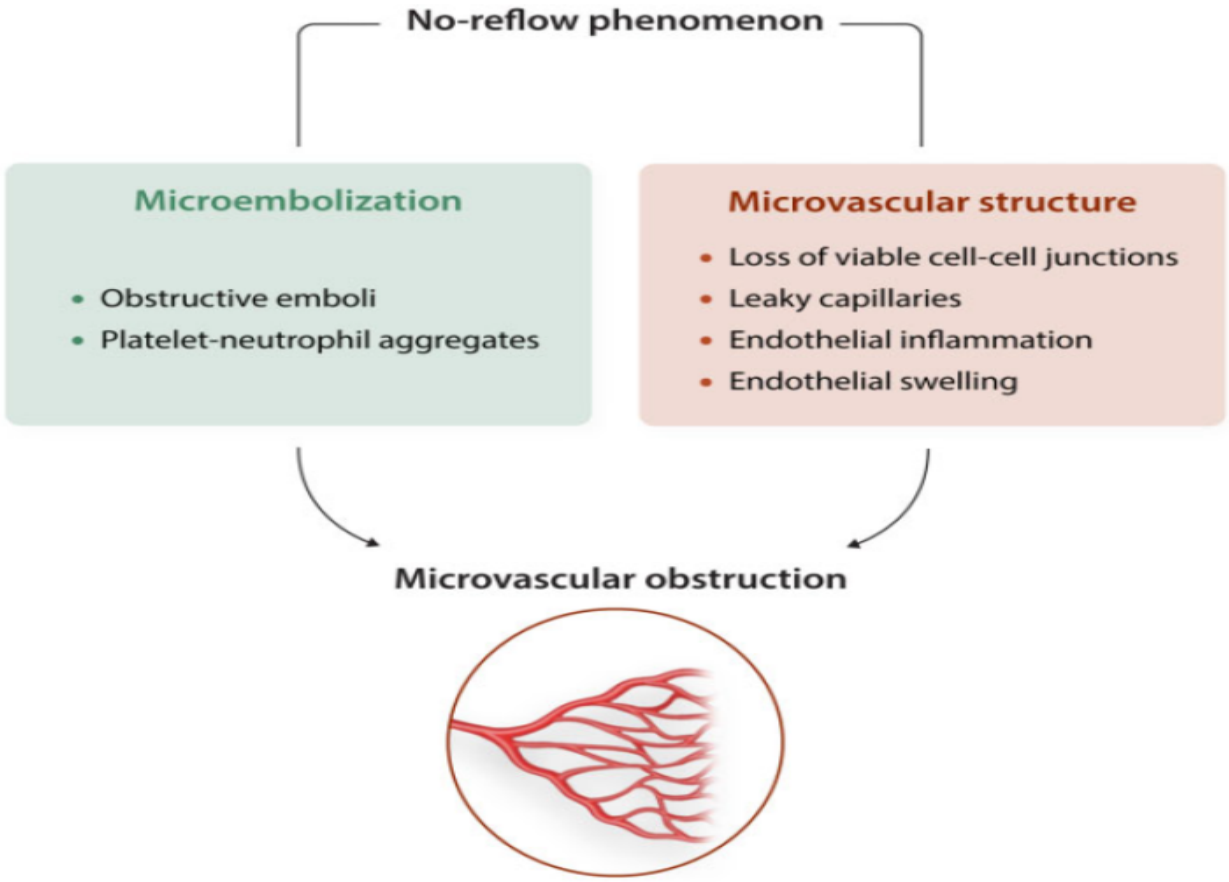


Figure 3 Pathophysiological mechanisms of microvascular dysfunction associated to the non-reflow phenomenon.

Predictive Value of the Index of Microcirculatory Resistance in Patients With ST-Segment Elevation Myocardial Infarction

William F. Fearon, MD, Maulik Shah, MD, Martin Ng, MD, Todd Brinton, MD, Andrew Wilson, MD, Jennifer A. Tremmel, MD, Ingela Schnittger, MD, David P. Lee, MD, Randall H. Vagelos, MD, Peter J. Fitzgerald, MD, PHD, Paul G. Yock, MD, Alan C. Yeung, MD

Stanford, California

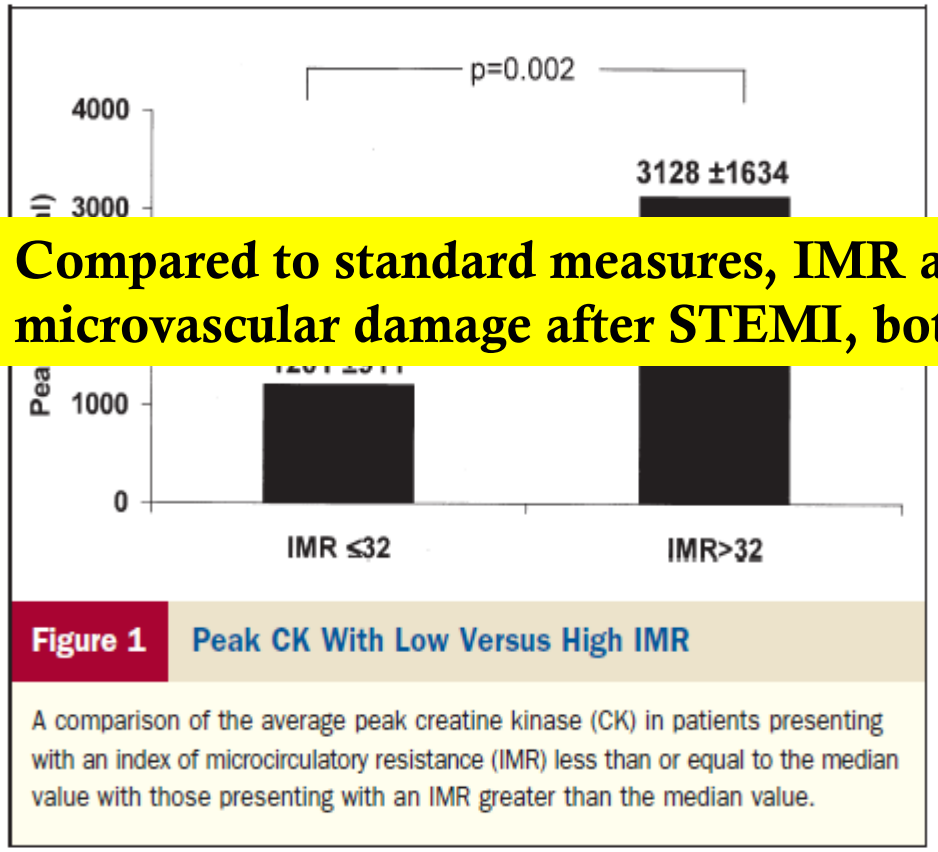


Figure 1 Peak CK With Low Versus High IMR

A comparison of the average peak creatine kinase (CK) in patients presenting with an index of microcirculatory resistance (IMR) less than or equal to the median value with those presenting with an IMR greater than the median value.

Compared to standard measures, IMR appears to be a better predictor of microvascular damage after STEMI, both acutely and in short term follow-up.

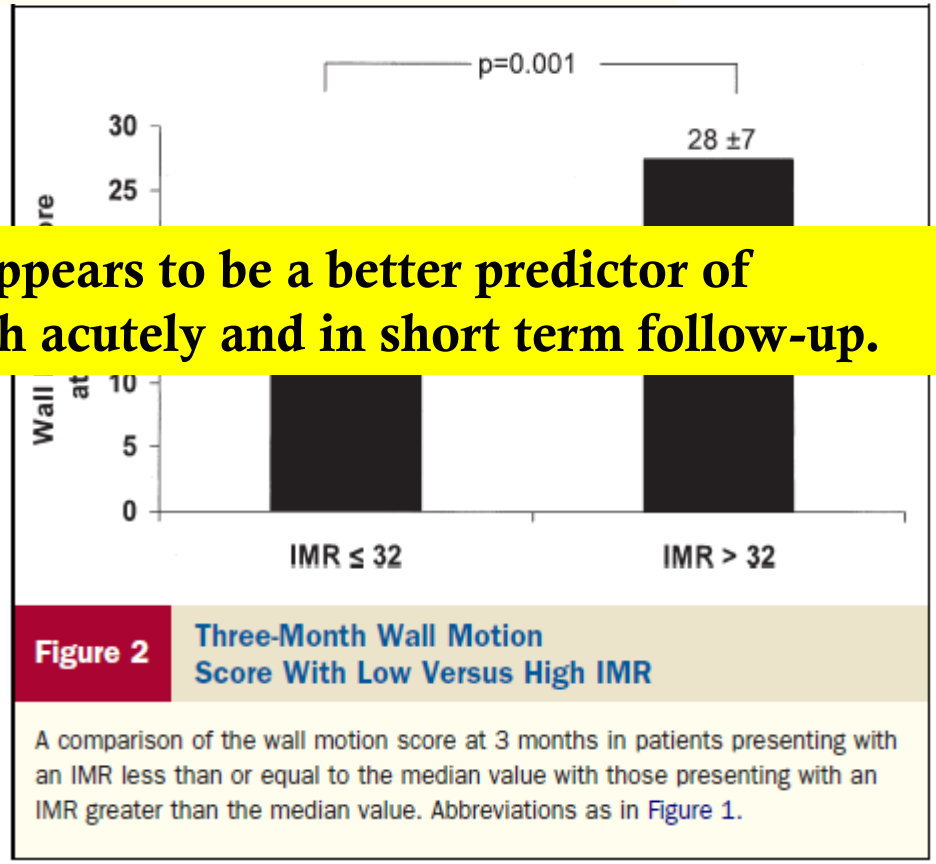


Figure 2 Three-Month Wall Motion Score With Low Versus High IMR

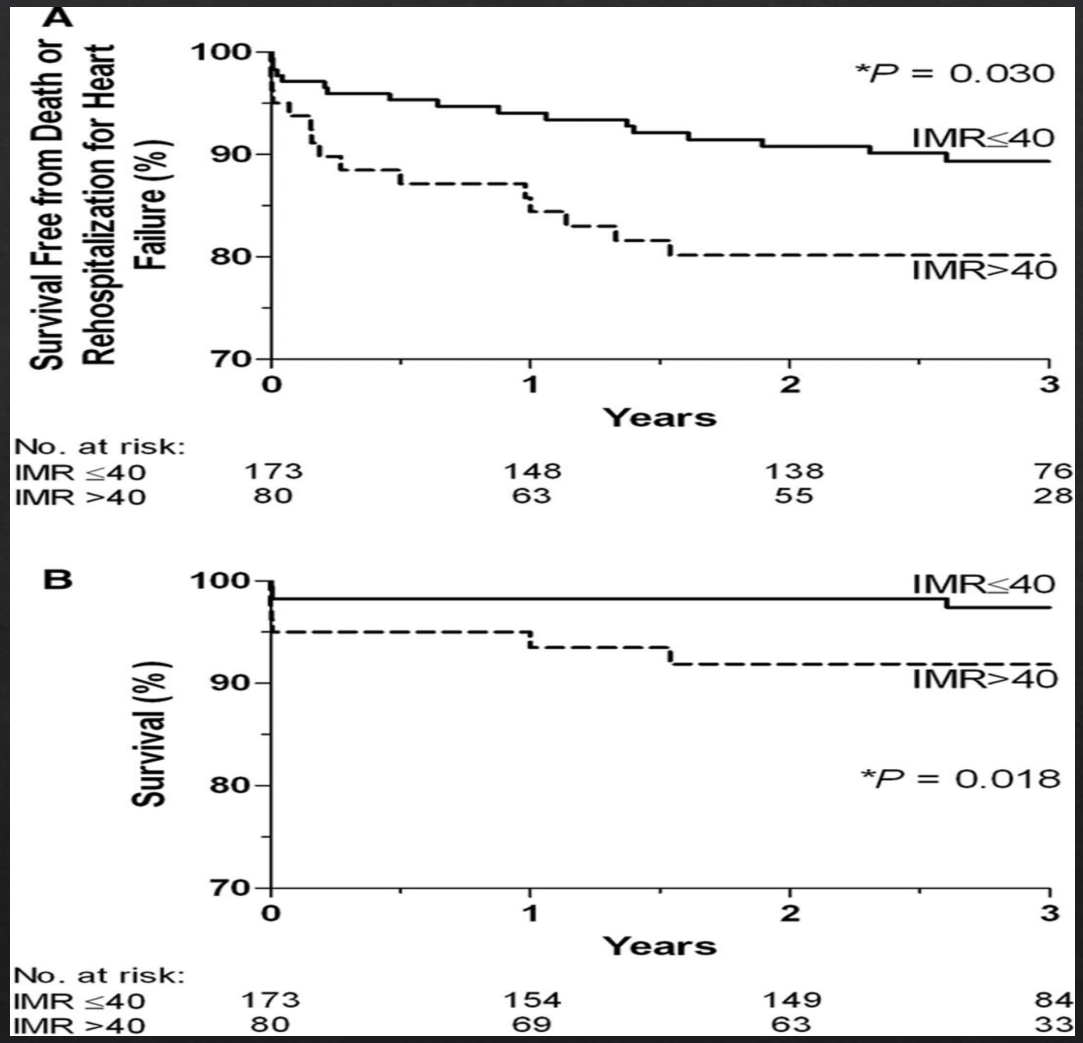
A comparison of the wall motion score at 3 months in patients presenting with an IMR less than or equal to the median value with those presenting with an IMR greater than the median value. Abbreviations as in Figure 1.

Journal of the American College of Cardiology

A, The Kaplan–Meier curves displaying the relationship between IMR >40 and survival free of death or rehospitalization for heart failure.

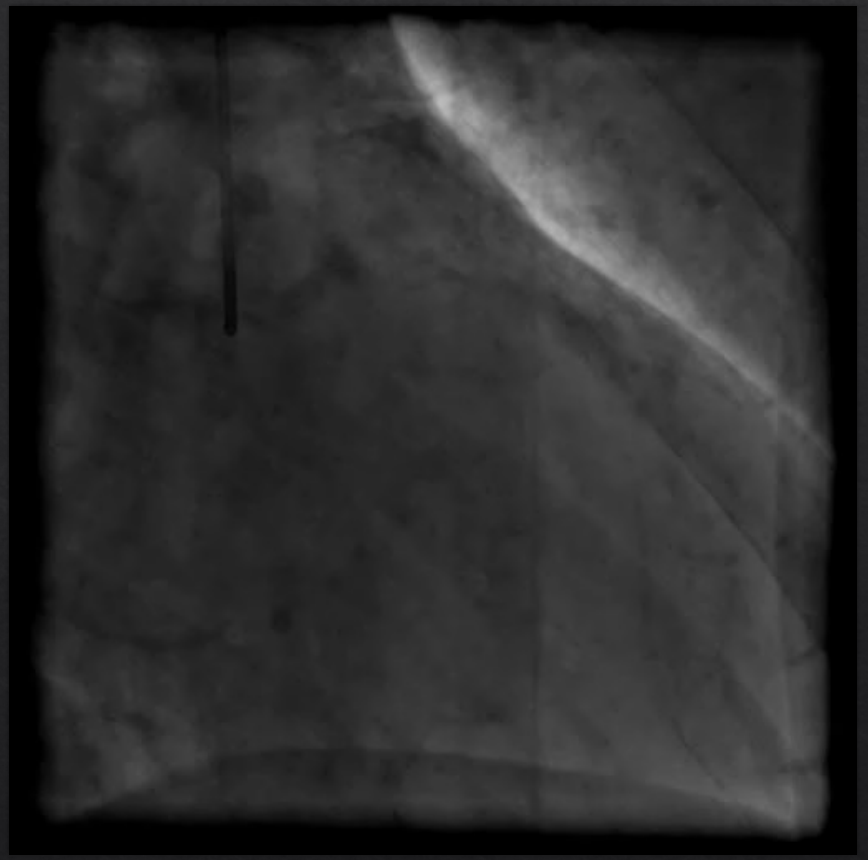
IMR - Décès et Hospitalisations pour IC

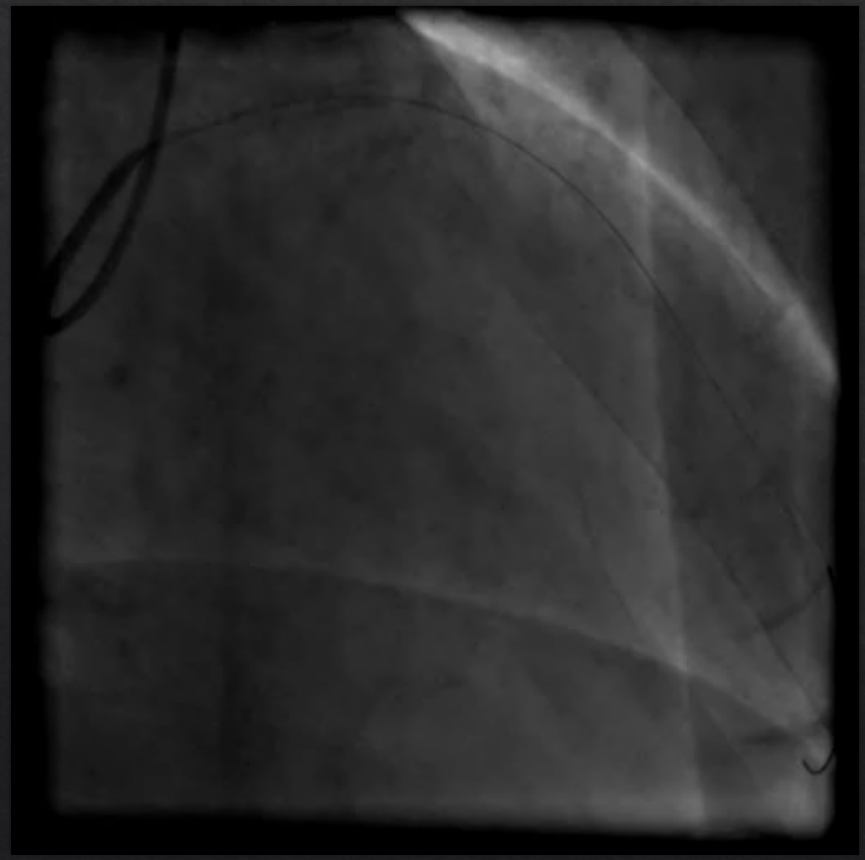
IMR -Mortalité



Fearon W F et al. Circulation. 2013;127:2436-2441

Patient 46 ans IDM ant H+3





IMR=48

MaR=42%

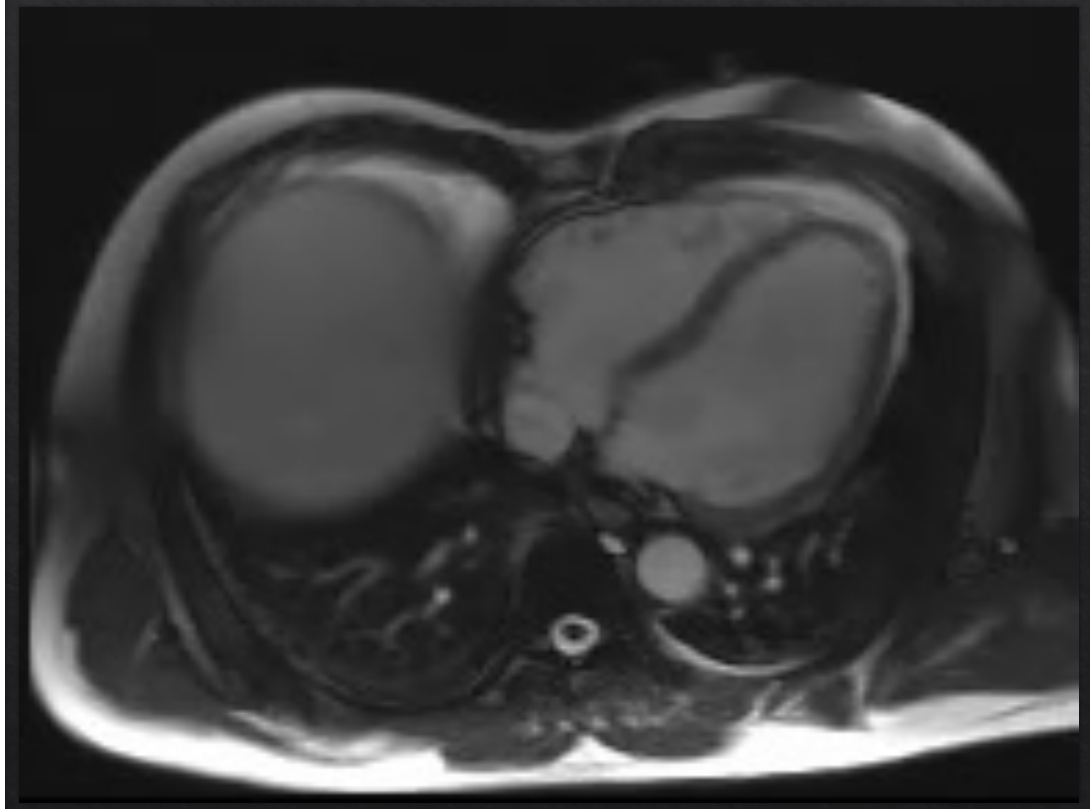
Patient 46 ans IDM ant H+3

Résultats

Le ventricule gauche n'est pas dilaté (VTDVGi : 72 mL/m²) ni hypertrophié (Masse VGi : 51 g/m²).
Séquelle ASA.
La FEVG est mesurée à 43%.
Pas d'hypoperfusion sur les séquences de 1er passage.
Rehaussement myocardique pathologique ASA quasi transmural sur les séquences tardives.
Pas d'anomalie endo cavitaire.
Aspect normal du ventricule droit.
Pas d'épanchement ou de rehaussement pathologique du péricarde
PA : 109/63

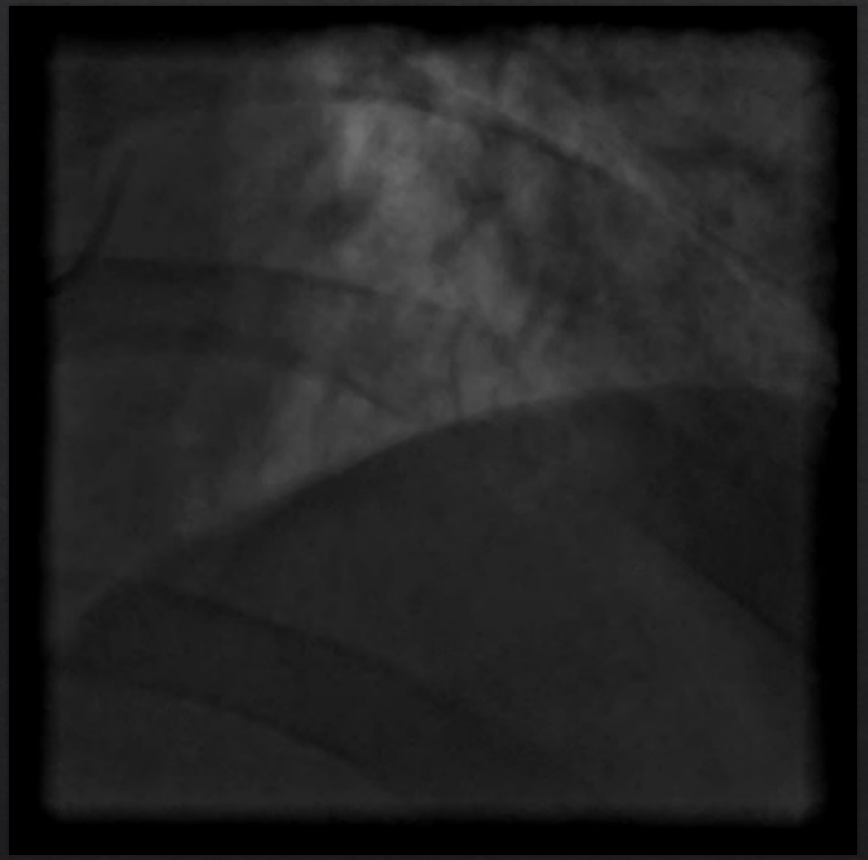
Conclusion

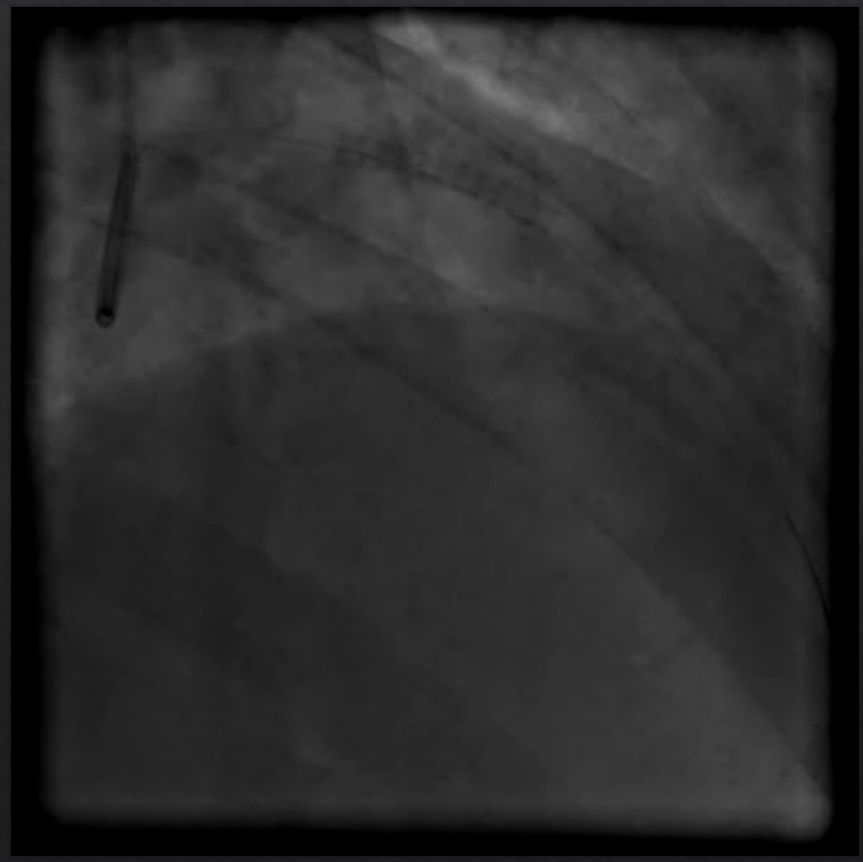
VG de dimensions normales.
Akinésie ASA.
FEVG 43%.
Rehaussement tardif ASA sous endocardique quasi transmural.



IRM à 6 mois FEVG=43%

Patient 56 ans IDM ant H+2





IMR=17

MaR=32%

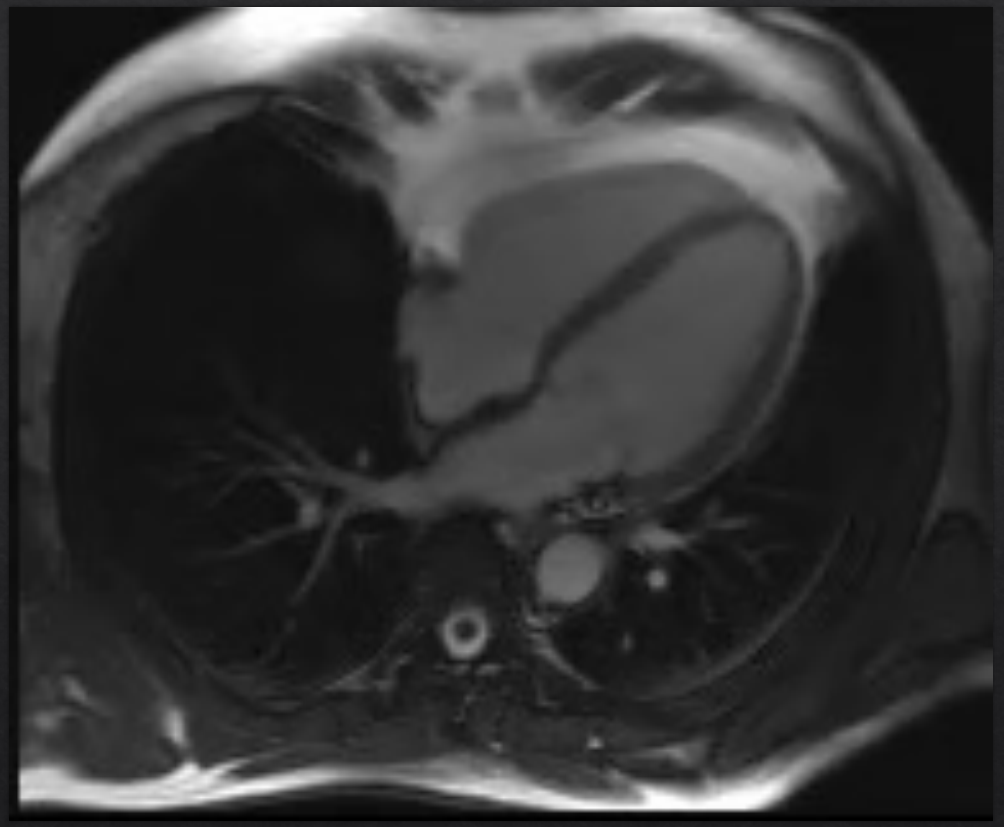
Patient 56 ans IDM ant H+2

Résultats

Ventricule gauche non dilaté, non hypertrophié avec volume télédiastolique mesuré à 64 ml/m2, volume télésystolique mesuré à 20 ml/m2.
La masse VG est évaluée à 52 g/m2.
Fraction d'éjection sub normale mesurée à plus de 60%.
Il existe une hypokinésie.
Absence d'oedeme en T2 STIR.
Absence d'hypoperfusion lors du 1er passage dynamique du produit de contraste.
10 minutes après injection, présence d'un rehaussement tarrdi pathologique essentiellement sous endocardique de la partie antéro septale moyenne et apicale.

Conclusion

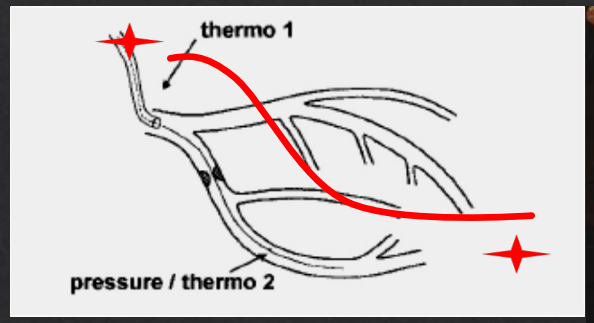
Cardiopathie ischémique avec fraction d'éjection ventriculaire gauche conservée associant une hypokinésie antéro septale très modérée essentiellement moyenne et apicale associée à un rehaussement sous endocardique témoignant d'une nécrose à ce niveau mais avec persistance d'une bonne viabilité de ce territoire.
Absence de thrombus apical.

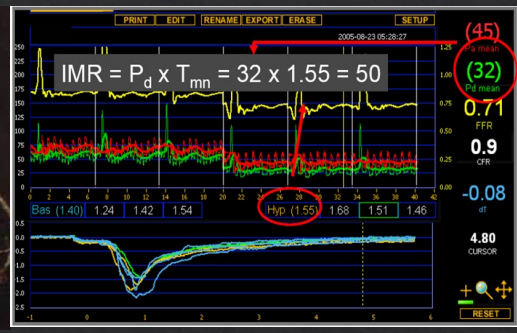


IRM à 6 mois FEVG=60%

Evaluation de la microcirculation en 2024

Pour quel patient ?





- **SCC INOCA**
- **SCA MINOCA**
- **SCA IDM no-Reflow**

Du syndrome X à l'angine microvasculaire…

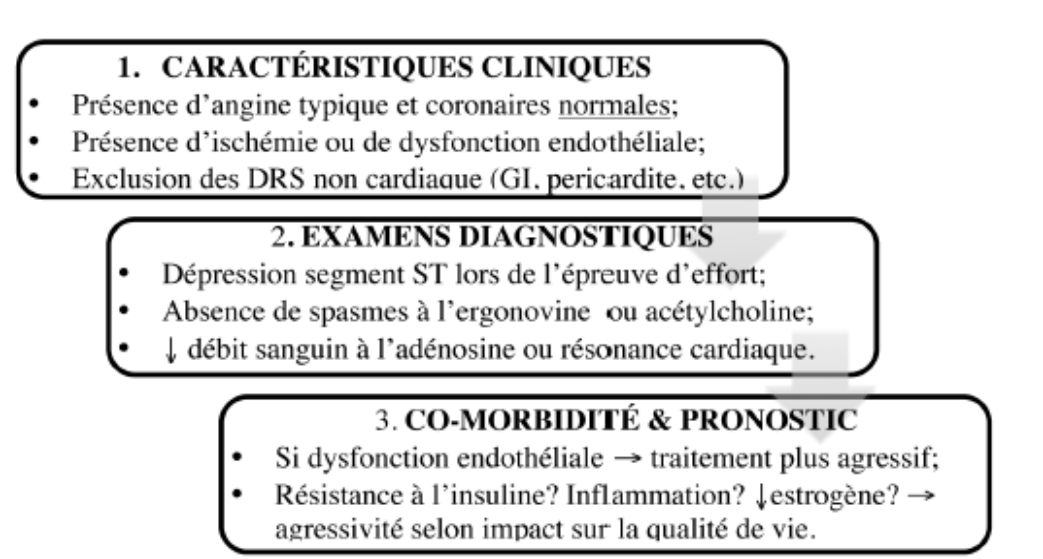


Figure 2. *Approche diagnostique du syndrome X cardiaque*[1-8,11]

Patients jeunes

Prédominance féminine

Discussion : L'hypothèse actuelle relative au syndrome X cardiaque postule une mauvaise réponse des microvaisseaux et une hypersensibilité aux stimuli douloureux, d'où également l'utilisation du terme « syndrome du cœur sensible ». Cette pathologie ne répond pas à tous les antiangineux. Le traitement actuel proposé consiste à rassurer le patient qui en est atteint, à introduire un bêtabloquant et de la nitroglycérine au besoin. Pour traiter en deuxième ligne la perception inadéquate de la douleur, on pourrait envisager l'imipramine. Le suivi clinique est souvent important. Les nombreux examens engendrés n'apportent pas toujours les réponses escomptées et provoquent chez le patient un sentiment de découragement ou d'anxiété.

INOCA

Pourquoi ?

Microvascular disease: très fréquente…

JACC: CARDIOVASCULAR IMAGING, VOL. 8, NO. 2, 2015
FEBRUARY 2015:210–20

Angina without coronary artery disease (CAD) has substantial morbidity and is present in 10% to 30% of patients undergoing angiography. Coronary microvascular dysfunction (CMD) is present in 50% to 65% of these patients. The optimal treatment of this cohort is undefined. We performed a systematic review to evaluate treatment strategies for objectively-defined CMD in the absence of CAD. We included studies assessing therapy in human subjects with angina and coronary flow reserve or myocardial perfusion reserve <2.5 by positron emission tomography, cardiac magnetic resonance imaging, dilution methods, or intracoronary Doppler in the absence of coronary artery stenosis ≥50% or structural heart disease. Only 8 papers met the strict inclusion criteria. The papers were heterogeneous, using different treatments, endpoints, and

Angina pectoris, the most common symptom of ischaemic heart disease (IHD), affects approximately 112 million people globally.[1]

management of patients with chronic coronary syndromes (CCS).[2] A large proportion of patients (up to 70%) undergoing coronary angiography because of angina and evidence of myocardial ischaemia do not have obstructive coronary arteries but have demonstrable ischaemia.[2,3] Studies carried out in the past two decades have

Coronary Microvascular Dysfunction, Microvascular Angina, and Treatment Strategies

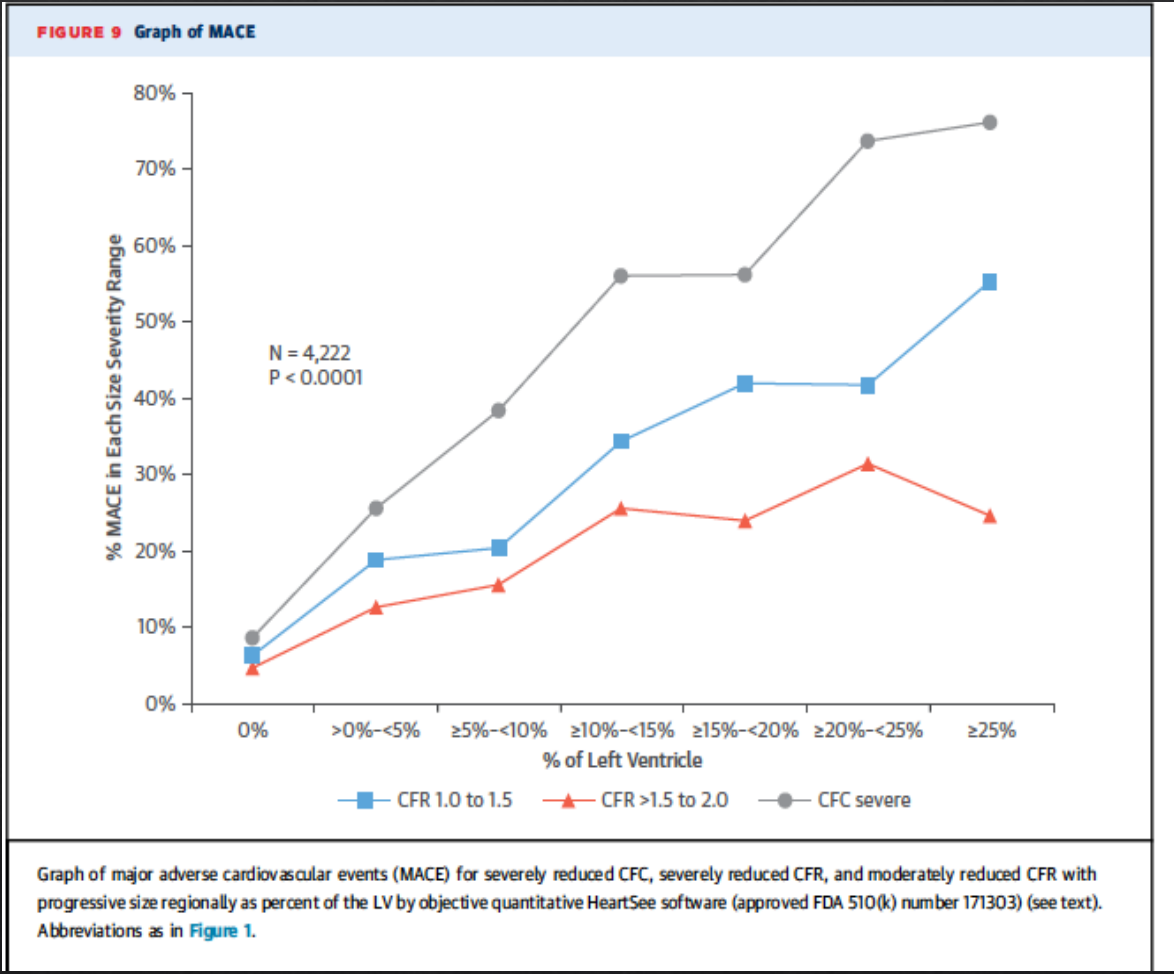
ESC European Society of Cardiology
European Heart Journal (2020) 41, 3504–3520
doi:10.1093/eurheartj/ehaa503
SPECIAL ARTICLE
Ischaemic heart disease

An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary

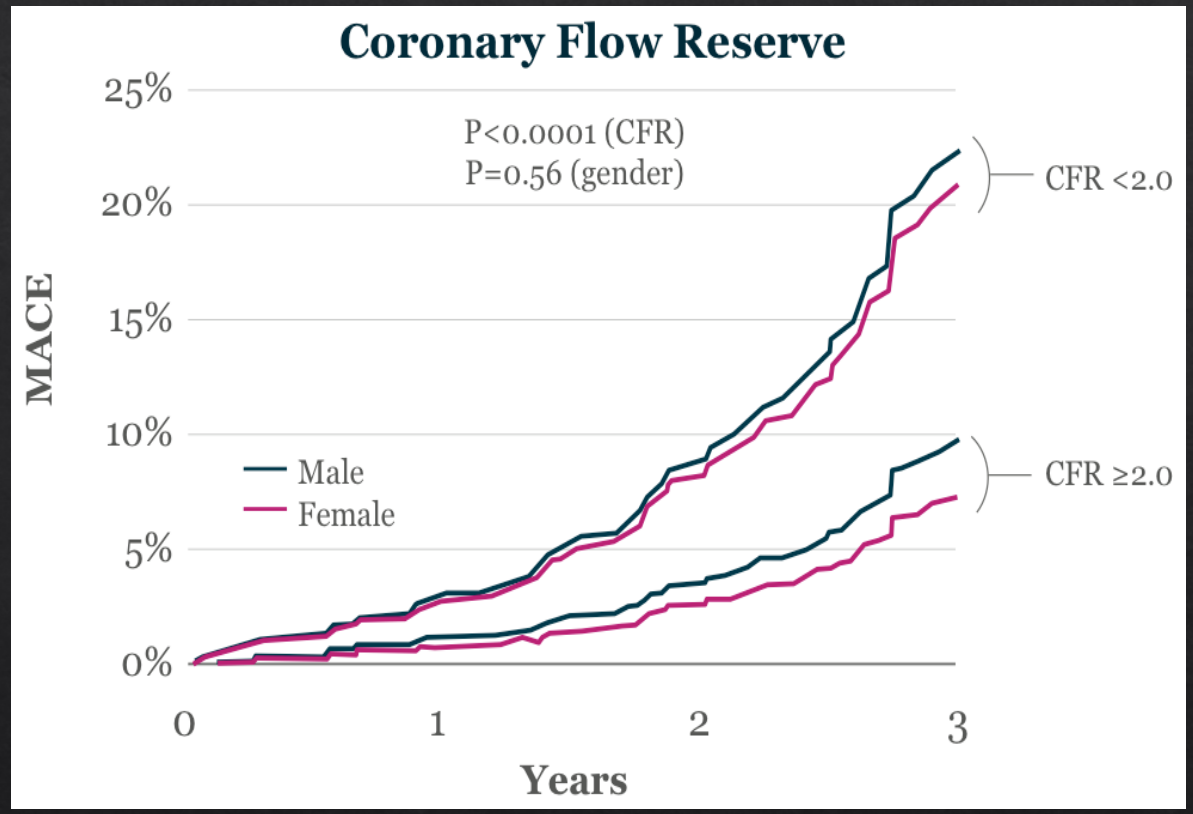
INOCA

Microvascular disease: MACE…

Pourquoi ?



Graph of major adverse cardiovascular events (MACE) for severely reduced CFC, severely reduced CFR, and moderately reduced CFR with progressive size regionally as percent of the LV by objective quantitative HeartSee software (approved FDA 510(k) number 171303) (see text). Abbreviations as in Figure 1.



Gould and Johnson
CFR and Microvascular Angina

JACC VOL. 72, NO. 21, 2018
NOVEMBER 27, 2018:2642-62

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Pourquoi ?

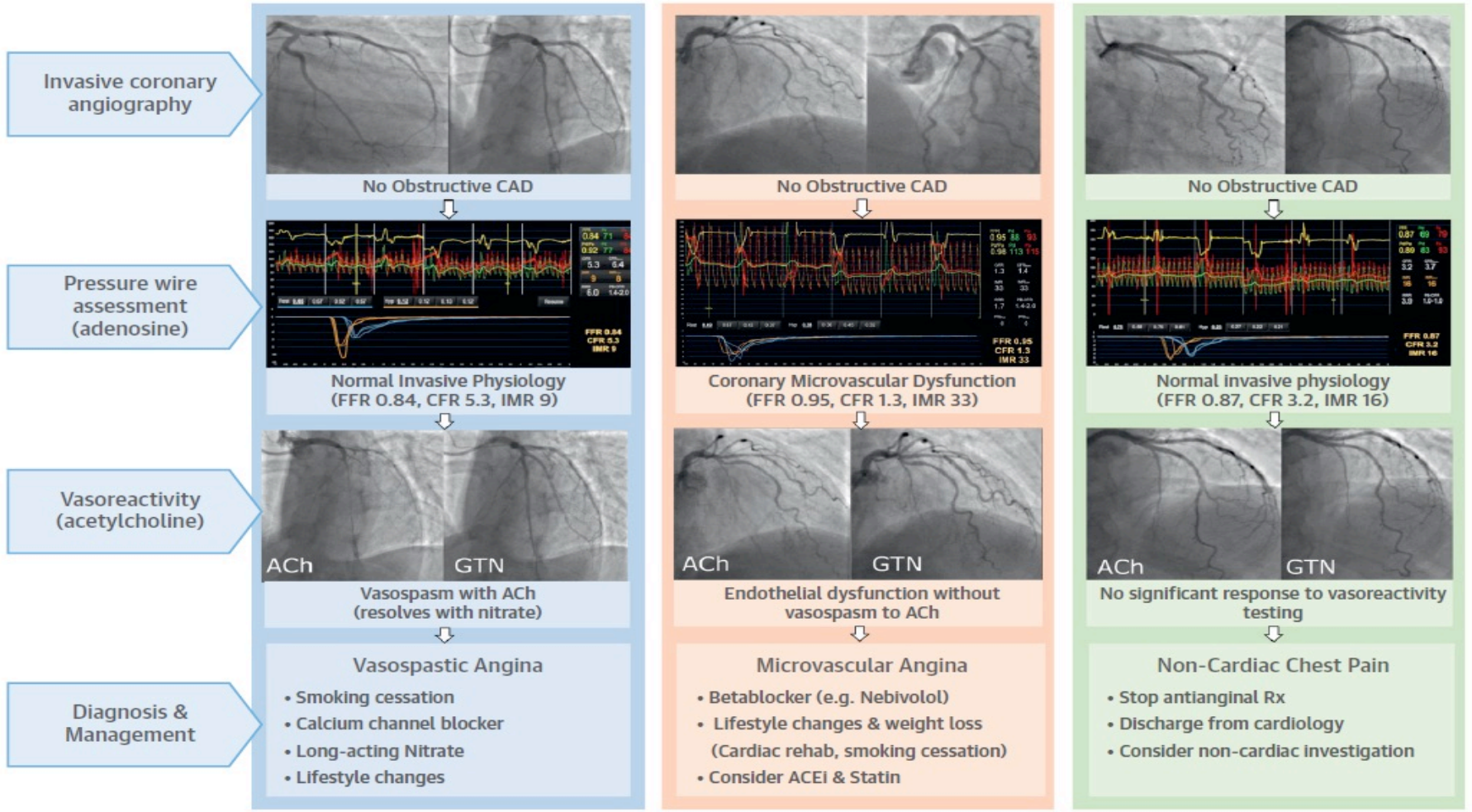
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 72, NO. 23, 2018

PUBLISHED BY ELSEVIER

Stratified Medical Therapy Using Invasive Coronary Function Testing in Angina

The CorMicA Trial

FIGURE 1 Stratified Medical Therapy Guided by an IDP in Patients With Angina but No Obstructive CAD



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Pourquoi ?

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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VOL. 72, NO. 23, 2018

Stratified Medical Therapy Using Invasive Coronary Function Testing in Angina

The CorMicA Trial

TABLE 3 Primary Outcome and Changes in Health Status at 6 Months

	Control (n = 75)		Intervention (n = 73)		Intervention Effect*		
	6 Months	Change From Baseline	6 Months	Change From Baseline	Estimate	95% CI	p Value
Primary efficacy endpoint—Seattle Angina Questionnaire							
Angina summary score	51.8 ± 26.1	3.1 ± 21.3	67.5 ± 23.0	14.4 ± 20.1	11.68	4.99 to 18.37	0.001
Angina limitation	50.9 ± 31.2	−1.6 ± 22.1	65.4 ± 27.7	12.6 ± 22.5	14.50	7.32 to 21.67	<0.001
Angina stability	46.3 ± 25.9	5.0 ± 37.2	57.2 ± 24.1	8.9 ± 33.4	4.31	−6.88 to 15.49	0.452
Angina frequency	55.9 ± 30.3	1.6 ± 27.1	74.5 ± 22.2	10.1 ± 27.5)	9.29	0.49 to 18.09	0.040
Treatment satisfaction	71.9 ± 23.6	−9.9 ± 25.8	83.9 ± 18.9	2.1 ± 19.0	12.05	4.73 to 19.37	0.002
SAQ quality of life	48.8 ± 28.2	9.3 ± 27.5	61.9 ± 27.9	19.5 ± 23.7	10.48	2.18 to 18.79	0.015
Clinical events (6 months)							
Major adverse cardiac and cerebrovascular events	2 (2.6)		2 (2.6)		1.01	0.14-7.39	1.000

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Ia ?

ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–71
doi:10.1093/eurheartj/ehz425

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

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.	IIa

CFR <2.0 or IMR ≥25 units

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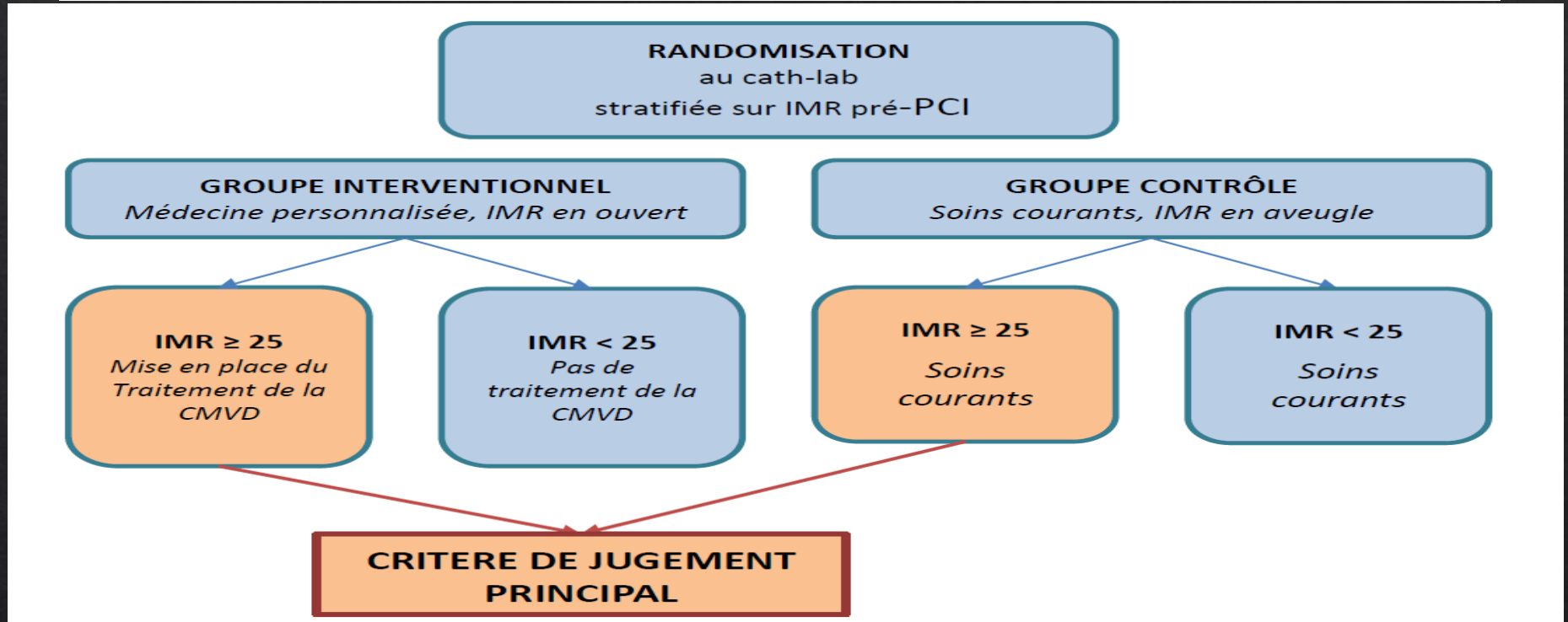
Pourquoi ?

Personalized Medicine Using Coronary Microvascular Function Measured in Patient with Percutaneous Coronary Intervention in Angina

DECISIONING

Etude Multicentrique



OBJECTIF PRINCIPAL	Démontrer un effet positif de la « médecine personnalisée » sur l'angine de poitrine chez les patients ayant eu une revascularisation épicardique par angioplastie et avec une CMVD significative mesurée par l'IMR pré-PCI.
CRITERE DE JUGEMENT PRINCIPAL	Le critère de jugement principal est la différence moyenne de sévérité de l'angor à 1 an, évaluée par le Seattle angina questionnaire summary score (SAQSS) entre les patients avec un IMR pré-PCI anormal dans le groupe interventionnel comparé avec les patients avec un IMR pré-PCI anormal dans le groupe contrôle.

MINOCA

Définition

Review

Pathophysiology and diagnostic pathway of myocardial infarction with non-obstructive coronary arteries

Jun Takahashi (MD, PhD, FJCC) *, Sho Onuma (MD), Kiyotaka Hao (MD, PhD), Shigeo Godo (MD, PhD), Takashi Shiroto (MD, PhD), Satoshi Yasuda (MD, PhD, FJCC)

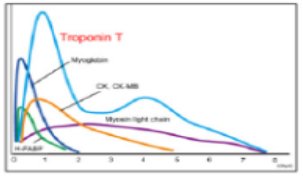
Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

Journal of Cardiology 83 (2024) 17–24

Definition of myocardial infarction with non-obstructive coronary arteries (MINOCA)

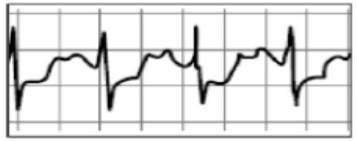
AMI defined by the 'Fourth Universal Definition of MI' criteria

Detection of a rise and/or fall in cTn values with at least one value above the 99th percentile upper reference limit



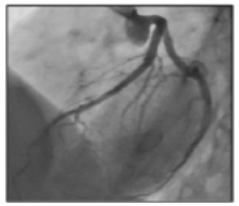
Clinical evidence of myocardial ischemia as shown at least 1 of the following:

- Symptoms of myocardial ischemia
- New ischemic ECG changes
- Development of pathological Q waves
- Imaging evidence of new loss of viable myocardium or new RWMA
- Identification of a coronary thrombus



Non-obstructive coronary arteries on angiography

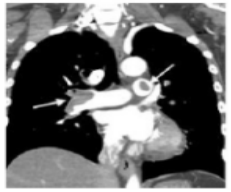
No stenotic lesion angiographically 50% or greater in the major epicardial coronary artery



No other cause of the acute presentation

Alternate diagnosis includes as follows;

- Sepsis
- Pulmonary embolism
- Cardiac Contusion
- Other conditions with non-cardiac causes of cardiac troponin elevation



MINOCA

2023 ESC Guidelines for the management of acute coronary syndromes

ESC European Society of Cardiology

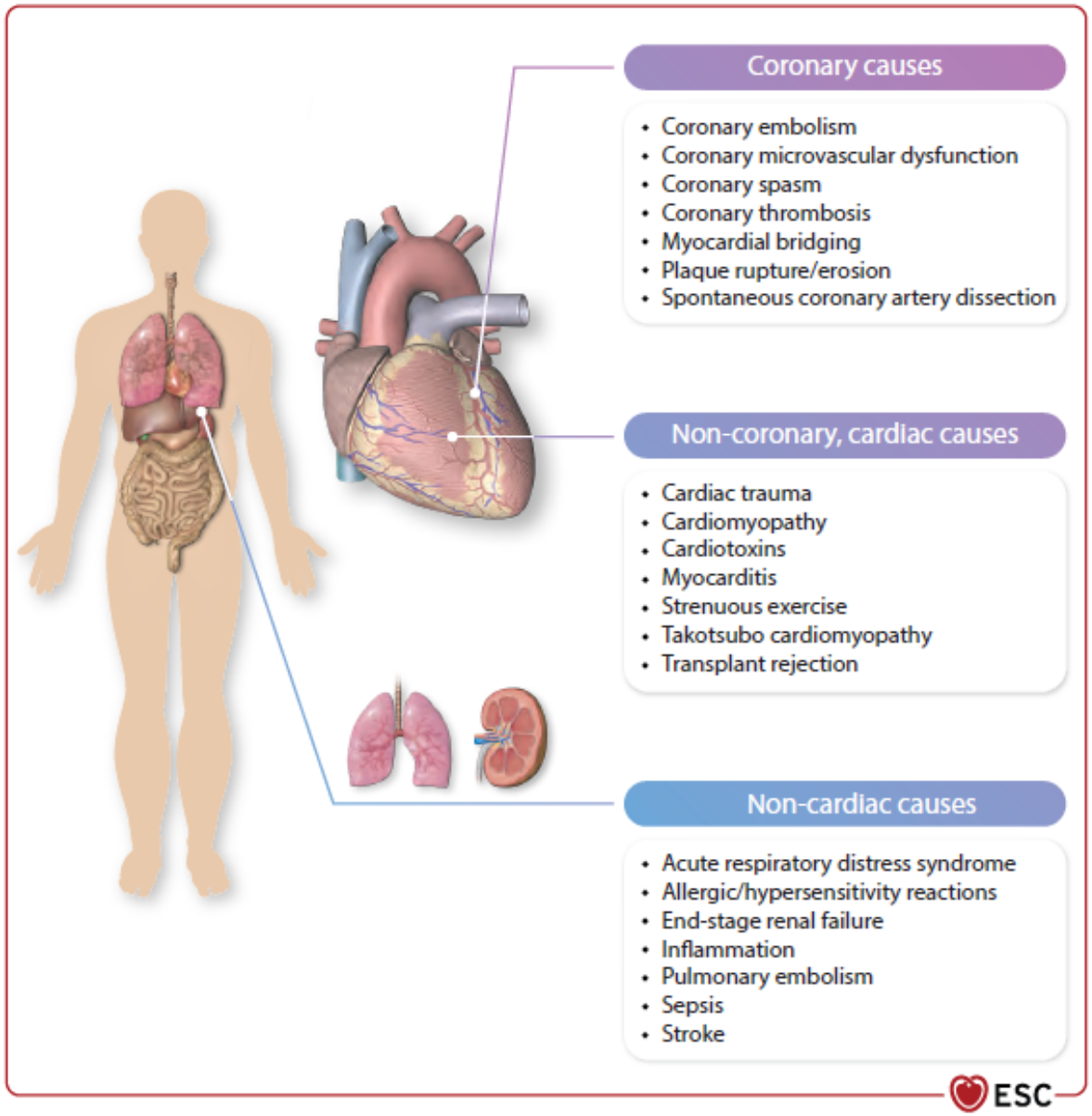


Figure 15 Underlying causes for patients with a working diagnosis of myocardial infarction with non-obstructive coronary arteries. This figure outlines some of the potential differential diagnoses in patients with a working diagnosis of MINOCA after coronary angiography, but this list is not exhaustive.

Etiologies

Umbrella term…

SCA avec coro 1%-14%….

MINOCA

Original Investigation | Cardiology

Mortality in ST-Segment Elevation Myocardial Infarction With Nonobstructive Coronary Arteries and Mimickers

Odayme Quesada, MD; Mehmet Yildiz, MD; Timothy D. Henry, MD; Seth Bergstedt, MS; Jenny Chambers, MBA; Ananya Shah; Larissa Stanberry, PhD; Lucas Volpenhein; Dalia Aziz, MD; Rebekah Lantz, DO; Cassady Palmer, BS; Justin Ugwu, MD; Muhammad J. Ahsan, MD; Ross F. Garberich, MS; Heather S. Rohm, BSN; Frank V. Aguirre, MD; Santiago Garcia, MD; Scott W. Sharkey, MD

Key Points

Question Is 5-year mortality different in patients with ST-segment elevation myocardial infarction (STEMI) presenting with nonobstructive coronaries (MINOCA) and MINOCA mimickers (takotsubo cardiomyopathy, myocarditis, or nonischemic cardiomyopathy) as compared with patients with obstructive disease?

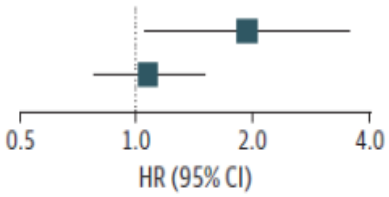
Findings In this cohort study of 8560 consecutive patients with STEMI, compared with obstructive disease, 5-year mortality hazard risk was higher in patients with MINOCA and similar in patients with MINOCA mimickers.

Meaning The findings of this study suggest that STEMI without obstructive disease is a morbid disease, emphasizing the need to diagnose the underlying cause of MINOCA and MINOCA mimickers at the time of the event.

Diagnostic avec IRM…

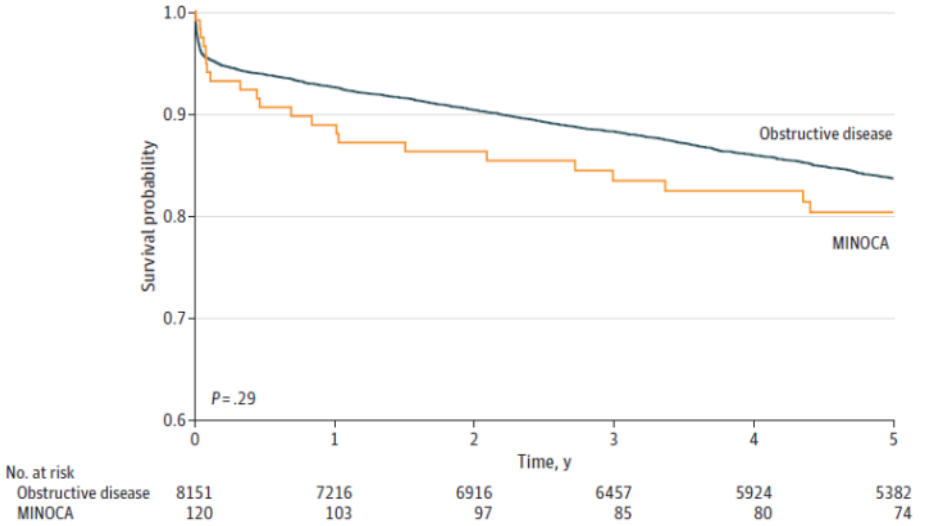
Figure 2. Adjusted 5-Year Mortality Risk in ST-Segment Elevation Myocardial Infarction (STEMI) Presenting With Nonobstructive Coronaries (MINOCA) and MINOCA Mimickers in Comparison With Obstructive Disease

STEMI diagnosis	HR (95% CI)
MINOCA	1.94 (1.06-3.54)
MINOCA mimicker	1.08 (0.78-1.49)



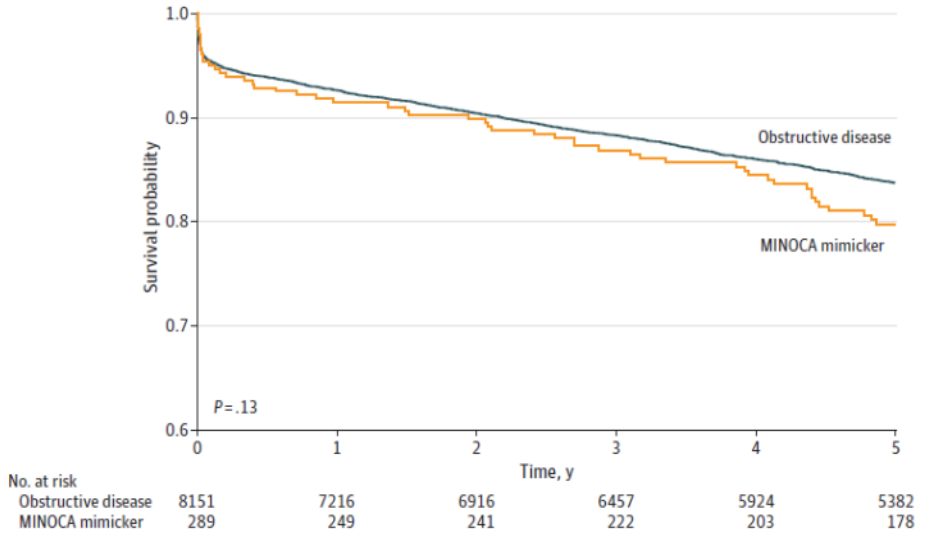
Gravité…

Figure 1. 5-Year Survival Probability in ST-Segment Elevation Myocardial Infarction (STEMI) Presenting With Nonobstructive Coronaries (MINOCA) and MINOCA Mimickers in Comparison With Obstructive Disease



No. at risk

Obstructive disease	8151	7216	6916	6457	5924	5382
MINOCA	120	103	97	85	80	74



No. at risk

Obstructive disease	8151	7216	6916	6457	5924	5382
MINOCA mimicker	289	249	241	222	203	178

MINOCA

Gravité…

Original article

Prognostic impact of coronary microvascular dysfunction in patients with myocardial infarction with non-obstructive coronary arteries

Fuad A. Abdu [a], Lu Liu [a], Abdul-Quddus Mohammed [a], Guoqing Yin [a], Bin Xu [a], Wen Zhang [a], Siling Xu [a], Xian Lv [a], Rui Fan [a], Cailin Feng [a], Tingting Shi [a], Yunlong Huo [b], Yawei Xu [a,*], Wenliang Che [a,c,*]

European Journal of Internal Medicine

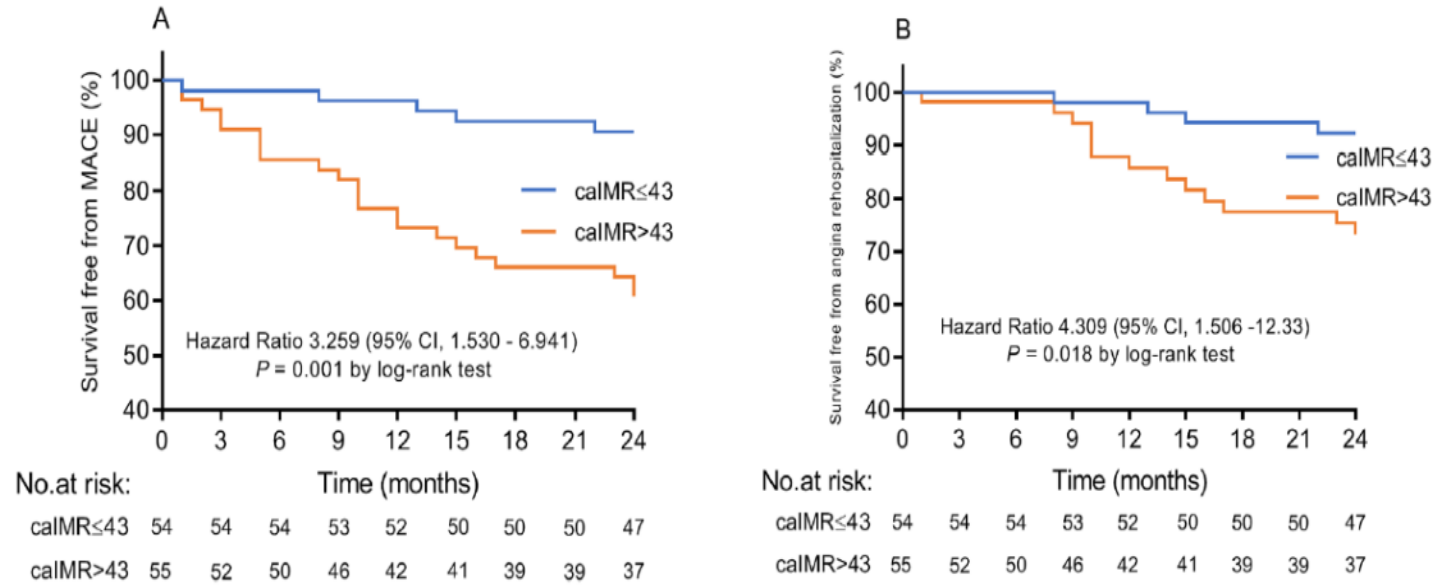


Fig. 3. (A) Kaplan-Meier curves for freedom from MACE according to the result of caIMR (≤ 43 and >43) in MINOCA patients. (B) Kaplan-Meier curves for freedom from angina rehospitalization according to the result of caIMR (≤43 and >43) in MINOCA patients. MACE, Major adverse cardiac events; caIMR, coronary angiography-derived index of microcirculatory resistance.

Surtout avec dysfonction caIMR…

MINOCA

Diagnostic

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Recommendations	Class[a]	Level[b]
In patients with a working diagnosis of MINOCA, CMR imaging is recommended after invasive angiography if the final diagnosis is not clear.[544,545]	I	B
Management of MINOCA according to the final established underlying diagnosis is recommended, consistent with the appropriate disease-specific guidelines.[546,550,552]	I	B
In all patients with an initial working diagnosis of MINOCA, it is recommended to follow a diagnostic algorithm to determine the underlying final diagnosis.	I	C

MINOCA

Diagnostic

2023 ESC Guidelines for the management of acute coronary syndromes

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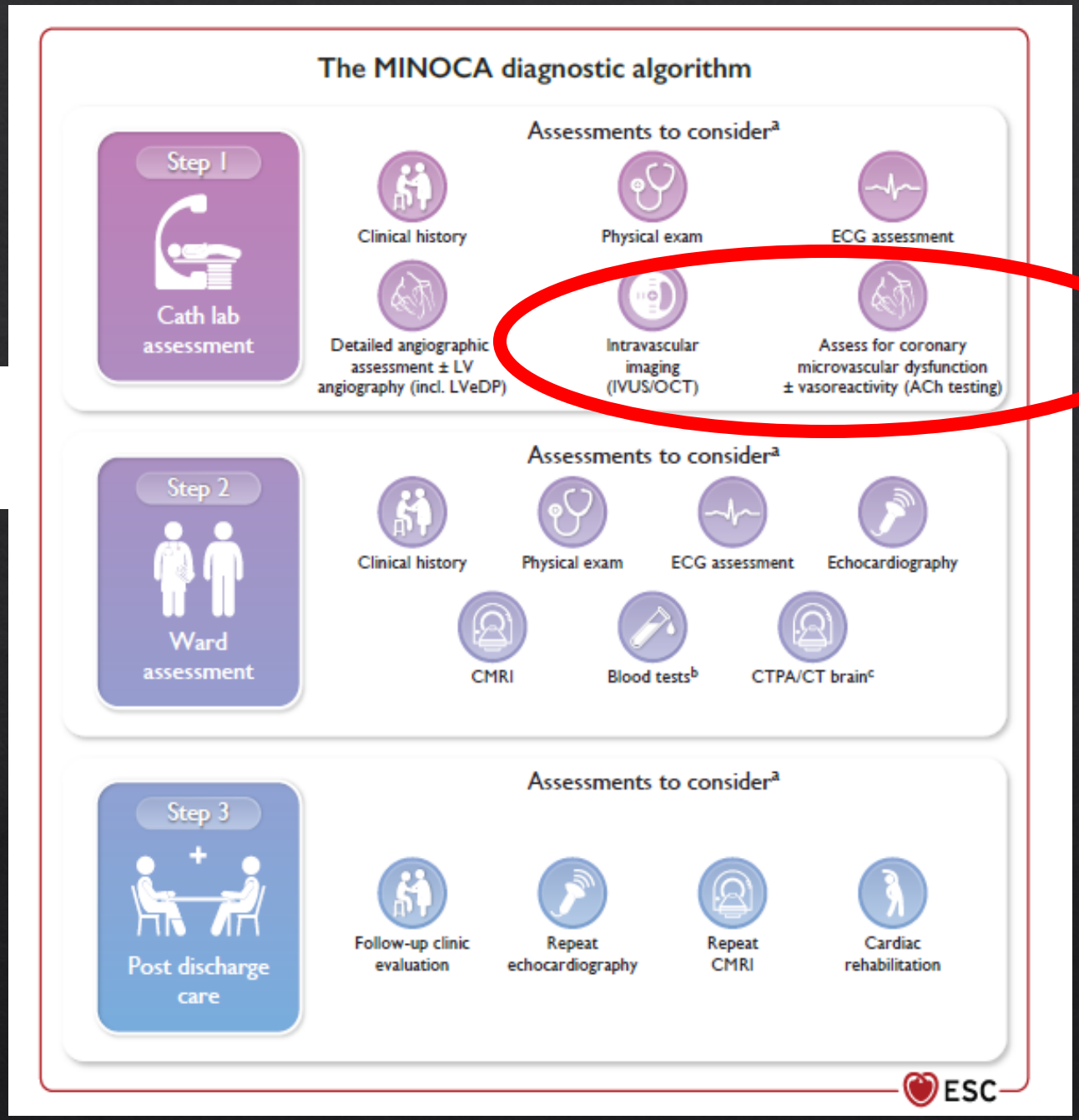
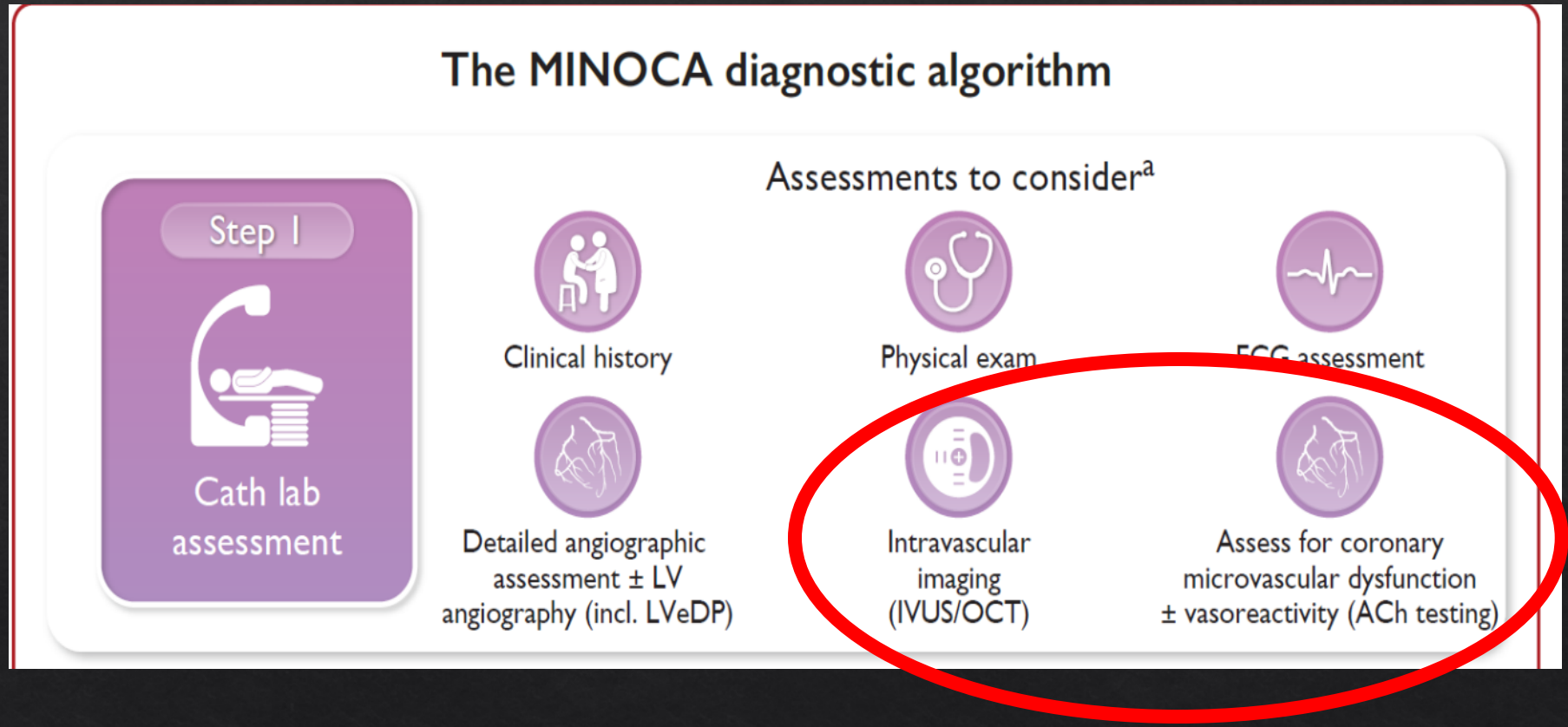


MINOCA

Cathlab



2023 ESC Guidelines for the management of acute coronary syndromes

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MINOCA

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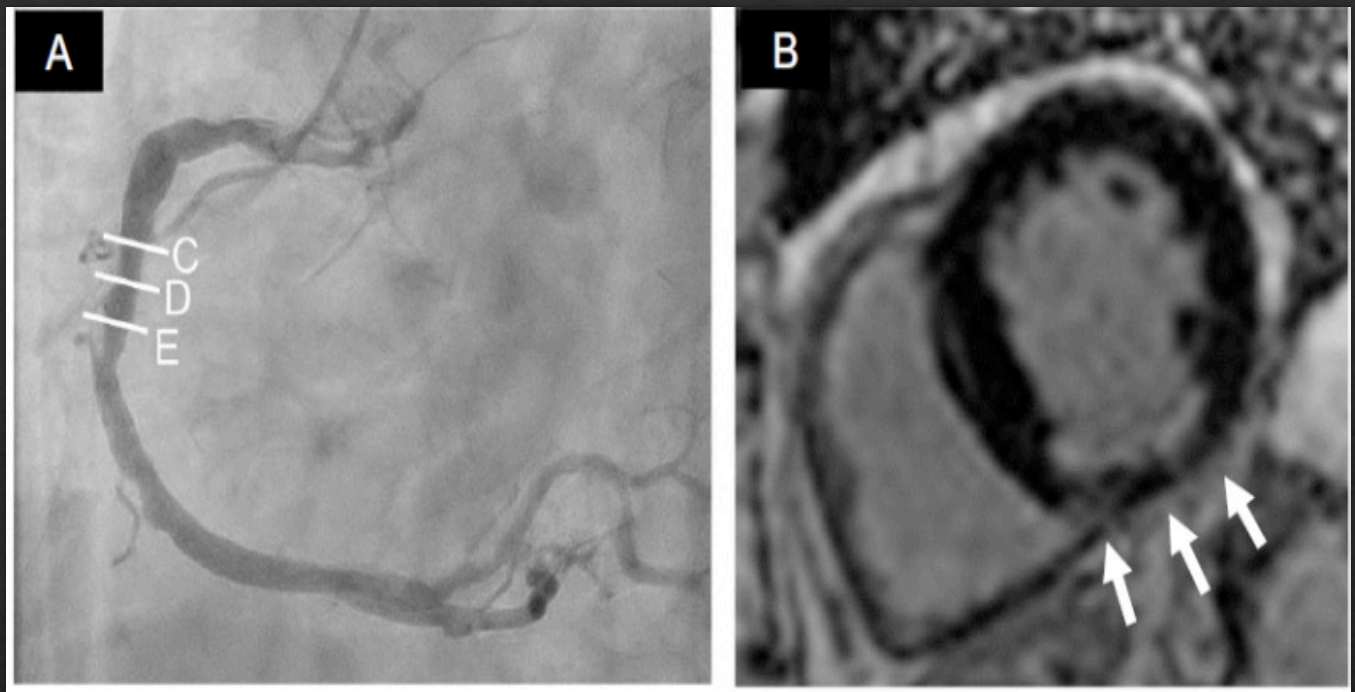
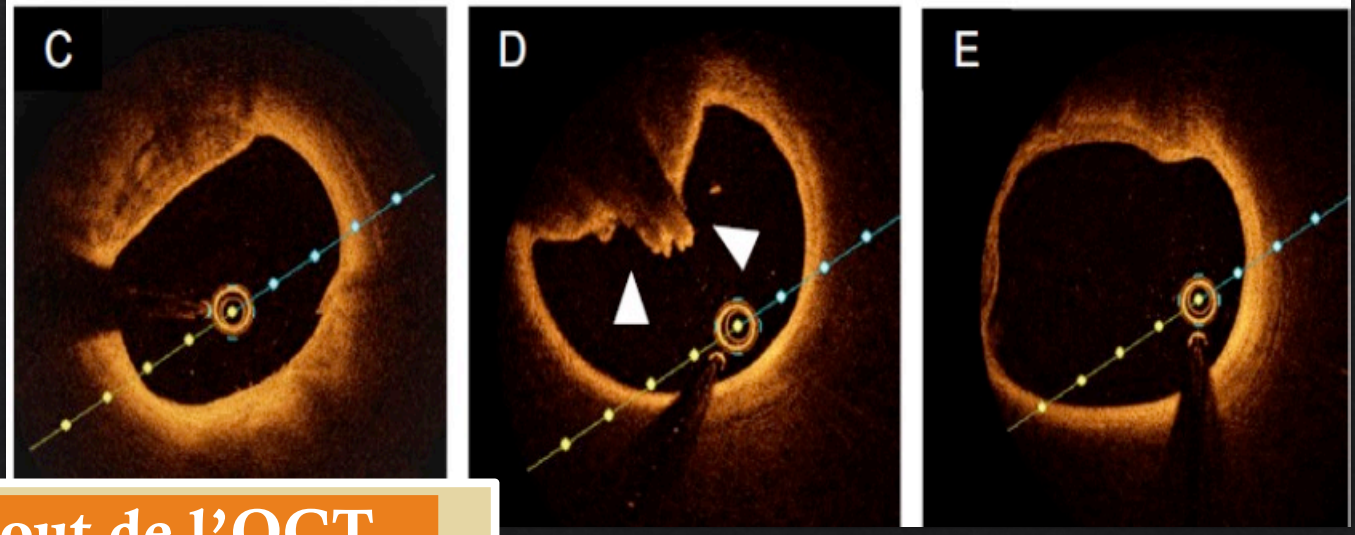




Review

Pathophysiology and diagnostic pathway of myocardial infarction with non-obstructive coronary arteries

Jun Takahashi (MD, PhD, FJCC) *, Sho Onuma (MD), Kiyotaka Hao (MD, PhD), Shigeo Godo (MD, PhD), Takashi Shiroto (MD, PhD), Satoshi Yasuda (MD, PhD, FJCC)

Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

Journal of Cardiology 83 (2024) 17–24

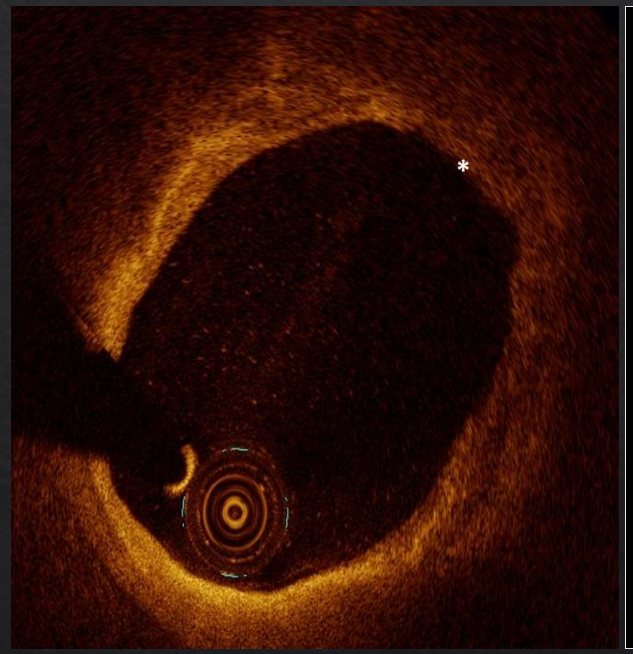
Fig. 3. Representative findings in coronary angiography, CMR, and OCT in a patient with plaque disruption causing MINOCA.
A 66-year-old man with hypertension and diabetes presented with chest pain and inferior T-wave inversions on ECG. Coronary angiography of the RCA showed <50 % stenosis (A). CMR performed 7 days later demonstrated a subendocardial LGE (white arrows) in the inferior wall (B). Serial OCT cross-sectional images from proximal (C) to distal (E) of the RCA on day 1 were demonstrated. There was a protruding mass with irregular surface indicating mural red thrombus (arrow heads in D). The final diagnosis of this case was inferior MINOCA caused by a plaque disruption. CMR, cardiac magnetic resonance; ECG, electrocardiogram; LGE, late gadolinium enhancement; MINOCA, myocardial infarction with non-obstructive coronary arteries; OCT, optical coherence tomography; RCA, right coronary artery.

Place de l'imagerie endocoronaire et surtout de l'OCT…

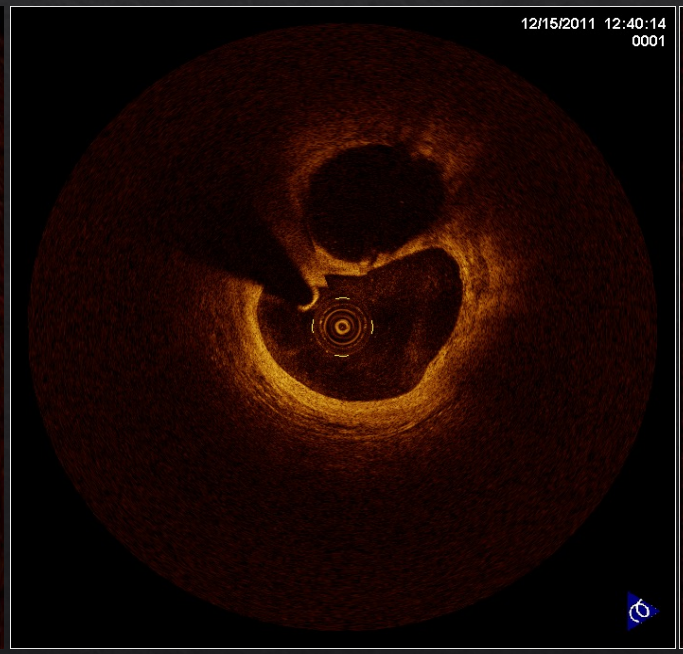
Microvascular disease

Ce qui n' est pas une dysfonction microvasculaire….

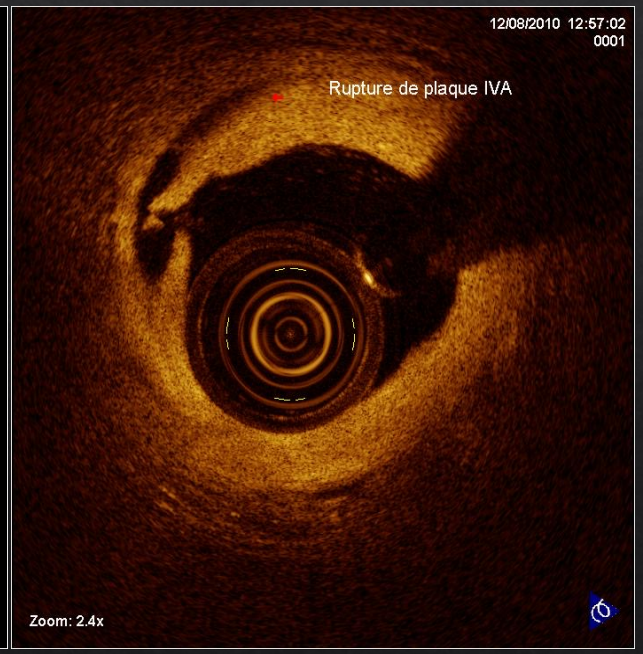
Erosion endothéliale



Dissection spontanée hématome disséquant



Plaque détergée

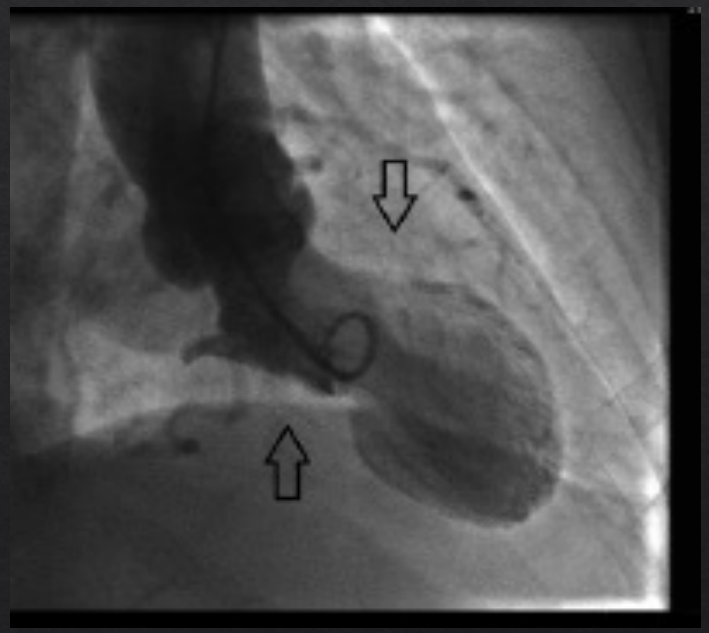


Intérêt de l'imagerie endocoronaire - OCT

Microvascular disease

Ce qui n' est pas une dysfonction microvasculaire….

Cardiomyopathie -TAKOTSUBO



Cardiovascular Revascularization Medicine
Volume 13, Issue 1, January–February 2012, Pages 66-68

Case Report

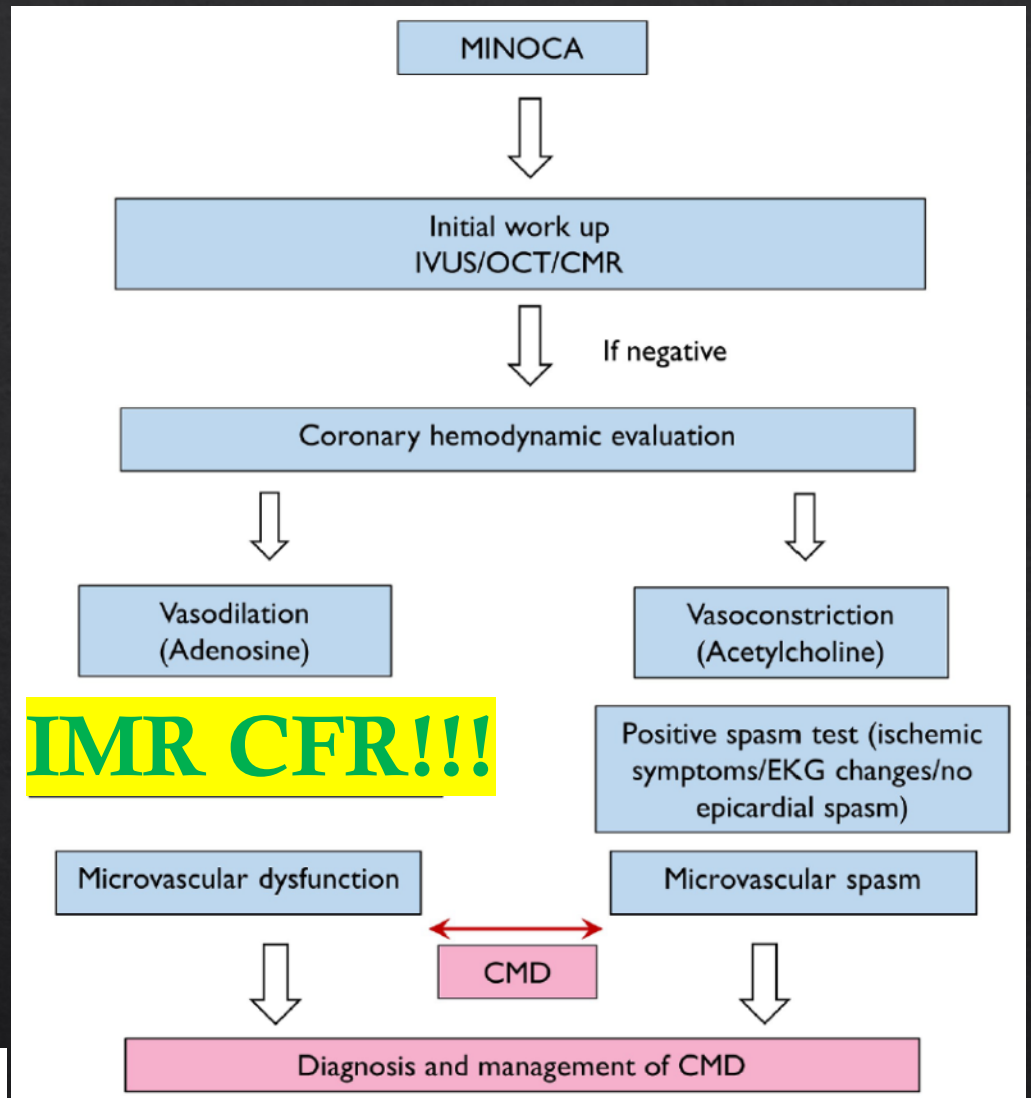
Takotsubo cardiomyopathy: reversible elevation in microcirculatory resistance ☆ ☆☆

Jamie Layland [a, b] ✉, Robert Whitbourn [a, b], Andrew MacIsaac [a, b], Jithendra Somaratne [a], Andrew Wilson [a, b]

Intérêt de l'angiographie et de l'échographie

MINOCA

Cathlab



Review Article

Coronary microvascular dysfunction and myocardial infarction with non-obstructive coronary arteries: Where do we stand?

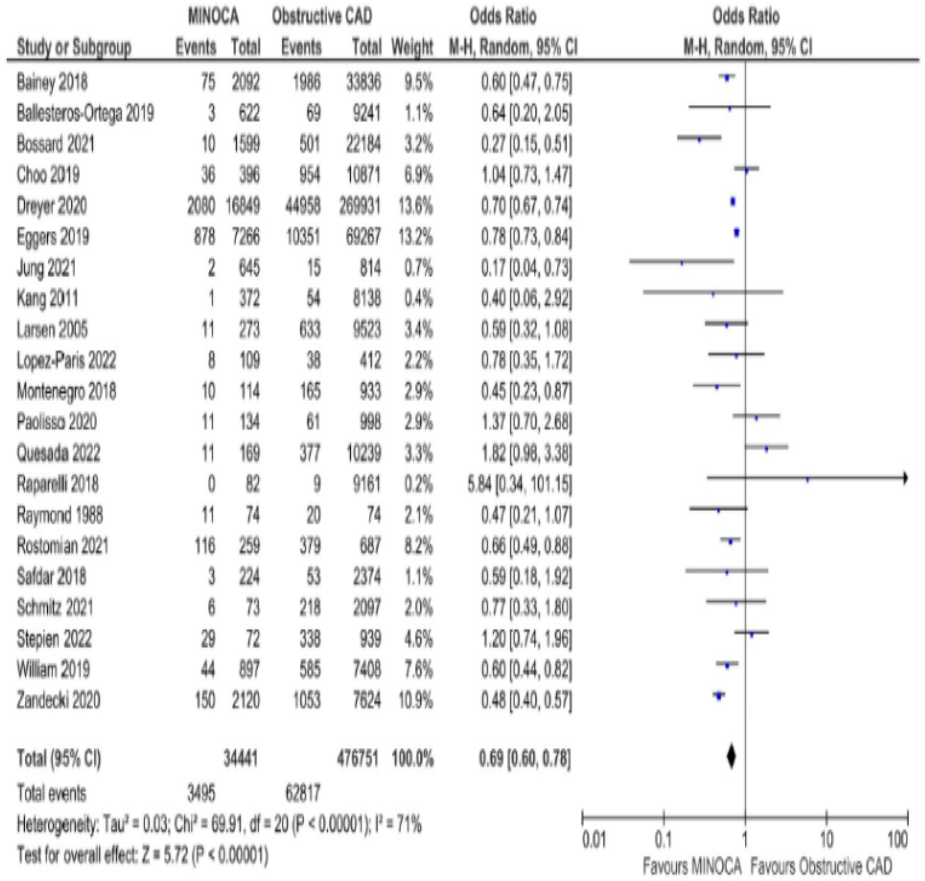
Abdul-Quddus Mohammed[a,†], Fuad A. Abdu[a,†], Lu Liu[a], Guoqing Yin[a], Redhwan M. Mareai[a], Ayman A. Mohammed[a], Yawei Xu[a], Wenliang Che[a,b,*]

European Journal of Internal Medicine 117 (2023) 8–20

Outcomes and Medical Therapy in Myocardial Infarction With Nonobstructive Coronary Arteries: A Systematic Review and Meta-Analysis

Am J Cardiol 2023;207:

Le traitement n'influence pas le pronostic

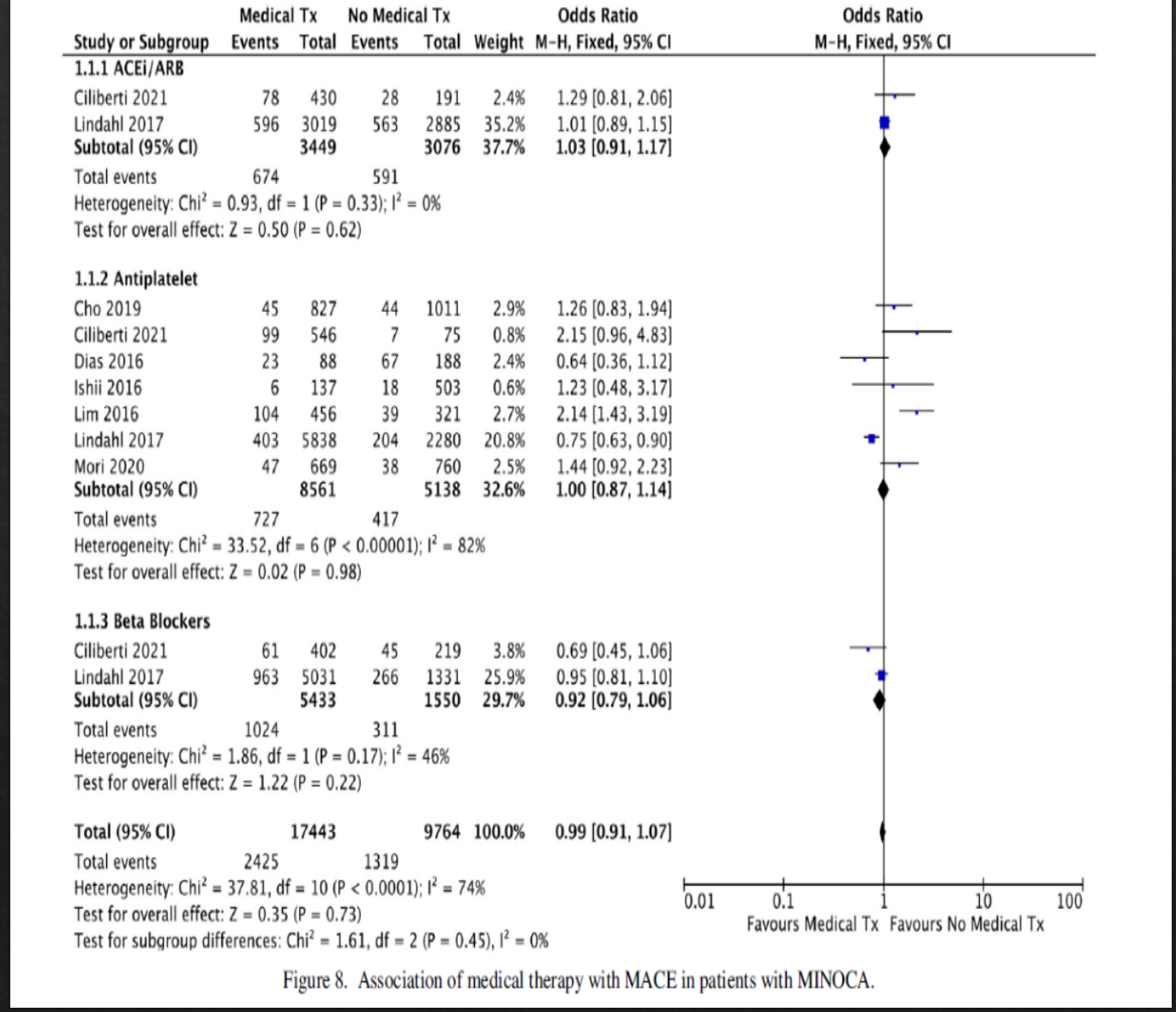


Study or Subgroup	MINOCA Events	MINOCA Total	Obstructive CAD Events	Obstructive CAD Total	Weight	Odds Ratio M-H, Random, 95% CI
Bainey 2018	75	2092	1986	33836	9.5%	0.60 [0.47, 0.75]
Ballesteros-Ortega 2019	3	622	69	9241	1.1%	0.64 [0.20, 2.05]
Bossard 2021	10	1599	501	22184	3.2%	0.27 [0.15, 0.51]
Choo 2019	36	396	954	10871	6.9%	1.04 [0.73, 1.47]
Dreyer 2020	2080	16849	44958	269931	13.6%	0.70 [0.67, 0.74]
Eggers 2019	878	7266	10351	69267	13.2%	0.78 [0.73, 0.84]
Jung 2021	2	645	15	814	0.7%	0.17 [0.04, 0.73]
Kang 2011	1	372	54	8138	0.4%	0.40 [0.06, 2.92]
Larsen 2005	11	273	633	9523	3.4%	0.59 [0.32, 1.08]
Lopez-Paris 2022	8	109	38	412	2.2%	0.78 [0.35, 1.72]
Montenegro 2018	10	114	165	933	2.9%	0.45 [0.23, 0.87]
Paolisso 2020	11	134	61	998	2.9%	1.37 [0.70, 2.68]
Quesada 2022	11	169	377	10239	3.3%	1.82 [0.98, 3.38]
Raparelli 2018	0	82	9	9161	0.2%	5.84 [0.34, 101.15]
Raymond 1988	11	74	20	74	2.1%	0.47 [0.21, 1.07]
Rostomian 2021	116	259	379	687	8.2%	0.66 [0.49, 0.88]
Safdar 2018	3	224	53	2374	1.1%	0.59 [0.18, 1.92]
Schmitz 2021	6	73	218	2097	2.0%	0.77 [0.33, 1.80]
Stepien 2022	29	72	338	939	4.6%	1.20 [0.74, 1.96]
William 2019	44	897	585	7408	7.6%	0.60 [0.44, 0.82]
Zandecki 2020	150	2120	1053	7624	10.9%	0.48 [0.40, 0.57]
Total (95% CI)		**34441**		**476751**	**100.0%**	**0.69 [0.60, 0.78]**
Total events	3495		62817			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 69.91$, df = 20 ($P < 0.00001$); $I^2 = 71\%$
Test for overall effect: $Z = 5.72$ ($P < 0.00001$)

Odds Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours MINOCA Favours Obstructive CAD

Figure 2. Association of MINOCA with all-cause mortality compared with MICAD.



Study or Subgroup	Medical Tx Events	Medical Tx Total	No Medical Tx Events	No Medical Tx Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.1.1 ACEi/ARB						
Ciliberti 2021	78	430	28	191	2.4%	1.29 [0.81, 2.06]
Lindahl 2017	596	3019	563	2885	35.2%	1.01 [0.89, 1.15]
Subtotal (95% CI)		**3449**		**3076**	**37.7%**	**1.03 [0.91, 1.17]**
Total events	674		591			
Heterogeneity: $Chi^2 = 0.93$, df = 1 ($P = 0.33$); $I^2 = 0\%$						
Test for overall effect: $Z = 0.50$ ($P = 0.62$)						
1.1.2 Antiplatelet						
Cho 2019	45	827	44	1011	2.9%	1.26 [0.83, 1.94]
Ciliberti 2021	99	546	7	75	0.8%	2.15 [0.96, 4.83]
Dias 2016	23	88	67	188	2.4%	0.64 [0.36, 1.12]
Ishii 2016	6	137	18	503	0.6%	1.23 [0.48, 3.17]
Lim 2016	104	456	39	321	2.7%	2.14 [1.43, 3.19]
Lindahl 2017	403	5838	204	2280	20.8%	0.75 [0.63, 0.90]
Mori 2020	47	669	38	760	2.5%	1.44 [0.92, 2.23]
Subtotal (95% CI)		**8561**		**5138**	**32.6%**	**1.00 [0.87, 1.14]**
Total events	727		417			
Heterogeneity: $Chi^2 = 33.52$, df = 6 ($P < 0.00001$); $I^2 = 82\%$						
Test for overall effect: $Z = 0.02$ ($P = 0.98$)						
1.1.3 Beta Blockers						
Ciliberti 2021	61	402	45	219	3.8%	0.69 [0.45, 1.06]
Lindahl 2017	963	5031	266	1331	25.9%	0.95 [0.81, 1.10]
Subtotal (95% CI)		**5433**		**1550**	**29.7%**	**0.92 [0.79, 1.06]**
Total events	1024		311			
Heterogeneity: $Chi^2 = 1.86$, df = 1 ($P = 0.17$); $I^2 = 46\%$						
Test for overall effect: $Z = 1.22$ ($P = 0.22$)						
Total (95% CI)		**17443**		**9764**	**100.0%**	**0.99 [0.91, 1.07]**
Total events	2425		1319			
Heterogeneity: $Chi^2 = 37.81$, df = 10 ($P < 0.0001$); $I^2 = 74\%$						
Test for overall effect: $Z = 0.35$ ($P = 0.73$)						
Test for subgroup differences: $Chi^2 = 1.61$, df = 2 ($P = 0.45$), $I^2 = 0\%$						

Odds Ratio M-H, Fixed, 95% CI
0.01 0.1 1 10 100
Favours Medical Tx Favours No Medical Tx

Figure 8. Association of medical therapy with MACE in patients with MINOCA.

Psychosocial Factors of Women Presenting With Myocardial Infarction With or Without Obstructive Coronary Arteries

Anaïs Hausvater, MD,[a,b] Tanya M. Spruill, PhD,[a,c] Yuhe Xia, MS,[c] Nathaniel R. Smilowitz, MD,[a,b,d] Milla Arabadjian, PhD,[a,c,e] Binita Shah, MD,[b,d] Ki Park, MD,[f] Caitlin Giesler, MD,[g] Kevin Marzo, MD,[h] Dwithiya Thomas, MD,[i] Janet Wei, MD,[j] Jeffrey Trost, MD,[k] Puja K. Mehta, MD,[l] Bryan Har, MD,[m] Kevin R. Bainey, MD,[n] Hua Zhong, PhD,[c] Judith S. Hochman, MD,[a,b] Harmony R. Reynolds, MD[a,b]

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

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ABSTRACT

BACKGROUND Women with myocardial infarction (MI) are more likely to have elevated stress levels and depression than men with MI.

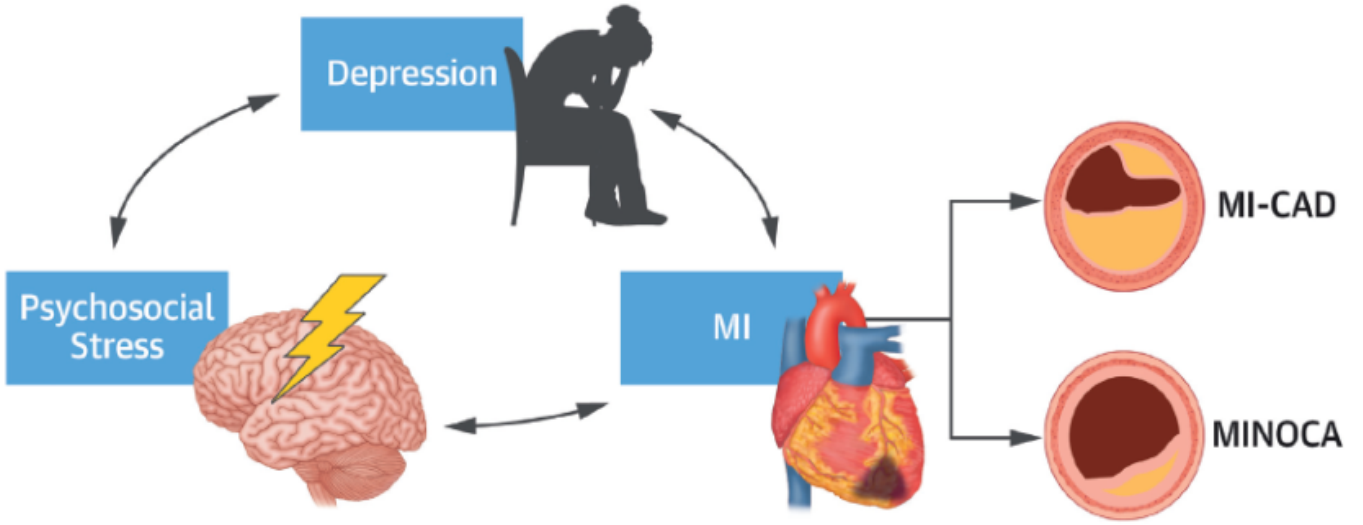
OBJECTIVES We investigated psychosocial factors in women with myocardial infarction with nonobstructive coronary arteries (MINOCA) and those with MI and obstructive coronary artery disease (CAD).

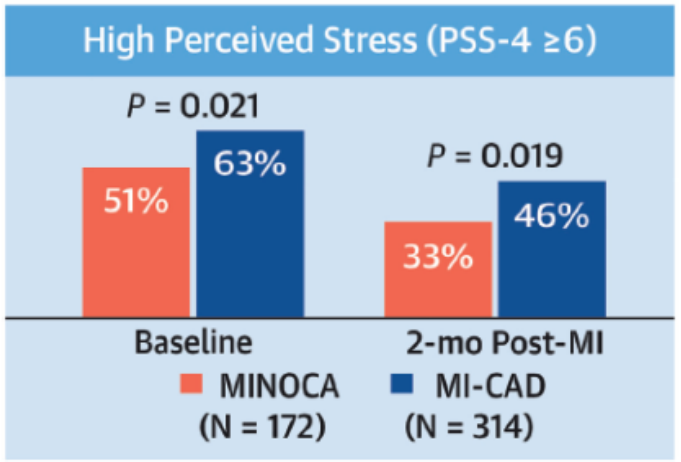
METHODS Women with MI enrolled in a multicenter study and completed measures of perceived stress (Perceived Stress Scale-4) and depressive symptoms (Patient Health Questionnaire-2) at the time of MI (baseline) and 2 months later. Stress, depression, and changes over time were compared between MI subtypes.

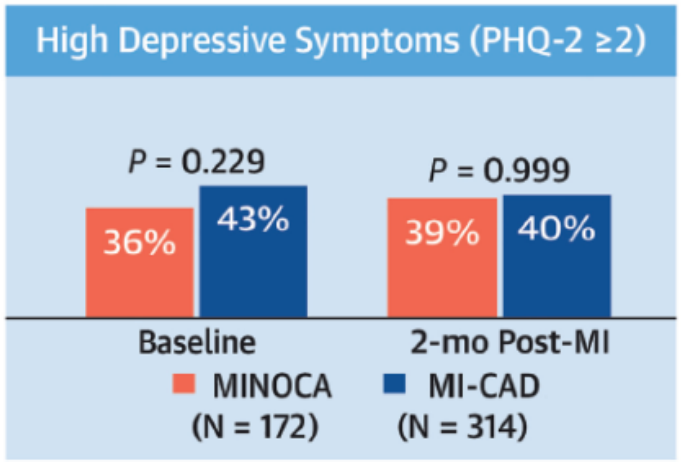
RESULTS We included 172 MINOCA and 314 MI-CAD patients. Women with MINOCA were younger (age 59.4 years vs 64.2 years; $P < 0.001$) and more diverse than those with MI-CAD. Women with MINOCA were less likely to have high stress (Perceived Stress Scale-4 ≥6) at the time of MI (51.0% vs 63.0%; $P = 0.021$) and at 2 months post-MI (32.5% vs 46.3%; $P = 0.019$) than women with MI-CAD. There was no difference in elevated depressive symptoms (Patient Health Questionnaire-2 ≥2) at the time of MI (36% vs 43%; $P = 0.229$) or at 2 months post-MI (39% vs 40%; $P = 0.999$). No differences in the rate of 2-month decline in stress and depression scores were observed between groups.

CONCLUSIONS Stress and depression are common among women at the time of and 2 months after MI. MINOCA patients were less likely to report high stress compared with MI-CAD patients, but the frequency of elevated depressive symptoms did not differ between the 2 groups. Stress and depressive symptoms decreased in both MI-CAD and MINOCA patients over time. (J Am Coll Cardiol 2023;82:1649-1658) © 2023 by the American College of Cardiology Foundation.

CENTRAL ILLUSTRATION Stress and Depression in Patients With Myocardial Infarction and Obstructive Coronary Artery Disease and Myocardial Infarction With Nonobstructive Coronary Arteries







Hausvater A, et al. J Am Coll Cardiol. 2023;82(17):1649-1658.

High perceived stress (Perceived Stress Scale [PSS-4] ≥6) around the time of myocardial infarction (MI) and 2 months after MI was significantly higher among women with myocardial infarction with obstructive coronary artery disease (MI-CAD) compared with those with myocardial infarction with nonobstructive coronary arteries (MINOCA). There was no difference between high depressive symptoms (Patient Health Questionnaire [PHQ-2] ≥2) among MINOCA and MI-CAD patients both at the time of MI and 2 months after MI.

Review Article

Coronary microvascular dysfunction and myocardial infarction with non-obstructive coronary arteries: Where do we stand?

Abdul-Quddus Mohammed [a,†], Fuad A. Abdu [a,†], Lu Liu [a], Guoqing Yin [a], Redhwan M. Mareai [a], Ayman A. Mohammed [a], Yawei Xu [a], Wenliang Che [a,b,*]

European Journal of Internal Medicine 117 (2023) 8–20

IMR : méthode simple, invasive, quantitative d'évaluation de la microcirculation coronaire. Spécifique de la microcirculation indépendante du tonus basal, hyperhémie,Cut-off…

Table 1
An overview of methods to assess CMD.

Methods	Measure/ Index	Pros	Cons
Invasive			
Coronary angiography	(TIMI-2/ TFC count>25 F/S)	Simple and readily available, without additional costs	Semi-quantitative, unable to elucidate information regarding the underlying mechanisms of CMD i.e. impaired vasodilation or microvascular spasms
Provocation spasm test (ACH/Erg)	–	Simple and safe can assess epicardial /microvascular spams, doesn't require additional equipment	Requires additional contrast, Lack of availability risk of potential arrhythmias
Intracoronary thermodilution	CFR $_{doppler}$ (<2–2.5)	Easily accessible, can assess vasodilatory capacity of microvessels	Not specific to microvascular compartment. Doesn't differentiate between epicardial and microvascular disease, affected by hemodynamic perturbations
Intracoronary thermodilution	IMR (>25) or (>40)	Widely used method, readily available, specific to microvascular compartment, and unaffected by resting hemodynamic or basal tone.	Requires guidewire manipulations, additional need for hyperemic agents, varying cut-off values among different patient population

Recherche MINOCA - Exploration de la fonctionnalité coronaire

- Redresser des diagnostics (faux positifs….)
- Amélioration pronostic et qualité de vie
- Amélioration thérapeutique
- Prévalence…
- Outils diagnostics (invasifs, non-invasifs)
- Pourquoi ne pas valider un jour le principe du BVS…..(INOCA)

Angor post PCI ?

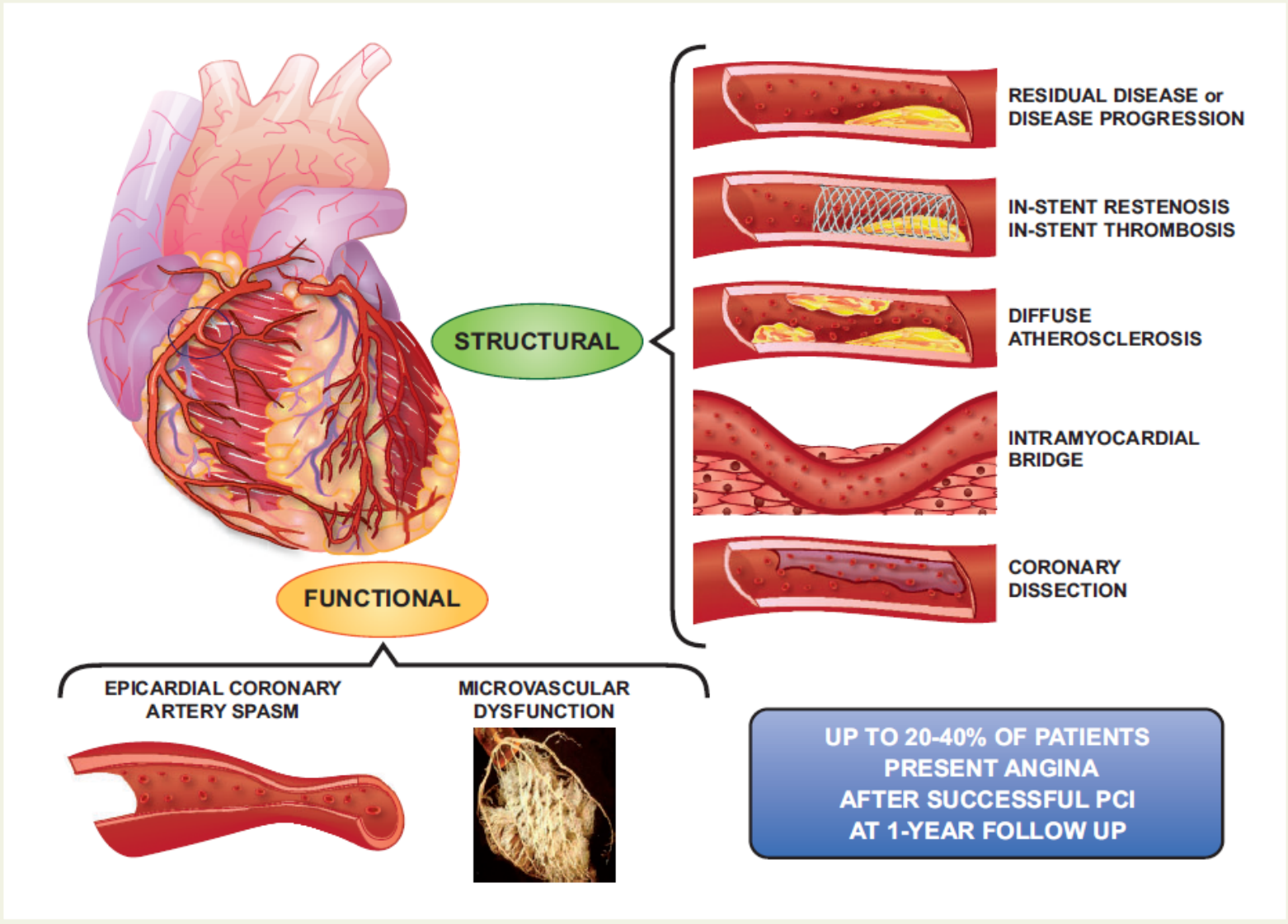


Figure 1 Structural and functional alterations of coronary circulation responsible for persistence or recurrence of angina after percutaneous coronary intervention.

Review

Pathophysiology and diagnostic pathway of myocardial infarction with non-obstructive coronary arteries

Jun Takahashi (MD, PhD, FJCC) *, Sho Onuma (MD), Kiyotaka Hao (MD, PhD), Shigeo Godo (MD, PhD), Takashi Shiroto (MD, PhD), Satoshi Yasuda (MD, PhD, FJCC)

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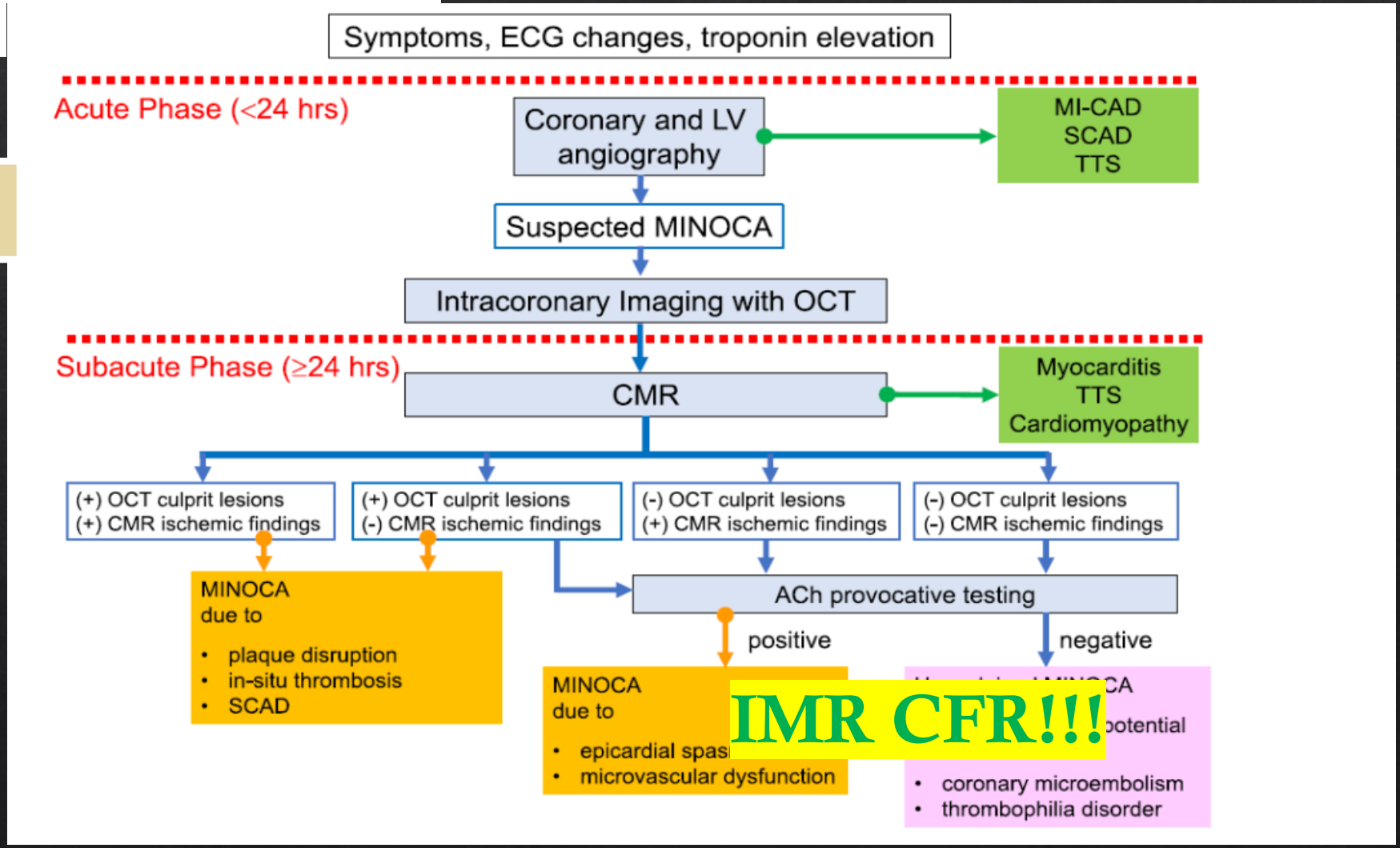
Journal of Cardiology 83 (2024) 17–24

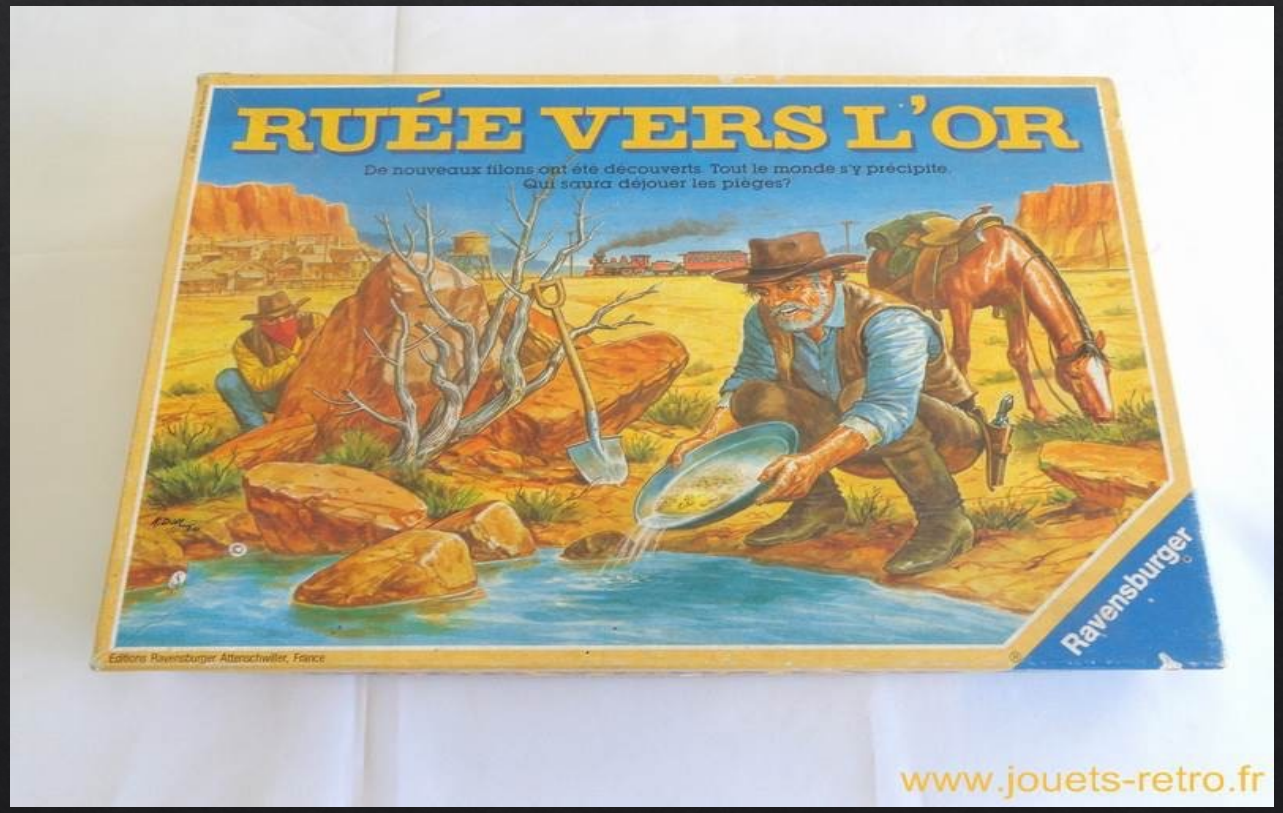
Cathlab

MINOCA



Perspectives

Recherche MINOCA - Exploration de la fonctionnalité coronaire



Perspectives

Recherche INOCA - Exploration de la fonctionnalité coronaire

Merci !

ESC Working Group on Coronary Pathophysiology and Microcirculation position paper on 'coronary microvascular dysfunction in cardiovascular disease'

ESC European Society of Cardiology
Cardiovascular Research (2020) 116, 741–755
doi:10.1093/cvr/cvaa003

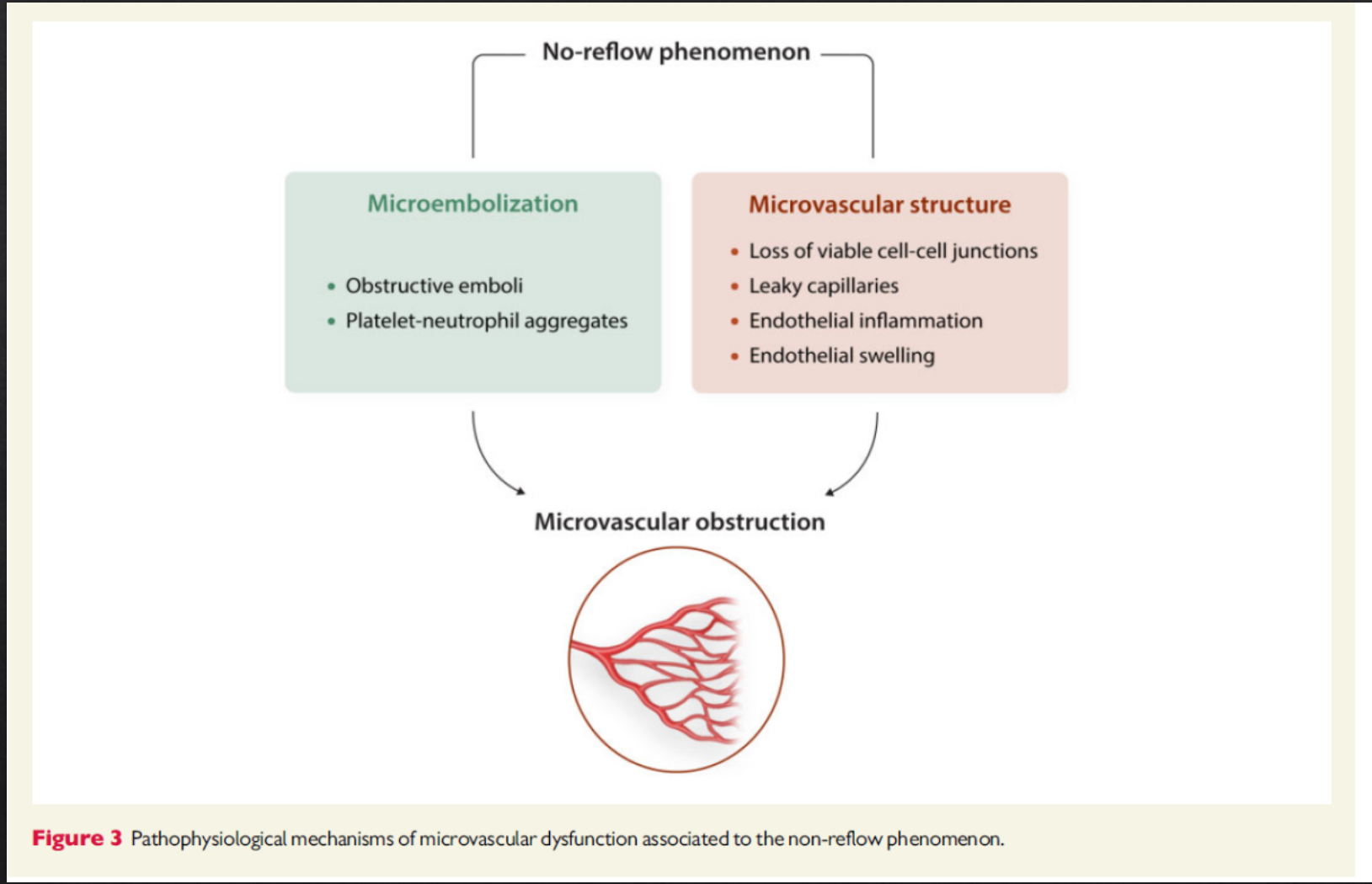
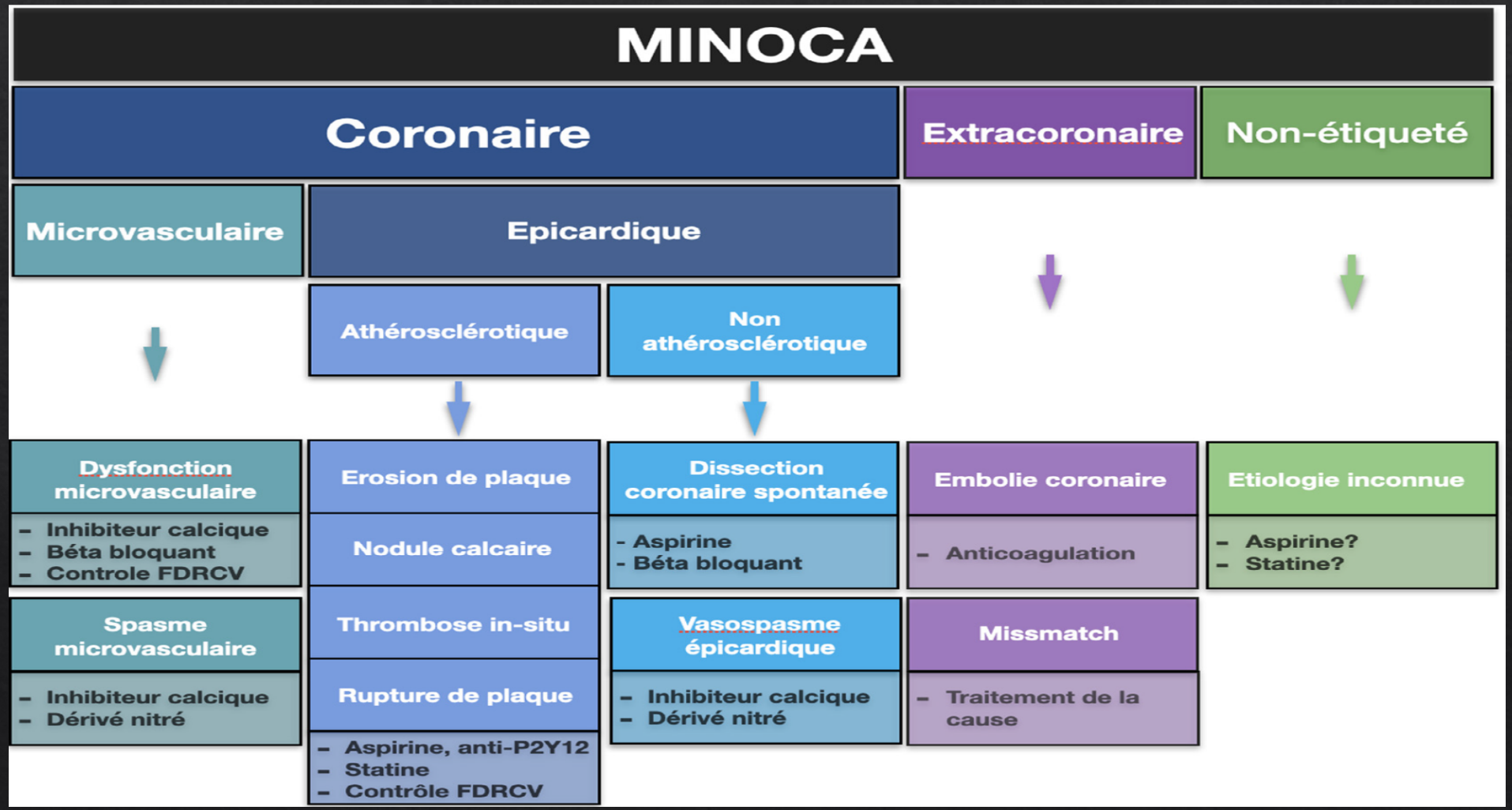


Figure 3 Pathophysiological mechanisms of microvascular dysfunction associated to the non-reflow phenomenon.

Annales de cardiologie et d'angeiologie 71 (2022) 381–390



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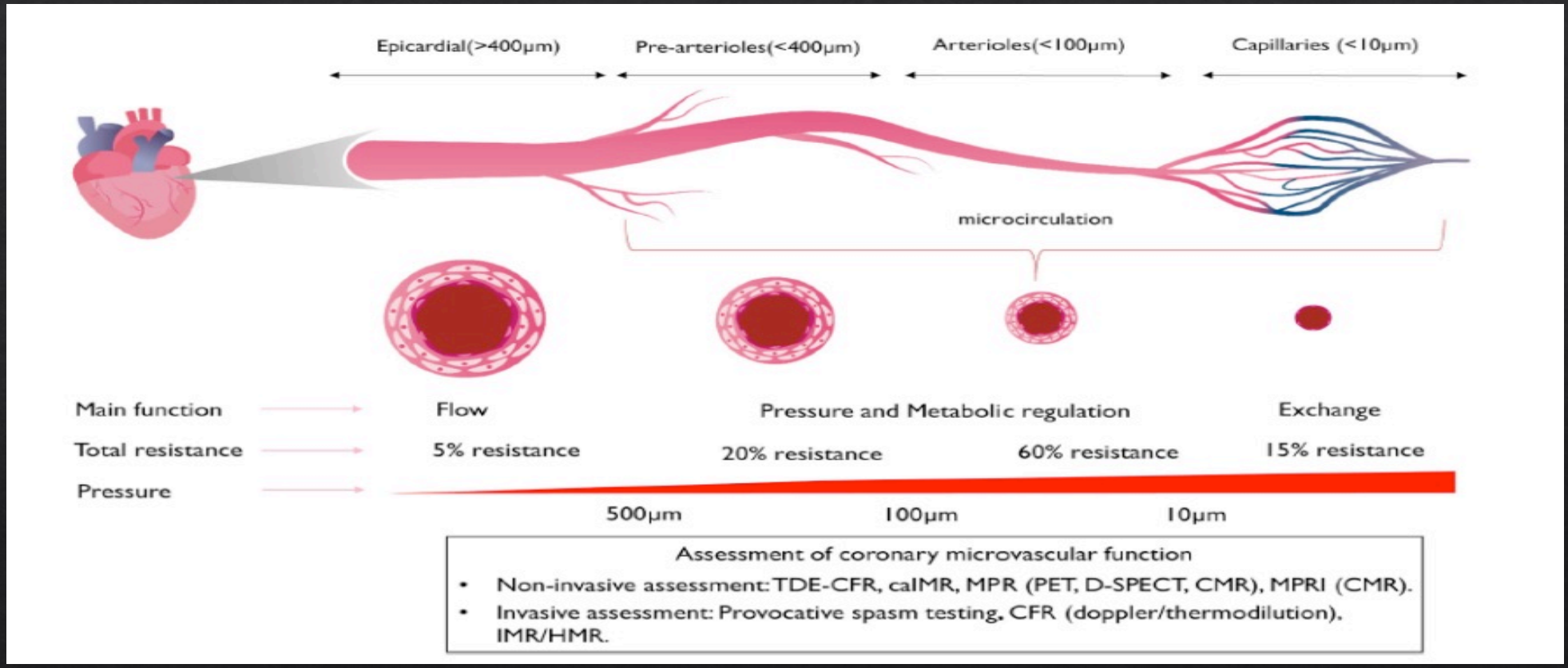

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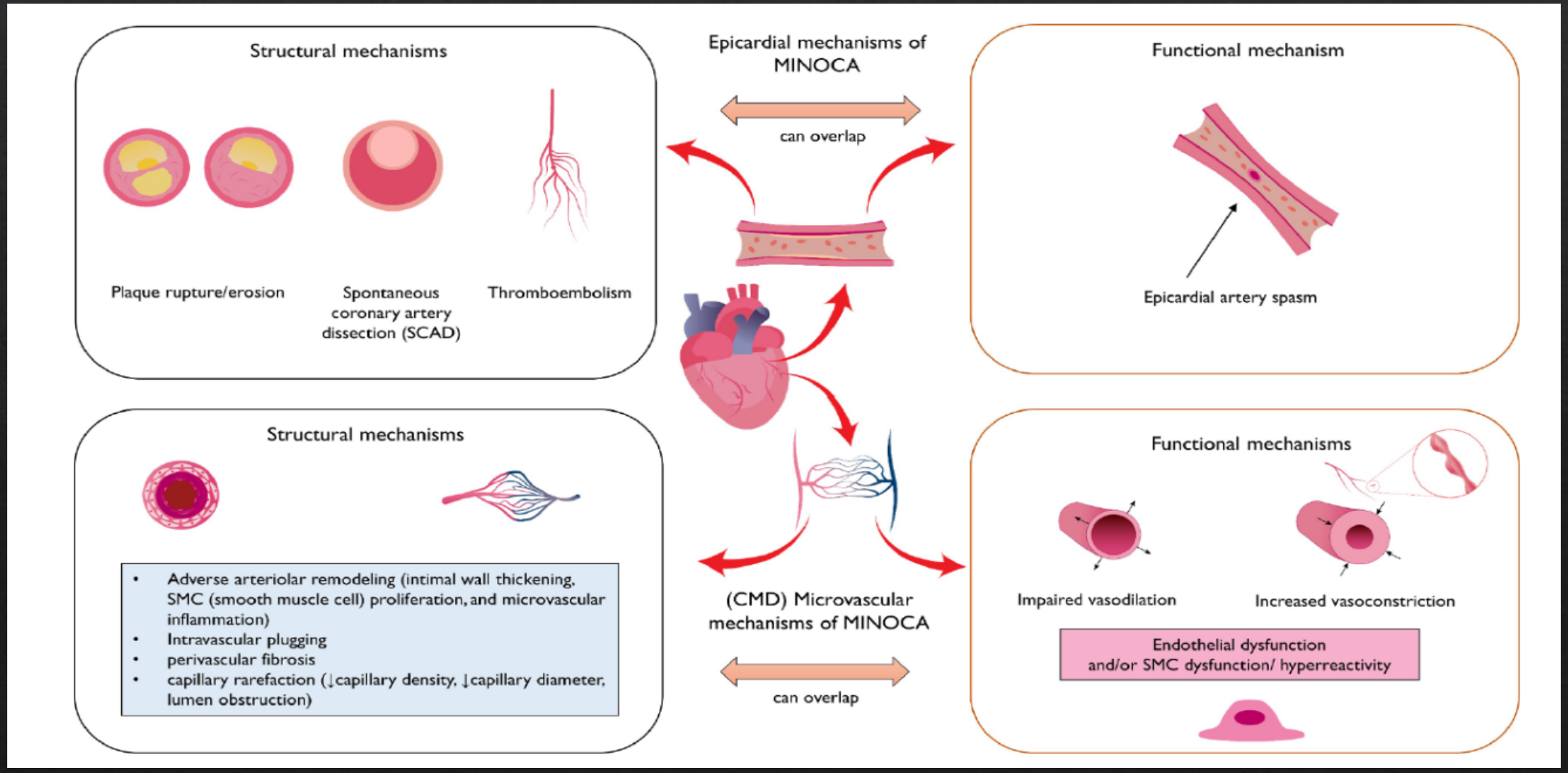

Original article

Prognostic impact of coronary microvascular dysfunction in patients with myocardial infarction with non-obstructive coronary arteries

Fuad A. Abdu [a], Lu Liu [a], Abdul-Quddus Mohammed [a], Guoqing Yin [a], Bin Xu [a], Wen Zhang [a], Siling Xu [a], Xian Lv [a], Rui Fan [a], Cailin Feng [a], Tingting Shi [a], Yunlong Huo [b], Yawei Xu [a,*], Wenliang Che [a,c,*]

European Journal of Internal Medicine

A B S T R A C T

Background: Myocardial infarction with non-obstructive coronary arteries (MINOCA) has been and remained a puzzling heterogeneous entity. The index of microcirculatory resistance (IMR) is a quantitative and specific index for the assessment of microvascular function. However, the role of IMR in MINOCA has not yet been studied. This study aimed to evaluate the prognostic value of coronary microvascular function, as assessed by coronary angiography-derived index of microvascular resistance (caIMR) in MINOCA patients.

Method: This study included 109 MINOCA patients. Microvascular function was assessed by caIMR and was analyzed in 280 coronary arteries. The primary endpoint of the study was MACE, defined as cardiovascular death, nonfatal MI, heart failure, stroke and angina rehospitalization. The best cut-off of caIMR was derived from ROC analysis based on MACE prediction.

Results: The patients were classified into high caIMR (caIMR>43U) and low caIMR (caIMR≤43U) based on a caIMR cut-off value of 43U. High caIMR was observed in 55 (50.5%) patients. A total of 27 MACE occurred during the 2 years of follow-up. MACE rate was significantly higher in patients with high caIMR than in patients with low caIMR (36.4% vs 13.0%, P=0.005). The Kaplan–Meier curves showed a significantly increased risk of MACE in patients with high caIMR (log-rank P=0.001). Cox multivariate analysis showed that caIMR>43 was a highly independent predictor of MACE (HR, 3.08; 95% CI, 1.13 - 8.35; P=0.027).

Conclusions: caIMR is a strong predictor of clinical outcome among MINOCA patients. The evaluation of IMR can provide an objective risk stratification method for patients with MINOCA.

Original article

Prognostic impact of coronary microvascular dysfunction in patients with myocardial infarction with non-obstructive coronary arteries

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European Journal of Internal Medicine

Fig. 1. Schematic representative performance of caIMR. (a) Reconstruction of 3D model from coronary angiography; (b) Flow velocity and microvascular resistance at diastole are proportional to those in hyperemia; (c) Aortic pressure as Pa, based on which to compute Pd; (d) Use CFD method to compute caIMR.

Coronary Microvascular Dysfunction Across the Spectrum of Cardiovascular Diseases

JACC State-of-the-Art Review

Marco Giuseppe Del Buono, MD,[a] Rocco A. Montone, MD, PhD,[b] Massimiliano Camilli, MD,[a] Salvatore Carbone, PhD,[c,d] Jagat Narula, MD, PhD,[e] Carl J. Lavie, MD,[f] Giampaolo Niccoli, MD, PhD,[g] Filippo Crea, MD[a,b]

ABSTRACT

Coronary microvascular dysfunction (CMD) encompasses several pathogenetic mechanisms involving coronary microcirculation and plays a major role in determining myocardial ischemia in patients with angina without obstructive coronary artery disease, as well as in several other conditions, including obstructive coronary artery disease, nonischemic cardiomyopathies, takotsubo syndrome, and heart failure, especially the phenotype associated with preserved ejection fraction. Unfortunately, despite the identified pathophysiological and prognostic role of CMD in several conditions, to date, there is no specific treatment for CMD. Due to the emerging role of CMD as common denominator in different clinical phenotypes, additional research in this area is warranted to provide personalized treatments in this "garden variety" of patients. The purpose of this review is to describe the pathophysiological mechanisms of CMD and its mechanistic and prognostic role across different cardiovascular diseases. We will also discuss diagnostic modalities and the potential therapeutic strategies resulting from recent clinical studies. (J Am Coll Cardiol 2021;78:1352–1371)

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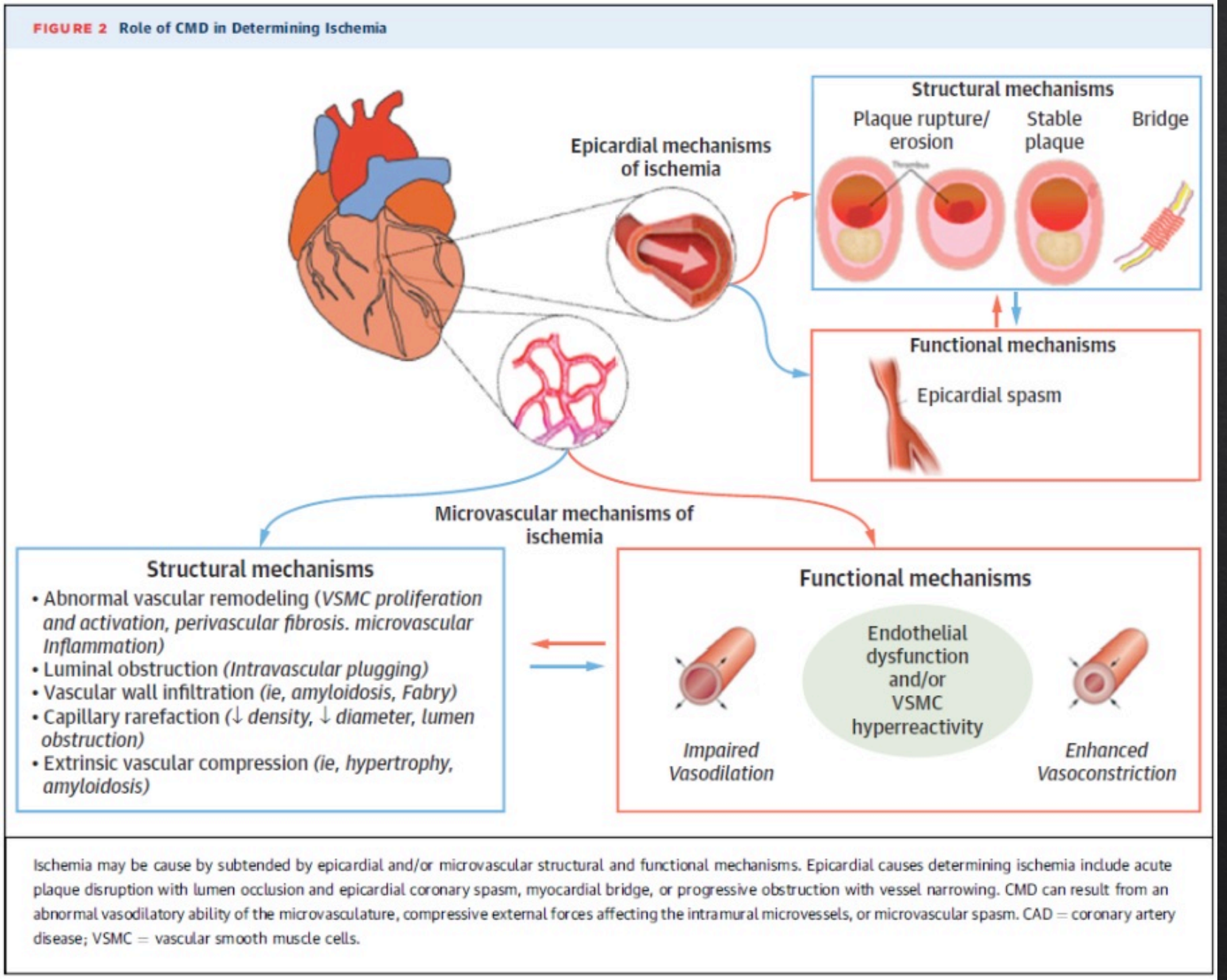
FIGURE 2 Role of CMD in Determining Ischemia



Ischemia may be cause by subtended by epicardial and/or microvascular structural and functional mechanisms. Epicardial causes determining ischemia include acute plaque disruption with lumen occlusion and epicardial coronary spasm, myocardial bridge, or progressive obstruction with vessel narrowing. CMD can result from an abnormal vasodilatory ability of the microvasculature, compressive external forces affecting the intramural microvessels, or microvascular spasm. CAD = coronary artery disease; VSMC = vascular smooth muscle cells.

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TABLE 2 Invasive Tools for Evaluation of CMD

Modality	Technique	Agent	Parameter	Diagnostic Threshold	Pros	Cons
Coronary angiography	Dynamic passage of angiographic contrast	Iodine-contrast agent	TIMI flow TFC	TIMI-2 TFC >25 frames	• Do not necessitate additional costs	• Do not provide information regarding the mechanism of CMD (impaired dilation vs microvascular spasm) • Semiquantitative parameter • Limited sensitivity • Usually calculated after coronary angiography
Intracoronary temperature-pressure wire	Estimate of coronary blood flow using bolus (calculating the mean transit time) or continuous thermodilution techniques (does not need pharmacological agents to induce hyperemia)	Adenosine Papaverine Saline solution	CFR IMR	CFR <2- 2.5 IMR >25 U	• CFR and IMR allow a combined assessment impaired vasodilation and microvascular hyperconstrictive response • IMR is specific for microcirculation and is not affected by resting hemodynamics • HMR is independent of resting coronary flow • FFR using the standard technique can be measured simultaneously	• CFR does not distinguish between microvascular and epicardial disease • Cut-off values for IMR still debated • Worse correlation with PET than HMR
Intracoronary Doppler flow-pressure wire	Direct measurement of coronary peak flow velocity	Adenosine	CFR HMR	CFR <2.5 HMR >1.7 mm Hg/cm/s	• CFR and HMR allow a combined assessment impaired vasodilation and microvascular hyperconstrictive response • HMR is independent of resting coronary flow • FFR using the standard technique can be measured simultaneously	• CFR does not distinguish between microvascular and epicardial disease • Cut-off values for HMR still debated
Intracoronary provocative testing	Intracoronary infusion of vasoactive agents	Acetylcholine Ergonovine	–	–	• Easy to assess • Evaluated at the time of coronary angiography • Do not necessitate additional equipment	• Additional contrast and radiation • Do not provide direct evidence of microvascular spasm • Risk of arrhythmias • Lack of availability

CFR = coronary flow reserve; ECG = electrocardiography; FFR = fractional flow reserve; HMR = hyperemic microvascular resistance; IMR = index of microvascular resistance; PET = positron emission tomography.

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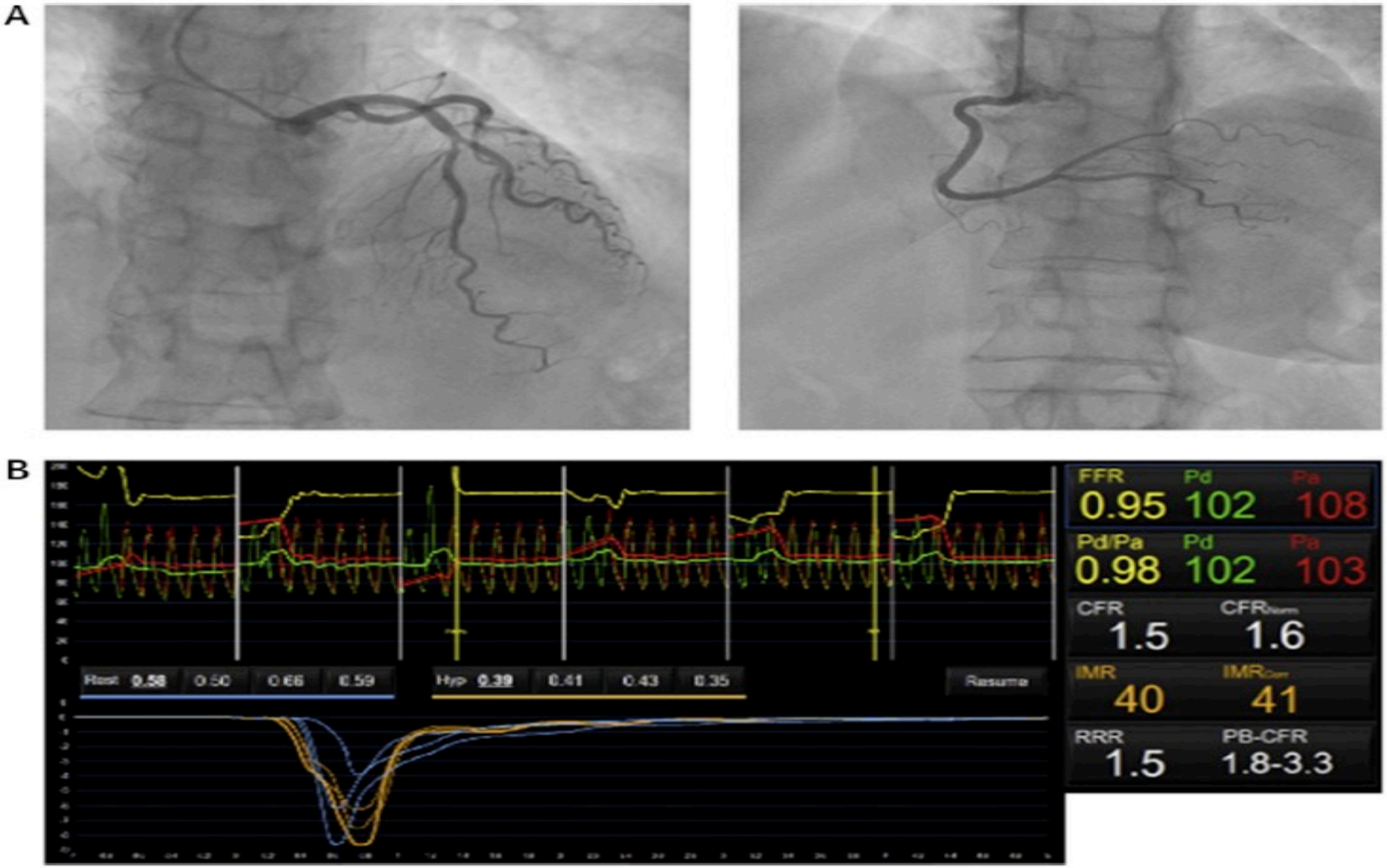
FIGURE 3 Assessment of CMD in a Patient With Microvascular Angina



Patient with effort angina and positive noninvasive stress testing. **(A)** Coronary angiography documented an angiographically normal right coronary artery **(right)** and intermediate coronary stenosis on mid-left anterior descending artery **(left)** without hemodynamic significance (FFR 0.95). **(B)** Microvascular function measured using a pressure wire coupled with thermodilution advanced into the distal part of the left anterior descending artery, at rest and during adenosine-induced maximal hyperemia, demonstrated an impaired coronary microvascular function (CFR 1.5 and IMR 40). Intracoronary provocative test with acetylcholine on left anterior descending artery was negative for epicardial and/or microvascular spasm, suggesting a mechanism of CMD caused by impaired vasodilation. CFR = coronary flow reserve; FFR = fractional flow reserve; IMR = index of microcirculatory resistance.

Review

Pathophysiology and diagnostic pathway of myocardial infarction with non-obstructive coronary arteries

Jun Takahashi (MD, PhD, FJCC) *, Sho Onuma (MD), Kiyotaka Hao (MD, PhD), Shigeo Godo (MD, PhD), Takashi Shiroto (MD, PhD), Satoshi Yasuda (MD, PhD, FJCC)

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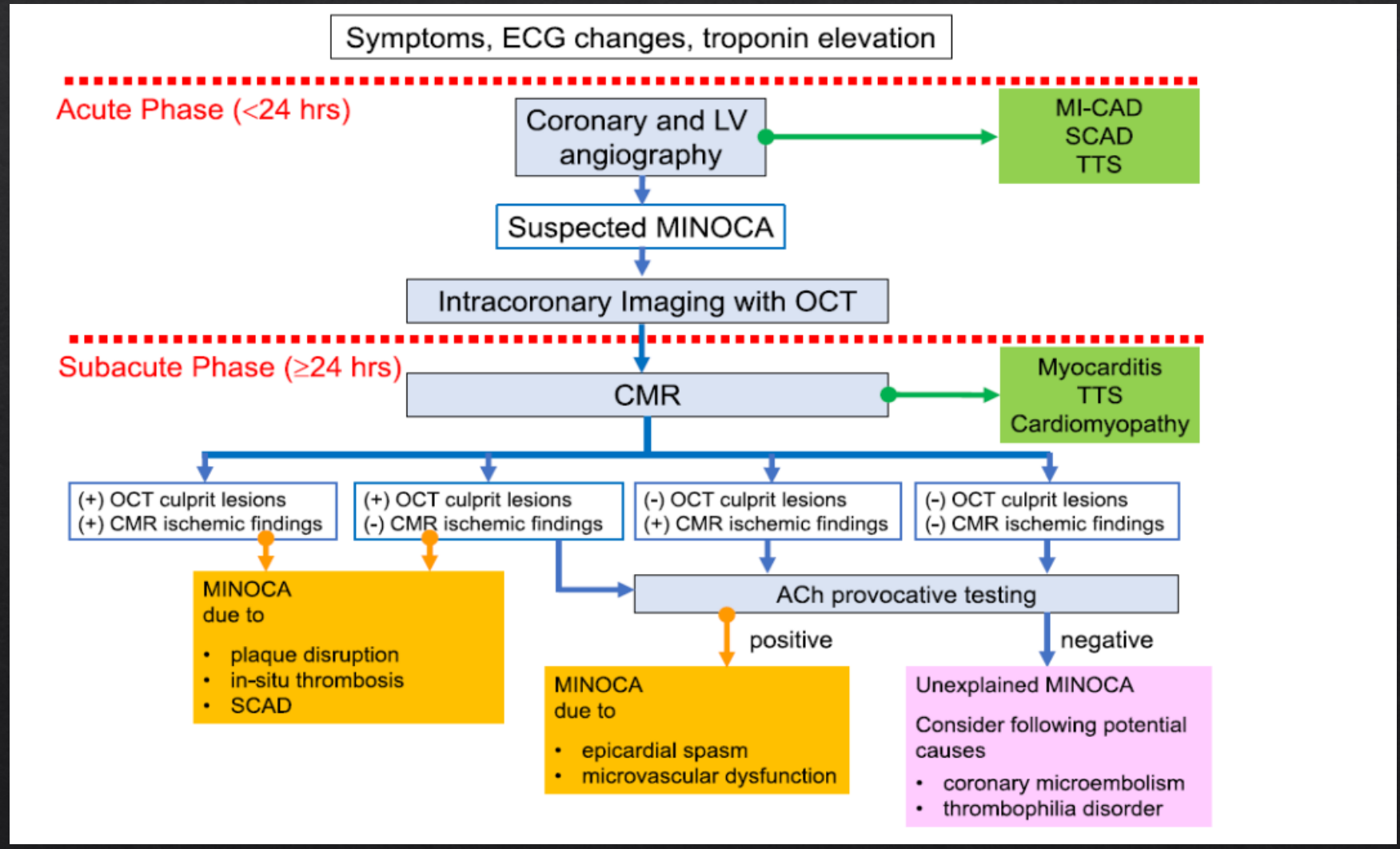
Journal of Cardiology 83 (2024) 17–24



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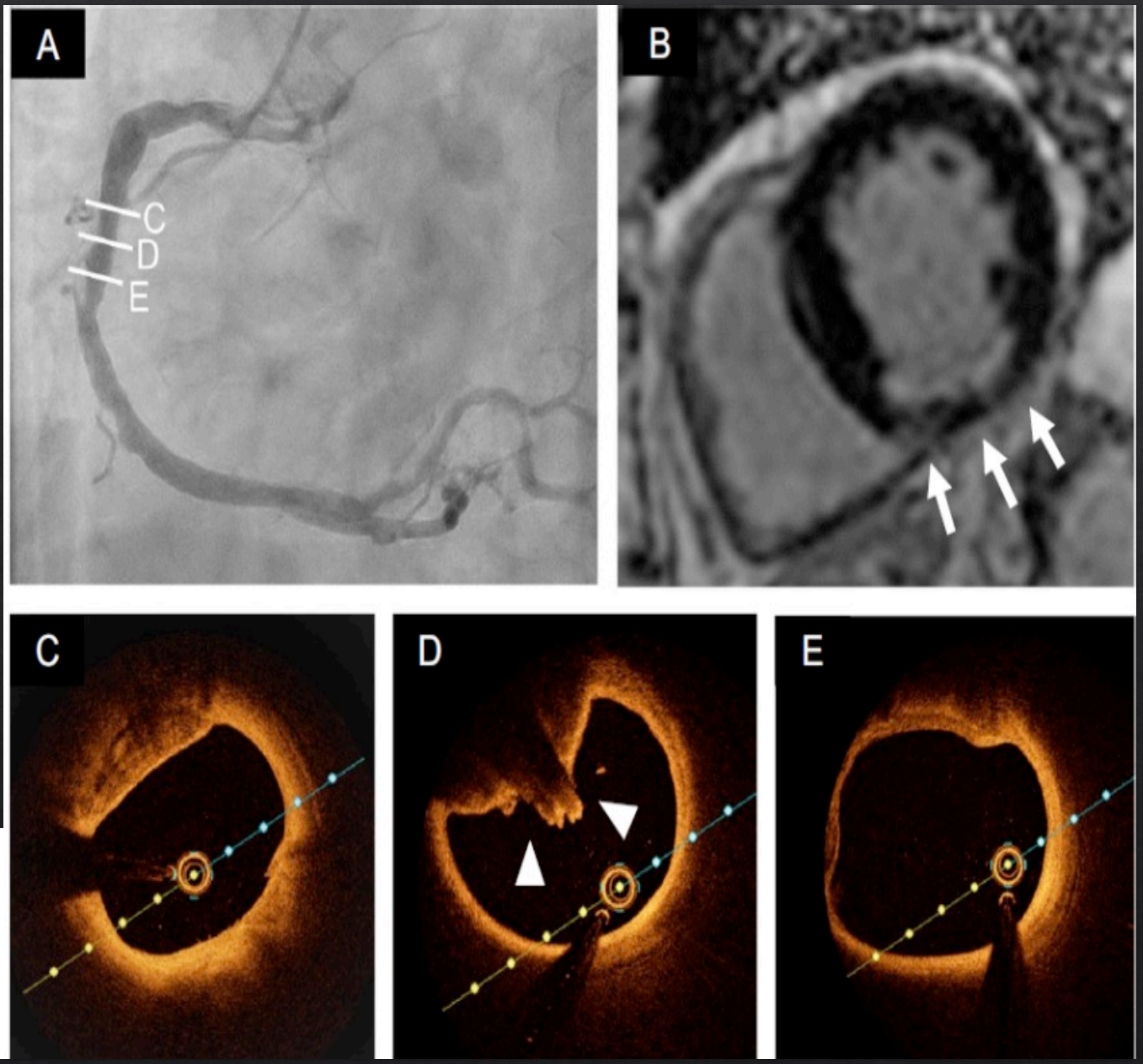

Fig. 3. Representative findings in coronary angiography, CMR, and OCT in a patient with plaque disruption causing MINOCA.
A 66-year-old man with hypertension and diabetes presented with chest pain and inferior T-wave inversions on ECG. Coronary angiography of the RCA showed <50 % stenosis (A). CMR performed 7 days later demonstrated a subendocardial LGE (white arrows) in the inferior wall (B). Serial OCT cross-sectional images from proximal (C) to distal (E) of the RCA on day 1 were demonstrated. There was a protruding mass with irregular surface indicating mural red thrombus (arrow heads in D). The final diagnosis of this case was inferior MINOCA caused by a plaque disruption. CMR, cardiac magnetic resonance; ECG, electrocardiogram; LGE, late gadolinium enhancement; MINOCA, myocardial infarction with non-obstructive coronary arteries; OCT, optical coherence tomography; RCA, right coronary artery.

Psychosocial Factors of Women Presenting With Myocardial Infarction With or Without Obstructive Coronary Arteries

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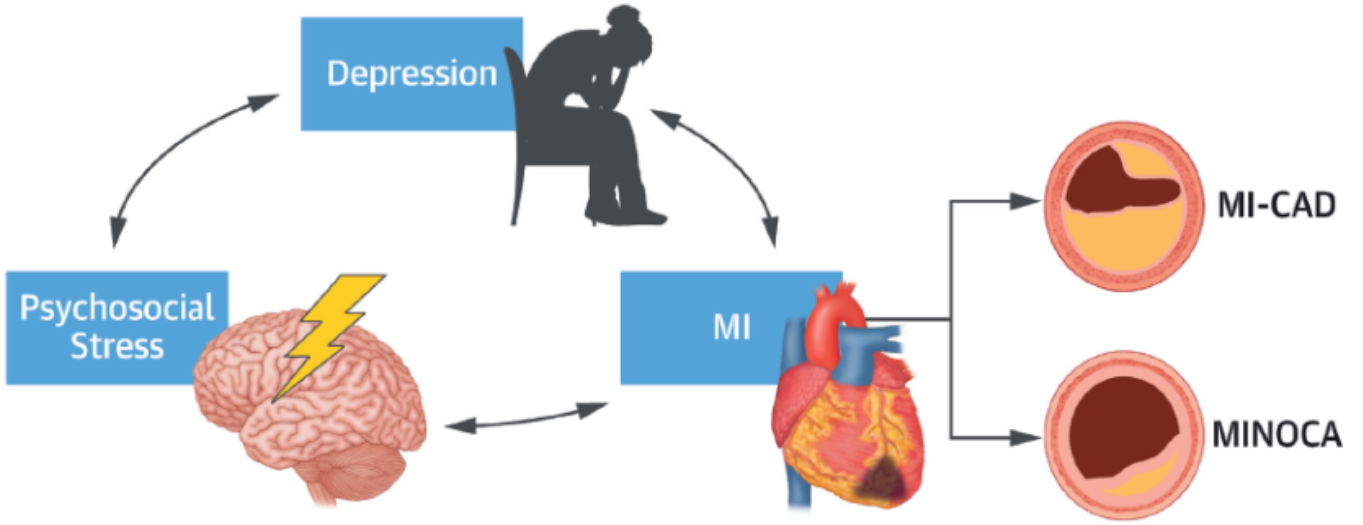
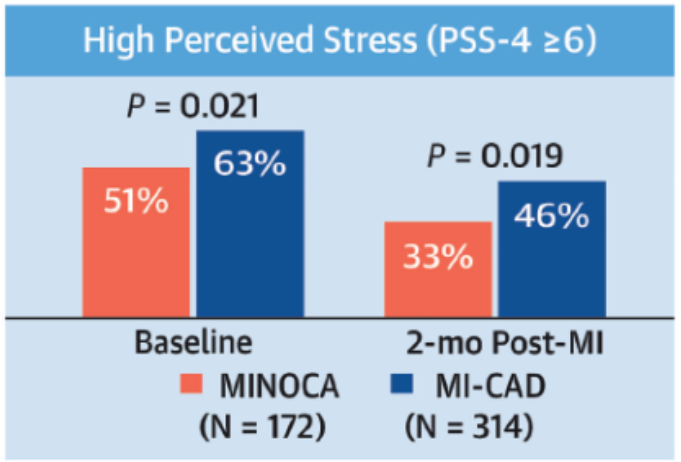
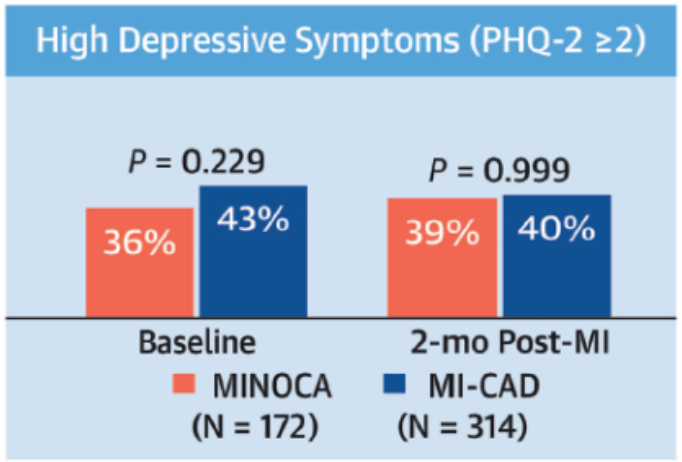
RESULTS We included 172 MINOCA and 314 MI-CAD patients. Women with MINOCA were younger (age 59.4 years vs 64.2 years; $P < 0.001$) and more diverse than those with MI-CAD. Women with MINOCA were less likely to have high stress (Perceived Stress Scale-4 ≥6) at the time of MI (51.0% vs 63.0%; $P = 0.021$) and at 2 months post-MI (32.5% vs 46.3%; $P = 0.019$) than women with MI-CAD. There was no difference in elevated depressive symptoms (Patient Health Questionnaire-2 ≥2) at the time of MI (36% vs 43%; $P = 0.229$) or at 2 months post-MI (39% vs 40%; $P = 0.999$). No differences in the rate of 2-month decline in stress and depression scores were observed between groups.

CONCLUSIONS Stress and depression are common among women at the time of and 2 months after MI. MINOCA patients were less likely to report high stress compared with MI-CAD patients, but the frequency of elevated depressive symptoms did not differ between the 2 groups. Stress and depressive symptoms decreased in both MI-CAD and MINOCA patients over time. (J Am Coll Cardiol 2023;82:1649-1658) © 2023 by the American College of Cardiology Foundation.

CENTRAL ILLUSTRATION Stress and Depression in Patients With Myocardial Infarction and Obstructive Coronary Artery Disease and Myocardial Infarction With Nonobstructive Coronary Arteries







Hausvater A, et al. J Am Coll Cardiol. 2023;82(17):1649-1658.

High perceived stress (Perceived Stress Scale [PSS-4] ≥6) around the time of myocardial infarction (MI) and 2 months after MI was significantly higher among women with myocardial infarction with obstructive coronary artery disease (MI-CAD) compared with those with myocardial infarction with nonobstructive coronary arteries (MINOCA). There was no difference between high depressive symptoms (Patient Health Questionnaire [PHQ-2] ≥2) among MINOCA and MI-CAD patients both at the time of MI and 2 months after MI.

Predicting the response to acetylcholine in ischemia or infarction with non-obstructive coronary arteries: The ABCD score

Atherosclerosis 391 (2024) 117503

551 consecutive patients with myocardial ischemia and non-obstructive CAD (371 INOCA and 180 MINOCA) underwent an intracoronary ACh provocation testing

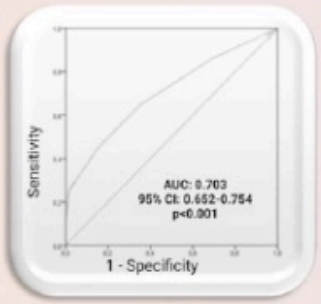
Time-based split

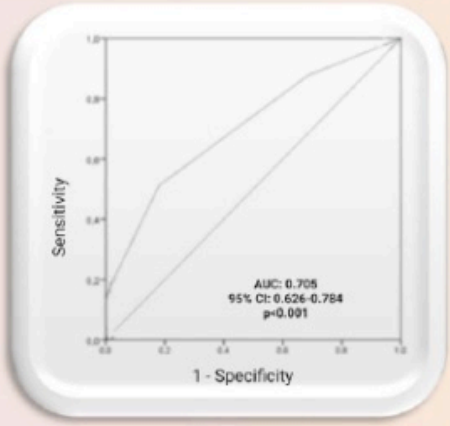
Derivation cohort (n = 386)

Validation cohort (n 165)

ABCD score

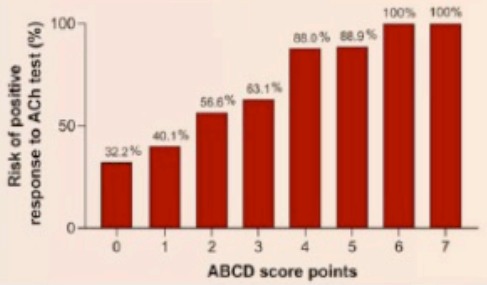
		Points
Acute clinical presentation	Yes (i.e. MINOCA)	2
	No (i.e. INOCA)	0
Presence of myocardial **B**ridge	Yes & lenght>20 mm	3
	Yes & lenght≤20 mm	1
	No	0
C-reactive protein	>5 mg/L	1
	≤5 mg/L	0
Dyslipidaemia	Yes	1
	No	0





- 94.3% with ABCD score ≥4 had a positive ACh test.
- All patients with an ABCD score ≥6 presented a positive ACh test response

Overall population



ESC Working Group on Coronary Pathophysiology and Microcirculation position paper on 'coronary microvascular dysfunction in cardiovascular disease'

ESC European Society of Cardiology
Cardiovascular Research (2020) 116, 741–755
doi:10.1093/cvr/cvaa003

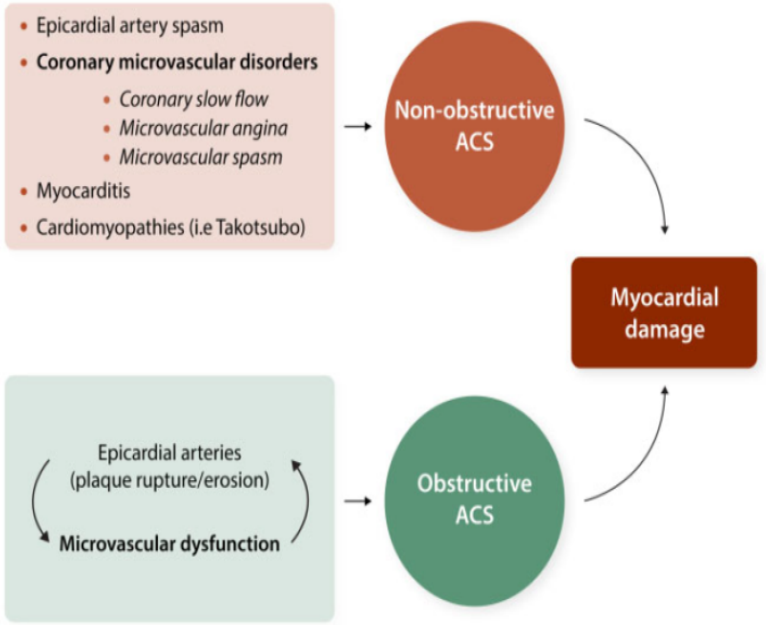
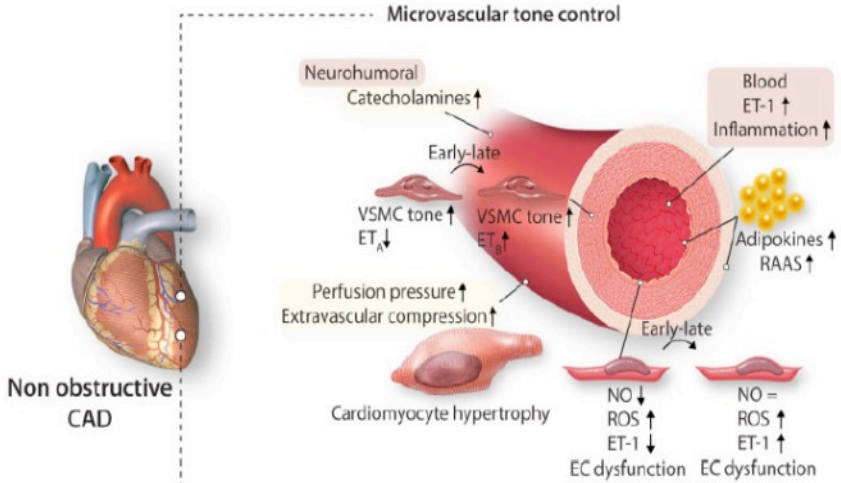


Figure 2 Microvascular dysfunction as underlying pathophysiological mechanism for acute coronary syndromes.



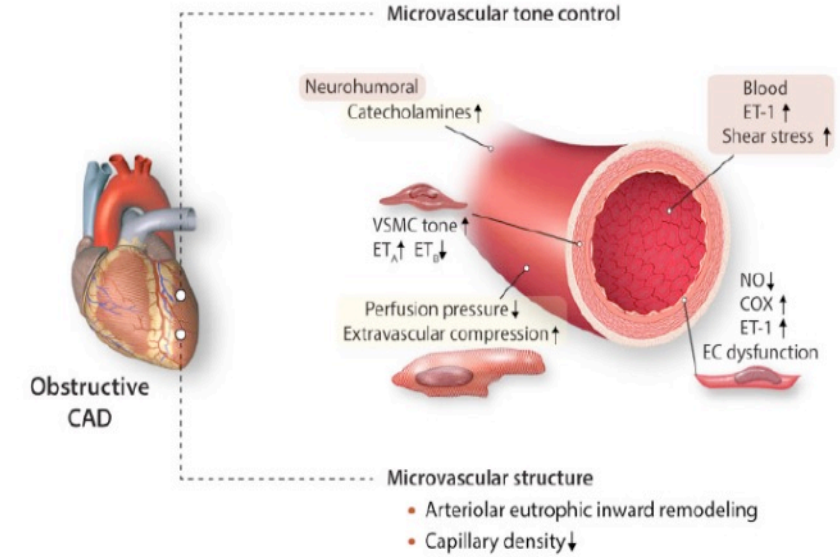


Figure 1 Coronary microvascular dysfunction in non-obstructive and obstructive coronary artery disease. COX, cyclooxygenase; EC, endothelial cell; ET-1, endothelin-1; ETA, endothelin receptor A; ETB, endothelin receptor B; NO, nitric oxide; RAAS, renin–angiotensin–aldosterone system; ROS, reactive oxygen species; VSMC, vascular smooth muscle cell.

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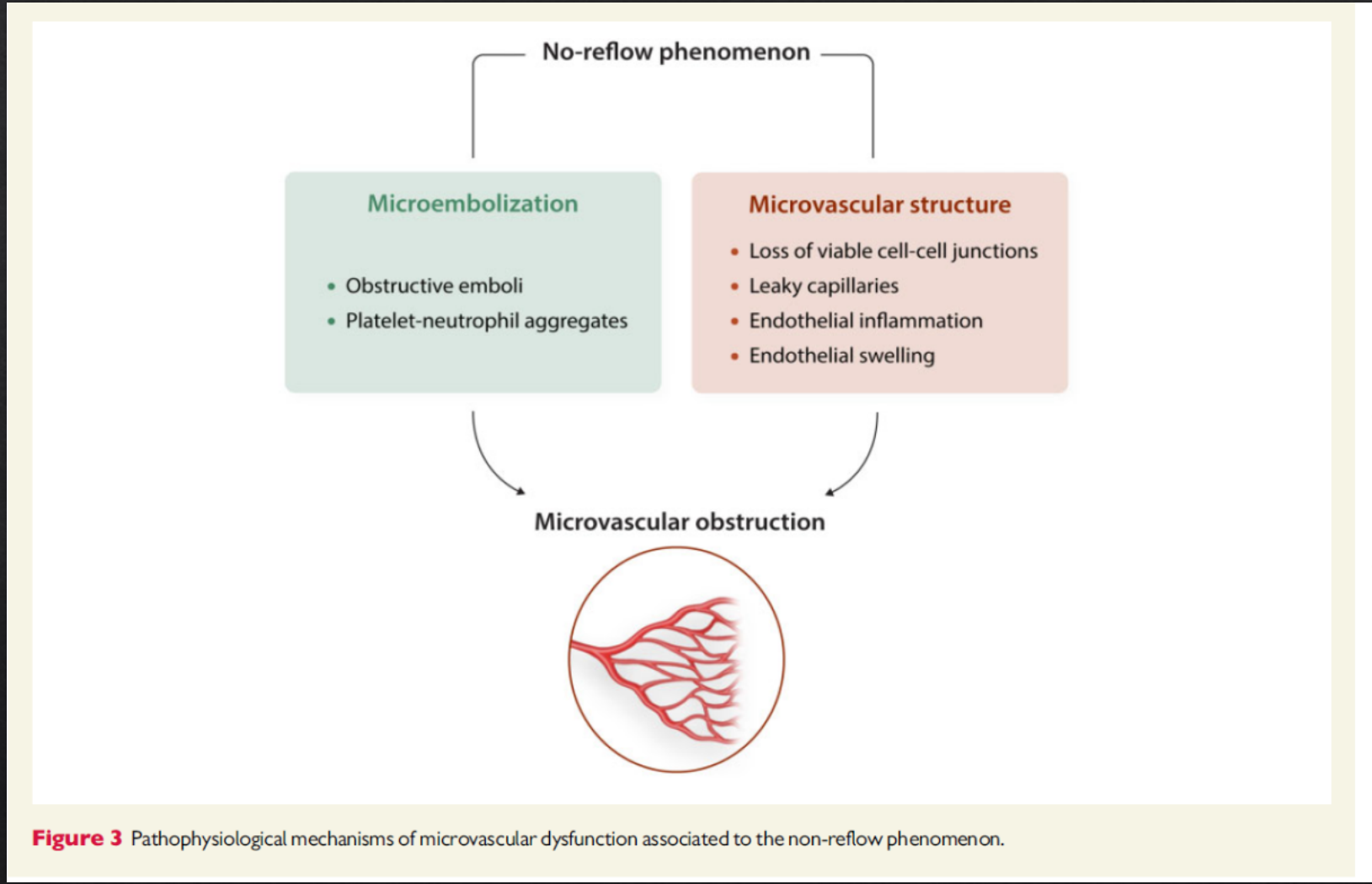

Figure 3 Pathophysiological mechanisms of microvascular dysfunction associated to the non-reflow phenomenon.

ESC Working Group on Coronary Pathophysiology and Microcirculation position paper on 'coronary microvascular dysfunction in cardiovascular disease'

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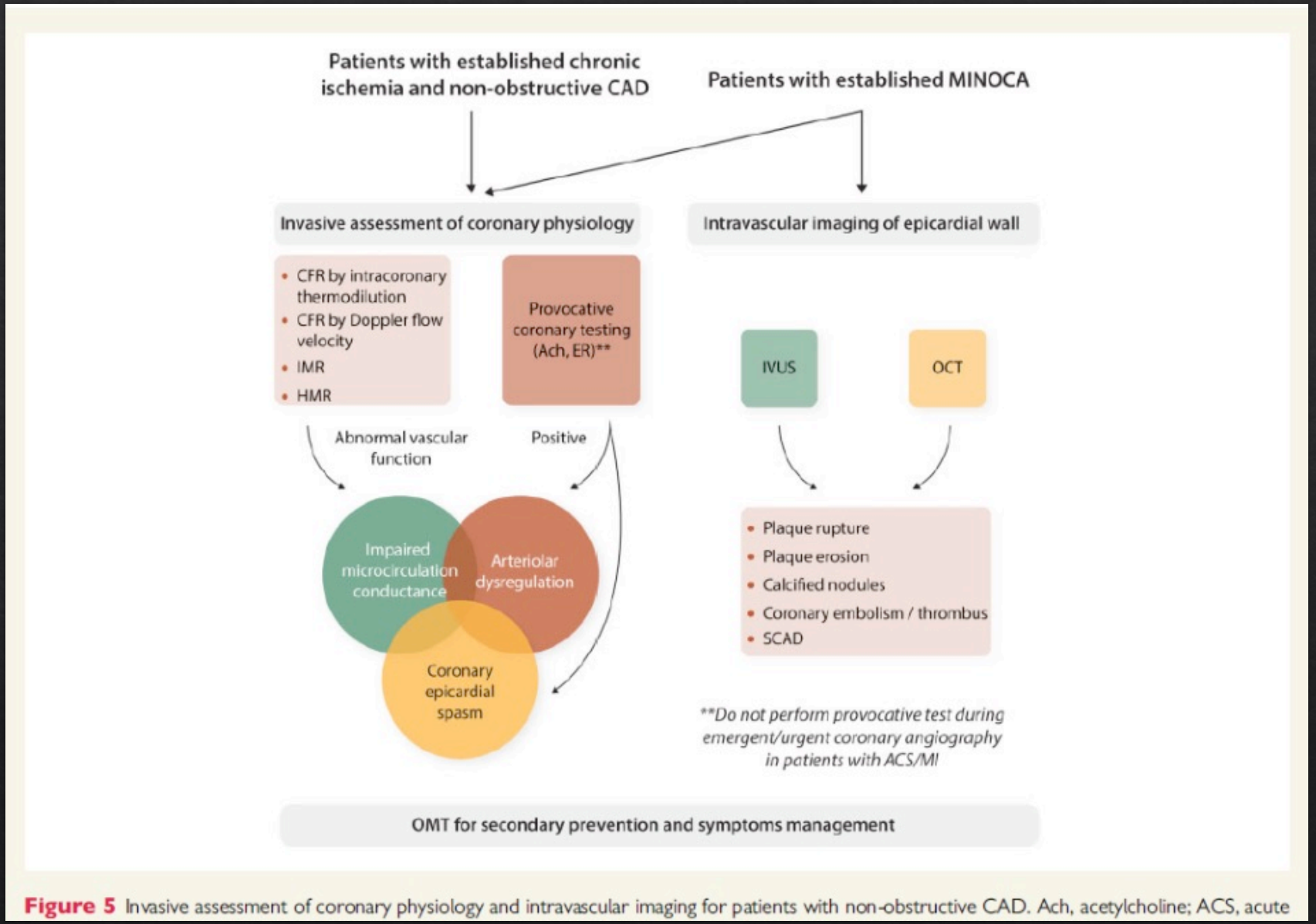

Figure 5 Invasive assessment of coronary physiology and intravascular imaging for patients with non-obstructive CAD. Ach, acetylcholine; ACS, acute

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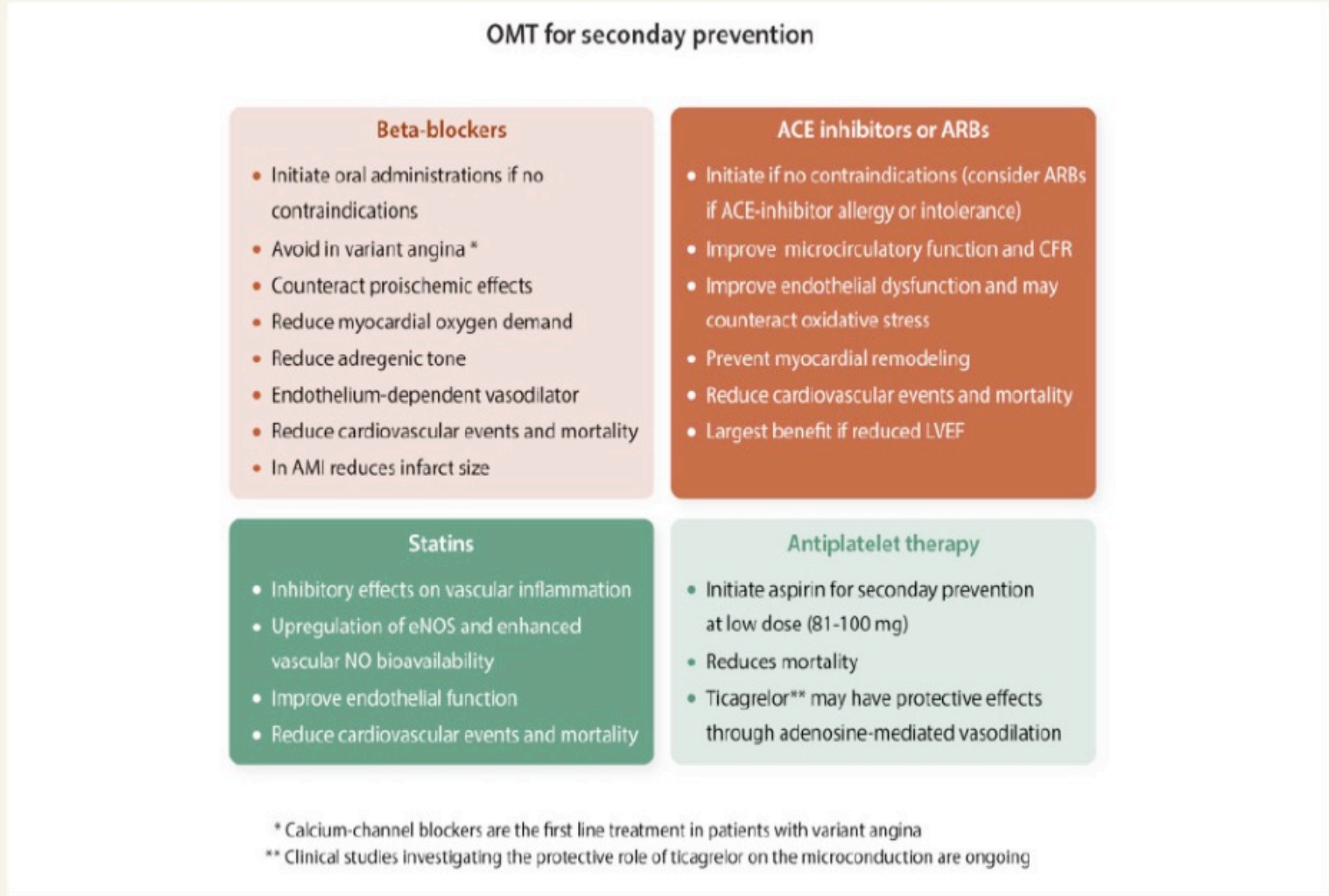

Figure 6 Secondary prevention strategies in patients with microvascular dysfunction or MINOCA. (i) Contraindications to beta-blockers include decom-

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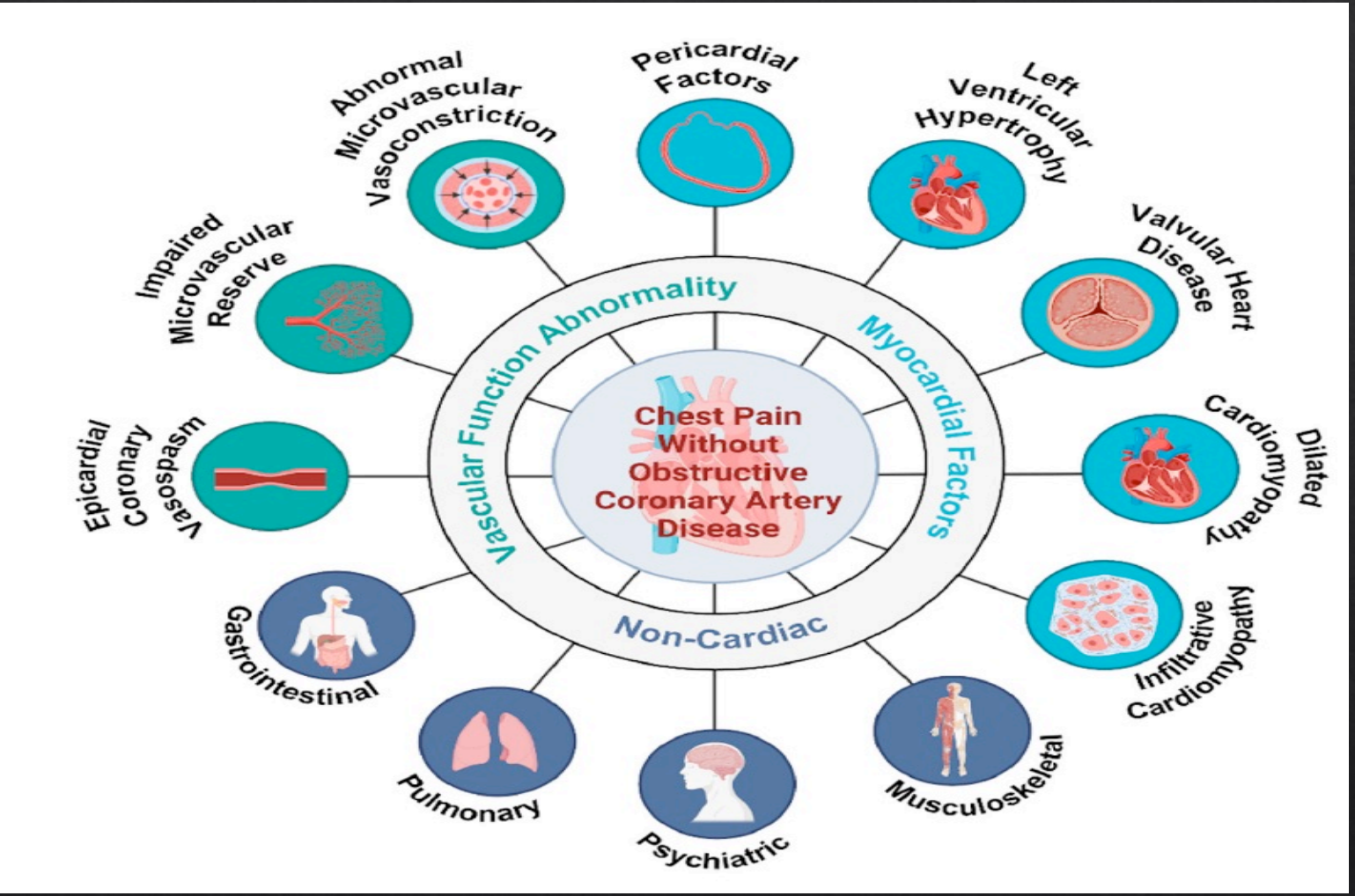
- Both structural and functional defects contribute and interact to cause a progressive impairment of coronary microvascular blood flow. There is a need to clarify the relative impact of each one in the diverse forms of presentation of CMD.
- There are no therapeutic strategies focused on specifically treating CMD and the microvasculature. There is an urgent need to identify novel and specific targets for therapy.
- There is a need to better understand the anatomic and physiologic features that predispose a higher burden of microvascular dysfunction in women.
- There is a need of new research to improve CMD assessment and the diagnostic methodologies now available.
- The management of patients with non-obstructive CAD and ACS or inducible myocardial ischaemia does not currently have a consensus strategy. These patients should be studied for the evaluation of endothelial and CMD , since they may influence outcome.
- Clinical studies and double-blind randomized clinical trials in patients with non-obstructive disease specifically designed to assess the effect of conventional and novel anti-ischaemic therapies are required.

Original Investigation | Cardiology

Mortality in ST-Segment Elevation Myocardial Infarction With Nonobstructive Coronary Arteries and Mimickers

Odayme Quesada, MD; Mehmet Yildiz, MD; Timothy D. Henry, MD; Seth Bergstedt, MS; Jenny Chambers, MBA; Ananya Shah; Larissa Stanberry, PhD; Lucas Volpenhein; Dalia Aziz, MD; Rebekah Lantz, DO; Cassady Palmer, BS; Justin Ugwu, MD; Muhammad J. Ahsan, MD; Ross F. Garberich, MS; Heather S. Rohm, BSN; Frank V. Aguirre, MD; Santiago Garcia, MD; Scott W. Sharkey, MD

INOCA



P.K. Mehta et al.

Atherosclerosis 363 (2022) 8–21

ESC European Society of Cardiology
European Heart Journal (2020) 41, 3504–3520 doi:10.1093/eurheartj/ehaa503
SPECIAL ARTICLE
Ischaemic heart disease

An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary

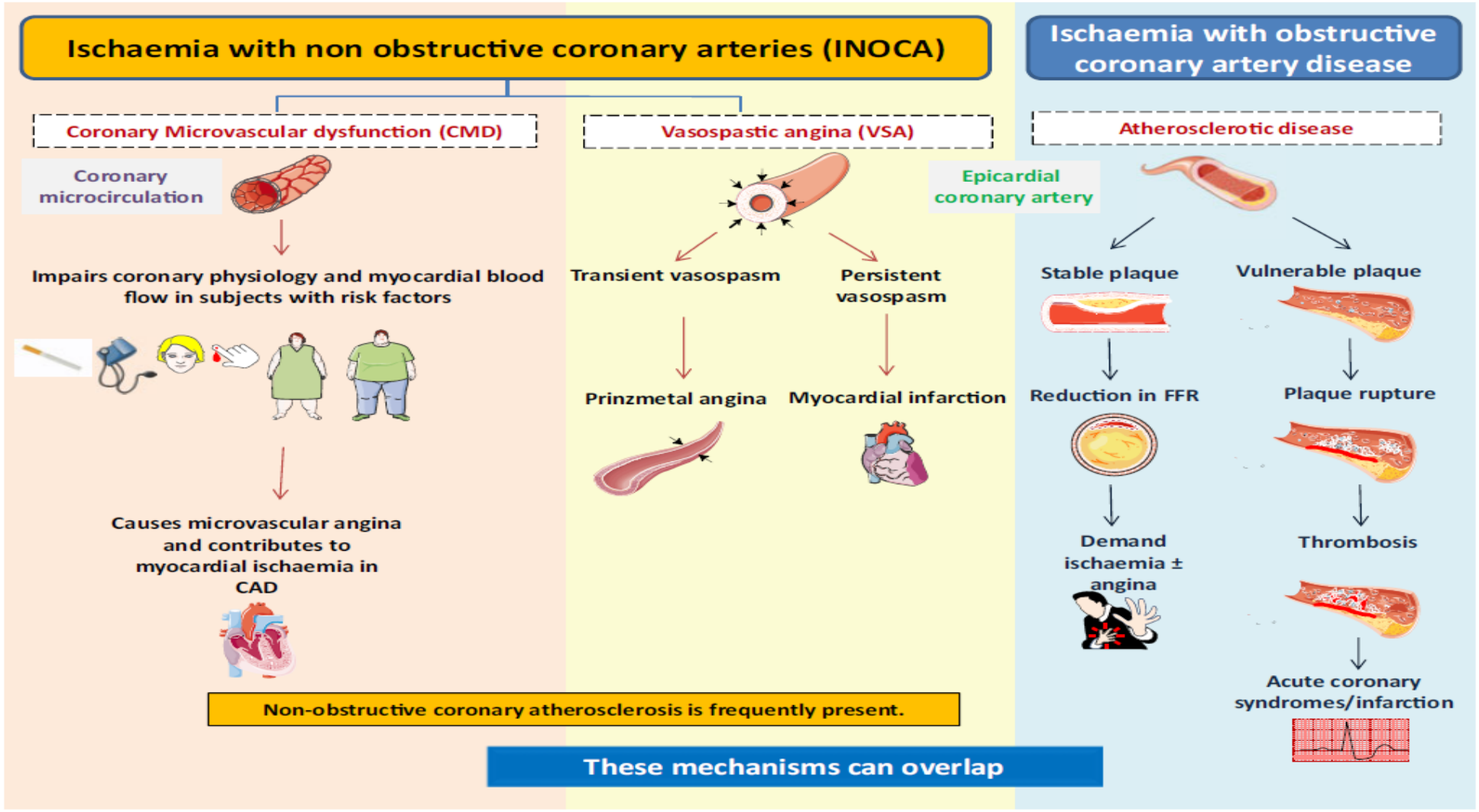


Figure 2 Mechanisms of myocardial ischaemia in INOCA and obstructive coronary artery disease. CAD, coronary artery disease; FFR, fractional flow reserve.

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SPECIAL ARTICLE
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representative of microvascular dysfunction.[97] The hyperaemic myocardial velocity resistance (HMR) index is a Doppler-based index, calculated by dividing intracoronary pressure by hyperaemic flow velocity. In a previous study of patients with angina and non-

Table 2 INOCA endotypes diagnostic criteria

	INOCA endotypes	Pathophysiology	Diagnostic criteria
1	Microvascular angina[a]	CMD	Diagnostic guidewire and Adenosine test • FFR > 0.8 • CFR < 2.0 • IMR ≥ 25[b] • HMR ≥ 1.9[b] Vasoreactivity (acetylcholine test) • No or <90% diameter reduction • + angina • + ischaemic ECG changes
2	Vasospastic angina	Epicardial spasm	Diagnostic guidewire and Adenosine test • FFR > 0.8 • CFR ≥ 2.0 • IMR < 25 • HMR < 1.9 Vasoreactivity (acetylcholine test) • ≥ 90% diameter reduction • + angina • + ischaemic ECG changes
3	Both microvascular and vasospastic angina	Both CMD and epicardial spasm	Diagnostic guidewire and Adenosine test • FFR > 0.8 • CFR < 2.0 • IMR ≥ 25 • HMR ≥ 1.9 Vasoreactivity (acetylcholine test) • No or <90% or ≥90% diameter reduction • + angina • + ischaemic ECG changes
4	Non-cardiac chest pain	None	Diagnostic guidewire and Adenosine test • FFR > 0.8 • CFR ≥ 2.0 • IMR < 25 • HMR < 1.9 Vasoreactivity (acetylcholine test) • No or <90% diameter reduction • No angina • No ischaemic ECG changes
5	Non-flow-limiting CAD[c]	Diffuse coronary artery atherosclerosis	Diagnostic guidewire and adenosine test • FFR > 0.8 • CFR ≥ 2.0 • IMR < 25 • HMR < 1.9 Vasoreactivity (acetylcholine test) • No or <90% diameter reduction • No angina • No ischaemic ECG changes

Angor microvasculaire

Angor spastique

Angor microvasculaire + Angor spastique

Non cardiaque

Sans limitation du flux coronaire….

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SPECIAL ARTICLE
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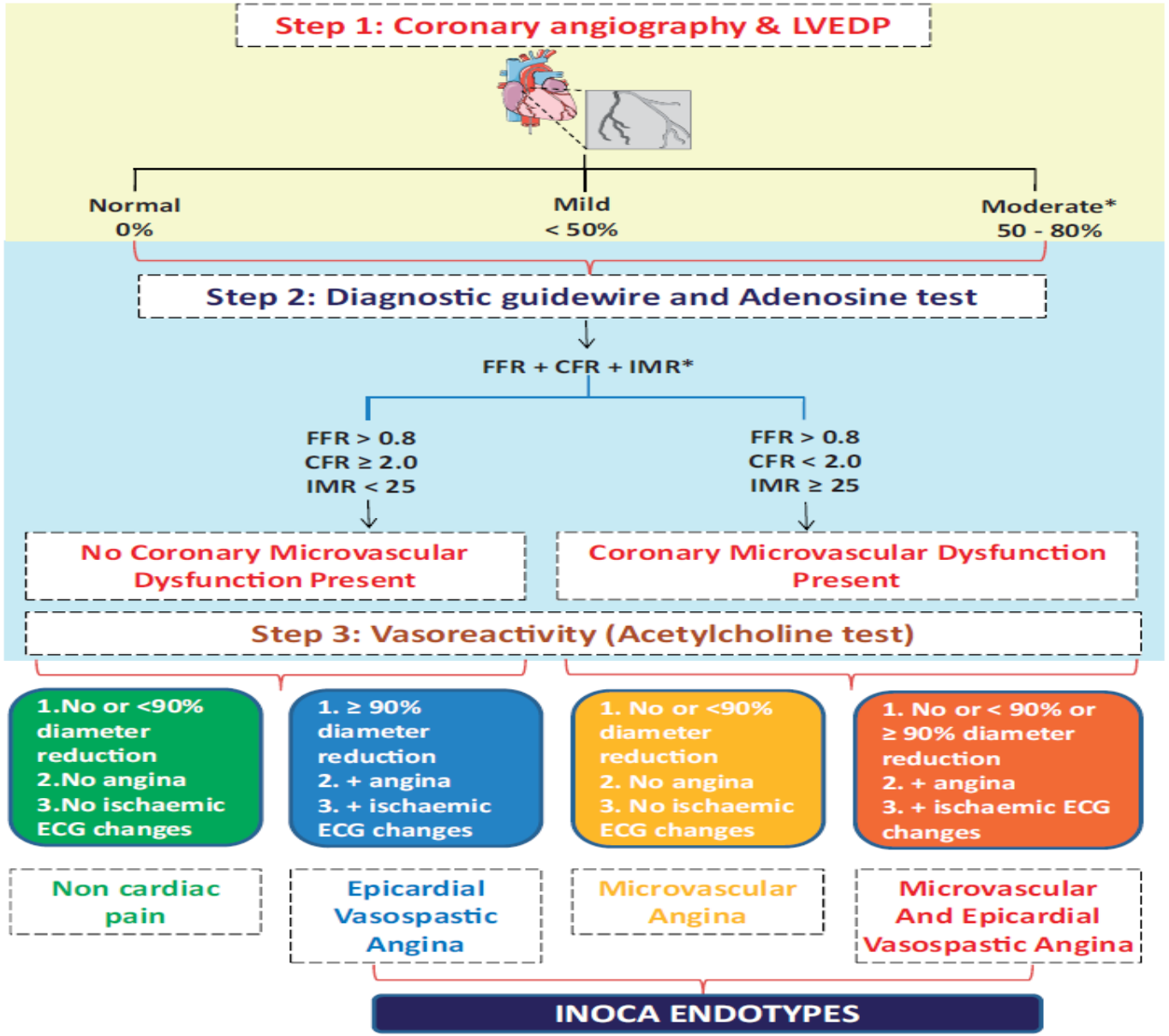

Figure 4 Invasive evaluation of INOCA. CFR, coronary flow reserve; FCA, functional coronary angiography; FFR, fractional flow reserve; IMR, index of microvascular resistance; LVEDP, left ventricular end-diastolic pressure. [a]And negative non-invasive or invasive testing for epicardial ischaemia. [b]Combo wire is an alternative option to measure FFR,CFR and IMR.

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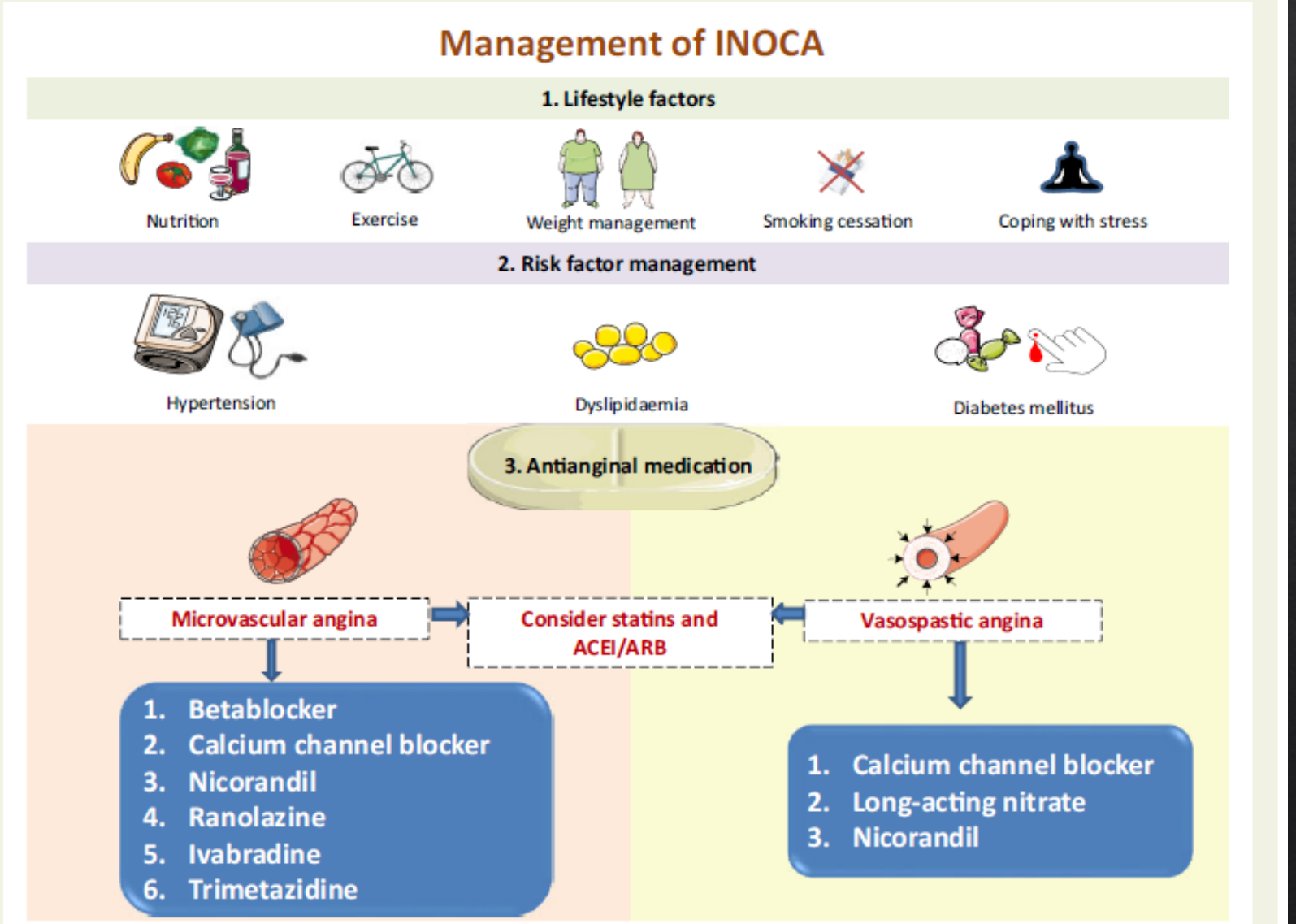

Figure 5 Management of INOCA. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

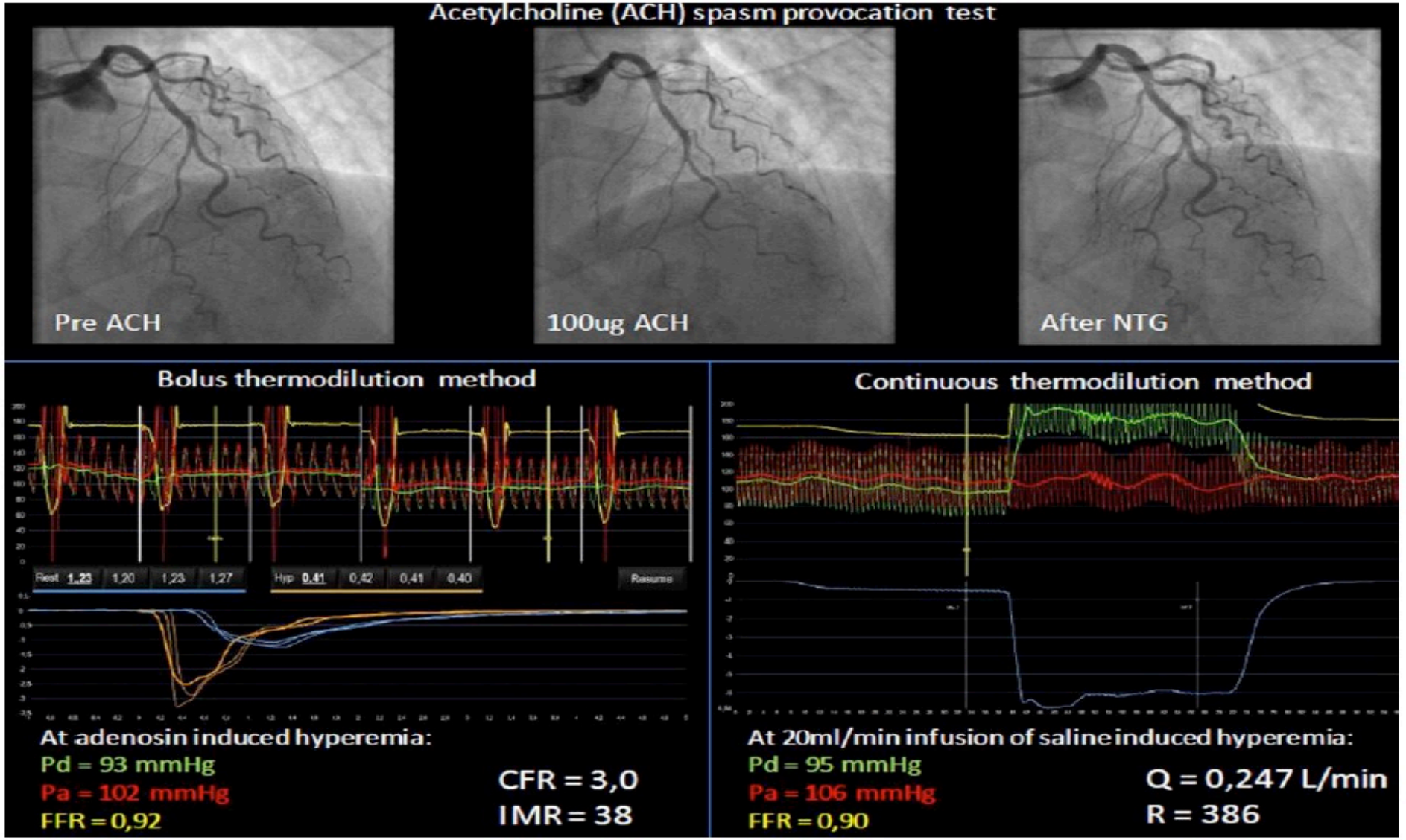

Figure 1 Example of a INOCA case (50-year-old female) with combined epicardial spasm and microvascular dysfunction.

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European Heart Journal (2021) 42, 4592–4600
doi:10.1093/eurheartj/ehab282
CLINICAL RESEARCH
Epidemiology and prevention

Clinical characteristics and prognosis of patients with microvascular angina: an international and prospective cohort study by the Coronary Vasomotor Disorders International Study (COVADIS) Group

Conclusions This first international study provides novel evidence that MVA is an important health problem regardless of sex or ethnicity that a diagnosis of MVA portends a substantial risk for MACE associated with hypertension and previous history of CAD, and that women have a lower quality of life than men despite the comparable prognosis.

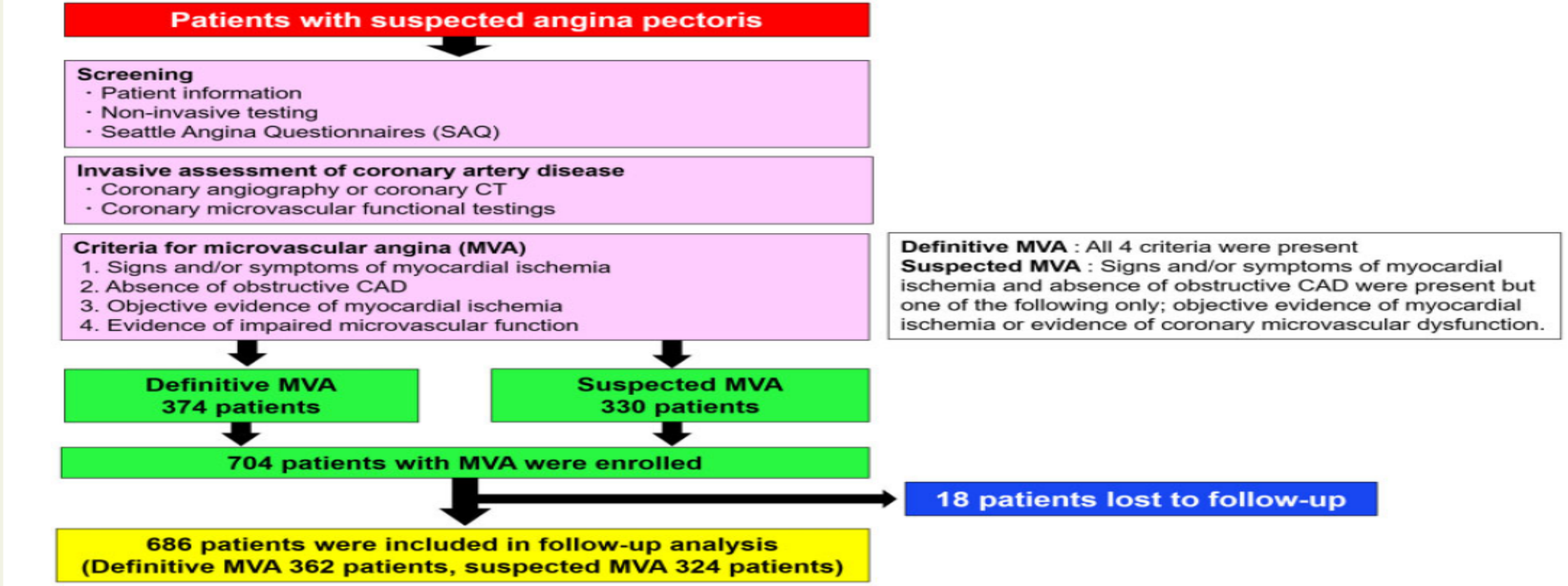

Figure 1 Patient enrolment and follow-up.

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European Heart Journal (2021) 42, 4592–4600
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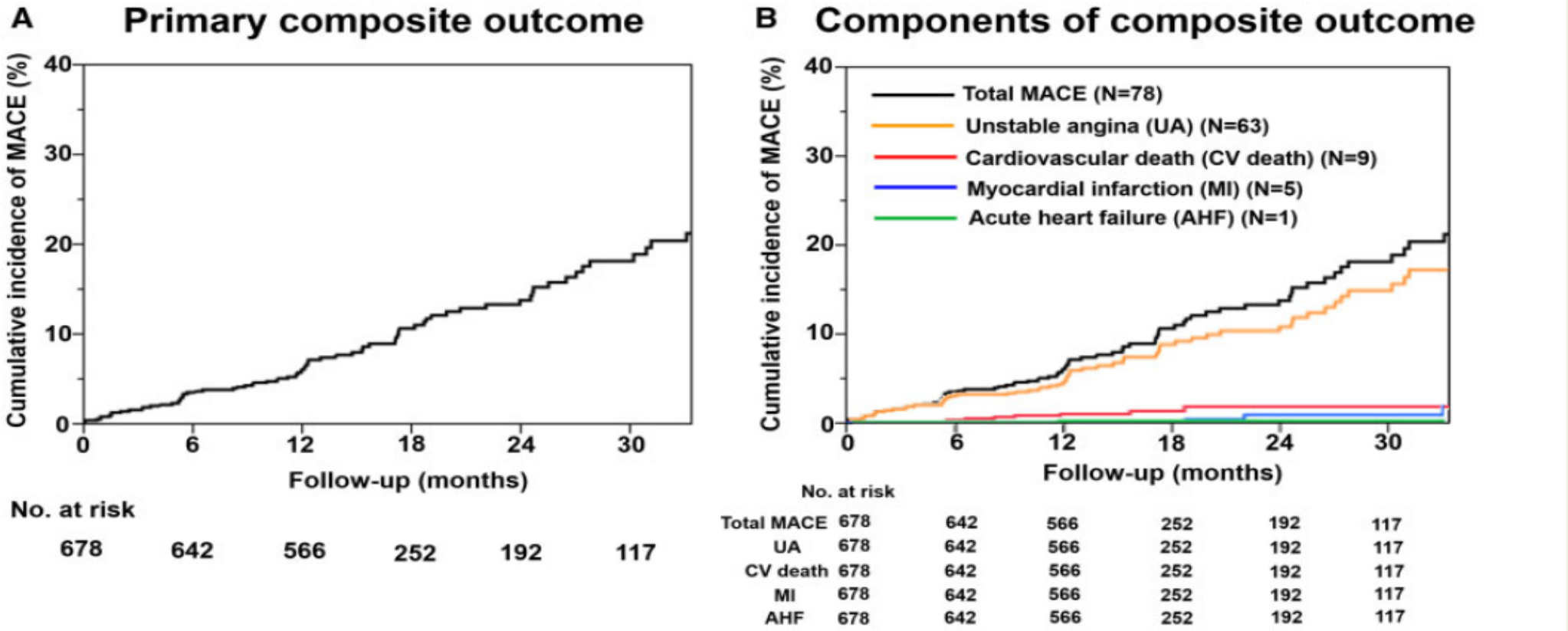

Figure 2 Kaplan–Meier curves for MACE in the overall cohort. Kaplan–Meier curve for (*A*) the primary composite outcome and (*B*) each component of the composite outcome.

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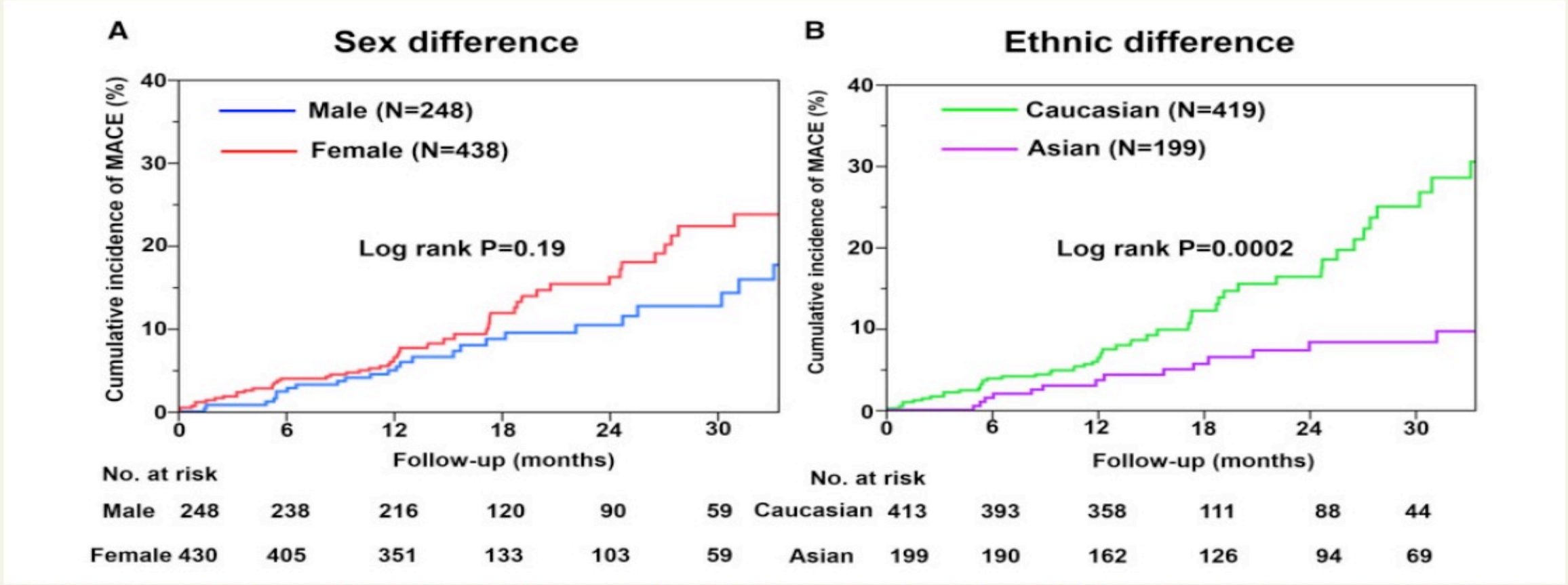

Figure 3 Kaplan–Meier curves for MACE by patient group. (*A*) Sex difference in the incidence of MACE. (*B*) Ethnic difference in the incidence of MACE (Caucasian vs. Asian).

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Clinical characteristics and prognosis of patients with microvascular angina: an international and prospective cohort study by the Coronary Vasomotor Disorders International Study (COVADIS) Group

Table 2 Prognostic factors for MACE in patients with MVA (Cox proportional hazard model)

	Univariable analysis			Multivariable analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Age	0.987	0.970–1.004	0.14			
Female sex	1.358	0.857–2.152	0.19			
Hypertension	1.802	1.148–2.831	0.01	1.692	1.067–2.681	0.03
Dyslipidaemia	1.362	0.877–2.115	0.17			
Diabetes mellitus	1.461	0.887–2.407	0.14			
Current smoking	0.868	0.479–1.572	0.64			
Previous history of CAD	2.233	1.448–3.442	0.005	2.032	1.312–3.147	0.001
Family history of CAD	1.700	1.093–2.645	0.02			

CAD, coronary artery disease including acute coronary syndrome and stable angina pectoris; CI, confidence interval; HR, hazard ratio; MVA, microvascular angina.

Angor post PCI ?

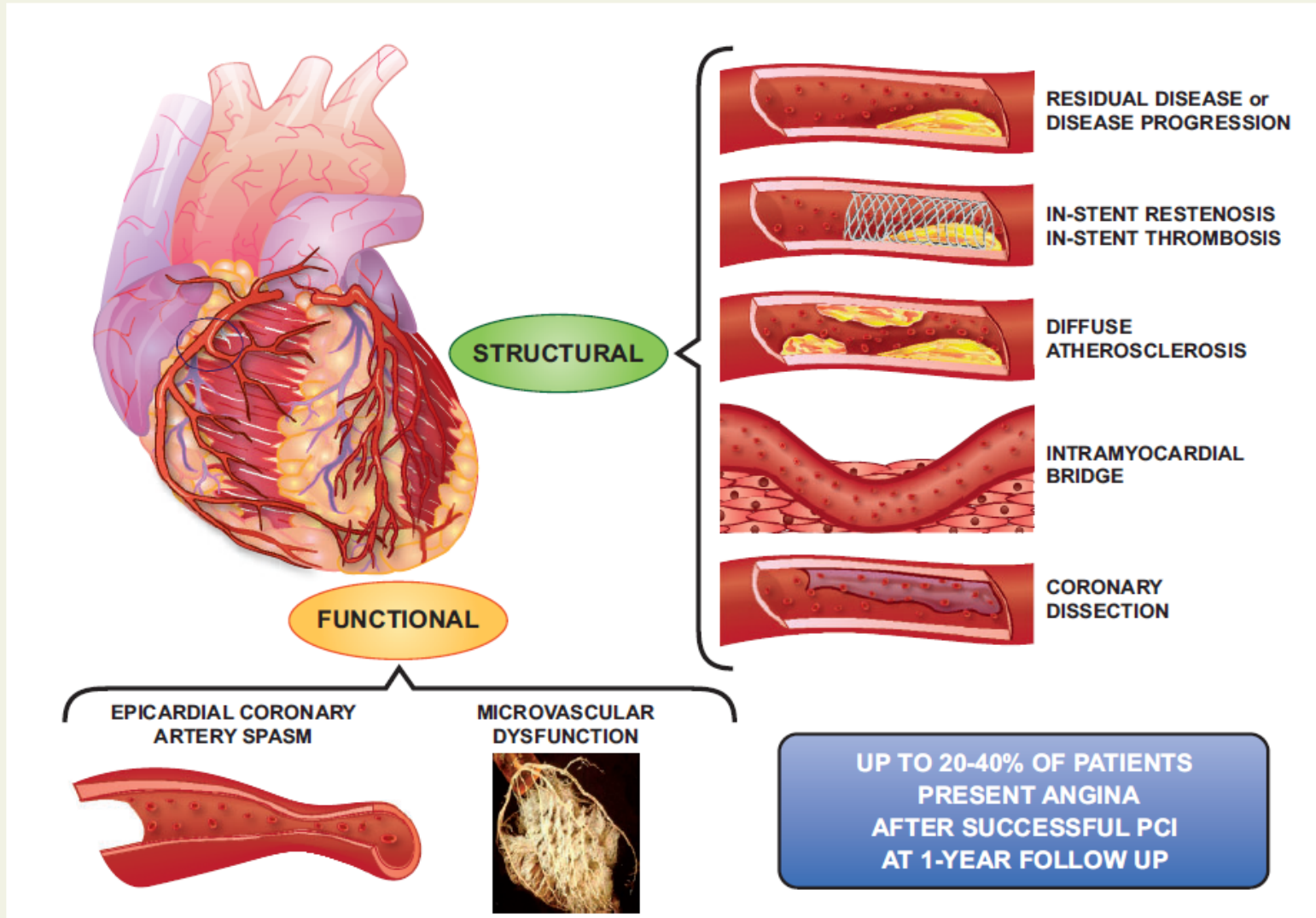
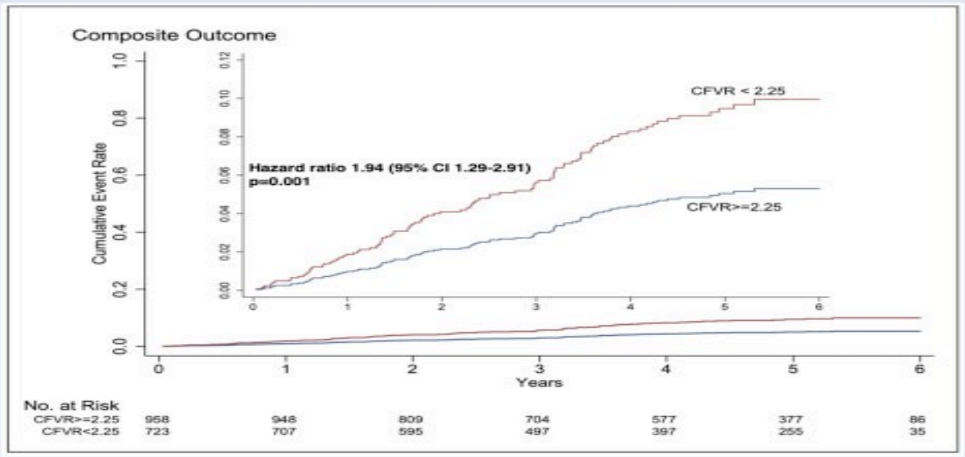


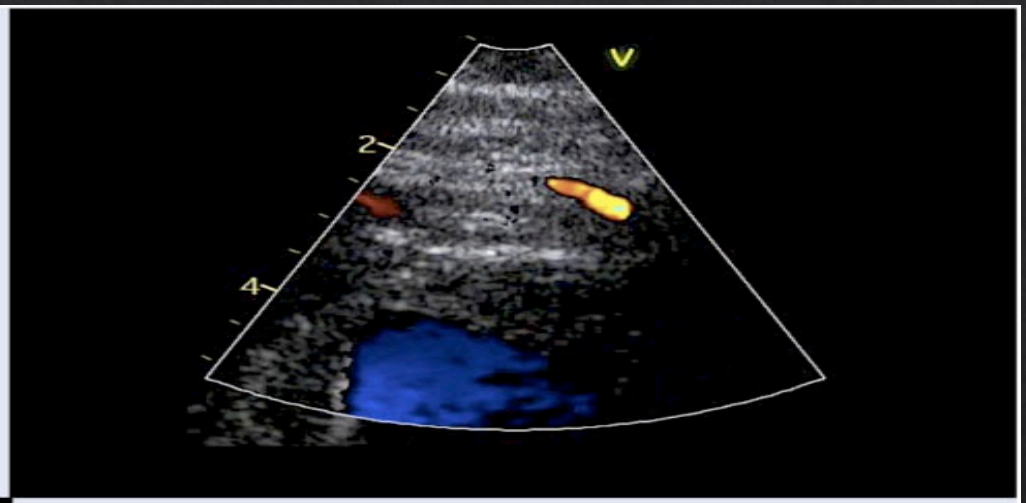
Figure 1 Structural and functional alterations of coronary circulation responsible for persistence or recurrence of angina after percutaneous coronary intervention.

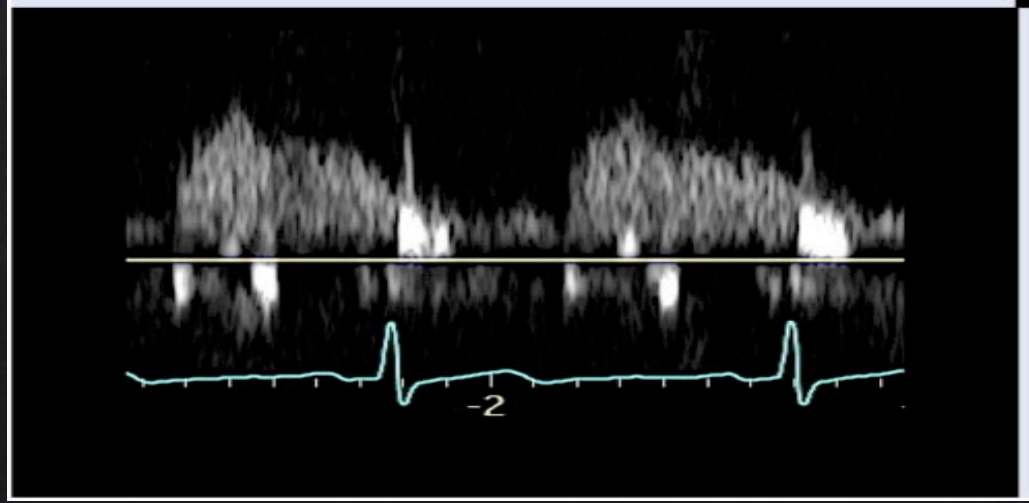
« If you wish to converse with me, define your terms. »

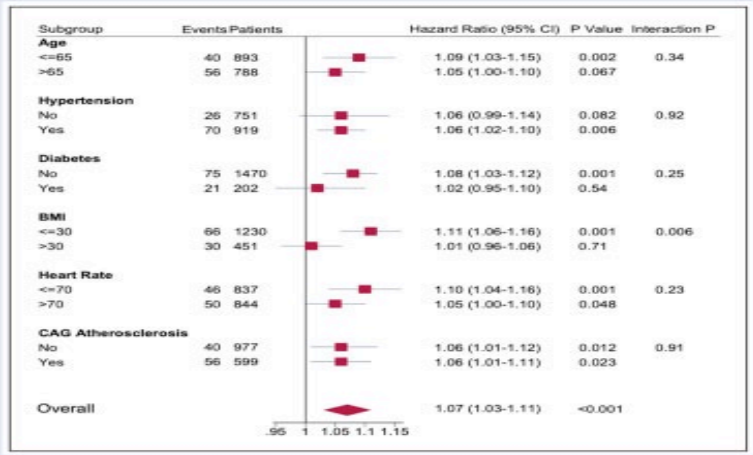
Coronary flow velocity reserve predicts adverse prognosis in women with angina and no obstructive coronary artery disease: results from the iPOWER study

ESC European Society of Cardiology
European Heart Journal (2021) 42, 228–239
doi:10.1093/eurheartj/ehaa944









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Conclusion Assessment of CFVR by echocardiography is feasible and predictive of adverse outcome in women with angina and no obstructive CAD. Results support a more aggressive preventive management of these patients and underline the need for trials targeting CMD.

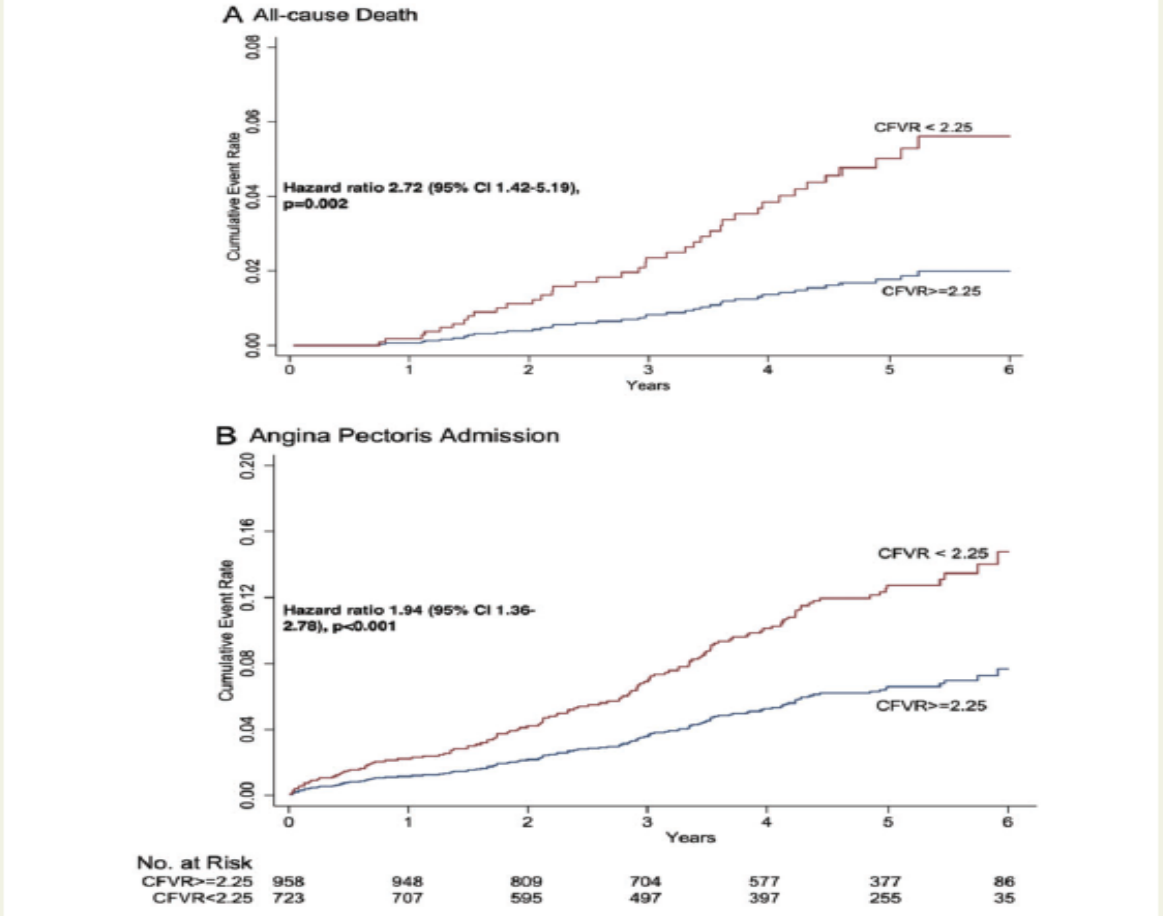
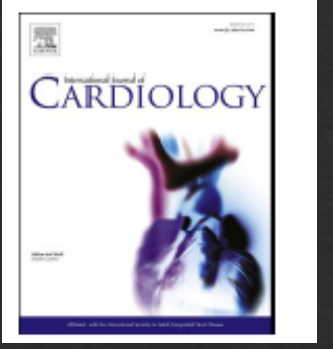


Figure 3 Time to event curves for secondary outcomes. CFVR, coronary flow velocity reserve.



Endothelial dysfunction in patients with angina and non-obstructed coronary arteries is associated with an increased risk of mayor cardiovascular events. Results of the Spanish ENDOCOR registry

Lilian Grigorian-Shamagian [a,b,c], Juan Francisco Oteo [d], Alejandro Gutiérrez-Barrios [e],

Endothelial dysfunction was defined by visually detectable vasoconstriction in any coronary segment (12). Vasoconstriction was assessed semi-quantitatively (Fig. 2) and defined as mild (10 — 30%), moderate (31–70%) and severe (>70%). Vasoconstriction was also further defined as local or diffuse depending on its distribution. Although, the assessment of the microvascular function was not an inclusion criterion, we also collected the results of those patients in whom the evaluation was done.

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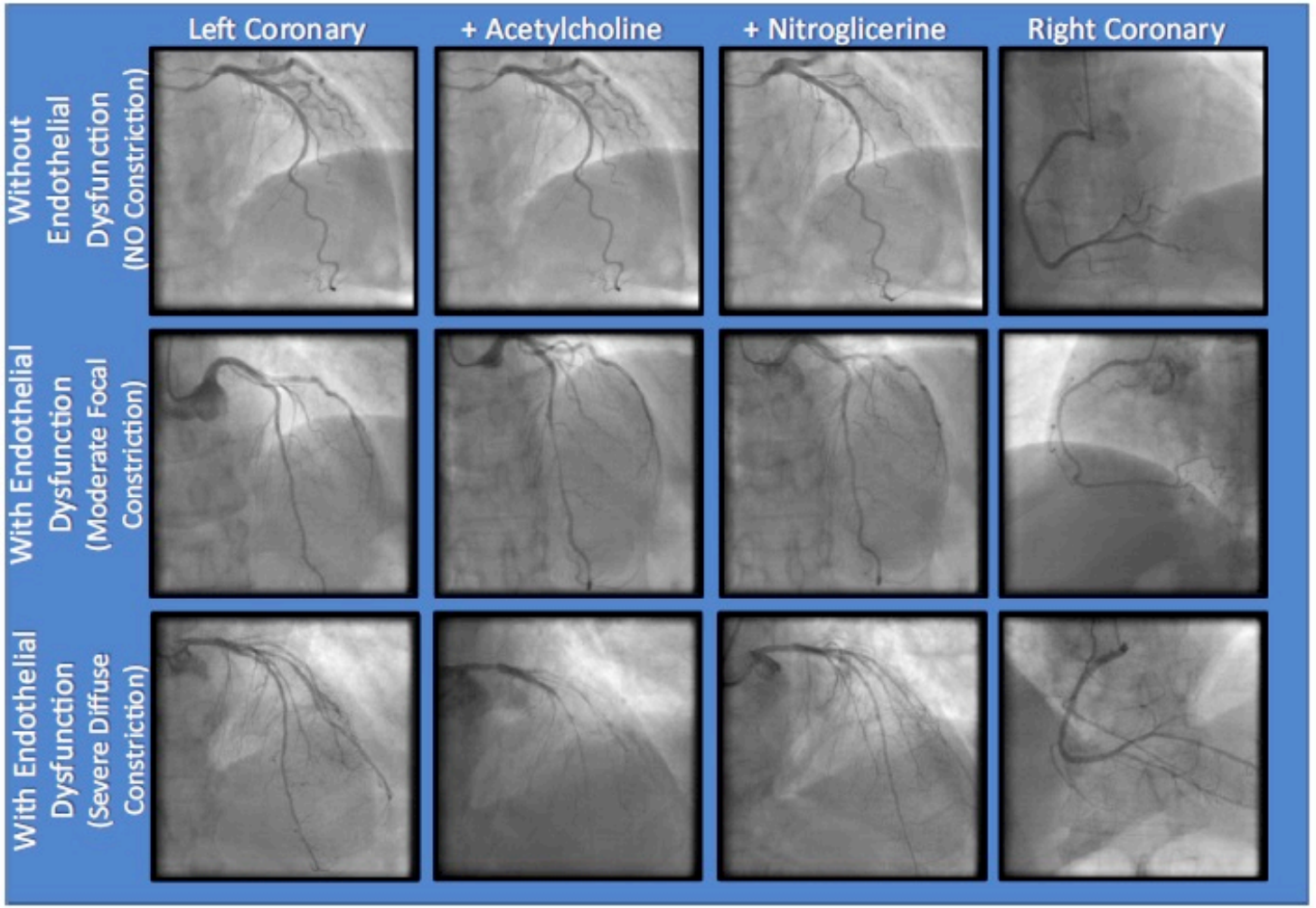

Fig. 2. Different degrees of vasoconstriction during acetylcholine test: mild (10–30%), moderate (30–70%), severe (> 70%).

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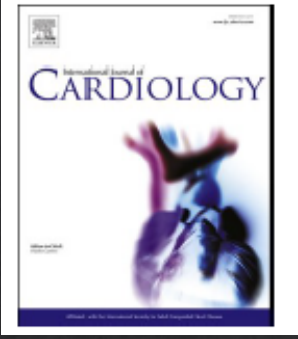

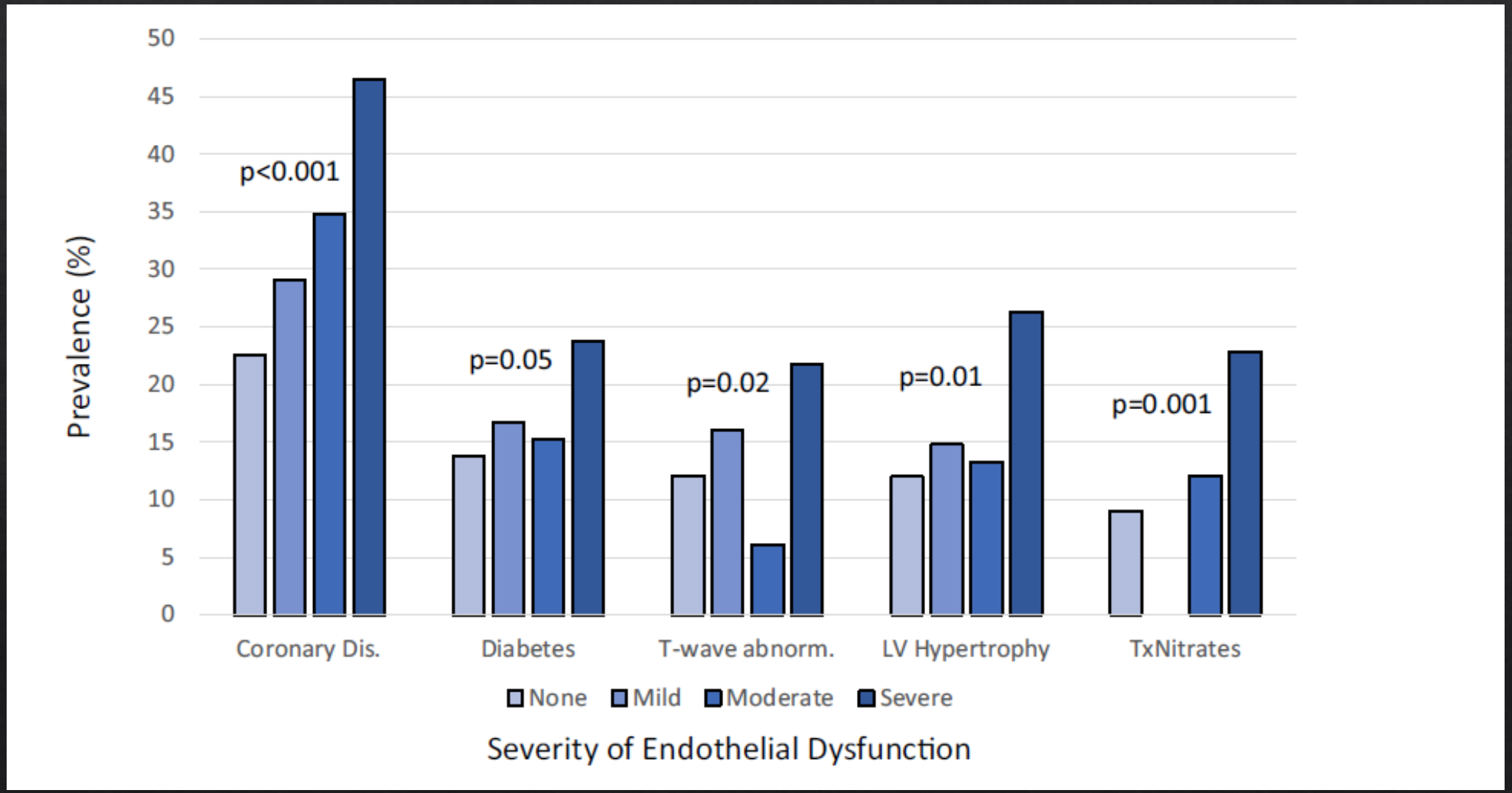

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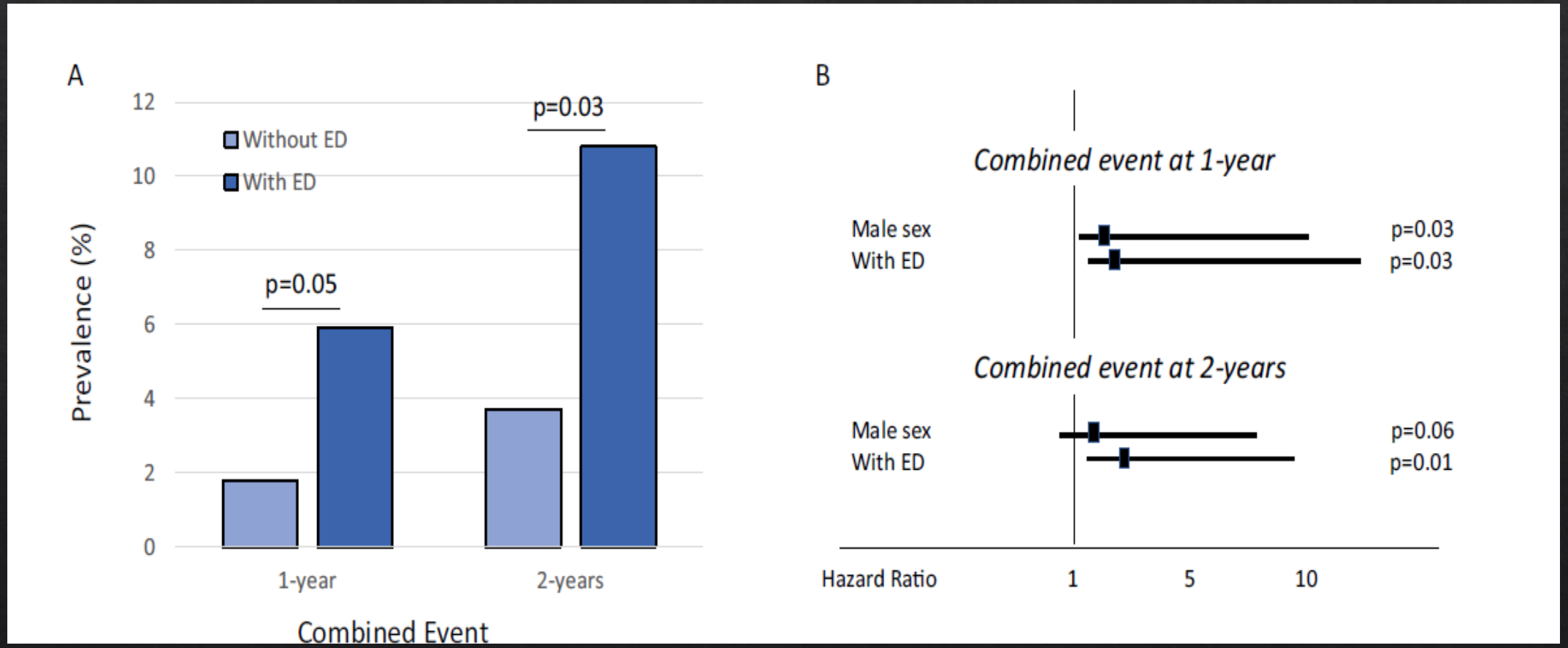
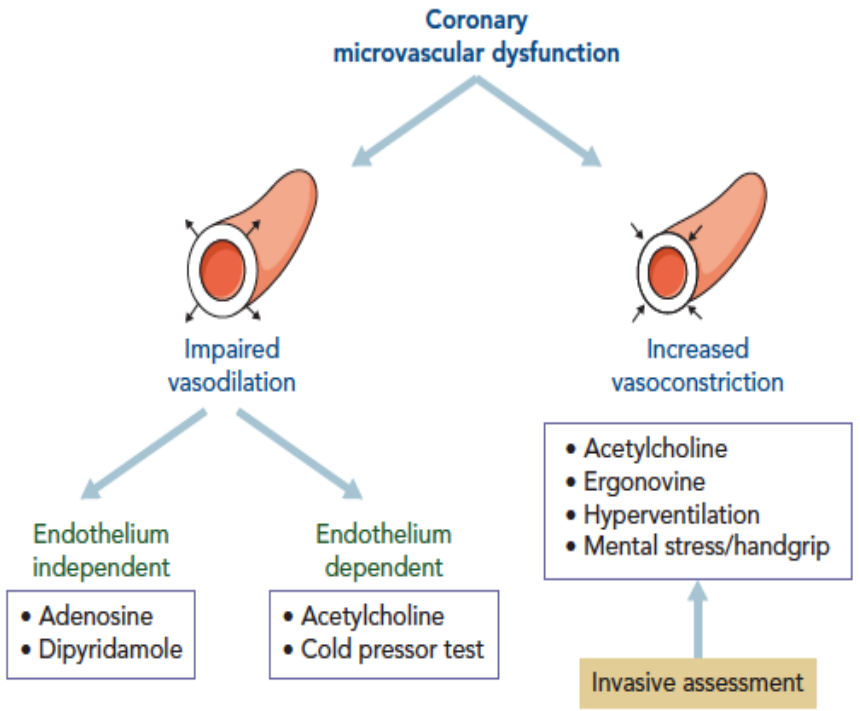


Microvascular disease

Tableau I. Mécanismes physiopathologiques de la dysfonction microvasculaire : causes structurales, fonctionnelles et extravasculaires
(Modifié de Camici PG, Crea F. N Engl J Med 2007[1]).

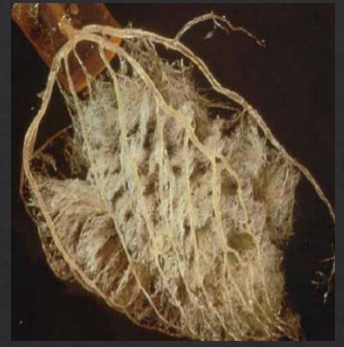
Causes structurales	
Obstruction luminale	• Microembolisation de matériel thrombotique suite à la recanalisation de la coronaire responsable d'un infarctus aigu
Raréfaction artériolaire et fibrose périvasculaire	• Cardiomyopathie hypertrophique • Sténose aortique • Hypertension artérielle
Infiltration de la paroi vasculaire	• Cardiopathies infiltratives (par exemple maladie de Fabry)
Causes fonctionnelles	
Dysfonction endothéliale	• Hyperlipidémie • Diabète • Tabagisme
Dysrégulation vasomotrice des cellules musculaires lisses	• Cardiomyopathie hypertrophique • Hypertension artérielle
Dysrégulation vasomotrice sur stimulation alpha-adrénergique	• Recanalisation de l'artère responsable d'un infarctus
Causes extravasculaires	
Compression extramurale	• Cardiomyopathie hypertrophique • Sténose aortique • Hypertension artérielle

Figure 1: Abnormalities of Coronary Microvascular Function and Tests Suggested to Investigate these Mechanisms in Patients with Suspected Microvascular Angina



'Primary' Microvascular Angina: Clinical Characteristics, Pathogenesis and Management

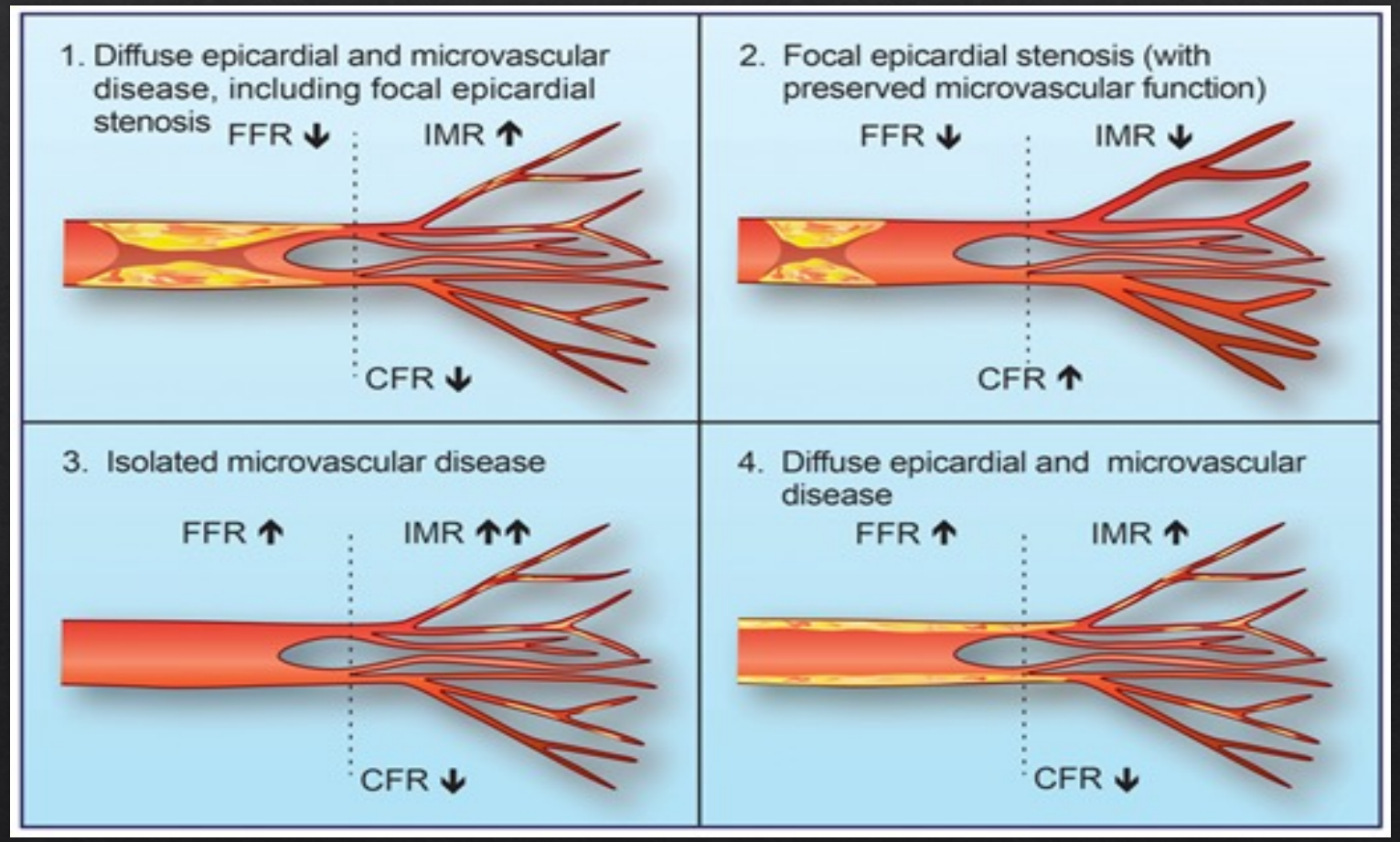
Gaetano Antonio Lanza[1], Antonio De Vita[1] and Juan-Carlos Kaski[2]



Coronary artery disease: physiology and prognosis

J. Ford, David Corcoran, Colin Berry Author Notes

Eur Heart J. (2017) 38(25), 1990–1992Thomas



Microvascular disease

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 7, NO. 5, 2014
MAY 2014:453–63

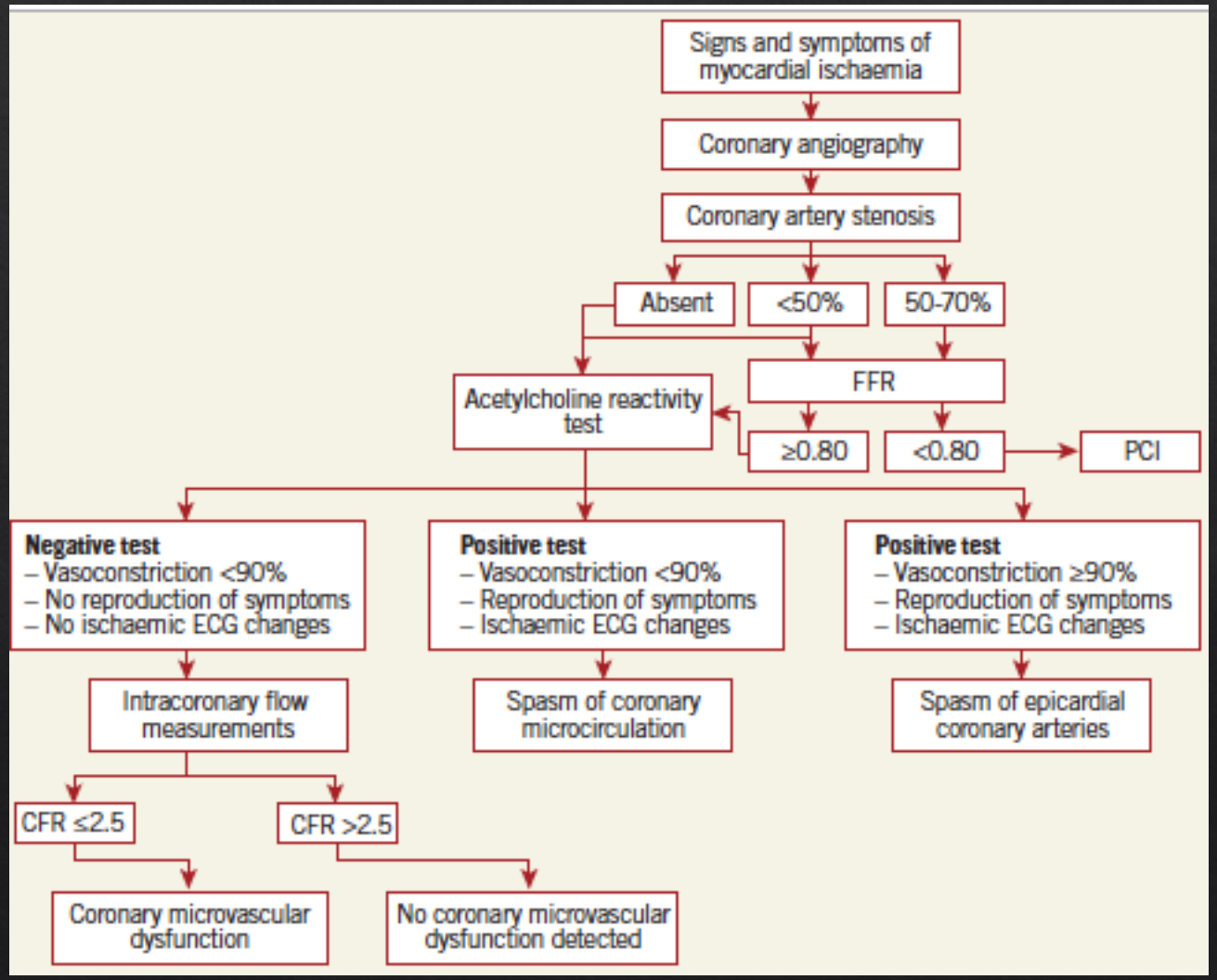
Table 3. Continued

Test	Protocol	Monitoring	Interpretation	Ref. #
Myocardial contrast echocardiography	Intravenous administration of an ultrasound contrast agent (microbubbles of sulfur hexafluoride surrounded by a phospholipid shell) and adenosine (0.14 mg/kg/min for 90 s).	Contrast images are acquired in an apical 4-chamber view, and myocardial opacification is quantified in the posterior interventricular septum and lateral left ventricular by a specific software. CFR assessment: comparison of contrast intensity at rest and at peak adenosine.	Positive for coronary microvascular endothelium-independent dysfunction: CFR <2.0 in the absence of significant epicardial coronary artery stenosis.	(46)
Adenosine stress perfusion cardiac magnetic resonance	Intravenous administration of gadolinium contrast and adenosine (0.14 mg/kg/min for 3 min).	Perfusion cardiac magnetic resonance images: adenosine gadolinium first-pass imaging for assessment of stress perfusion repeated after 15 min for assessment of rest perfusion.	Positive for coronary microvascular dysfunction: Reduced or even absent gadolinium enhancement in the corresponding subendocardial layer.	(47)
Positron emission tomography perfusion imaging	Intravenous administration of a specific cardiovascular radioisotopic tracer ($^{13}NH_3$, $H_2{}^{15}O$, and ^{82}Rb) and adenosine (or dipyridamole).	MBF assessment is achieved by the quantification of the myocardial radioisotopic-tracer uptake. CFR assessment: ratio of MBF in hyperemic conditions and at rest.	Positive for coronary microvascular endothelium-independent dysfunction: CFR <2.5 in the absence of significant epicardial coronary artery stenosis.	(48)
Multislice detector computed tomography	Intravenous administration of iodinated contrast and adenosine (0.14 mg/kg/min for 5 min).	Images are analyzed by measuring the attenuation changes over time in basal and hyperemic conditions and plotting time-attenuation curves. CFR: ratio of area under the curve for the hyperemic territory to the remote territory.	Positive for coronary microvascular endothelium-independent dysfunction: CFR <2.5 in the absence of significant epicardial coronary artery stenosis.	(50)

CFR = coronary flow reserve; CFV = coronary flow velocity; ECG = electrocardiographic; FFR = fractional flow reserve; GTN = glyceryl trinitrate, nitroglycerin; IMR = index of microcirculatory resistance; ISDN = isosorbide dinitrate; LCA = left coronary artery; MBF = myocardial blood flow; RCA = right coronary artery.

Microvascular disease, what little we know

Yolande Appelman*, MD, PhD
Chair Thinktank Women & Health VU University Medical Center, Member of EAPCI-Women

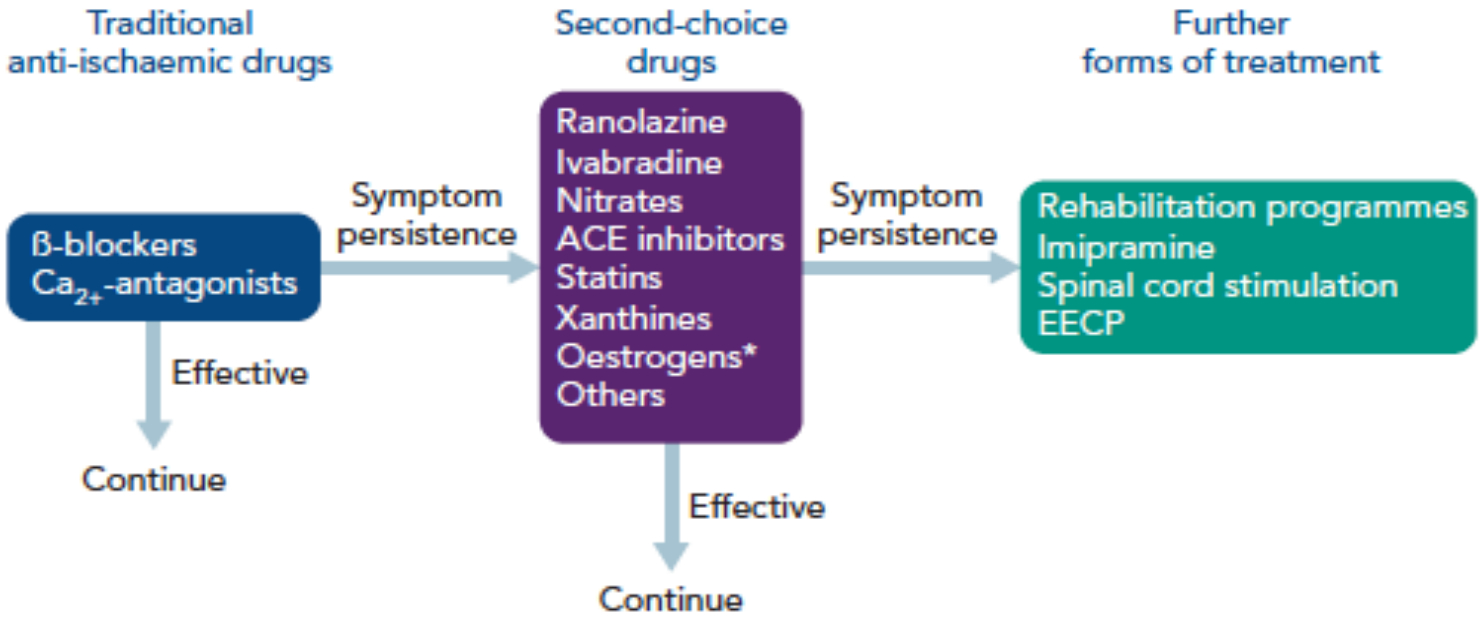


EuroIntervention 2018;

‘Primary’ Microvascular Angina: Clinical Characteristics, Pathogenesis and Management

Gaetano Antonio Lanza[1], Antonio De Vita[1] and Juan-Carlos Kaski[2]

Figure 2: Therapeutic Approach in Patients with Primary Stable Microvascular Angina



*In selected subgroups of post-menopausal women.

ESC European Society of Cardiology
European Heart Journal (2021) 42, 4592–4600
doi:10.1093/eurheartj/ehab282

Clinical characteristics and prognosis of patients with microvascular angina: an international and prospective cohort study by the Coronary Vasomotor Disorders International Study (COVADIS) Group

Initial treatment after diagnosis, *n* (%)				
Statin	424 (62)	141 (57)	283 (65)	0.04
Nitrate	295 (43)	83 (33)	212 (48)	0.0001
Calcium channel blocker	249 (36)	106 (43)	143 (33)	0.009
Beta-blocker	249 (36)	83 (33)	166 (38)	0.25
Angiotensin-converting enzyme inhibitor	169 (25)	57 (23)	112 (26)	0.49
Angiotensin II receptor blocker	117 (17)	41 (17)	76 (17)	0.78

Table 1
Differences between INOCA and MINOCA.

	INOCA	MINOCA
Symptoms	Yes	Yes
Resting EKG abnormalities	Possible	Possible
Exercise EKG abnormalities	Usually	N/A[a]
Abnormal wall motion on stress echo	Possible, but usually not	N/A
Abnormal perfusion on SPECT	Possible, but usually "breast artifact" or "probably normal"	N/A
Abnormal PET-derived myocardial flow reserve	If yes, diagnose CMD If no, could still be CMD due to a vasocontrictor problem; definitive diagnosis requires invasive coronary function testing	N/A
Troponin elevation	May have a prior history of troponin elevation, and now recurrent non-MI chest pain	Yes

[a] Not applicable in acute coronary syndrome.

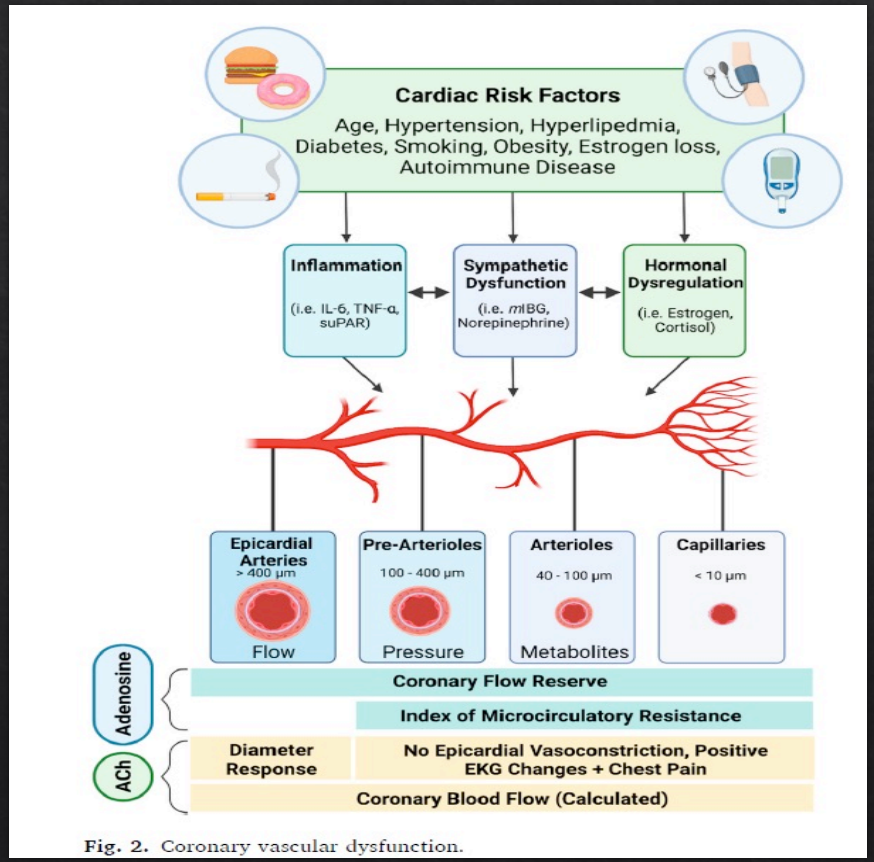
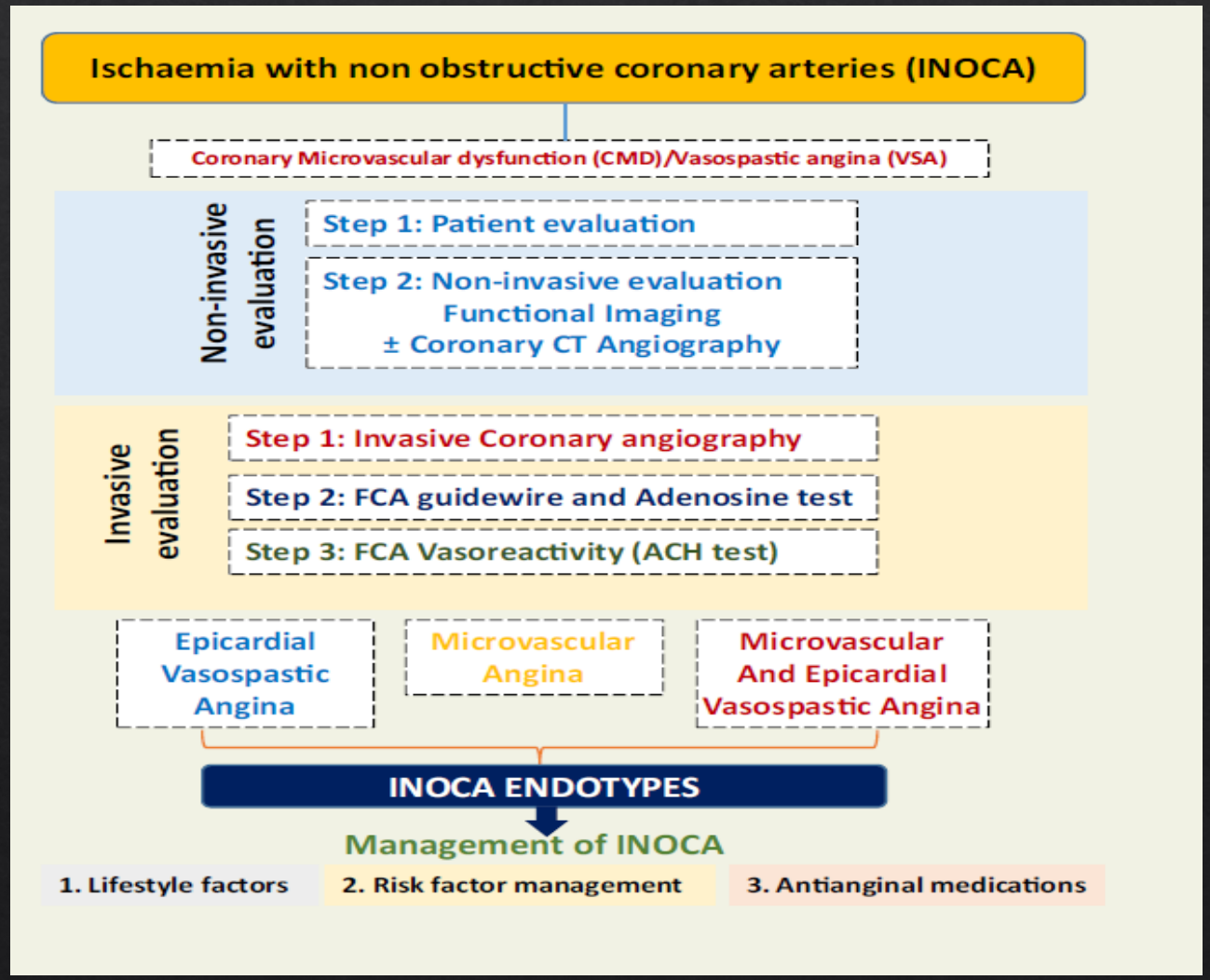


Fig. 2. Coronary vascular dysfunction.

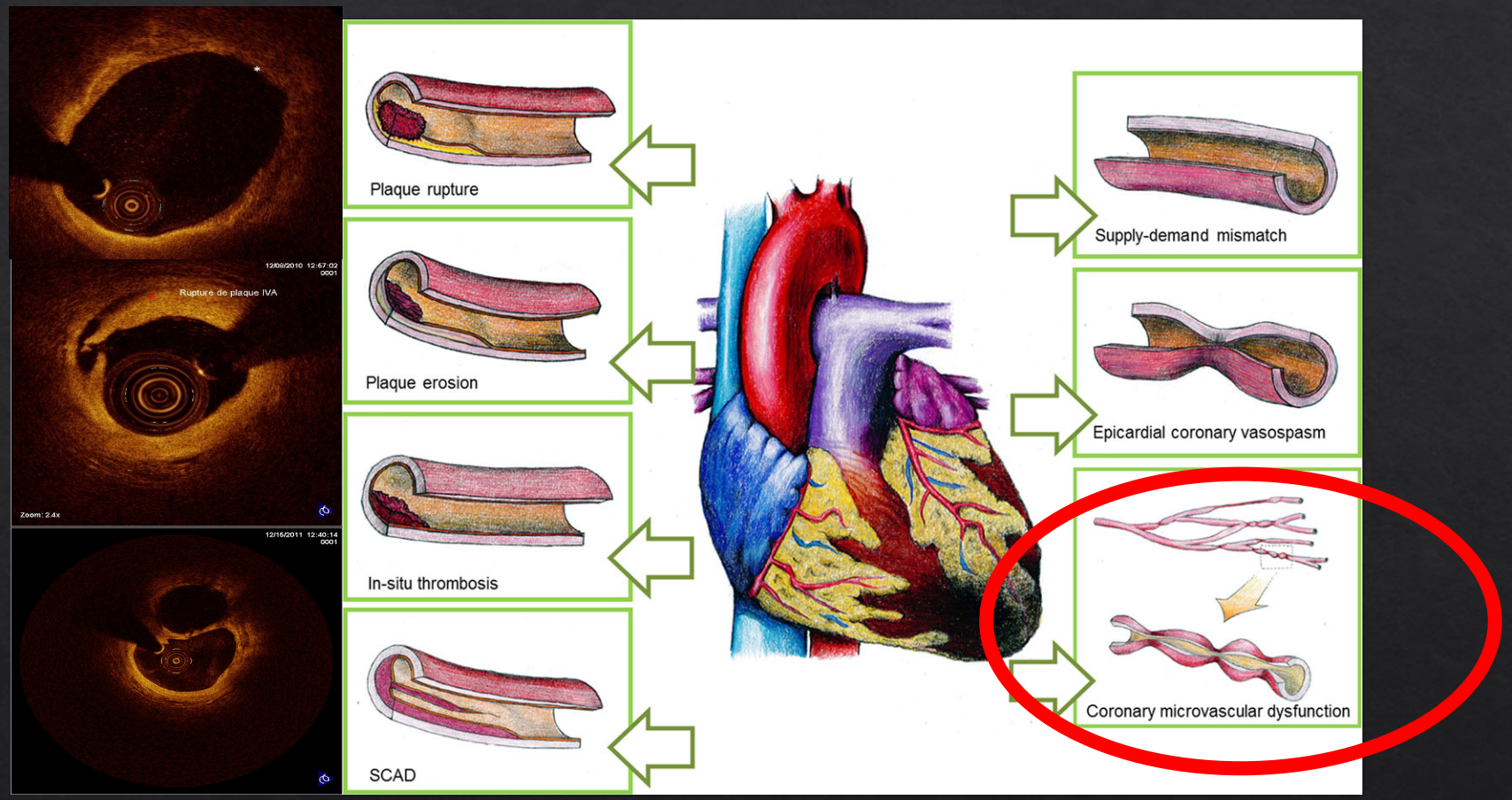
ESC European Society of Cardiology
European Heart Journal (2020) 41, 3504–3520
doi:10.1093/eurheartj/ehaa503

SPECIAL ARTICLE
Ischaemic heart disease

An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary



Chest pain without obstructive CAD- (M)INOCA

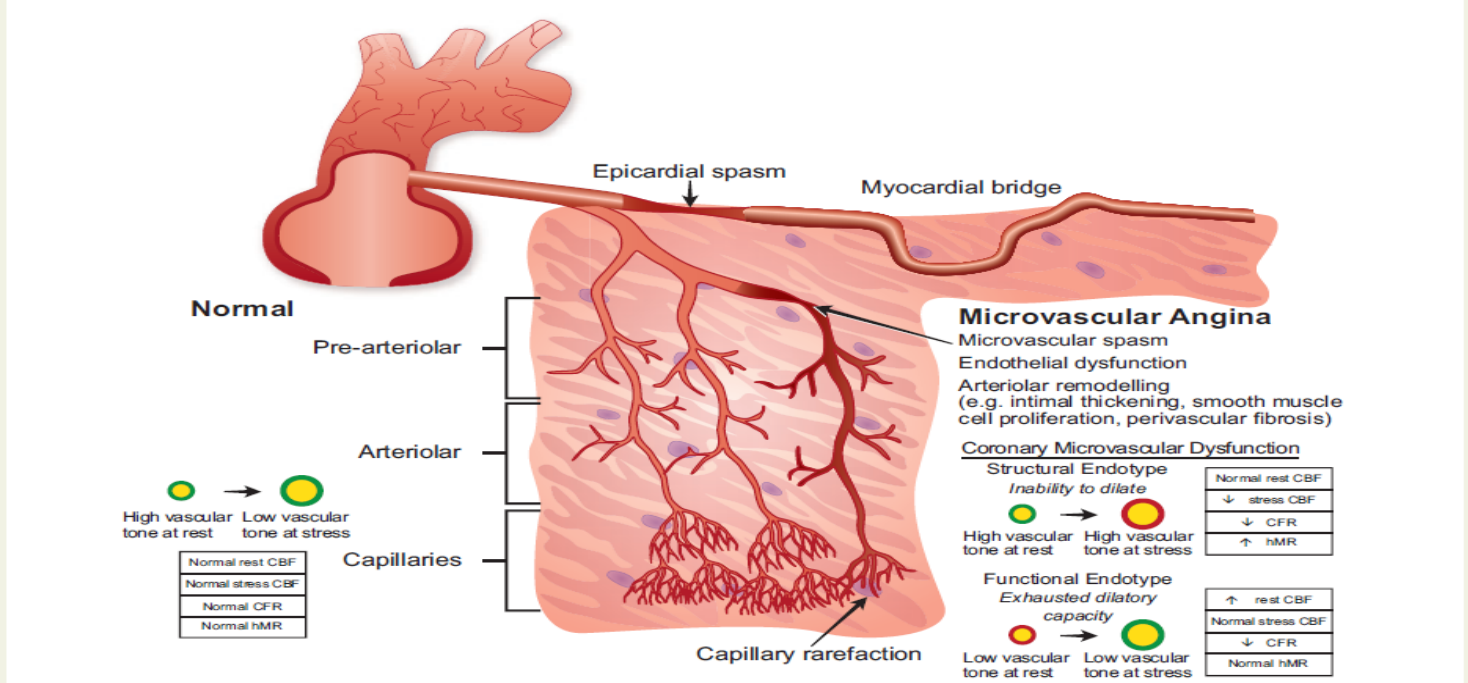


Tamis-Holland et al
Diagnosis and Management of Patients With MINOCA
Circulation. 2019;139:e891–e908

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 4601–4604
doi:10.1093/eurheartj/ehab534

EDITORIAL

Microvascular angina: quo tendimus?



Graphical abstract Summary of known mechanisms that cause ischaemia with normal coronary arteries at the level of both the epicardial coronary arteries (coronary vasospasm and intramyocardial muscle bridging) and the coronary microcirculation [microvascular spasm, endothelial dysfunction, arteriolar remodelling, two endotypes of coronary microvascular dysfunction (structural due to failure to maximally vasodilate and functional due to exhausted vasodilatory capacity), and capillary rarefaction]. cMVD, coronary microvascular dysfunction; CBF, coronary blood flow; CFR, coronary flow reserve; hMR, hyperaemic index of microcirculatory resistance.

Microvascular disease

Ce qui est une dysfonction microvasculaire….

Coronary Microvascular dysfunction:

endothelium-independent decreased ability for dilatation of the microvascular coronary arteries

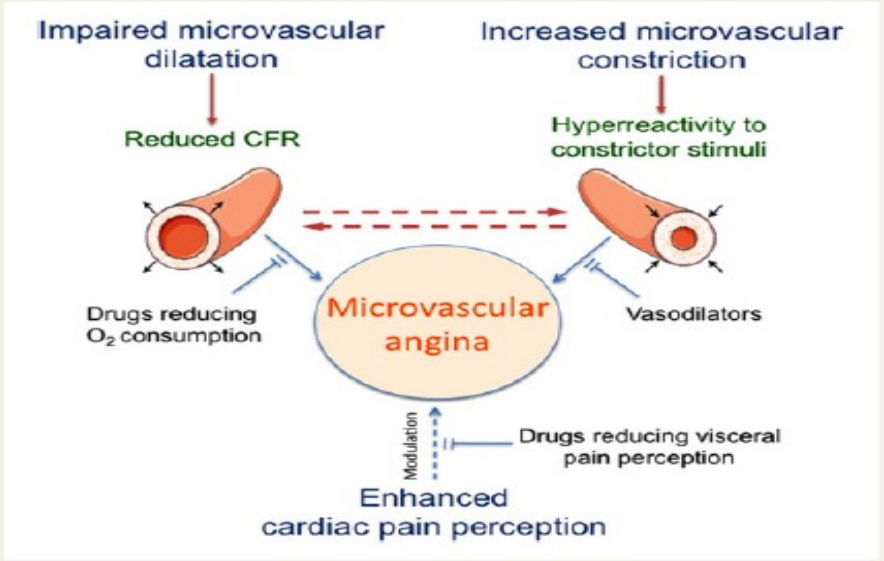


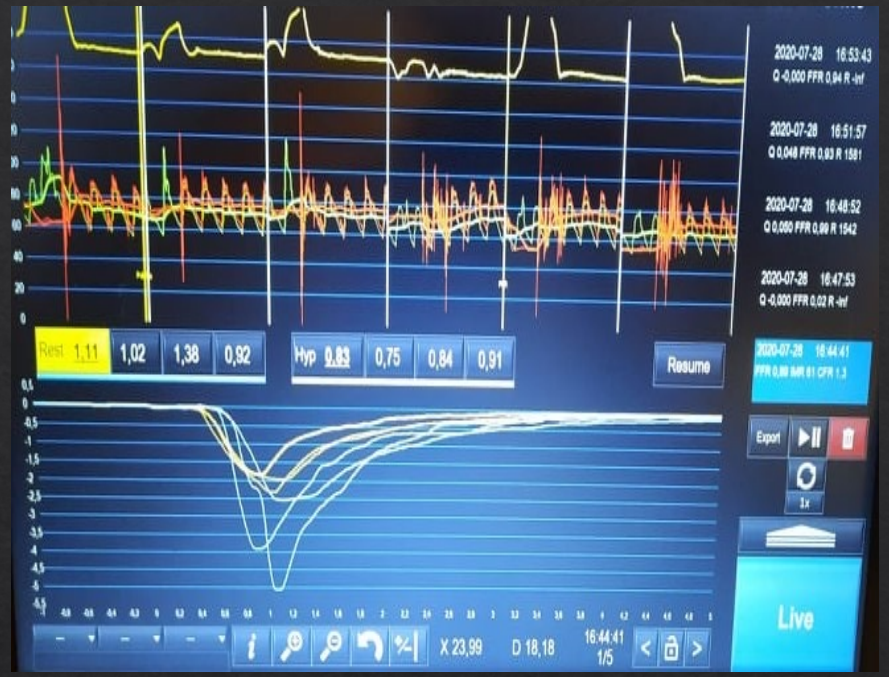
Figure 1 Pathophysiological mechanisms that can variably be involved in determining microvascular angina. CFR, coronary flow reserve.

Treatment of microvascular angina: the need for precision medicine

Filippo Crea* and Gaetano Antonio Lanza

European Heart Journal (2016) **37**, 1514–1516
doi:10.1093/eurheartj/ehw021

CASE 4



IMR:61

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