



HOT TOPICS IN CARDIOLOGIA 2022

28 e 29 Novembre 2022

Aula Magna - Centro Congressi Federico II
Via Partenope, 36 - Napoli

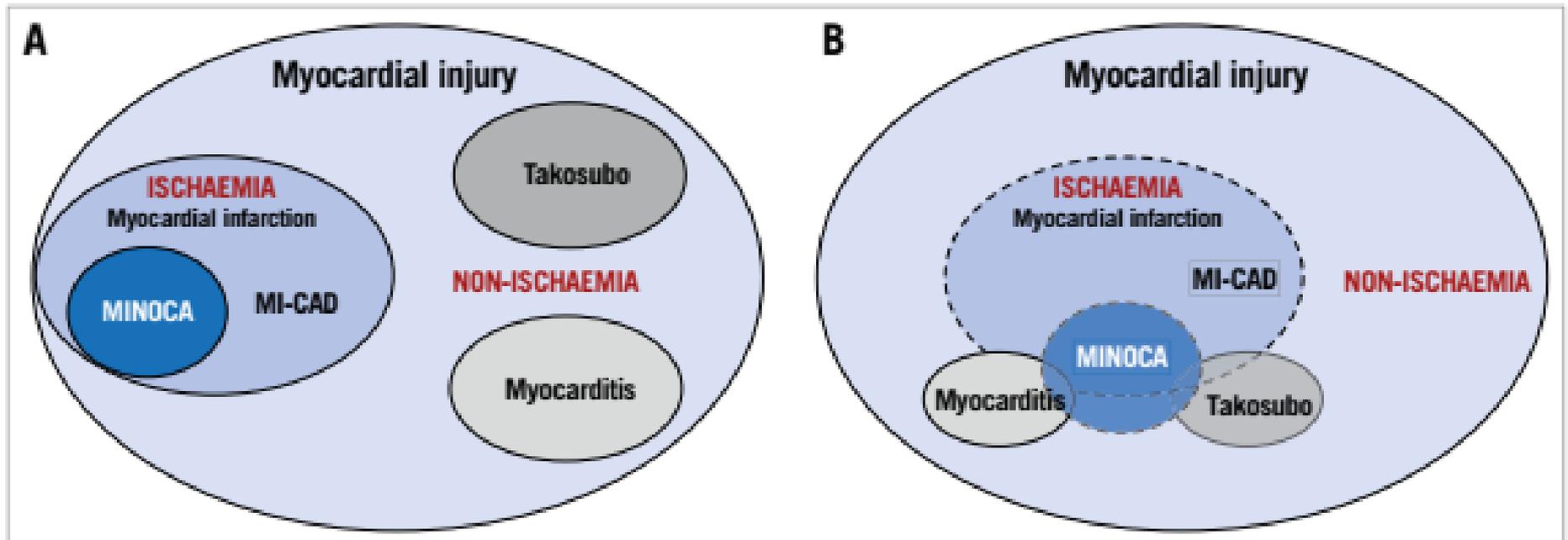
**MINOCA al
termine del
percorso
diagnostico:
quale la terapia
migliore**

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MINOCA diagnostic criteria

1. Acute myocardial infarction (modified from the "Fourth Universal Definition of Myocardial Infarction" Criteria)
Detection of a rise or fall of cTn with at least 1 value above the 99th percentile upper reference limit
and
Corroborative clinical evidence of infarction evidenced by at least 1 of the following:
Symptoms of myocardial ischemia
New ischemic electrocardiographic changes
Development of pathological Q waves
Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic cause
Identification of a coronary thrombus by angiography or autopsy
2. Nonobstructive coronary arteries on angiography:
Defined as the absence of obstructive disease on angiography (ie, no coronary artery stenosis $\geq 50\%$) in any major epicardial vessel*
This includes patients with:
Normal coronary arteries (no angiographic stenosis)
Mild luminal irregularities (angiographic stenosis $< 30\%$ stenoses)
Moderate coronary atherosclerotic lesions (stenoses $> 30\%$ but $< 50\%$)
3. No specific alternate diagnosis for the clinical presentation:
Alternate diagnoses include but are not limited to nonischemic causes such as sepsis, pulmonary embolism, and myocarditis

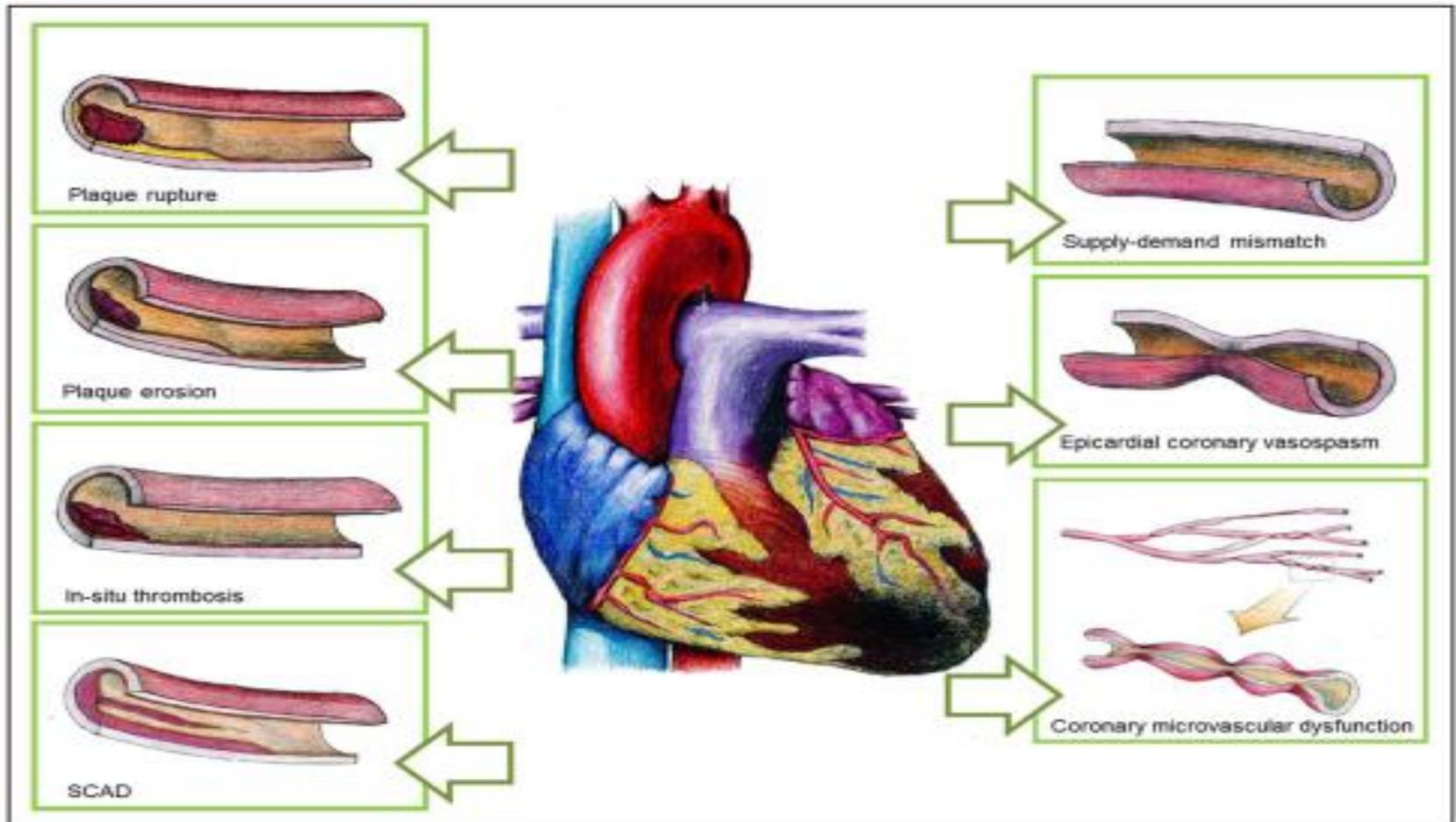
Causes of myocardial injury



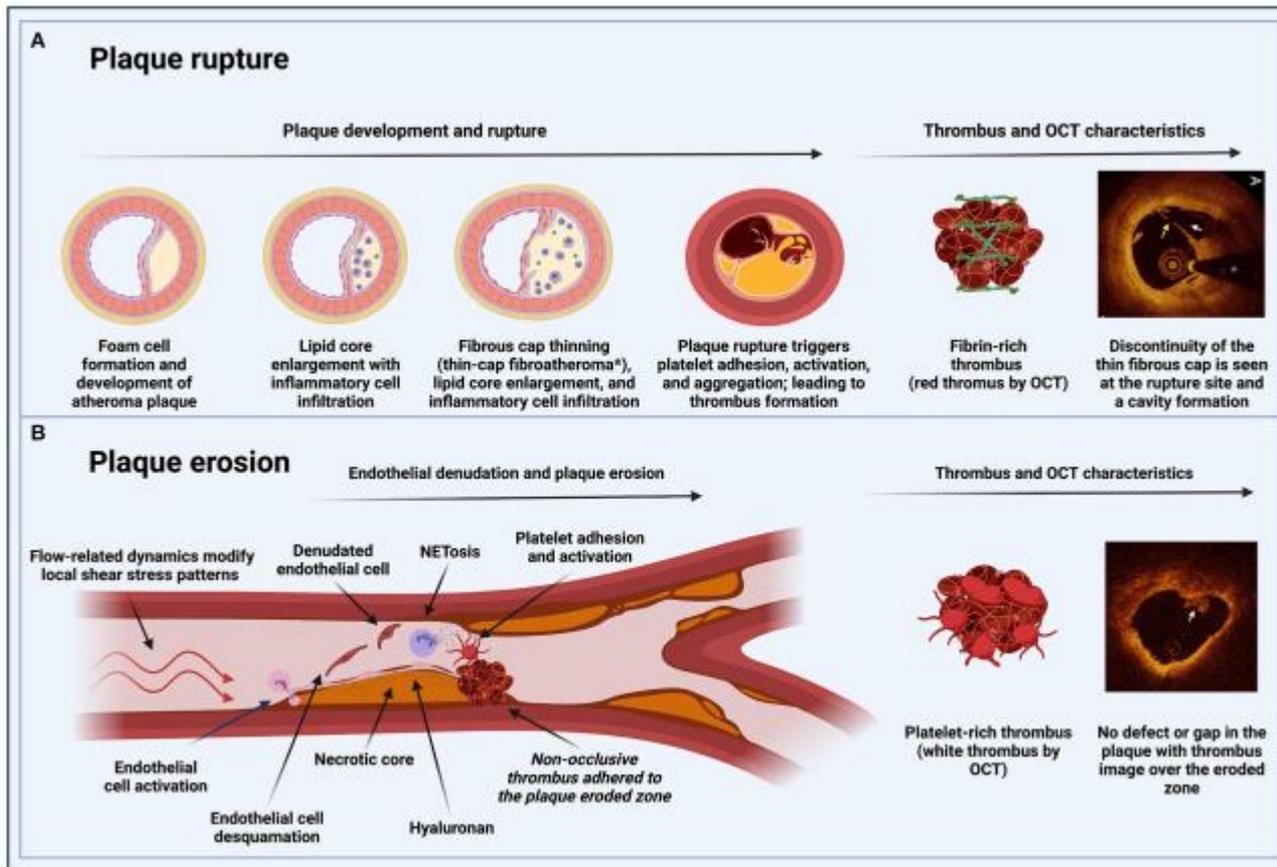
MINOCA Epidemiological data

- ▶ Accounts for 5-11% of all MIs
- ▶ No real gender differences
- ▶ Patients slightly younger than MI-CAD pts
- ▶ Fewer traditional risk factors except for hypertension
- ▶ Increased risk of death and new cardiovascular events
- ▶ Annual mortality rate 2%
- ▶ Cardiac maximal troponin level is related with prognosis
- ▶ 8-25% of MINOCA cause remains undetermined

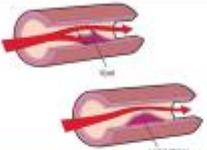
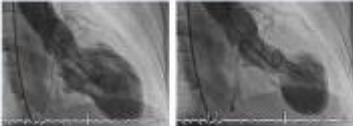
Pathogenesis



Atherosclerotic patients

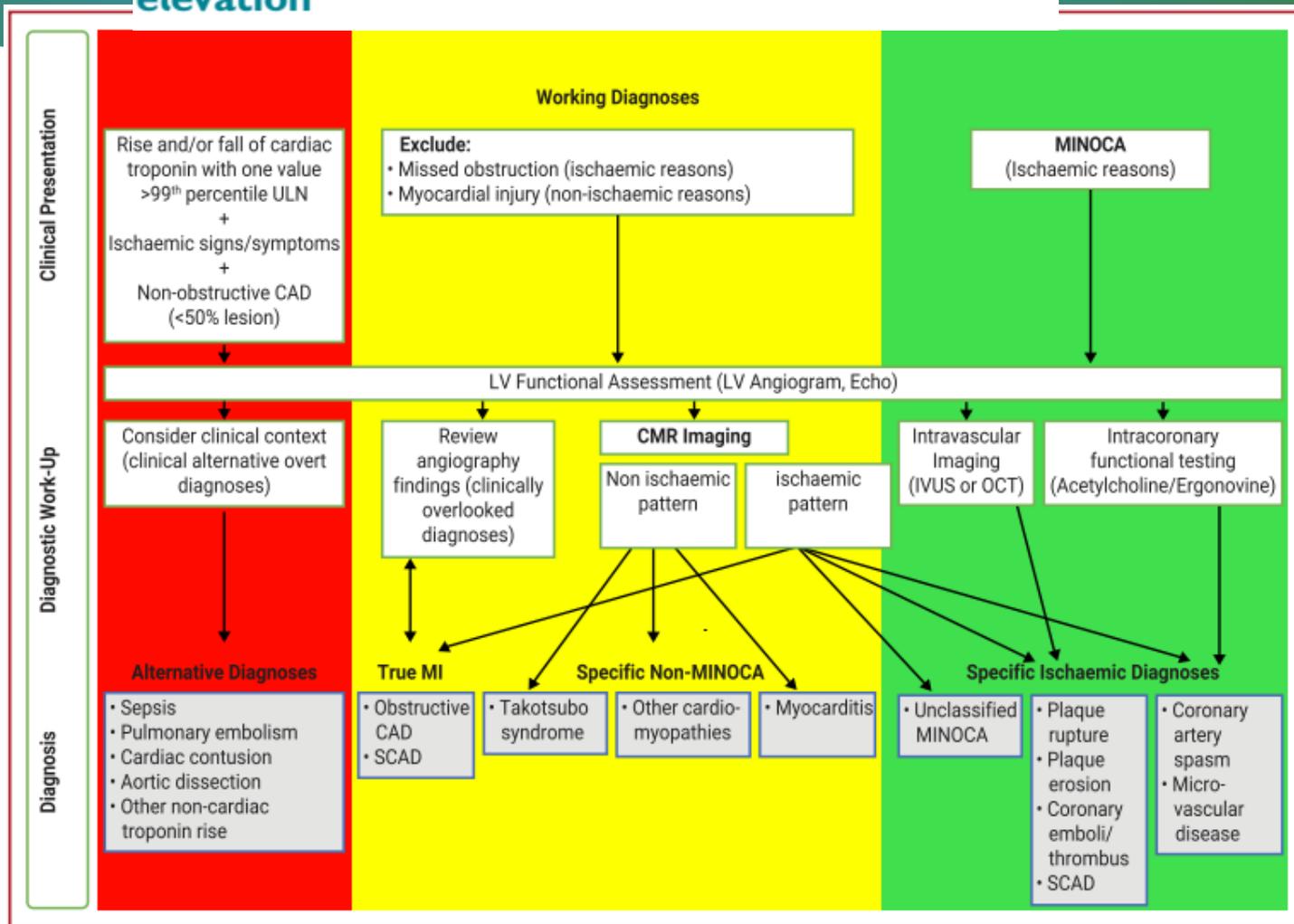


No atherosclerotic patients

Coronary microvascular dysfunction		 <p>Due to endothelial dysfunction or reperfusion injury, the intense inflammatory reactions produce NETosis, followed by microvascular spasm may lead to platelet adhesion, activation, and thrombus formation</p>
Spontaneous coronary artery dissection		<p>Flow obstruction may be related to platelet adhesion, activation, and aggregation with the subsequent thrombus formation</p>
Takotsubo syndrome		<p>No clear relationship between Takotsubo syndrome and platelet function</p>
Epicardial coronary artery spasm		<p>No clear relationship between epicardial coronary spasm and platelet function. However, some authors have suggested that coronary spasm associated with MI causes platelet activation and aggregation</p>



2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation



2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Pharmacological therapy with aspirin, statins, angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs), and calcium channel blockers (in case vasospasm is still suspected) as routine treatment may be suggested.³⁹⁶ These medications have shown significant long-term beneficial effects in terms of all-cause mortality (statins, beta-blockers), cardiovascular death (statins), AMI (beta-blockers), stroke (statins), and MACE (statins, ACE inhibitor/ARB) at 12 months in a national registry.³⁹⁷ However, this registry did not apply current MINOCA criteria,³⁹⁷ therefore, the conclusions drawn must be interpreted with caution.

Recommendations

Recommendations	Class ^a	Level ^b
In all patients with an initial working diagnosis of MINOCA, it is recommended to follow a diagnostic algorithm to differentiate true MINOCA from alternative diagnoses.	I	C
It is recommended to perform CMR in all MINOCA patients without an obvious underlying cause. ³⁷⁰	I	B
It is recommended to manage patients with an initial diagnosis of MINOCA and a final established underlying cause according to the disease-specific guidelines.	I	C
Patients with a final diagnosis of MINOCA of unknown cause may be treated according to secondary prevention guidelines for atherosclerotic disease.	IIb	C

MINOCA

Observational studies on pharmacological secondary treatment

Drug class	Study	Association with outcome (MACE)
Dual antiplatelet therapy/P2Y ₁₂ inhibitors	Lindahl et al ⁸³	Non-significant
	Kovach et al ⁸⁴	Non-significant
	Abdu et al ⁸⁵	Non-significant
	Ciliberti G. et al ⁸⁶	Non-significant
	Paolisso P. et al ⁸⁷	Non-significant
Statins	Lindahl et al ⁸³	Decrease
	Kovach et al ⁸⁴	Decrease
	Abdu et al ⁸⁵	Decrease
	Ciliberti G. et al ⁸⁶	Non-significant
	Paolisso P. et al ⁸⁷	Non-significant
Beta-blockers	Lindahl et al ⁸³	Non-significant
	Kovach et al ⁸⁴	Non-significant
	Abdu et al ⁸⁵	Non-significant
	Ciliberti G. et al ⁸⁶	Decrease
	Paolisso P. et al ⁸⁷	Non-significant
ACEI/ARB	Lindahl et al ⁸³	Decrease
	Kovach et al ⁸⁴	Decrease
	Abdu FA. et al ⁸⁵	Decrease
	Ciliberti G. et al ⁸⁶	Non-significant
	Paolisso P. et al ⁸⁷	Decrease
Calcium channel blockers	Kovach et al ⁸⁴	Non-significant
	Ciliberti G. et al ⁸⁶	Non-significant

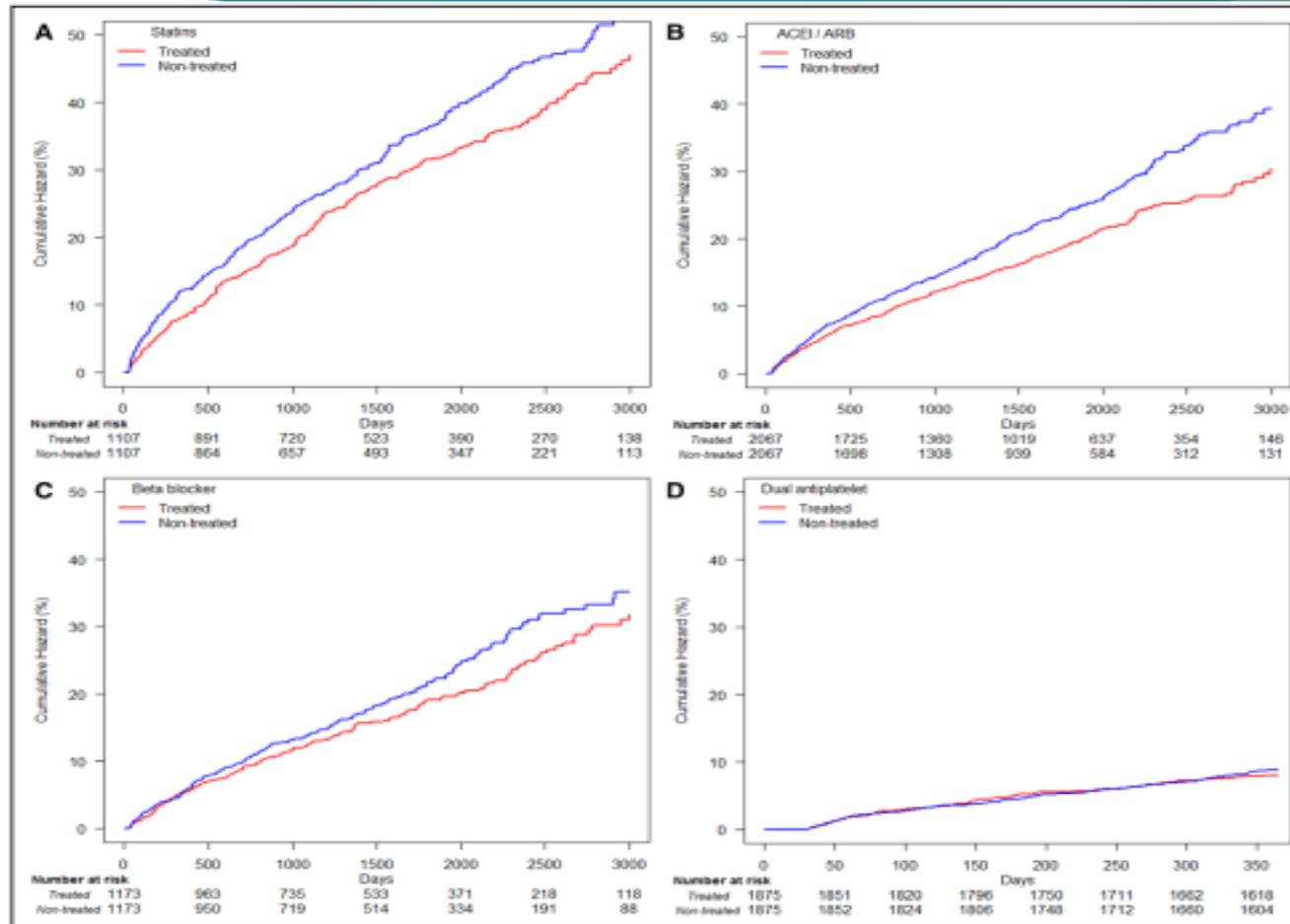
MACE: major adverse cardiac events

Medical Therapy for Secondary Prevention and Long-Term Outcome in Patients With Myocardial Infarction With Nonobstructive Coronary Artery Disease

Total, n	9136
Demographics	
Age, y (\pm SD)	65.3 \pm 11.4
Female, %	61.0
Medical history, %	
Hypertension	57.6
Diabetes mellitus	16.5
History of CHF	6.6
History of AMI	7.6
History of stroke	7.0
History of bleeding	6.7
History of cancer	1.8
Dementia	0.2
COPD	8.0
Peripheral vascular disease	1.8
Atrial fibrillation	11.1
Current smoking	20.0
ECG changes on admission, %	
ST-segment elevation	17.1
Laboratory values on admission	
Creatinine, μ mol/L (\pm SD)	80.7 \pm 39.8
LDL cholesterol, mmol/L (\pm SD)	3.1 \pm 1.0

Medications on admission, %	
Aspirin	22.9
Other antiplatelets	3.6
Warfarin	5.1
β -Blockers	27.4
ACE -inhibitors	16.5
ARB	12.0
Statins	19.0
Medications at discharge, %	
Aspirin	90.1
Other antiplatelets	69.7
Warfarin	8.9
β -Blockers	83.4
ACE inhibitors	49.5
ARB	13.7
Statins	84.5

Medical Therapy for Secondary Prevention and Long-Term Outcome in Patients With Myocardial Infarction With Nonobstructive Coronary Artery Disease



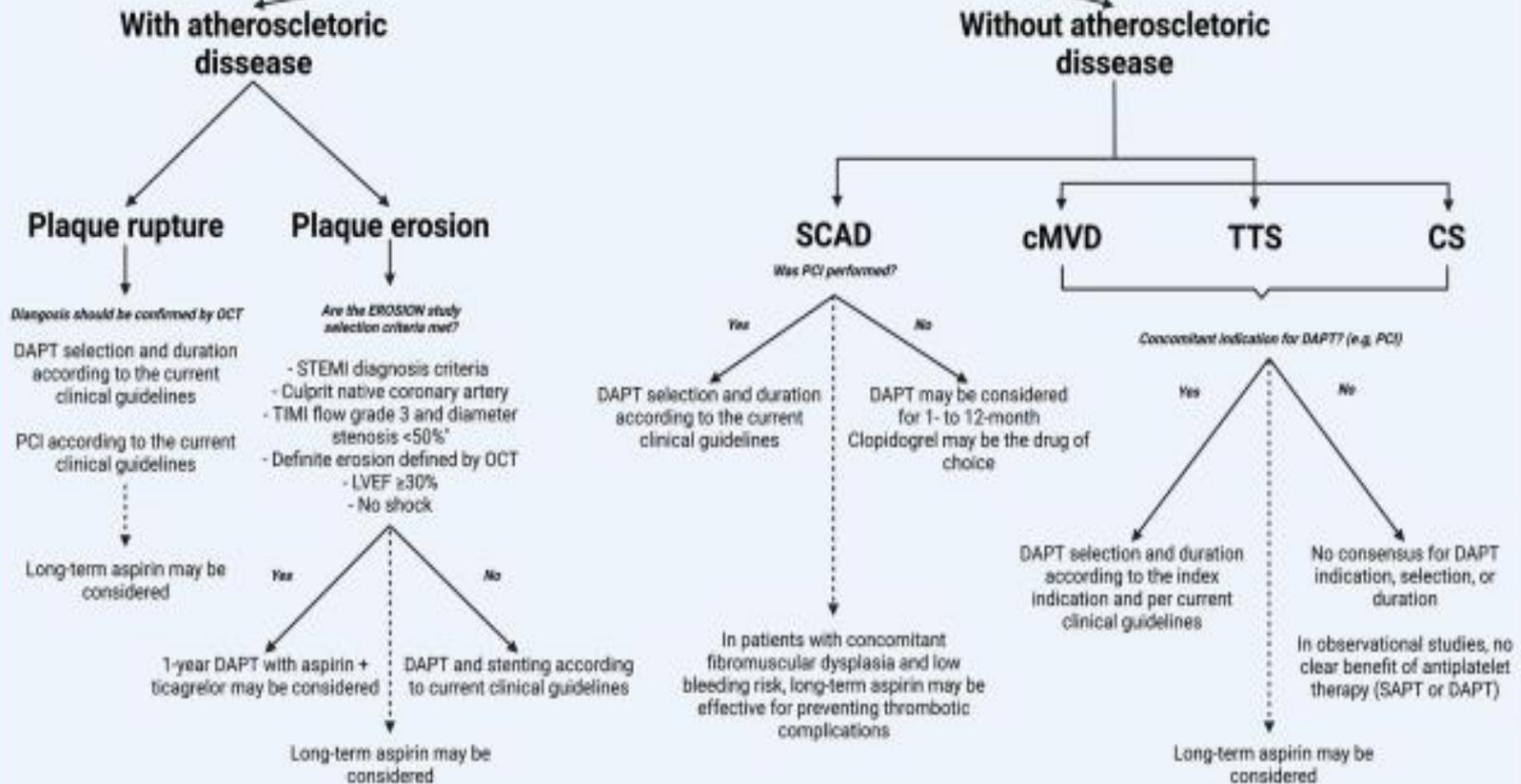
Medical Therapy for Secondary Prevention and Long-Term Outcome in Patients With Myocardial Infarction With Nonobstructive Coronary Artery Disease



	Statins n=7512	ACEI/ARB n=5904	β -Blockers n=6362	DAPT* n=8118
MACE	0.77 (0.68–0.87)	0.82 (0.73–0.93)	0.86 (0.74–1.01)	0.90 (0.74–1.08)
All-cause mortality	0.66 (0.57–0.77)	0.87 (0.74–1.02)	0.81 (0.66–0.99)	0.75 (0.56–1.01)
CV mortality	0.59 (0.47–0.75)	0.91 (0.70–1.18)	0.80 (0.57–1.14)	0.87 (0.54–1.40)
AMI	0.88 (0.68–1.13)	0.83 (0.67–1.03)	0.74 (0.56–0.97)	1.02 (0.71–1.47)
Stroke	0.67 (0.50–0.90)	0.80 (0.60–1.06)	0.97 (0.66–1.41)	0.82 (0.52–1.30)
CHF	0.88 (0.70–1.12)	0.92 (0.70–1.21)	0.88 (0.62–1.23)	0.83 (0.58–1.17)
Bleeding events	0.99 (0.70–1.39)	1.04 (0.75–1.43)	0.92 (0.63–1.35)	1.33 (0.73–2.42)

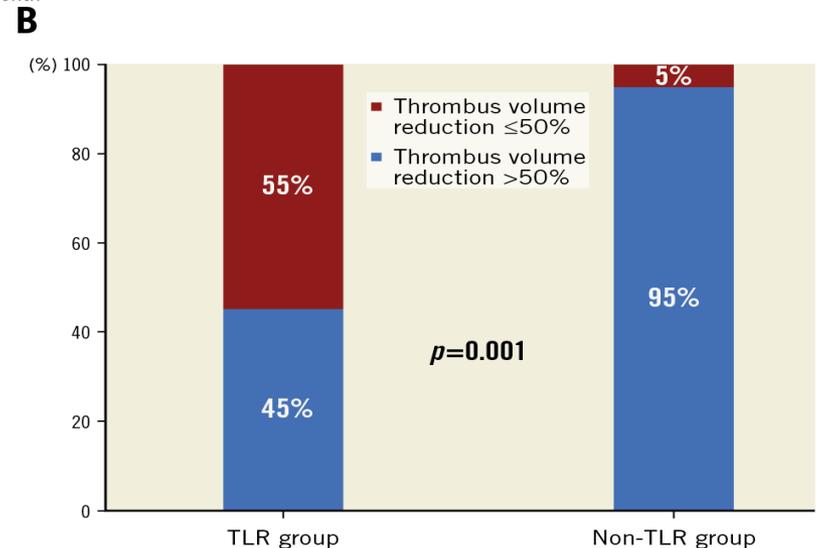
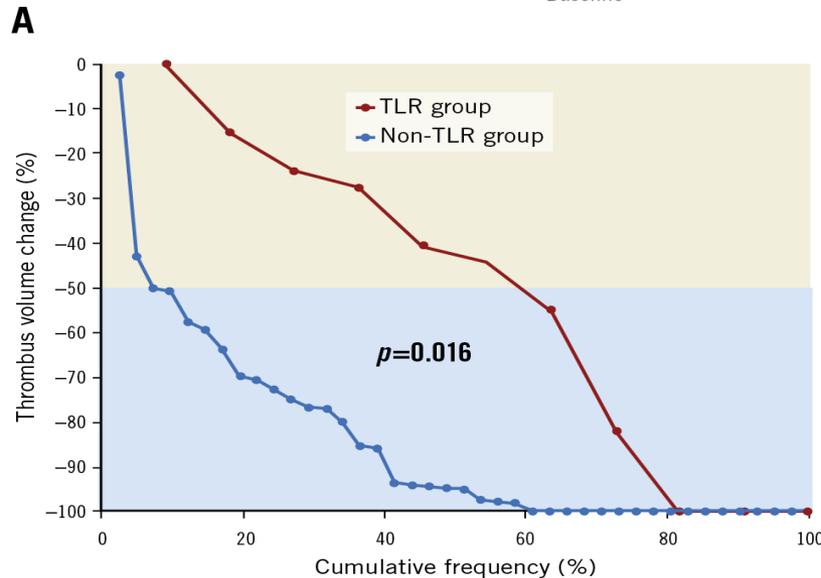
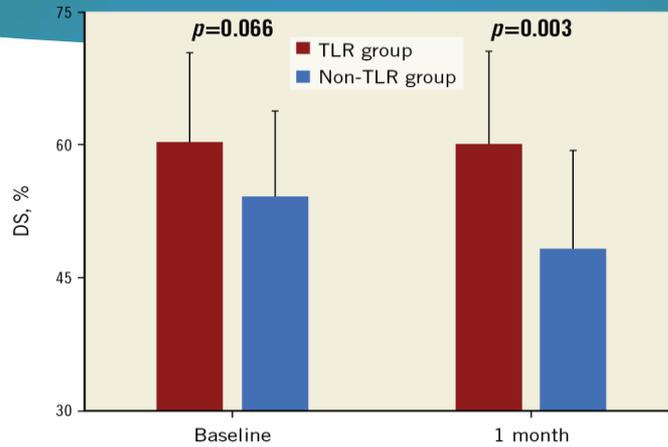
	Statins	ACEI/ARB	β -Blockers	DAPT*
Women	0.80 (0.69–0.94) n=4550	0.75 (0.64–0.88) n=3557	0.89 (0.73–1.08) n=3817	0.86 (0.68–1.09) n=4995
Men	0.70 (0.57–0.85) n=2967	0.95 (0.78–1.16) n=2347	0.82 (0.64–1.06) n=2545	0.92 (0.68–1.25) n=3123
<70 y	0.73 (0.60–0.90) n= 4718	0.96 (0.80–1.15)† n=3861	0.88 (0.70–1.10) n=4192	0.83 (0.60–1.13) n=5066
\geq 70 y	0.85 (0.72–0.99) n=2799	0.74 (0.63–0.87)† n=2043	0.83 (0.68–1.03) n=2170	0.96 (0.76–1.21) n=3052

Antiplatelet therapy in MINOCA patients



	ACEi/ ARB	Beta Blockers	Antiplat./ Anticoag.	CCB	Statins	PCI	Others
Plaque disruption/erosion	+++	++-	+++	+--	+++	++- Sel. cases	
Spontaneous Coronary Artery Dissection	? *	++- **	++- (ASA) **	?	?	+-- Sel. cases	DISCO Registry failed *SAFER SCAD Trial ongoing **BA-SCAD Trial ongoing
Coronary artery spasm	?	---	+-- (ASA low dose)	+++	+--	+-- Sel Cases	Red. Stress, physical activity. Long acting nitrates ++- Nicorandil +--, Cilostazol
Coronary Embolism/Thrombosys	?	?	+++ (Anticoagulant)	?	+--	+--	Remove etiological factor Aspiration thrombectomy
Microvascular Dysfunction	++-	+--	?	+--	++-	?	Unconventional therapies (ranolazine, l-arginine, dipyridamole, etc) SGLT2 inhibitors ?
Supply/demand mismatch							Treat underlying disease

Predictors of non-stenting strategy for acute coronary syndrome caused by plaque erosion: four-year outcomes of the EROSION study



Antiplatelet therapy in patients with conservatively managed spontaneous coronary artery dissection from the multicentre DISCO registry

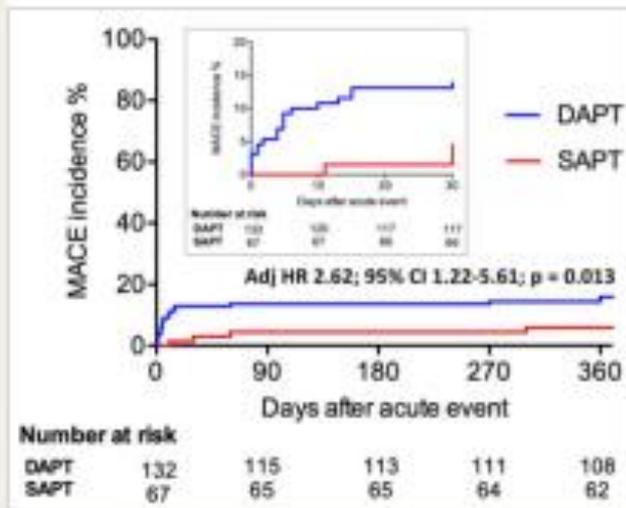


International DISCO SCAD Registry SCAD conservatively treated* (n=199)

Antiplatelet regimen according to physician's choice

DAPT
N = 132 (66%)

SAPT
N = 67 (34%)



AHA SCIENTIFIC STATEMENT

Contemporary Diagnosis and Management of Patients With Myocardial Infarction in the Absence of Obstructive Coronary Artery Disease

A Scientific Statement From the American Heart Association

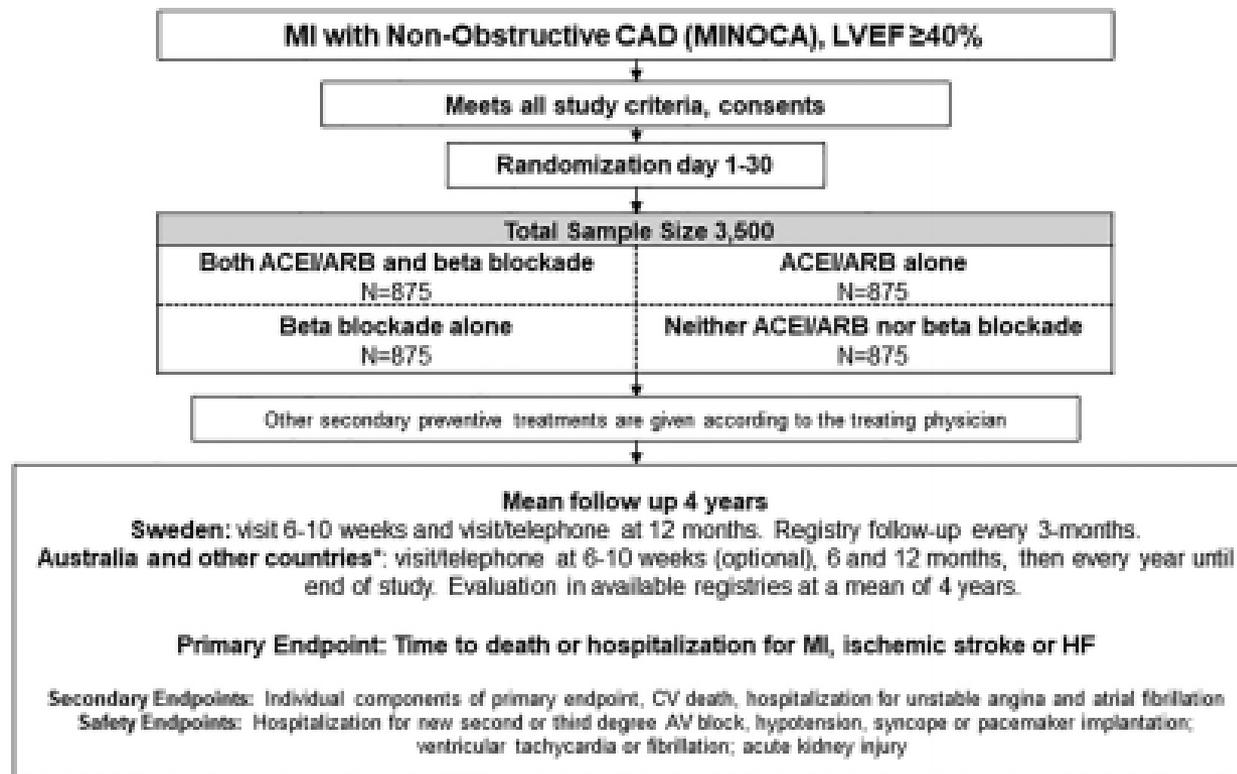
Ischemic presentation (MINOCA)		
Plaque disruption	Angiographic review Intravascular imaging (IVUS or OCT)	Aspirin High-intensity statin β -blockers (in presence of left ventricular dysfunction, and possibly with preserved EF) ACE inhibitors/ARBs (in presence of left ventricular dysfunction, and possibly with preserved EF) Consider clopidogrel/ticagrelor
Coronary artery spasm	Resolution with coronary vasodilators (eg, intracoronary nitroglycerin) Provocative spasm testing Blood toxicology testing Review of medication and nonprescription drug use (eg, migraine medications, cocaine)	Calcium channel blockers Other antispastic agents (nitrates, nicorandil, cilostazol) Consider statin
Coronary microvascular dysfunction	Angiographic review Coronary microvascular functional testing	Conventional antianginal therapies (eg, calcium channel blocker, β -blocker) Unconventional antianginal therapies (eg, L-arginine, ranolazine, dipyridamole, aminophylline, imipramine, α -blockers)
Coronary embolism/thrombus	Angiographic review Intravascular imaging (IVUS or OCT) Thrombophilia screen	Antiplatelet or anticoagulant therapy Other targeted therapies for hypercoagulable condition
Spontaneous coronary artery dissection	Angiographic review Intravascular imaging (IVUS or OCT)	Aspirin β -blocker Consider clopidogrel
Supply-demand mismatch	Review history for potential stressors	Treatment for underlying condition





Randomized evaluation of beta blocker and ACE-inhibitor/angiotensin receptor blocker treatment in patients with myocardial infarction with non-obstructive coronary arteries (MINOCA-BAT): Rationale and design

Anna M Nordenskjöld, MD, PhD,^a Stefan Agewall, MD, PhD,^b Dan Atar, MD, PhD,^b Tomasz Baron, MD, PhD,^c John Beltrame, BMBS, PhD,^d Olle Bergström, MD,^e David Erlinge, MD, PhD,^f Chris P Gale, PhD, FRCP,^g Javier López-Pais, MD,^h Tomas Jernberg, MD, PhD,ⁱ Pelle Johansson,^j Annica Ravn-Fisher, MD, PhD,^k Harmony R. Reynolds, MD,^l Jithendra B. Somaratne, MBChB, FRACP, PhD,^m Per Tornvall, MD, PhD,ⁿ and Bertil Lindahl, MD, PhD^c Örebro, Uppsala, Lund, Stockholm, Sweden Adelaide, Australia Leeds, UK and NYU Grossman School of Medicine, New York



*Additional countries to be recruited may require customized follow up schedules, which will be accommodated as long as the overall trial goals can be achieved.

Ongoing trials with antiplatelet agents

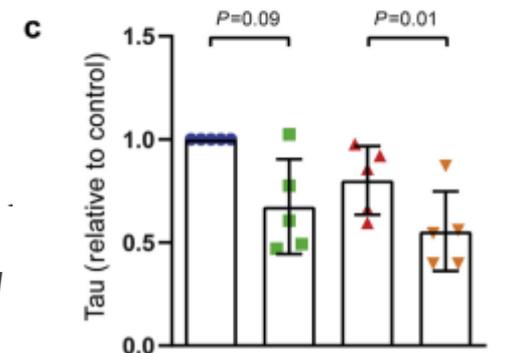
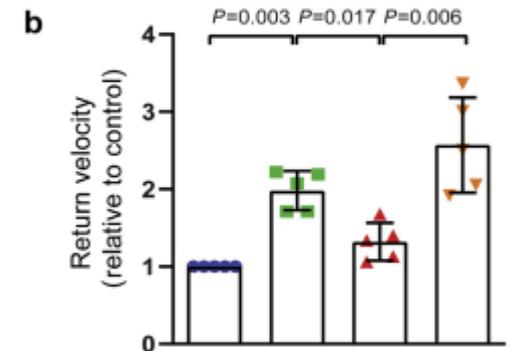
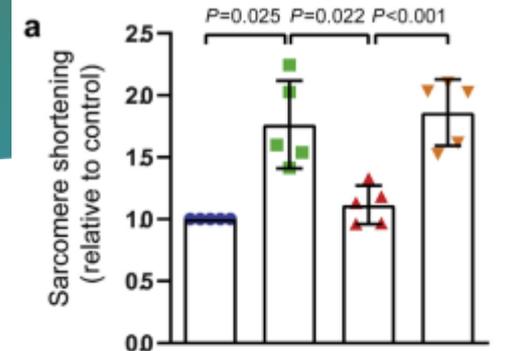
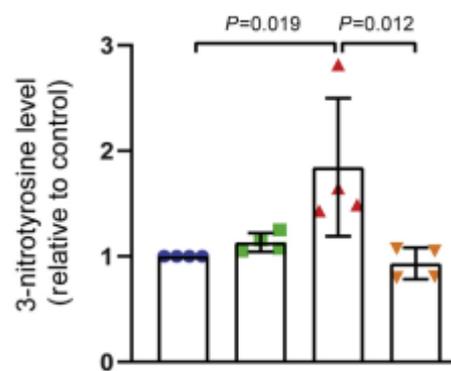
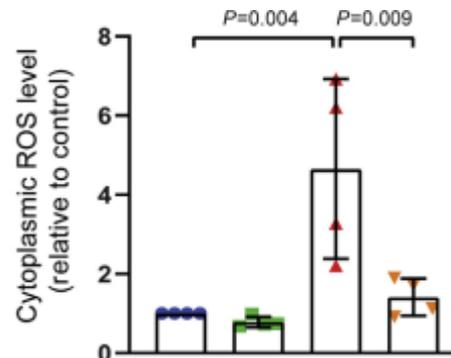
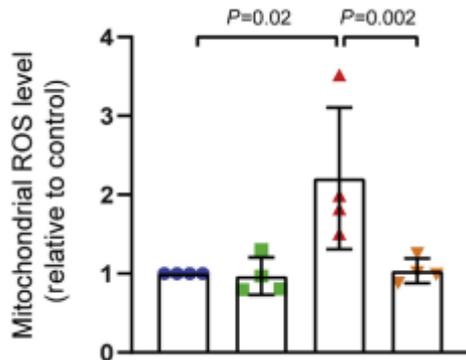
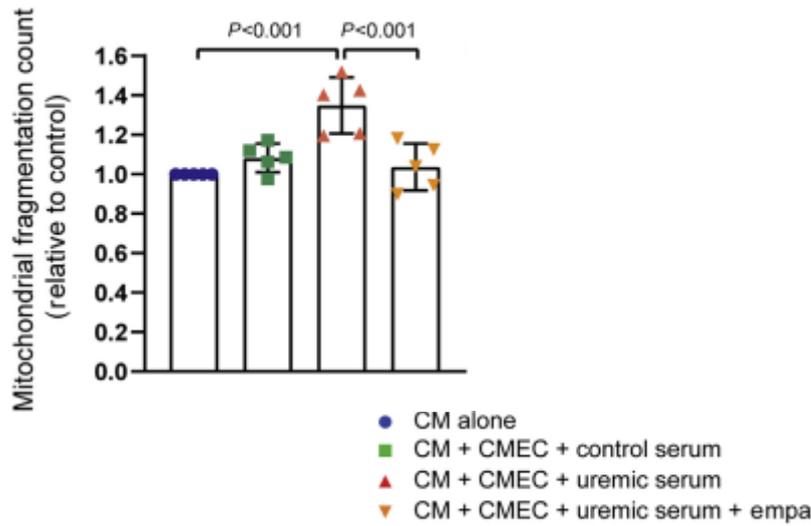
Serpytis R et al Am J Med . 2022 Jan;135(1):103-109

Randomized Pilot Trial on Optimal Treatment Strategy, Myocardial Changes, and Prognosis of Patients with Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA)

Alfonso F et al Rev Esp Cardiol 2022 Jun;75(6):515-522.

Rationale and design of the BA-SCAD (Beta-blockers and Antiplatelet agents in patients with Spontaneous Coronary Artery Dissection) randomized clinical trial

Empagliflozin restores chronic kidney disease–induced impairment of endothelial regulation of cardiomyocyte relaxation and contraction



Myocardial infarction with non obstructive coronary artery
MINOCA

Perform IVUS or OCT

Plaque disruption:

Plaque erosion
Plaque rupture
Calcified nodule

Perform CMR
Ischemic pattern

Treat with DAPT (prefer ticagrelor) and statin

Coronary thromboembolism

Embolic source assessment

Search for causes (TEE, CMR, thrombophilic screening)

Treat with OAC antiplatelet therapy if CAD

Coronary vasospasm

Endothelial damage and microthrombi

Perform provocative test

CCB, nitrates, cilostazol

Takotsubo syndrome

Exclusion of CAD

Perform CMR (no LGE)

ACEi, ARB, BB, SAPT and statin if CAD

Spontaneous coronary dissection

Imaging characterization of true and false lumen

Treat with SAPT or DAPT, BB

Conclusions and Future Directions

- ▶ **Gap in our knowledge of this heterogeneous entity**
- ▶ **Determine the specific cause for every patient**
- ▶ **Once the cause is established targeted evidence based treatment should be instituted to improve clinical outcomes and lower the cost**
- ▶ **Large therapy trials population is needed for every pathophysiological mechanism to test drug efficacy**
- ▶ **New specific code for MINOCA in the ongoing revision of *ICD Classification of Disease-Tenth Revision* to facilitate patients individuation**