MINOCA Consensus Statement. Myocardial Infarction with Nonobstructive Coronary Arteries / Abridged version

Supplementary Material

Table 1. Differences between plaque rupture and erosion

Plaque rupture	Plaque erosion
Fibrous cap rupture	Intact fibrous cap
Large necrotic nucleus	Small necrotic nucleus
High macrophage density, scant collagen	Presence of smooth muscle cells; rich in hyaluronic acid
Underlying thrombus rich in red blood cells and fibrin (red thrombus)	Underlying thrombus rich in platelets (grey thrombus)
More frequent in STEMI	More frequent in NSTEMI

Table 2. Technical characteristics and sensitivity of OCT and IVUS to detect atherosclerotic lesions

Technical differences	OCT	IVUS
Wave length	Light waves; 1.3 µ	Sound wave; 20-40 MHz
Resolution	12-15 µm axial 20-40 µm lateral	35-80 µm 100-200 µm axial 200-300 µm lateral
Images	100 frames/s	30 frames/s
"Pull-back" velocity	20 mm/s	0.5-1 mm/s
Maximum visible diameter	9.7 mm	15 mm
Tissue penetration	1.0-2.5 mm	10 mm
Characterization of atherosclerotic lesions according to the method		
Necrortic core	++	+
Cap	+++	–
Thrombus	+++	+
Dissection	+++	++
Calcium	++	+++

Tabla 3. Differential diagnosis between plaque rupture and erosion by OCT

Plaque rupture	Fibrous cap rupture, with or without intraluminal thrombi. A cavity may be observed for necrotic nucleus drainage.
Definite plaque erosion	Intact fibrous cap, with or without intraluminal thrombi (images show absence of rupture).
Probable plaque erosion	Type 1: when the fibrous cap is intact, no thrombosis but an irregular surface is observed. Type 2: when thrombosis does not allow to see the underlying plaque and there is no lipid deposit or proximal or distal thrombus calcification.

Tabla 4. Differential diagnosis between embolism and thrombosis on a ruptured plaque

Major criteria
• Angiographic evidence of embolism/coronary thrombus.
• Coronary emboli in multiple coronary vessels.
• Associated left ventricular systemic embolization without thrombi, attributable to an acute myocardial infarction.
• Histological evidence of the venous origin of coronary embolism.
• Evidence of an associated embolic source (based on TTE, TEE, CT scan and CMR imaging studies. For example: Thrombus in left atrial appendage).
Minor criteria
• Angiographic stenosis <25% in non-culprit coronary vessels.
• Atrial fibrillation.
• Embolic risk factors, cardiomyopathy, rheumatic heart disease, prosthetic valve, patent foramen ovale, atrial septal defect, history of heart surgery, infective endocarditis or hypercoagulability states.
Diagnosis (adapted from diagnostic criteria by Shibata et al.):
• **Definite:** 2 or more major criteria or 1 major and 2 minor criteria, or 3 minor criteria.
• **Probable:** 1 major criterion and 1 minor criterion or 2 minor criteria.

Tabla 5. Diagnostic criteria of vasospastic angina (COVADIS) (58)

1. Angina respondent to nitrates, spontaneous episodes with at least one of the following criteria:
- Angina at rest (especially between night and dawn).
- Marked daytime change in the tolerance to exercise (especially in the morning).
- Hyperventilation may trigger the episodes.
- Episodes can be avoided with calcium blockers (but not with betablockers).
2. Transient ECG changes during spontaneous episodes, including some of the following criteria in two contiguous leads:
- ST-segment elevation ≥0.1 mV.
- ST-segment depression ≥0.1 mV.
- New negative U waves.
3. Definite epicardial coronary artery spasm:
- Spontaneous total or subtotal occlusion (>90%), with angina and electrocardiographic changes or in response to pharmacological (ACh/ERGO) or physiological (hyperventilation) stimuli.
Definite vasospastic angina: when all the criteria are met.
Suspicion of vasospastic angina: it responds to nitrates, but without confirmatory evidence of points 2 and 3.

Tabla 6. Diagnostic criteria of microvascular angina (COVADIS) (65)

1. Symptoms of myocardial ischemia a. Exercise- or rest-induced angina. b. Anginal equivalent (i.e., shortness of breath).
2. Absence of obstructive coronary disease (stenosis <50% or FFR >0.80) a. Coronary computed tomography angiography b. Invasive coronary angiography.
3. Objective evidence of myocardial ischemia a. Ischemic ECG changes during an episode of spontaneous chest pain. b. Chest pain induced by stress and/or ischemic ECG changes in the presence and/ or absence of transient myocardial hypoperfusion and/or reversible wall motion abnormality.
4. Evidence of coronary microvascular dysfunction a. Impaired coronary flow reserve (cut-off values according to the methodology used between ≤2.0 and ≤2.5). b. Microvascular coronary spasm, defined as reproduction of symptoms, ischemic ECG changes, but without epicardial spasm during acetylcholine testing. c. Abnormal coronary microvascular resistance indices (>25). d. Slow coronary flow, defined as CA frame count. (>25).
Definite microvascular angina: when all the criteria are met (1 to 4). **Suspicion of microvascular angina:** if ischemic symptoms are present (criterion1) with absence of obstruction (criterion 2), buy only with evidence of myocardial ischemia (criterion 3) or evidence of microvascular dysfunction (criterion 4).

1. Acetylcholine and ergonovine testing. Protocol for use

1.1 Acetylcholine testing

Protocol

- Perform in the hemodynamics lab with 12-lead electrocardiographic and invasive pressure monitoring.
- Transient right ventricular pacemaker implantation is suggested, as acetylcholine may trigger extreme bradycardias, more frequently when injected in the right coronary artery.
- Perform angiographic control in a position that allows viewing all the branches.
- Left coronary artery: A dilution of 20 µg, 50 µg, 100 µg and 200 µg Ach will be injected.
- Right coronary artery: A dilution of 20 µg, 50 µg and 80 µg Ach will be injected. (Table 7)

The injections will be completed in 20 seconds at 3-minute intervals. The electrocardiogram, arterial pressure and symptoms (angor) will be recorded 1 or 2 minutes after injection.

Table 7. Doses for Ach vasoreactivity testing

Artery	Doses	Duration of injection	Interval
Left cor.	20 µg, 50 µg, 100 µg, 200 µg	20 seconds	3 minutes
Right cor.	20 µg, 50 µg, 80 µg	20 seconds	3 minutes

1.2 Ergonovine testing

There are several protocols published. (78) For safety reasons, ERGO provocative testing is recommended with IC instead of IV injection.

Protocol

It is performed in the hemodynamics lab with 12-lead electrocardiographic and invasive pressure monitoring. The electrocardiogram, arterial pressure and symptoms (angor) will be recorded 1 minute after injection.

- Left coronary artery: a dilution of 20 µg, 50 µg and100 µg ergonovine will be injected, with a 3-minute interval between doses.
- Right coronary artery: a dilution of 20 µg and 50 µg ergonovine will be injected, with a 3-minute interval between doses. (Tables 8 and 9)

In case of symptoms or signs, the injections will be suspended and the spasm will be reversed with IC nitroglycerine 2.5 µg to 5 µg; in case of using adenosine, it will be injected at a dose of 60 µg for the left coronary artery or 40 µg for the right coronary artery. (77) (Table 10)

Table 8. Doses for ERGO vasoreactivity testing

Artery	Doses	Duration of injection	Injection interval
Left cor.	20 µg, 50 µg, 100 µg	20 seconds	3 minutes
Right cor.	20 µg, 50 µg	20 seconds	3 minutes

Tabla 9. Ergonovine preparation

Ergonovine, IM or IV injectable solution, 0.2 mg/ml.
0.2 mg/ml = 200 µg/ml.
Dilution in 10 cc of saline solution yields 20 µg per cc.
With this dilution, IC injections can be performed with a smaller syringe.
With this dilution: 1 cc = 20 µg; 2.5 cc = 50 µg y 5 cc = 100 µg.

Table 10. Reversion of ergonovine-induced spasm

Artery	NTG	Adenosine
Left cor.	2.5 to 5 µg	60 µg
Right cor.	2.5 to 5 µg	40 µg

Table 11. Safety of vasospasm testing

Complication	%	OCT	IVUS
Bradycardia or transiente atrioventricular block	3.23%	More frequent at high doses and with fast administration, especially in the right coronary artery.	Stop the infusion for a few seconds, until rhythm is recovered. Evaluate resuming the test at a slower infusion rate.
Atrial fibrillation	2.38%	Usually self-limited, although it is generally fast and poorly clinically tolerated. This will motivate test interruption which will have an undefined result.	In case of good hemodynamic tolerance, treat with antiarrhythmic drugs; in case of poor tolerance, evaluate electrical cardioversion.
Atrial fibrillation, ventricular tachycardia or need for reanimation	1.00%	Caused by acute ischemia due to flow-limiting vasospasm.	Nitroglycerin and defibrillation.
Shock and/or myocardial infarction	0.07%	Caused by multivessel or common trunk flow-limiting spasm.	Nitroglycerin and inotropic support +/– ventricular support.
Transient hypotension	0.05%	It is usually of little importance.	Stop the infusion for a few seconds, until rhythm is recovered. Evaluate resuming the test at a slower infusion rate.
Coronary dissection	0.02%	Catheter-induced coronary dissection.	Stent implantation.
Air embolism	0.02%	Operator-dependent complication, more frequently when the infusion is performed with a microcatheter. It can be severe if not treated immediately.	Administer 100% oxygen and perform several arterial lavages with saline solution (after ensuring there is no more air). It may require inotropic or ventricular support (or both).
Catheter spasms	0.02%	More frequent in the right coronary artery.	Try not to administer nitroglycerin if there is no flow loss. It is generally transient.

Table 12. Advantages and limitations of coronary flow reserve assessment by echocardiography

Advantages	Limitations
- Non-invasive assessment - Non-expensive - Reproducible - Functional information independent of contractility disorders - Results equivalent to those of the intracoronary Doppler guideline - Prognostic value independent of FFR evaluated by coronary catheterization	- Only assessment of the anterior descending artery in most patients - Velocities, not flows are determined - Feasibility is not 100% (although it is very high) - It does not allow to differentiate coronary obstruction from microvascular dysfunction - The results may be influenced by hemodynamic conditions or associated pathologies