Sociedad Médica de Santiago
Sociedad Chilena de Medicina Interna
150 años al Servicio de la Medicina

IX CURSO MEDICINA INTERNA HOSPITALARIA 2019

Infarto agudo al miocardio con arterias coronarias normales (MINOCA)

Dr. Gonzalo Pérez Díaz
Pontificia Universidad Católica de Chile

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Infarto agudo al miocardio sin enfermedad coronaria obstructiva (MINOCA)

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Declaración de interés

- Sin conflicto de interés para esta presentación

Objetivos

- Reconocer la importancia tanto diagnóstica como pronóstica y terapéutica
- Revisar la evolución de la aproximación diagnóstica de esta entidad
- Conocer algunas de sus principales etiologías
- Enfatizar la necesidad de estudios complementarios

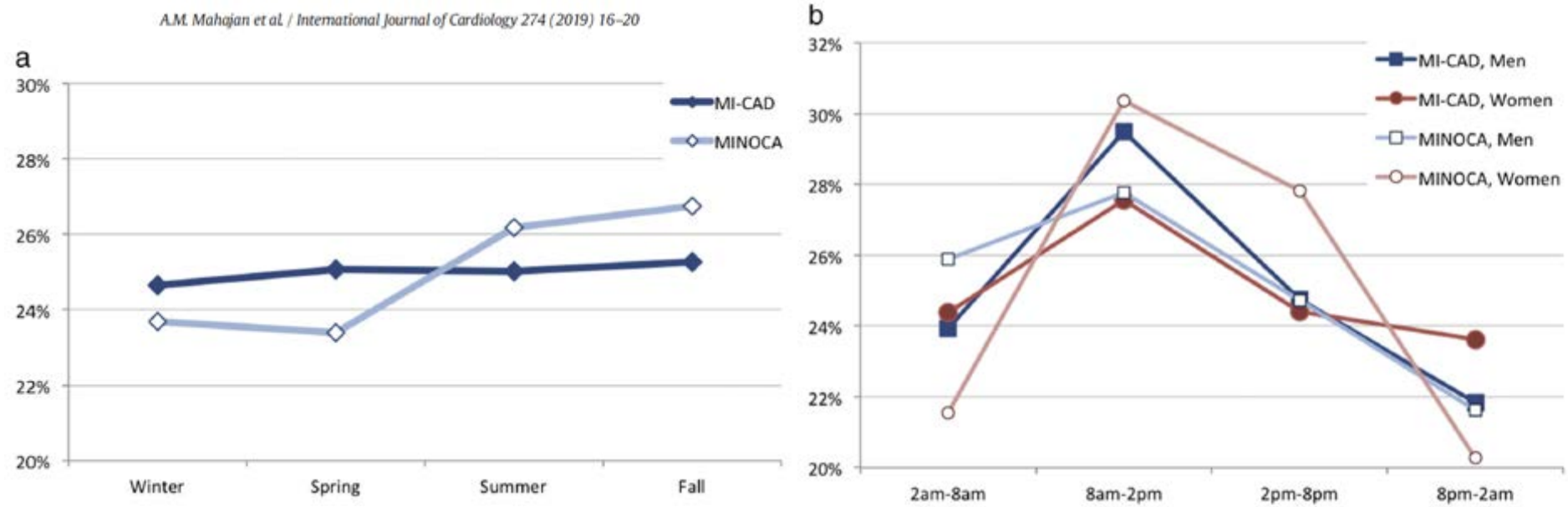
Epidemiología

- En la población general: cerca de 5% de angina estable.
- En EEUU se estiman 3-4 millones de personas con “INOCA”
- Hasta 40% de mujeres y 8% de hombres evaluados por isquemia presentan EAC no obstructiva (incluso hay estudios que muestran 59%). O sea, **5 veces más frecuente en mujeres**
- Las mujeres con síntomas de isquemia tienen más probabilidad de tener enfermedad no obstructiva, en cuadros agudos y crónicos.
- Cerca de **10% de los IAM** no tienen enfermedad obstructiva.
- En seguimientos (ej cohorte WISE) la tasa de eventos cardíacos adversos mayores es cercana a 2,5% a 5 años, y hasta 12,8% a 10 años

Bairey Merz et al. Ischemia and No Obstructive Coronary Disease (INOCA). Developing Evidence-Based Therapies and Research Agenda for the Next Decade. Circulation 2017; 135:1075-1092

Epidemiología

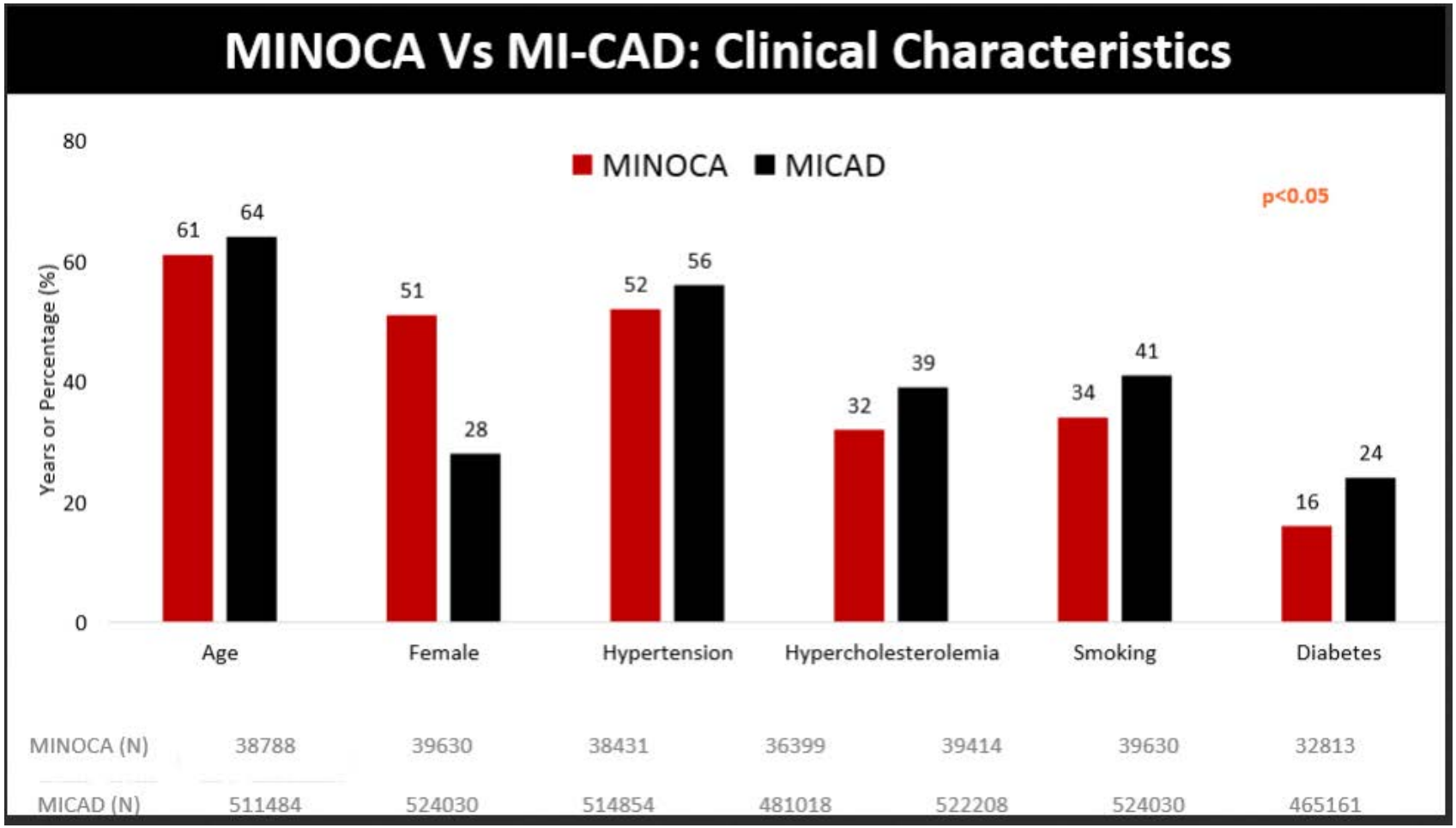
- Pacientes generalmente más jóvenes
- Menor prevalencia de dislipidemia, HTA y DM respecto a enfermedad obstructiva



Tanis-Holland et al. Diagnosis and Management of Patients with MINOCA. Circulation 2019

Mahajan et al. Seasonal and circadian patterns of myocardial infarction. Int J Cardiol 2019

Epidemiología



Tomado de presentación: Pasupathy. Survival after myocardial infarction with non-obstructive coronary arteries (MINOCA)- A comprehensive systematic review and meta-analysis. ESC Congress Paris 2019

Definición MINOCA (2013)

- Antes catalogado como un estudio “falso positivo”
- Es más bien un **diagnóstico de trabajo**

Table 1 Diagnostic criteria for myocardial infarction with non-obstructive coronary arteries

The diagnosis of MINOCA is made immediately upon coronary angiography in a patient presenting with features consistent with an acute myocardial infarct, as detailed by the following criteria:

(1) AMI criteria.[1]
  (a) Positive cardiac biomarker (preferably cardiac troponin) defined as a rise and/or fall in serial levels, with at least one value above the 99th percentile upper reference limit.
  and
  (b) Corroborative clinical evidence of infarction evidenced by at least one of the following:
    (i) Symptoms of ischaemia
    (ii) New or presumed new significant ST-T changes or new LBBB
    (iii) Development of pathological Q waves
    (iv) Imaging evidence of new loss of viable myocardium or new RWMA
    (v) Intracoronary thrombus evident on angiography or at autopsy

(2) Non-obstructive coronary arteries on angiography:
  - Defined as the absence of obstructive CAD on angiography, (i.e. no coronary artery stenosis ≥50%), in any potential infarct-related artery.
  - This includes both patients with:
    - normal coronary arteries (no stenosis >30%)
    - mild coronary atheromatosis (stenosis >30% but <50%).

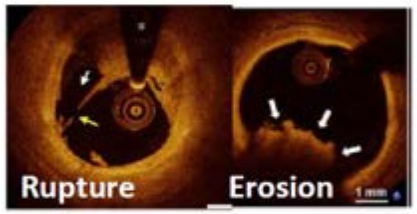
(3) No clinically overt specific cause for the acute presentation:
  - At the time of angiography, the cause and thus a specific diagnosis for the clinical presentation is not apparent.
  - Accordingly, there is a necessity to further evaluate the patient for the underlying cause of the MINOCA presentation.

LBBB, left bundle branch block. RWMA, regional wall motion abnormality.

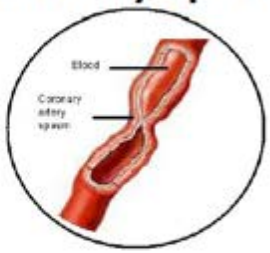
Agewall et al. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. Eur Heart J. 2017 Jan 14;38(3):143-153

Diagnósticos diferenciales

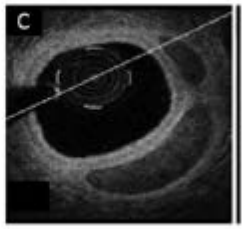
Plaque Rupture/Erosion



Coronary Spasm

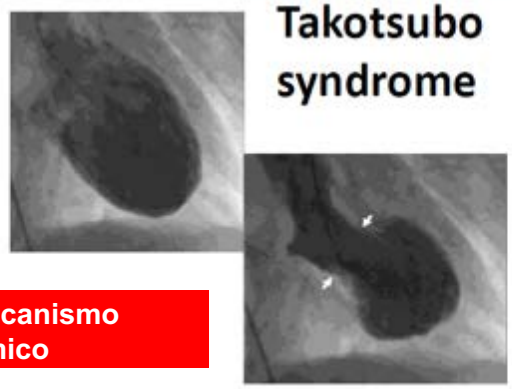


Dissection



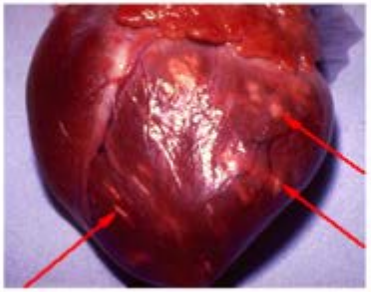
Embolism

Takotsubo syndrome



No sería mecanismo isquémico

Myocarditis

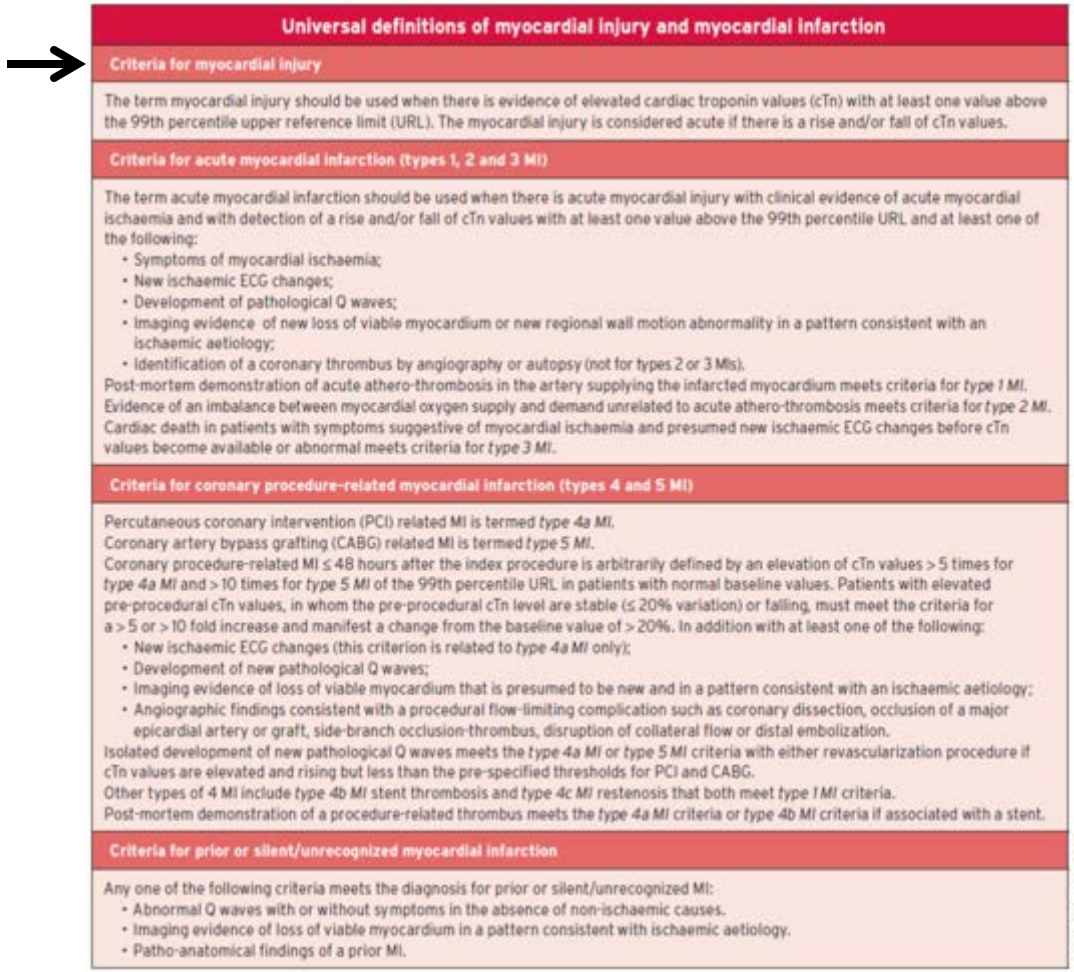


Clinical Research Center
ool of Medicine
ONE MEDICAL CENTER

PPT Harmony Reynolds, NYU School of Medicine. Myocardial Infarction with Non-Obstructive CAD (MINOCA): Management Strategies

No sería mecanismo isquémico

4ª Definición IAM (2018)



Universal definitions of myocardial injury and myocardial infarction

Criteria for myocardial injury

The term myocardial injury should be used when there is evidence of elevated cardiac troponin values (cTn) with at least one value above the 99th percentile upper reference limit (URL). The myocardial injury is considered acute if there is a rise and/or fall of cTn values.

Criteria for acute myocardial infarction (types 1, 2 and 3 MI)

The term acute myocardial infarction should be used when there is acute myocardial injury with clinical evidence of acute myocardial ischaemia and with detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and at least one of the following:

- Symptoms of myocardial ischaemia;
- New ischaemic ECG 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 ischaemic aetiology;
- Identification of a coronary thrombus by angiography or autopsy (not for types 2 or 3 MIs).

Post-mortem demonstration of acute athero-thrombosis in the artery supplying the infarcted myocardium meets criteria for *type 1 MI*.
Evidence of an imbalance between myocardial oxygen supply and demand unrelated to acute athero-thrombosis meets criteria for *type 2 MI*.
Cardiac death in patients with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes before cTn values become available or abnormal meets criteria for *type 3 MI*.

Criteria for coronary procedure-related myocardial infarction (types 4 and 5 MI)

Percutaneous coronary intervention (PCI) related MI is termed *type 4a MI*.
Coronary artery bypass grafting (CABG) related MI is termed *type 5 MI*.
Coronary procedure-related MI ≤ 48 hours after the index procedure is arbitrarily defined by an elevation of cTn values > 5 times for *type 4a MI* and > 10 times for *type 5 MI* of the 99th percentile URL in patients with normal baseline values. Patients with elevated pre-procedural cTn values, in whom the pre-procedural cTn level are stable (≤ 20% variation) or falling, must meet the criteria for a > 5 or > 10 fold increase and manifest a change from the baseline value of > 20%. In addition with at least one of the following:

- New ischaemic ECG changes (this criterion is related to *type 4a MI* only);
- Development of new pathological Q waves;
- Imaging evidence of loss of viable myocardium that is presumed to be new and in a pattern consistent with an ischaemic aetiology;
- Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow or distal embolization.

Isolated development of new pathological Q waves meets the *type 4a MI* or *type 5 MI* criteria with either revascularization procedure if cTn values are elevated and rising but less than the pre-specified thresholds for PCI and CABG.
Other types of 4 MI include *type 4b MI* stent thrombosis and *type 4c MI* restenosis that both meet *type 1 MI* criteria.
Post-mortem demonstration of a procedure-related thrombus meets the *type 4a MI* criteria or *type 4b MI* criteria if associated with a stent.

Criteria for prior or silent/unrecognized myocardial infarction

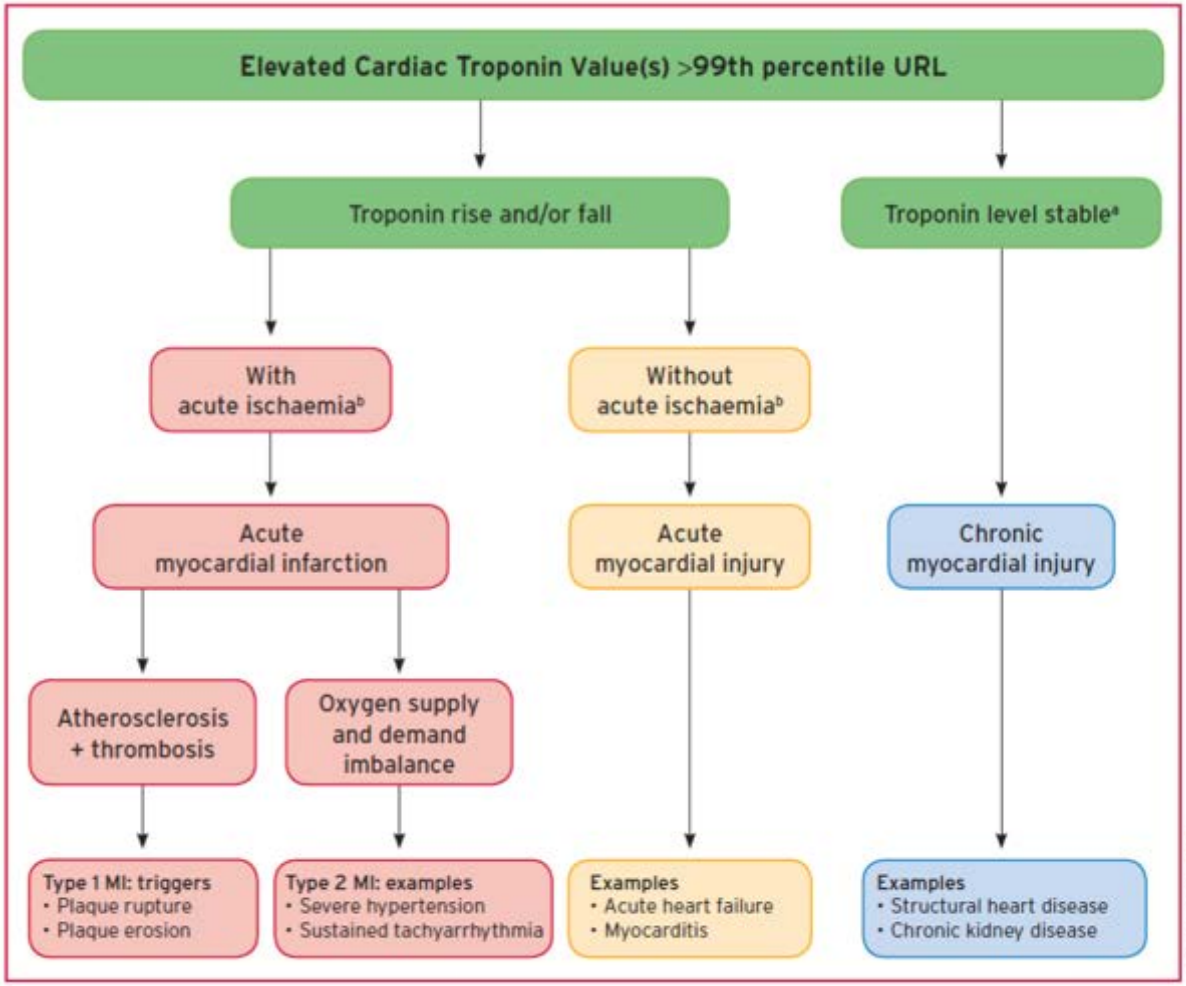
Any one of the following criteria meets the diagnosis for prior or silent/unrecognized MI:

- Abnormal Q waves with or without symptoms in the absence of non-ischaemic causes.
- Imaging evidence of loss of viable myocardium in a pattern consistent with ischaemic aetiology.
- Patho-anatomical findings of a prior MI.

ESC/ACC/AHA/WHF 2018

Fourth Definition of Myocardial Infarction. EHJ 2018

4ª Definición IAM (2018)



Fourth Definition of Myocardial Infarction. EHJ 2018

Definición MINOCA (2019)

1)IAM (Según 4ta definición)

2)Enfermedad no obstructiva en angiografía (< 50% estenosis)

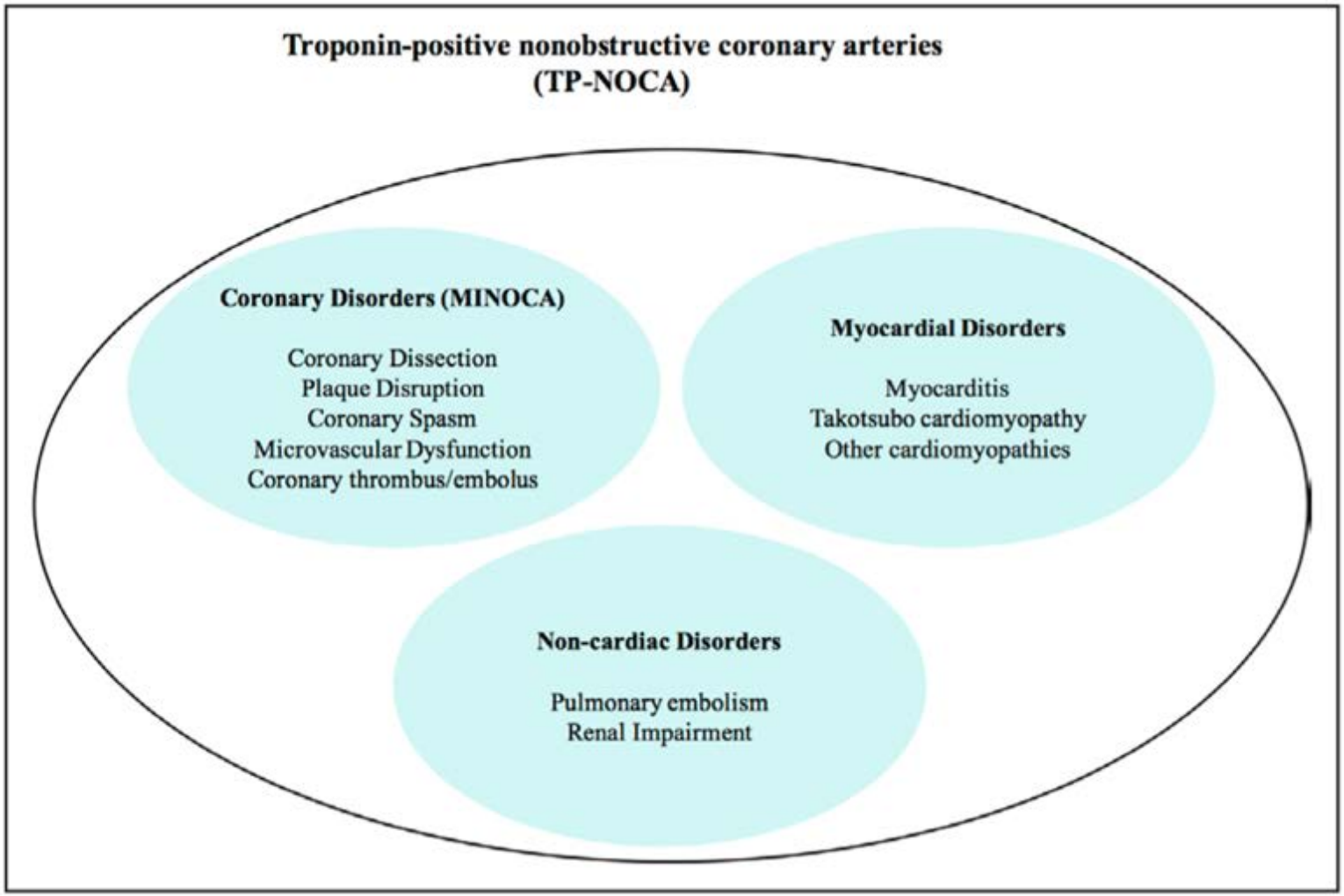
3)Sin diagnósticos alternativos específicos

Table 1. MINOCA Diagnostic Criteria

The diagnosis of MINOCA is made in patients with acute myocardial infarction that fulfills the following 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 ≥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

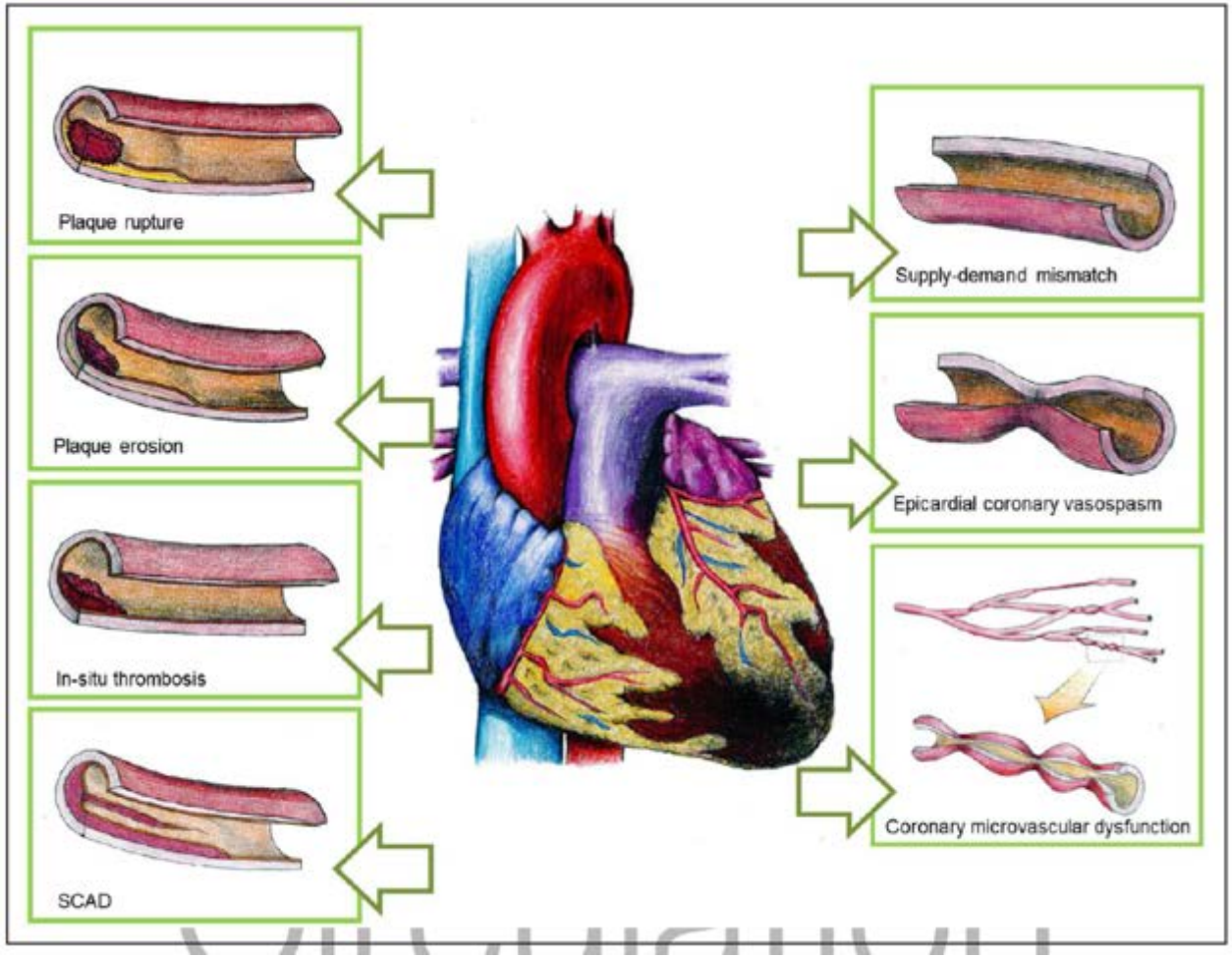
Tanis-Holland et al. Diagnosis and Management of Patients with MINOCA. Circulation 2019

Causas específicas



Pasupathy et al. MINOCA: The Past, Present, and Future Management Circulation 2017

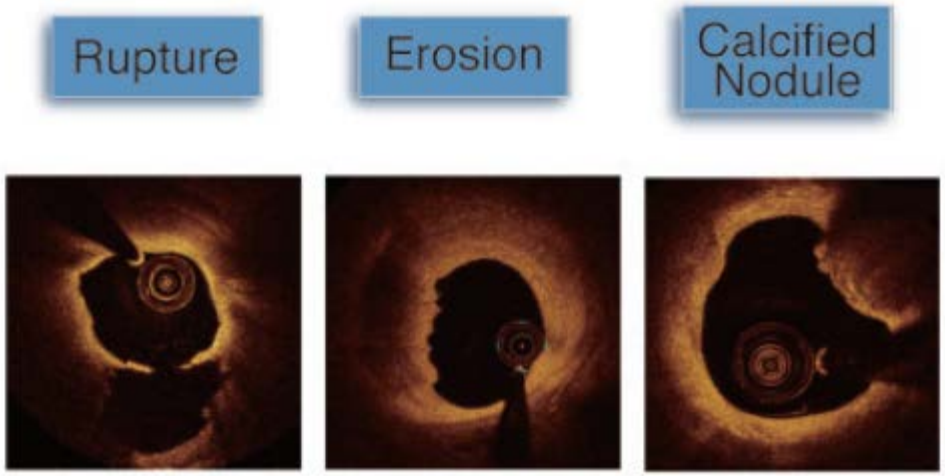
Causas específicas



Tanis-Holland et al. Diagnosis and Management of Patients with MINOCA. Circulation 2019

Disrupción de placa

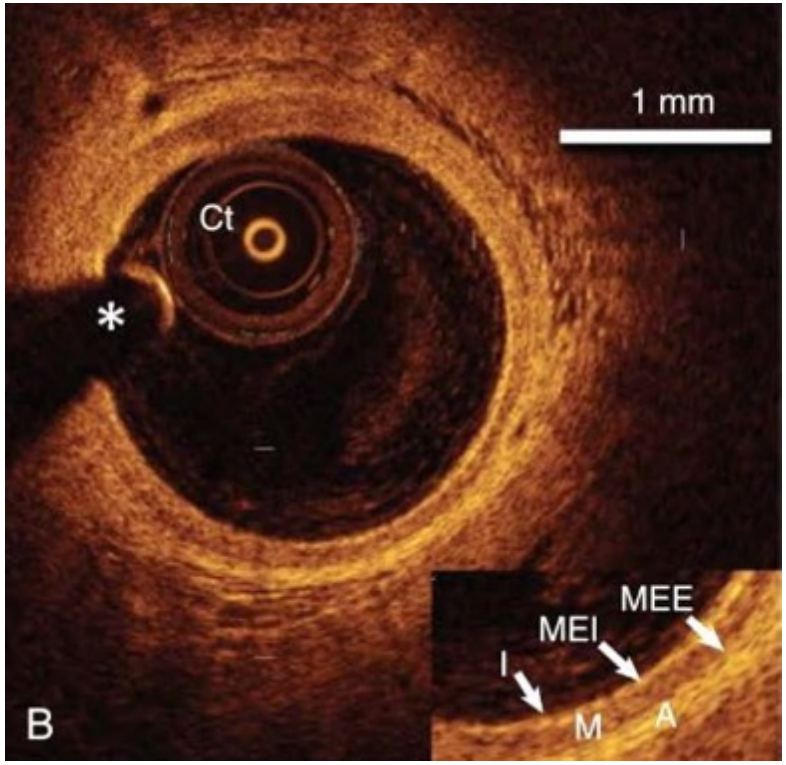
- Incluye erosión, rotura, nódulos calcificados
- Más común en mujeres, fumadores, enfermedad de un vaso, jóvenes
- Hasta 40% de pacientes en estudios con imágenes intracoronarias (ej IVUS)



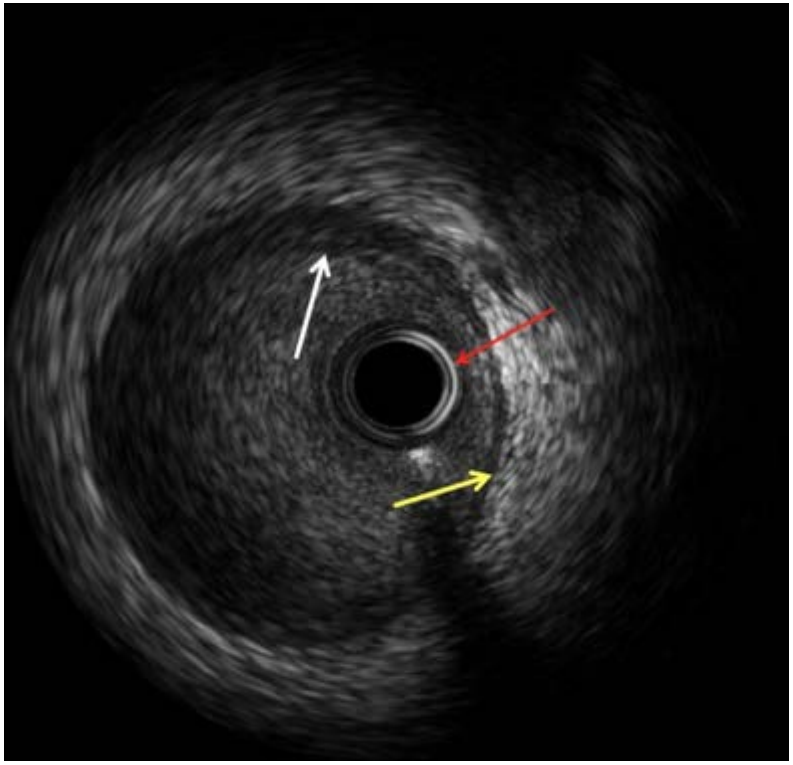
Tanis-Holland et al. Diagnosis and Management of Patients with MINOCA. Circulation 2019

Imágenes intracoronarias

OCT



IVUS



Disrupción de placa

- Necrosis miocárdica mediada por trombosis, tromboembolia, vasoespasmo, o combinación
- Podría haber trombólisis espontánea o autolisis del trombo
- Manejo: Se propone DAPT por un año

Tanis-Holland et al. Diagnosis and Management of Patients with MINOCA. Circulation 2019

Espasmo coronario

- Vasoconstricción intensa (> 90%) de arteria epicárdica con compromiso de flujo
- En respuesta a drogas o toxinas que generan hiperreactividad de musculatura lisa o espontáneamente por alteraciones en tono vasomotor
- Más frecuente en asiáticos
- Podría llegar hasta 27% de los casos de MINOCA

Espasmo coronario

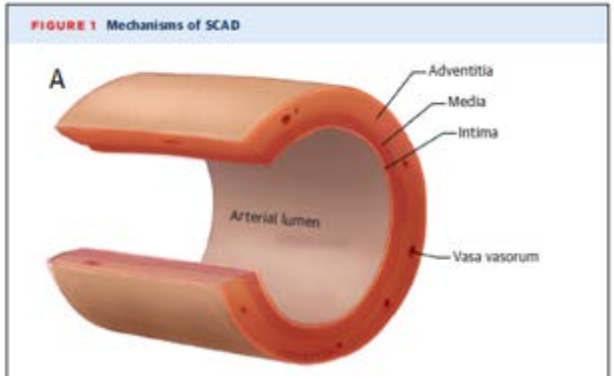
- Episodios recurrentes de angina de reposo con rápida respuesta a nitratos
- Patrón circadiano (mayor en la noche)
- Diagnóstico: test de provocación con acetilcolina
- Manejo: bloqueadores de canales de calcio, otros antiespásticos

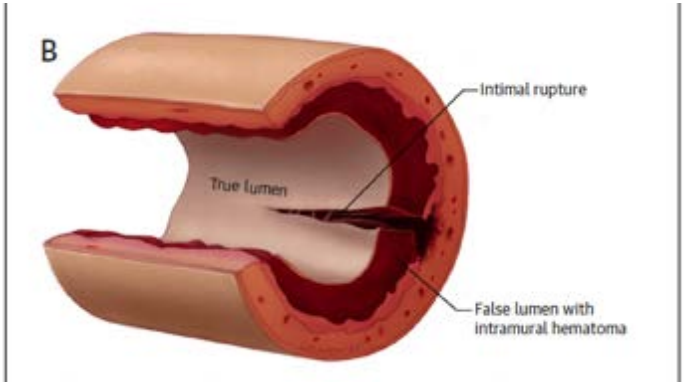
Disección espontánea de arterias coronarias

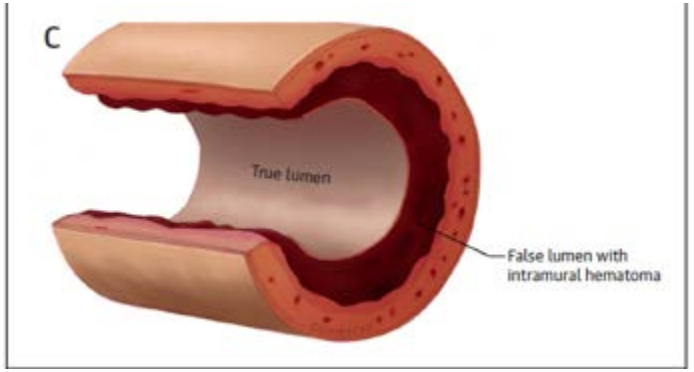
- Definición: separación espontánea de la pared de la arteria coronaria, no debida a iatrogenia o trauma
- Prevalencia: 1,4 a 4% de SCA
- Afecta a mujeres en > 90% de los casos
- Edad promedio 44-55 años
- En Norteamérica: 81-83% raza caucásica
- Se estima que cerca de un 20% afectaría a más de un vaso
- Puede no ser aparente en la coronariografía

Saw et al. Contemporary Review on Spontaneous Coronary Artery Dissection. J AM Coll Cardiol 2016;68: 297-312

Fisiopatología



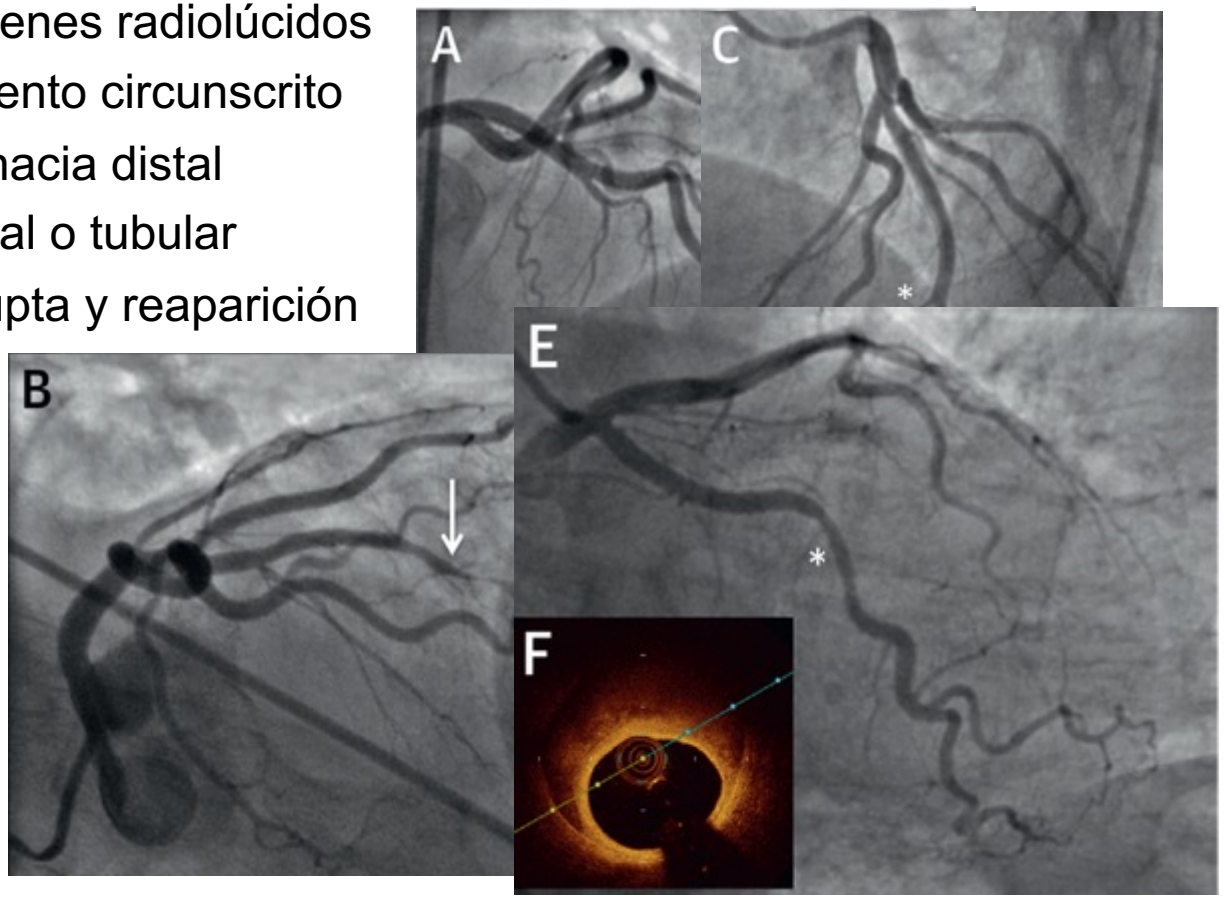




Saw et al. Contemporary Review on Spontaneous Coronary Artery Dissection. J AM Coll Cardiol 2016;68: 297-312

Tipos (Clasificación de Saw)

- I: múltiples lúmenes radiolúcidos
- 2a: Adelgazamiento circunscrito
- 2b: Extensión hacia distal
- 3: estenosis focal o tubular
- 4: oclusión abrupta y reaparición



Factores de riesgo

Predisponentes
Displasia fibromuscular
Relacionado a embarazo
Embarazos recurrentes
Enfermedad del tejido conectivo
Enfermedad inflamatoria sistémica
Terapia hormonal
Espasmo coronario
Idiopático

Precipitantes
Ejercicio intenso
Estrés emocional intenso
Parto
Maniobas de valsalva intensas
Drogas recreacionales
Terapia hormonal intensa

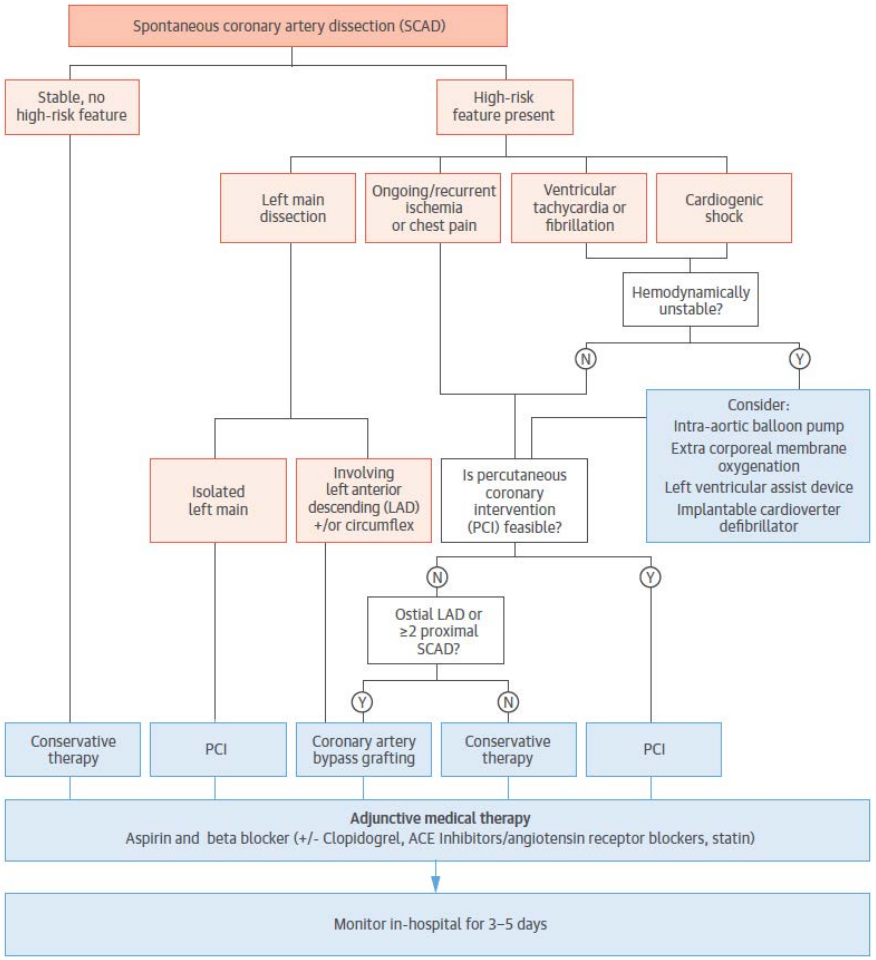
Adaptado de: Saw et al. Contemporary Review on Spontaneous Coronary Artery Dissection. J AM Coll Cardiol 2016;68: 297-312

Factores de riesgo

Predisponentes	Precipitantes
Displasia fibromuscular	**Ejercicio intenso**
Relacionado a embarazo	**Estrés emocional intenso**
Embarazos recurrentes	**Parto**
Enfermedad del tejido conectivo: Marfan, Loeys-Dietz, Ehler-Danlos tipo 4, necrosis medial quística, déficit alfa 1 antitripsina, riñón poliquístico	**Maniobas de valsalva intensas**
Enfermedad inflamatoria sistémica: LES, Crohn, colitis ulcerosa, PAN, sarcoidosis, Churg-Strauss, Wegener, AR, Kawasaki, Arteritis células gigantes, enfermedad celíaca	**Drogas recreacionales**
Terapia hormonal: ACO, testosterona, corticoides	**Terapia hormonal intensa**
Espasmo coronario	
Idiopático	

Manejo

CENTRAL ILLUSTRATION Management Algorithm for Spontaneous Coronary Artery Dissection



Saw et al. Contemporary Review on Spontaneous Coronary Artery Dissection. J AM Coll Cardiol 2016;68: 297-312

Embolía coronaria

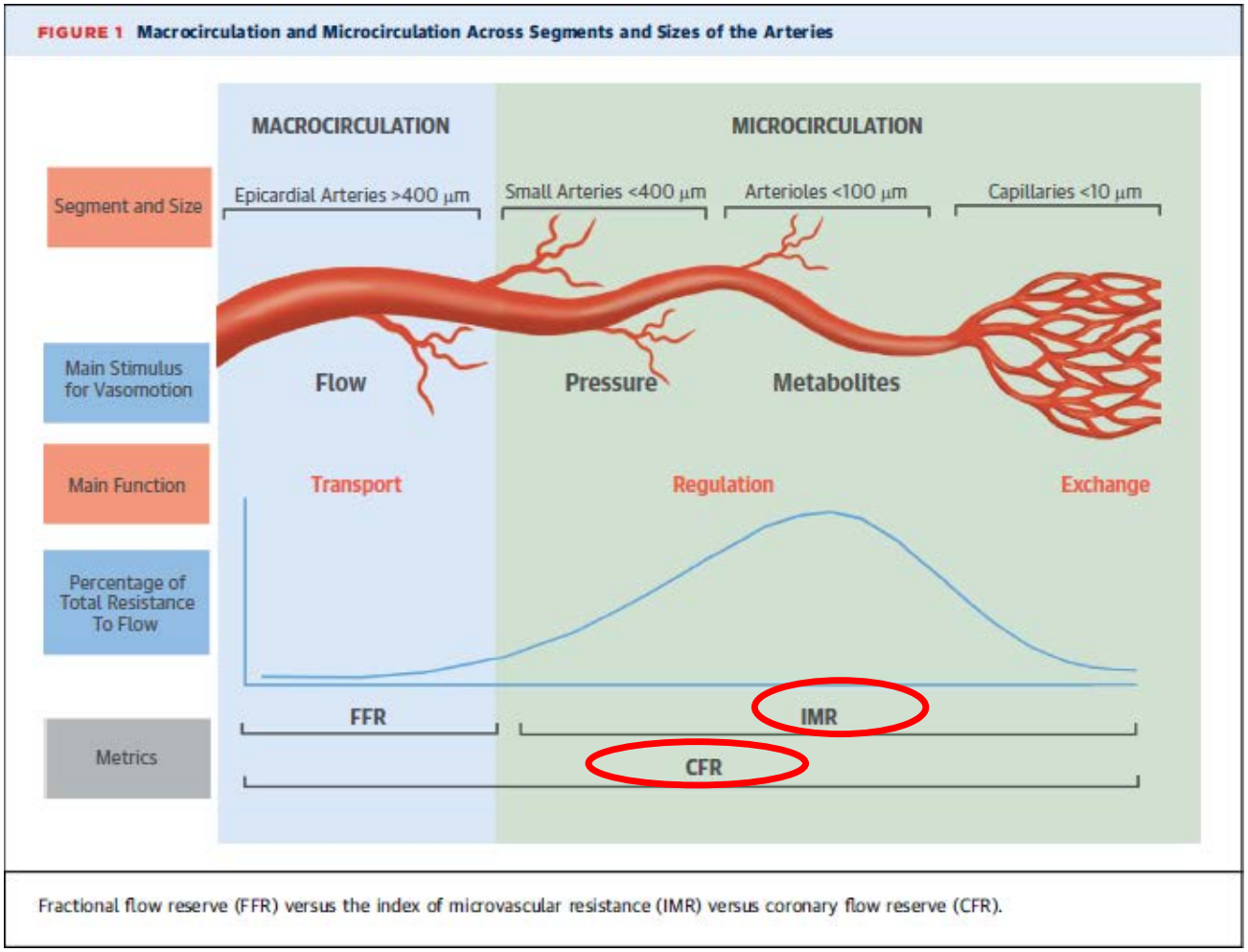
- Hasta 14% del total de pacientes con MINOCA
- No siempre aparentes en coronariografía
- Puede deberse a desórdenes trombóticos hereditarios o adquiridos
- Origen en coronarias mismas o a nivel sistémico

Table 4 Diagnostic work-up cardiac thromboembolism

Patient history	Atrial fibrillation, cardiomyopathy, prosthetic valve, prothrombotic risk factors, (cardiac) tumour, valvular heart disease, recent endocarditis, recent TVT or pulmonary embolism, concomitant stroke, or systemic embolism
Signs	Fever, signs of systemic thromboembolism
Laboratory analysis	Inflammatory markers, factor V Leiden, protein C, protein S, lupus anticoagulant, anti-cardiolipin antibodies, INR (in patients on vitamin K antagonists), and blood cultures
Echocardiography	Left ventricular function and ventricular thrombus, myxoma and papillary fibroelastoma and other cardiac tumours, assessment of atrial shunt, valvular heart disease with particular focus on signs of endocarditis, calcified valves, mobile plaques in ascending aorta, right-to-left shunt (microbubbles) to look for patent foramen ovale; consider transoesophageal echocardiography to look for patent foramen ovale
Coronary angiography	Non-occluded coronary arteries or distal stops, intervention-related air emboli. Intravascular ultrasound or OCT may be useful to identify atherosclerotic plaque disruption and plaque erosion as well as coronary dissection or thrombosis, which may not have been appreciated during angiography, in particular in patients with signs of atherosclerosis

Agewall et al. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. Eur Heart J. 2017 Jan 14;38(3):143-153

Disfunción microvascular



J Am Coll Cardiol. 2016 Mar 15;67(10):1170-1172.

Criterios diagnósticos angina microvascular

- Propuestos recientemente por la COVADIS: *the Coronary Vasomotion Disorders International Study Group.*
- AMV definitiva: 4 criterios- sospechada: 1 y 2, 3 o 4

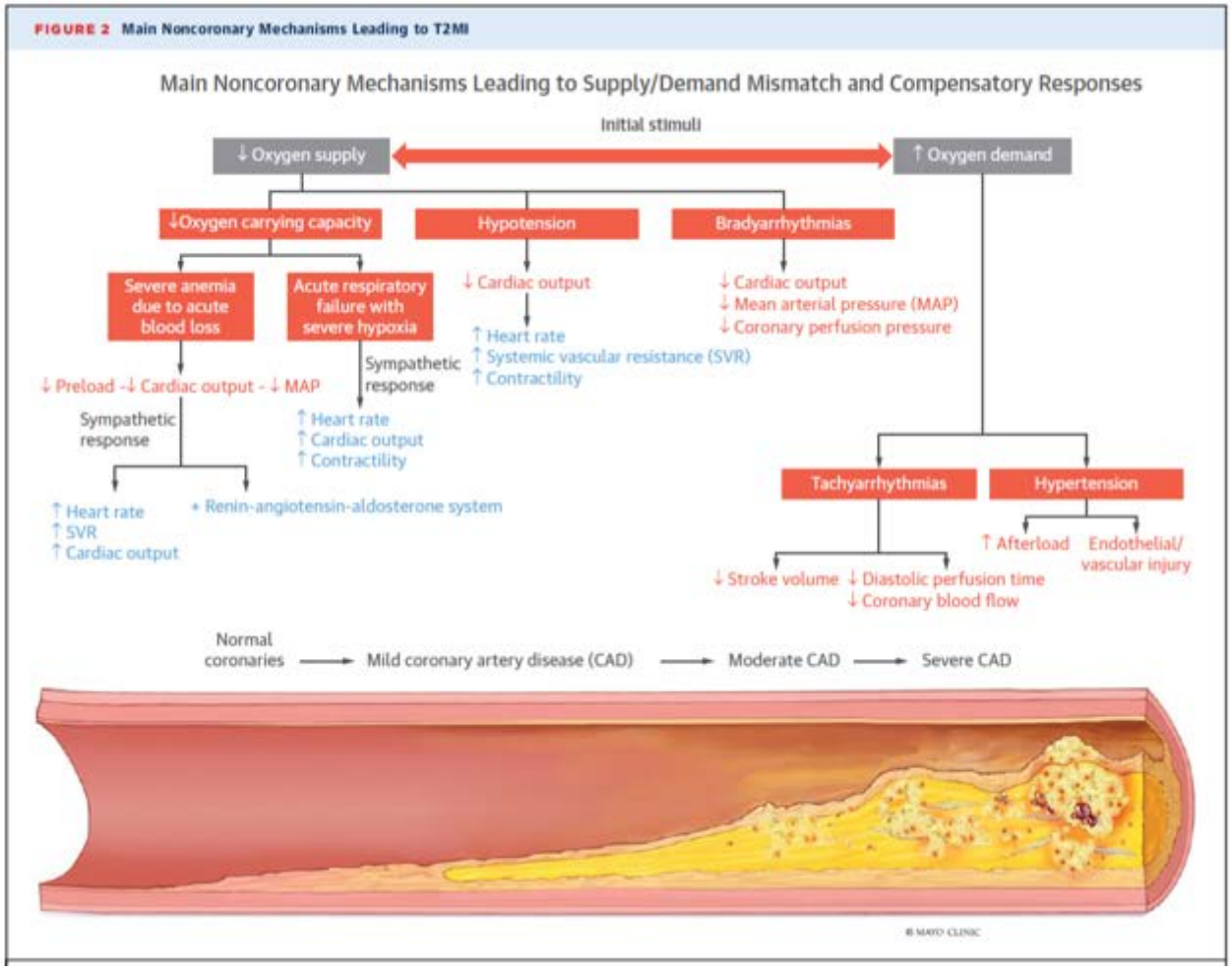
1.Síntomas de isquemia miocárdica a) Angina de esfuerzo o reposo b) Equivalentes anginosos (ej disnea)
2.**Ausencia de EC obstructiva (< 50% reducción de diámetro o FFR > 0,80)** por a. angioTC b. Coronariografía
3. **Evidencia objetiva de isquemia miocárdica** a) Cambios ECG isquémicos durante un episodio de dolor torácico b) Dolor inducido por estrés y/o cambios isquémicos en presencio o ausencia de anormalidades en perfusión transitorias/reversibles y/o alteraciones de motilidad
4. **Evidencia de alteración en función de microcirculación coronaria** a) Alteración FRC (puntos de corte entre ≤2,0 y ≤2,5) b) Espasmo coronario microvascular, definido como reproducción de síntomas, cambios ECG sin cambios epicárdicos, en test de acetilcolina c) Índices de resistencia microvascular coronaria alterados (IMR > 25) d) Fenómeno de flujo lento, definido como TIMI “frame count” > 25

Adaptado de Ong et al. International standardization of diagnostic criteria for microvascular angina. International Journal of Cardiology 250 (2018) 16-20.

Discordancia oferta demanda

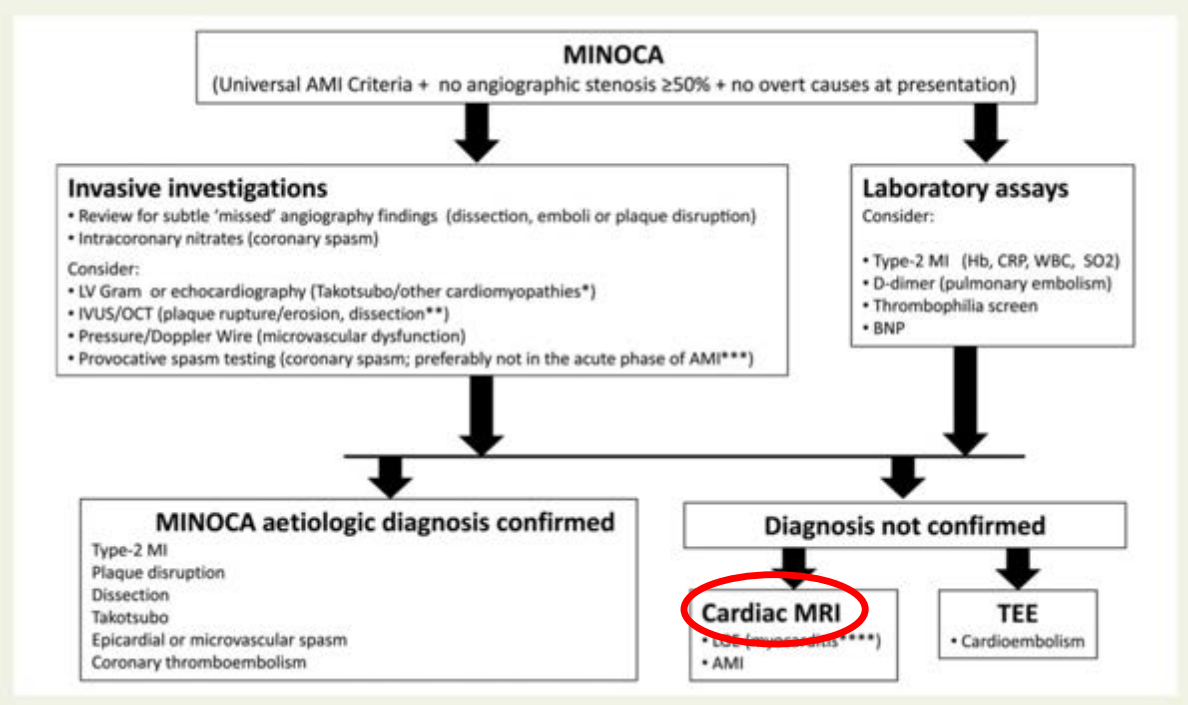
- Arritmias: lo más frecuente
- Anemia
- Hipotensión
- Tirotoxicosis
- Algunos autores proponen no considerarlo dentro de MINOCA

Discordancia oferta demanda



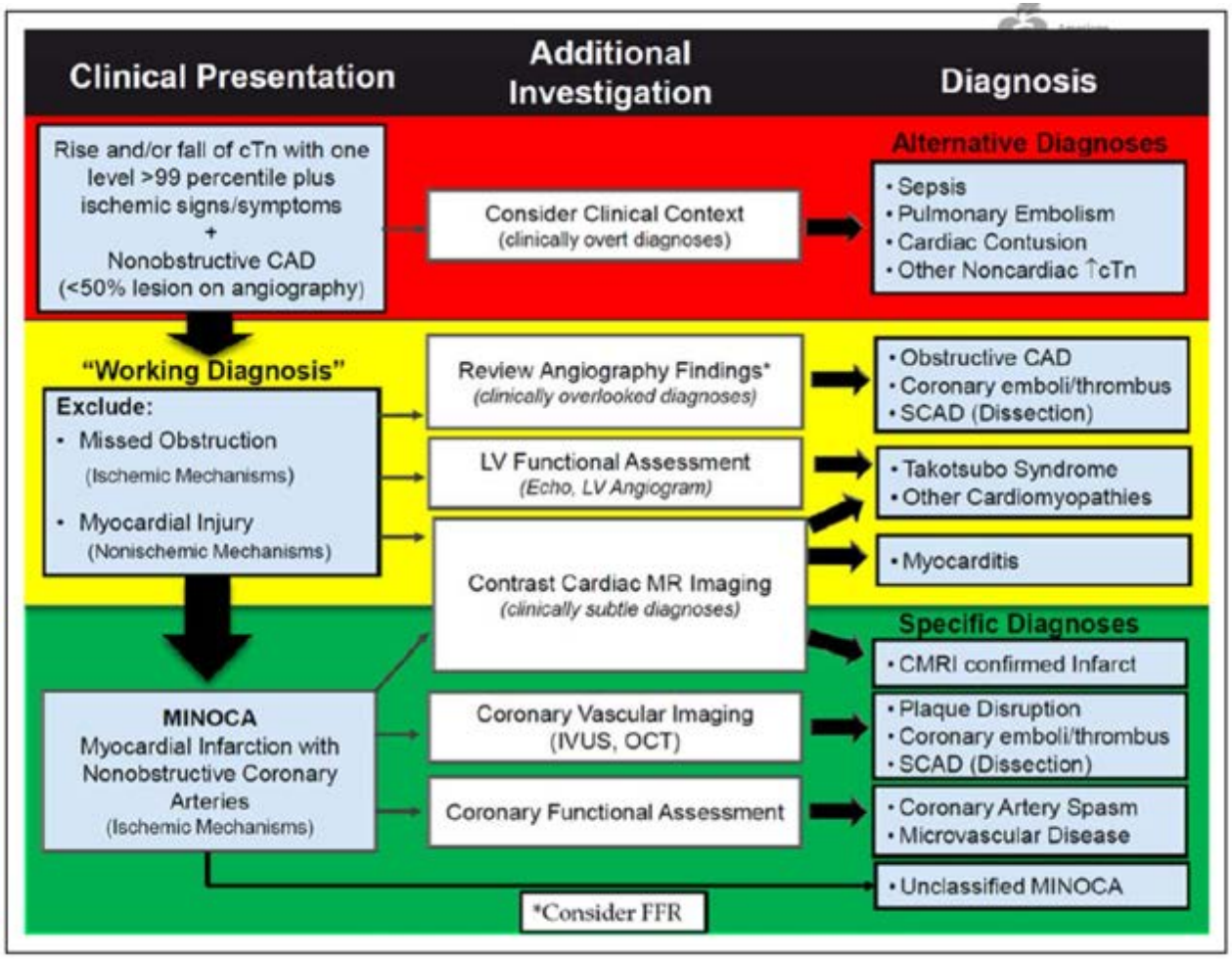
Sandoval, Jaffe. Type 2 Myocardial Infarction. JACC 2019

Aproximación (ESC 2013)



Agewall et al. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. Eur Heart J. 2017 Jan 14;38(3):143-153

"Semáforo" (AHA 2019)



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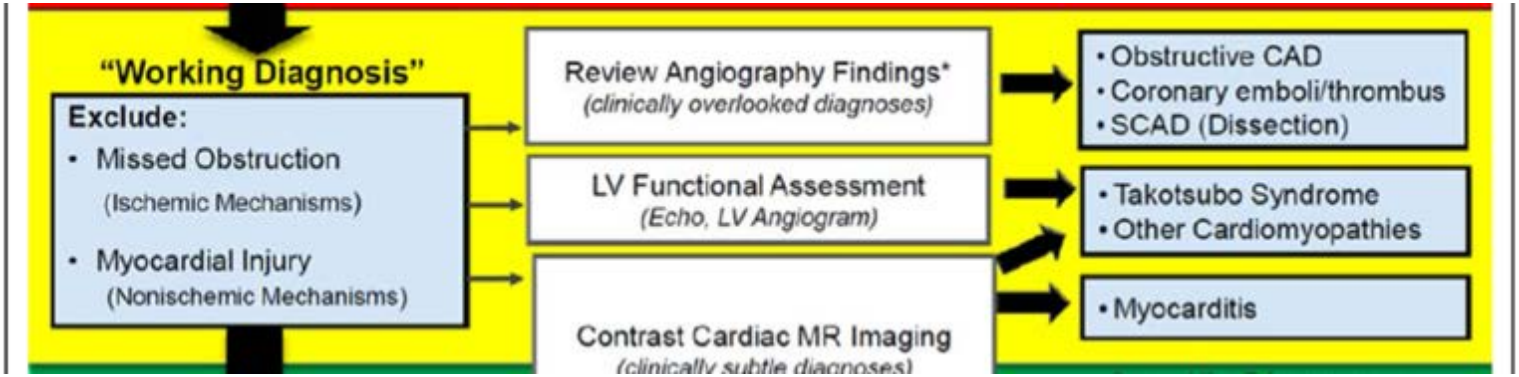
"Semáforo" (AHA 2019)

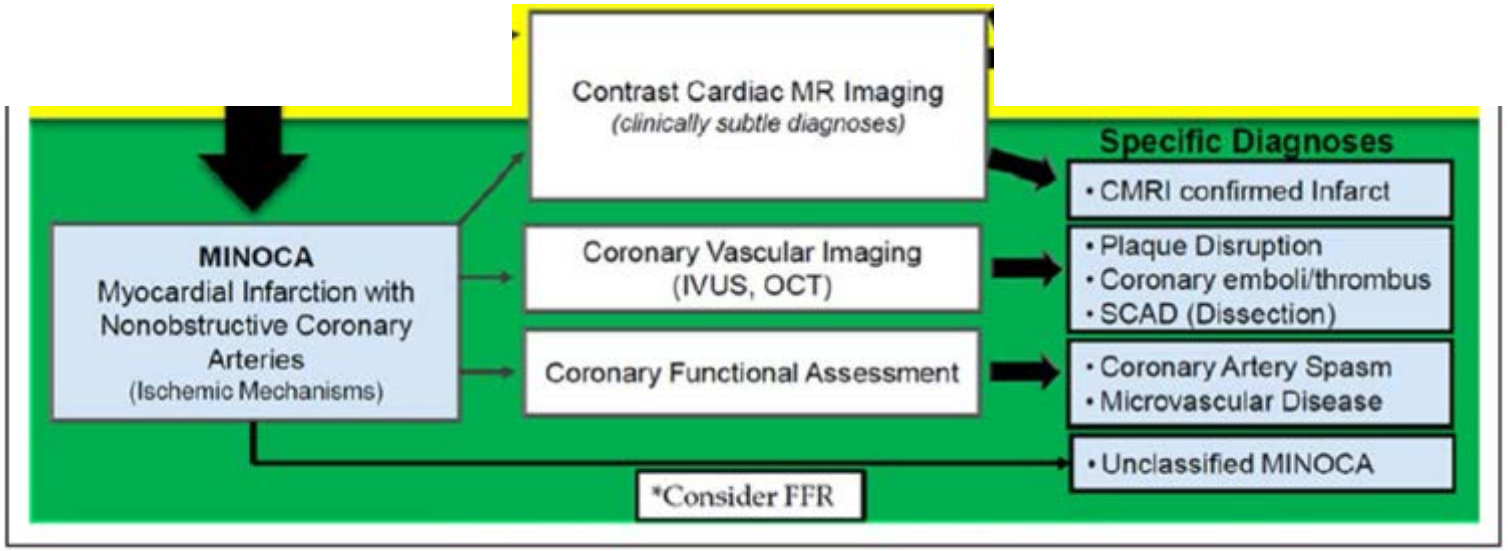
Tanis-Holland et al. Diagnosis and Management of Patients with MINOCA. Circulation 2019

"Semáforo" (AHA 2019)



Tanis-Holland et al. Diagnosis and Management of Patients with MINOCA. Circulation 2019

"Semáforo" (AHA 2019)



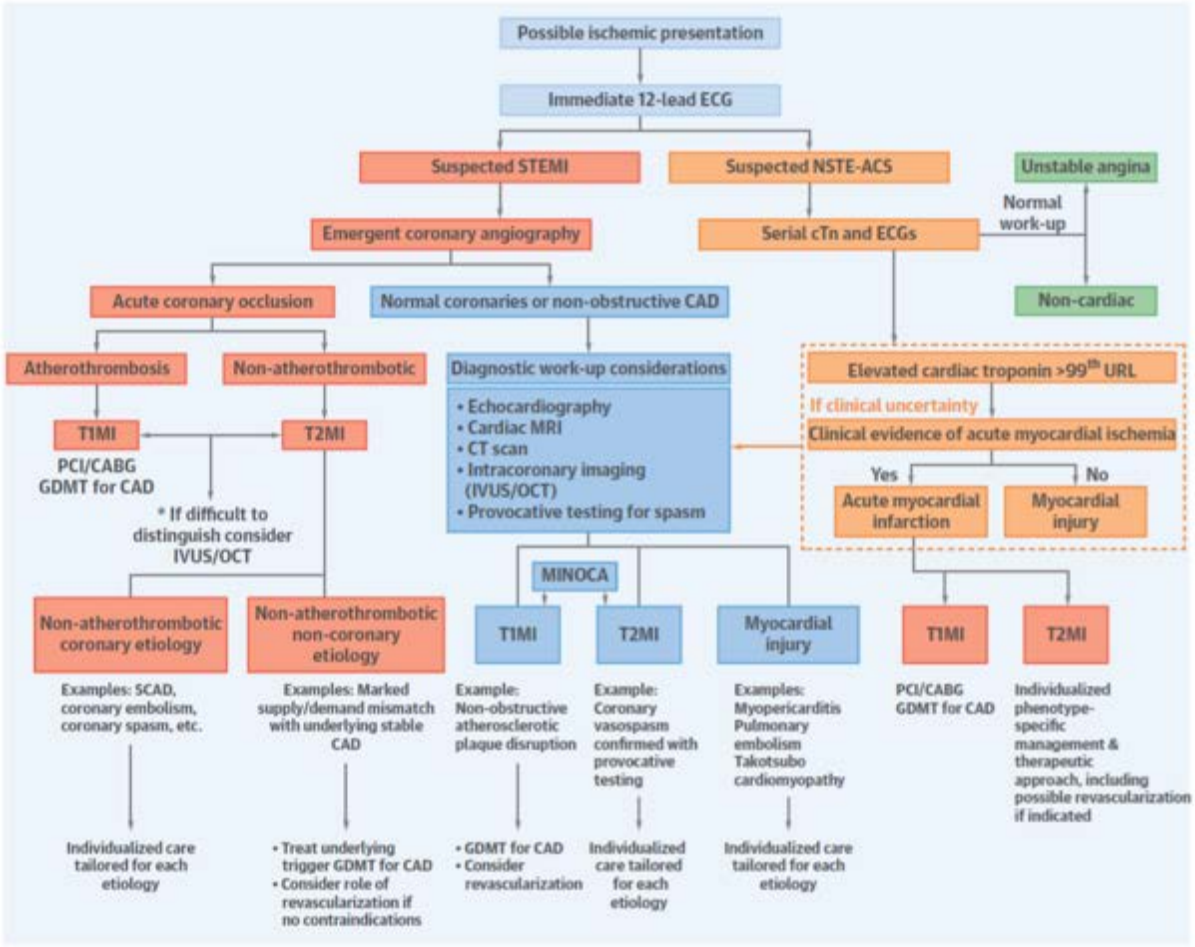
Tanis-Holland et al. Diagnosis and Management of Patients with MINOCA. Circulation 2019

Resonancia magnética

Fourth Definition of Myocardial Infarction. EHJ 2018

Aproximación general

CENTRAL ILLUSTRATION Diagnostic Approach for Patients With Suspected Acute Myocardial Ischemia



Sandoval, Jaffe. Type 2 Myocardial Infarction. JACC 2019

Tratamiento

ORIGINAL RESEARCH ARTICLE

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

Lindahl et al. Secondary Prevention in patients with MINOCA. Circulation 2017

Tratamiento

Estatinas:
HR 0,77 (0,68-0,77)

Beta bloqueo:
HR 0,86(0,74-1,01)

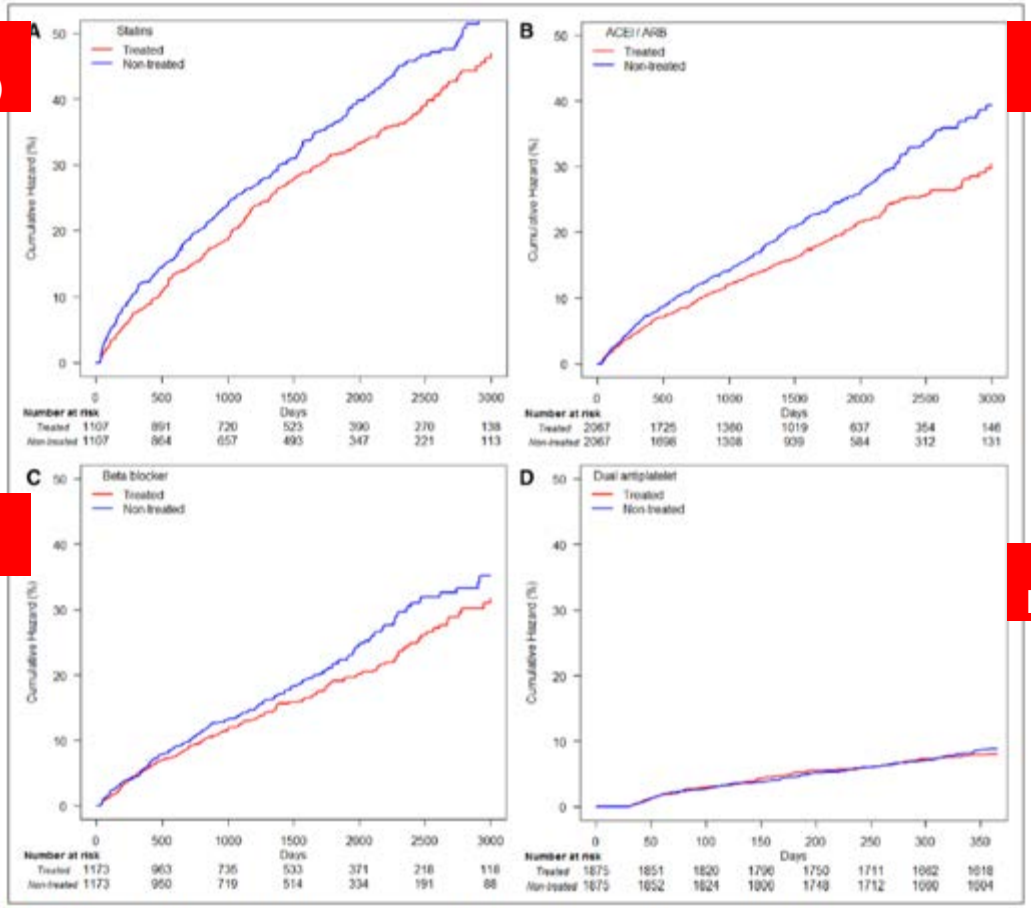


Figure 2. Survival curves for treated and untreated in the 1:1 propensity score–matched populations.
A, Statins. **B,** angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB). **C,** β-blockers. **D,** Dual antiplatelet treatment.

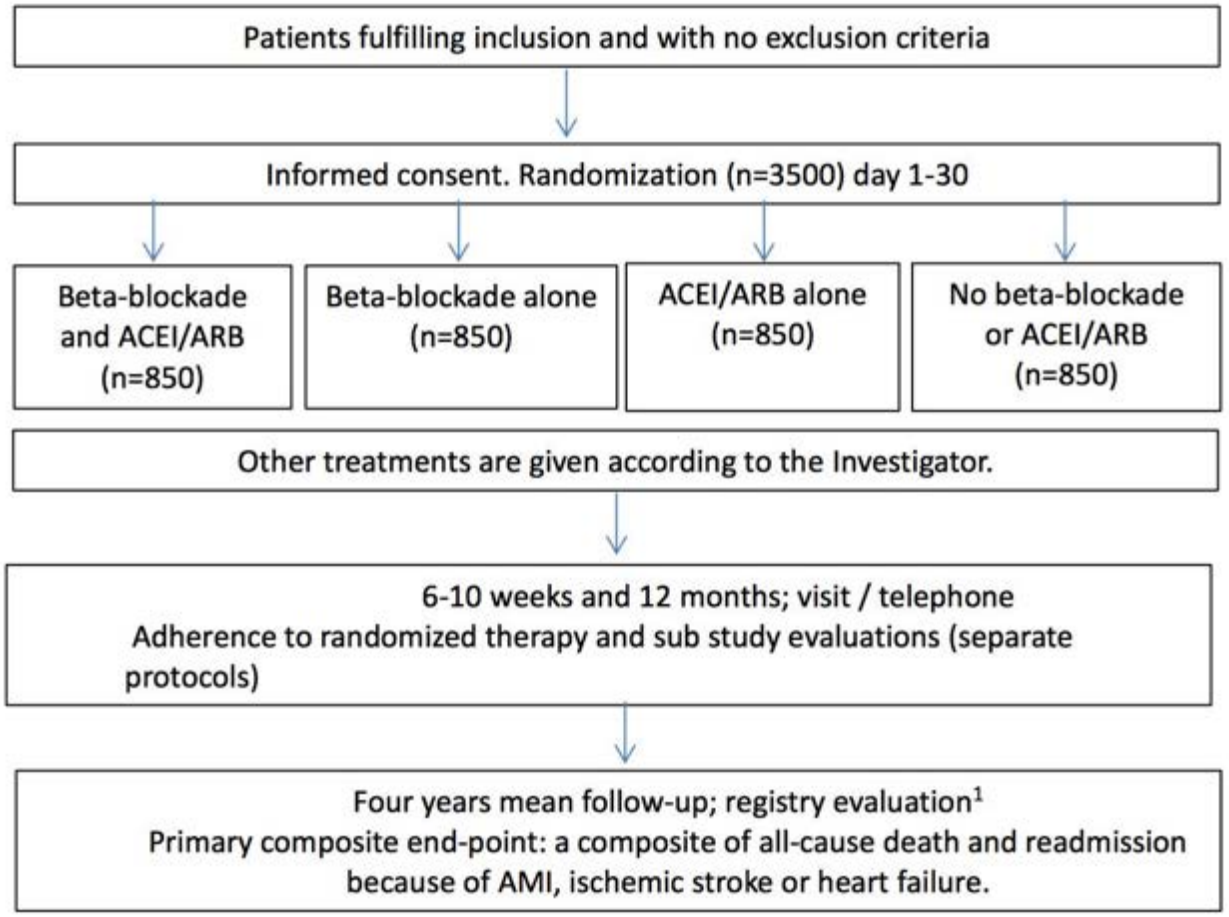
iECA/ARA2:
HR 0,82 (0,73-0,93)

DAPT:
HR 0,90(0,74-1,08)

Lindahl et al. Secondary Prevention in patients with MINOCA. Circulation 2017

Tratamiento

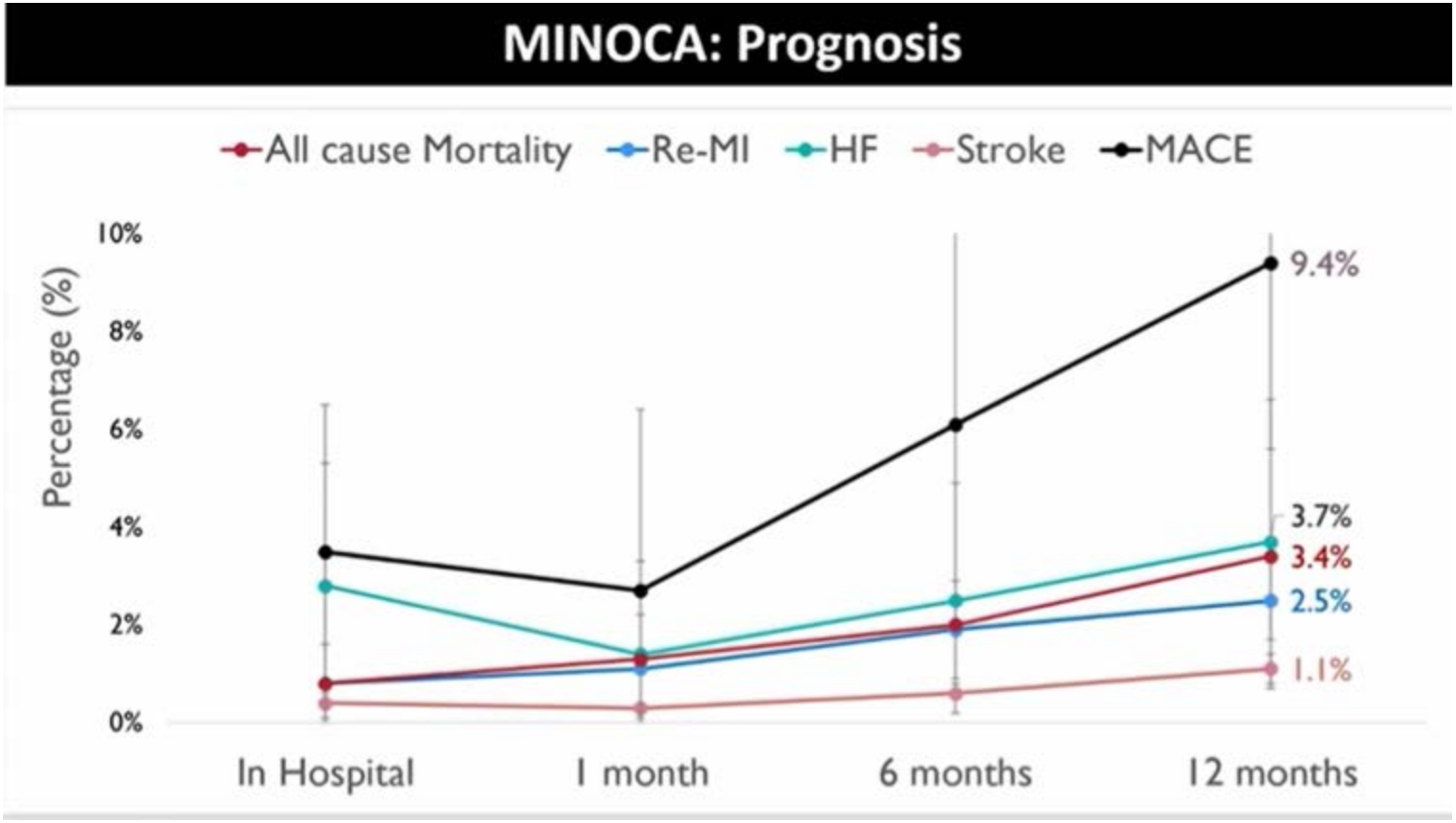
MINOCA -BAT



Pronóstico

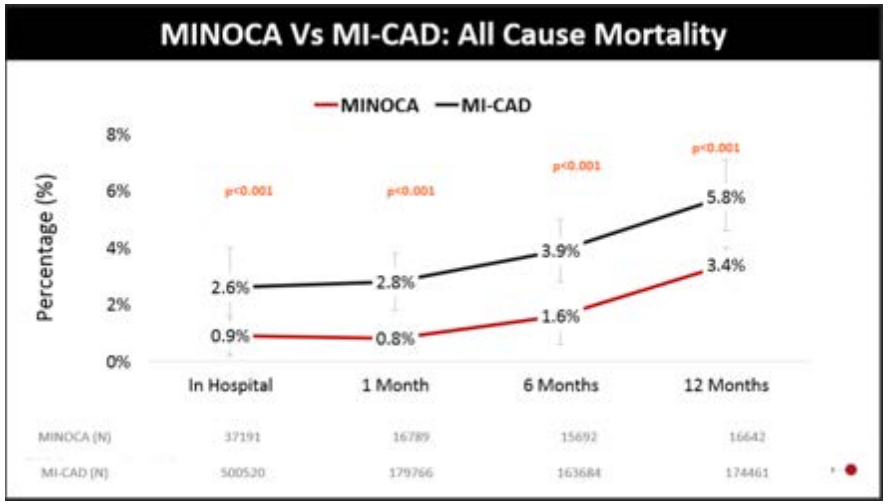
- Se ha descrito pronóstico mejor que enfermedad obstructiva, pero peor que sujetos controles
- Recurrencia: hasta 25% pacientes sufrirán angina dentro de 12 meses

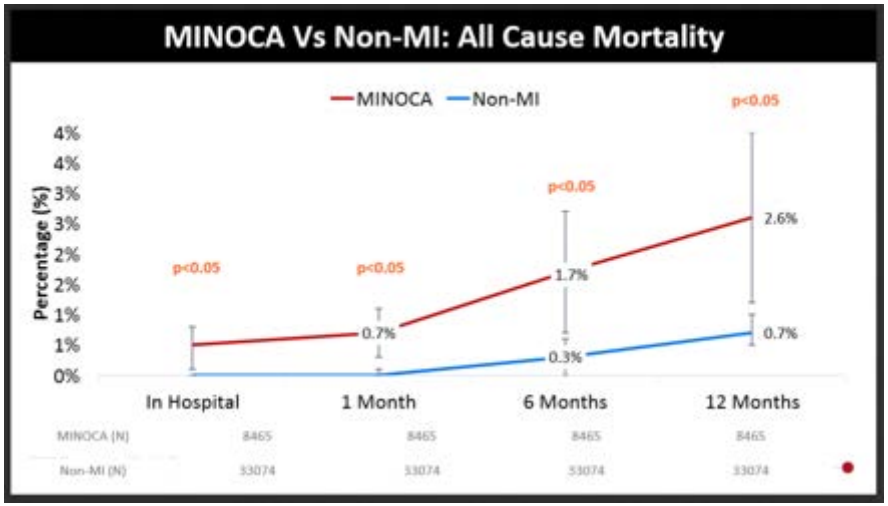
Pronóstico



Tomado de presentación: Pasupathy. Survival after myocardial infarction with non-obstructive coronary arteries (MINOCA)- A comprehensive systematic review and meta-analysis. ESC Congress Paris 2019

Pronóstico





Tomado de presentación: Pasupathy. Survival after myocardial infarction with non-obstructive coronary arteries (MINOCA)- A comprehensive systematic review and meta-analysis. ESC Congress Paris 2019

Mensajes clave

- MINOCA es un diagnóstico de trabajo
- Etiologías heterogéneas
- La aproximación inicial pasa por una revisión cuidadosa de la coronariografía, con apoyo de imágenes intracoronarias
- Uso de la RM cada vez más recomendado en casos de duda diagnóstica
- El tratamiento debe ser orientado a la causa de base (“personalizado”)

Bibliografía

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¡Gracias por su atención!