Β' ΠΑΝΕΠΙΣΤΗΜΙΑΚΗ
ΚΑΡΔΙΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ
Α.Π.Θ.

Προκάρδιο άλγος και κινητοποίηση τροπονίνης χωρίς αποφρακτική στεφανιαία νόσο. Πώς την προσεγγίζουμε;

Ε. Καραγιαννίδης
Β' Πανεπιστημιακή Καρδιολογική Κλινική
Γ.Ν.Θ. «Ιπποκράτειο

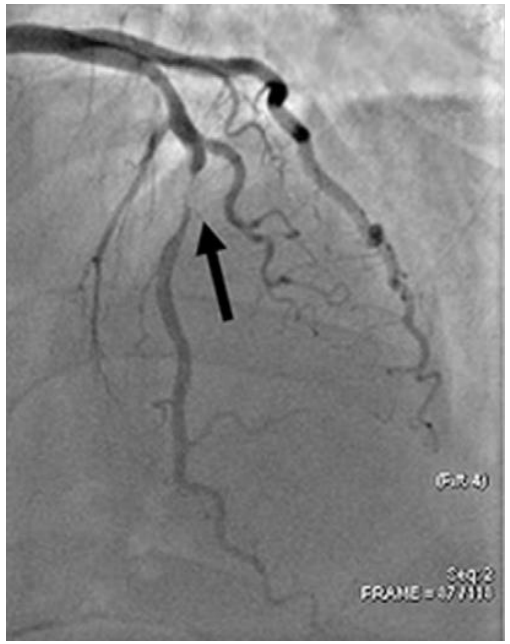
Symptoms: chest pain
Biomarkers: Δ troponin

→

Provisional diagnosis: Acute MI

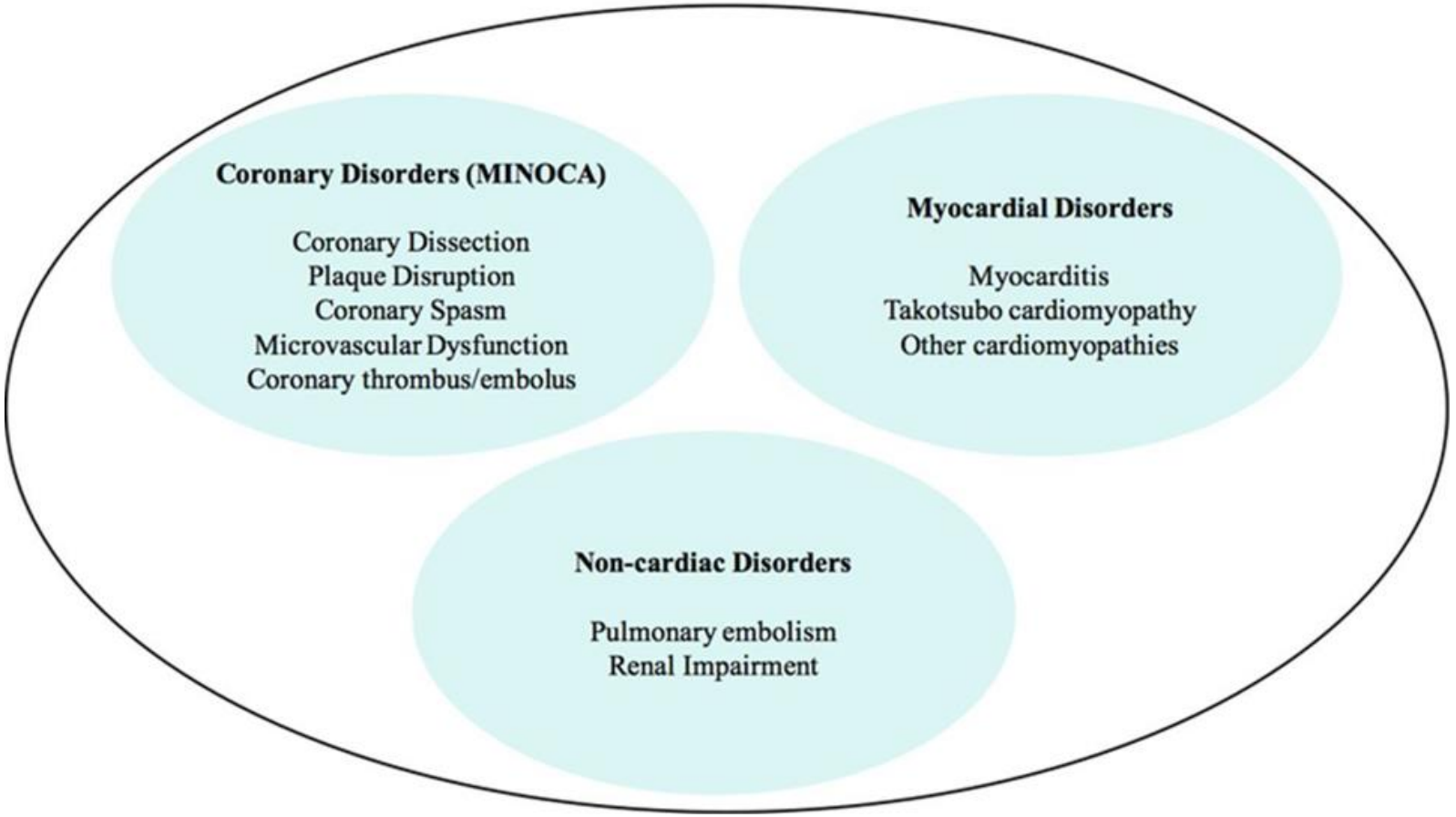
↓

Coronary angiogram



Troponin positive nonobstructive coronary arteries (TP-NOCA)

↑ troponin→ **organ specific** rather than ischemic specific



Pasupathy et al . Circulation.2017

Standardized Diagnostic Criteria for MINOCA

1. **AMI criteria -** 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 type 2 or 3 MIs).

2. **Nonobstructive coronary arteries** on angiography:

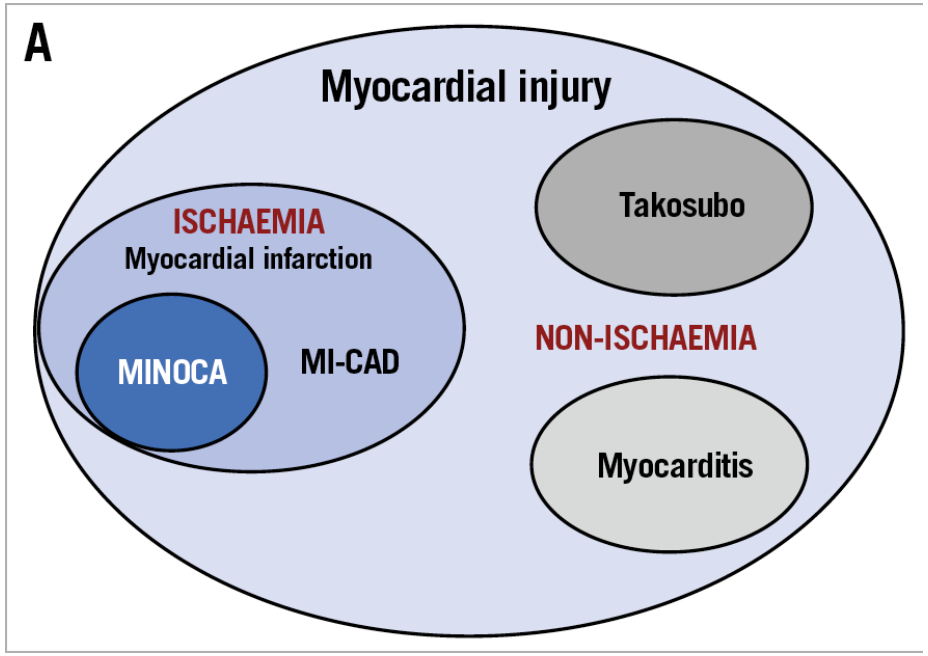
   Defined as the absence of obstructive disease on angiography (ie, no coronary artery stenosis ≥50%) in any major epicardial vessel

   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 other clinically overt specific cause** that can serve an alternative cause for the acute presentation (eg. sepsis, pulmonary embolism, myocarditis)

In theory

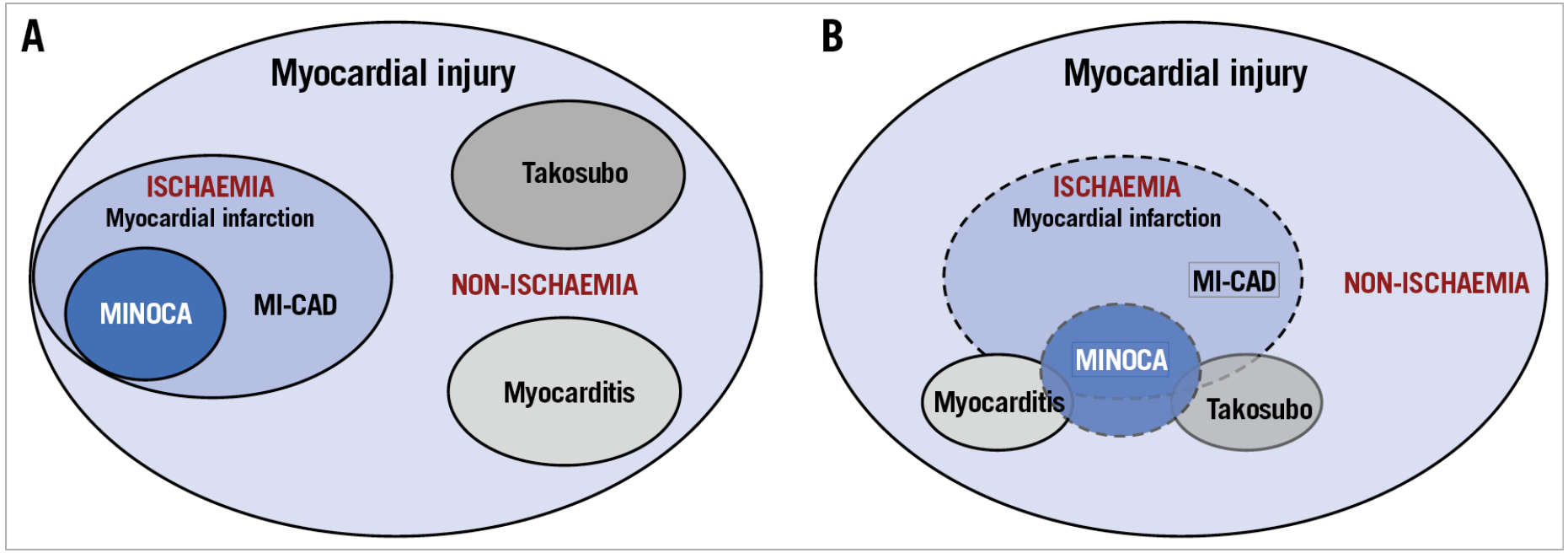


EuroIntervention 2021;17:e875-e887

In the real world, the situation is much less clear…

In theory

In clinical practice

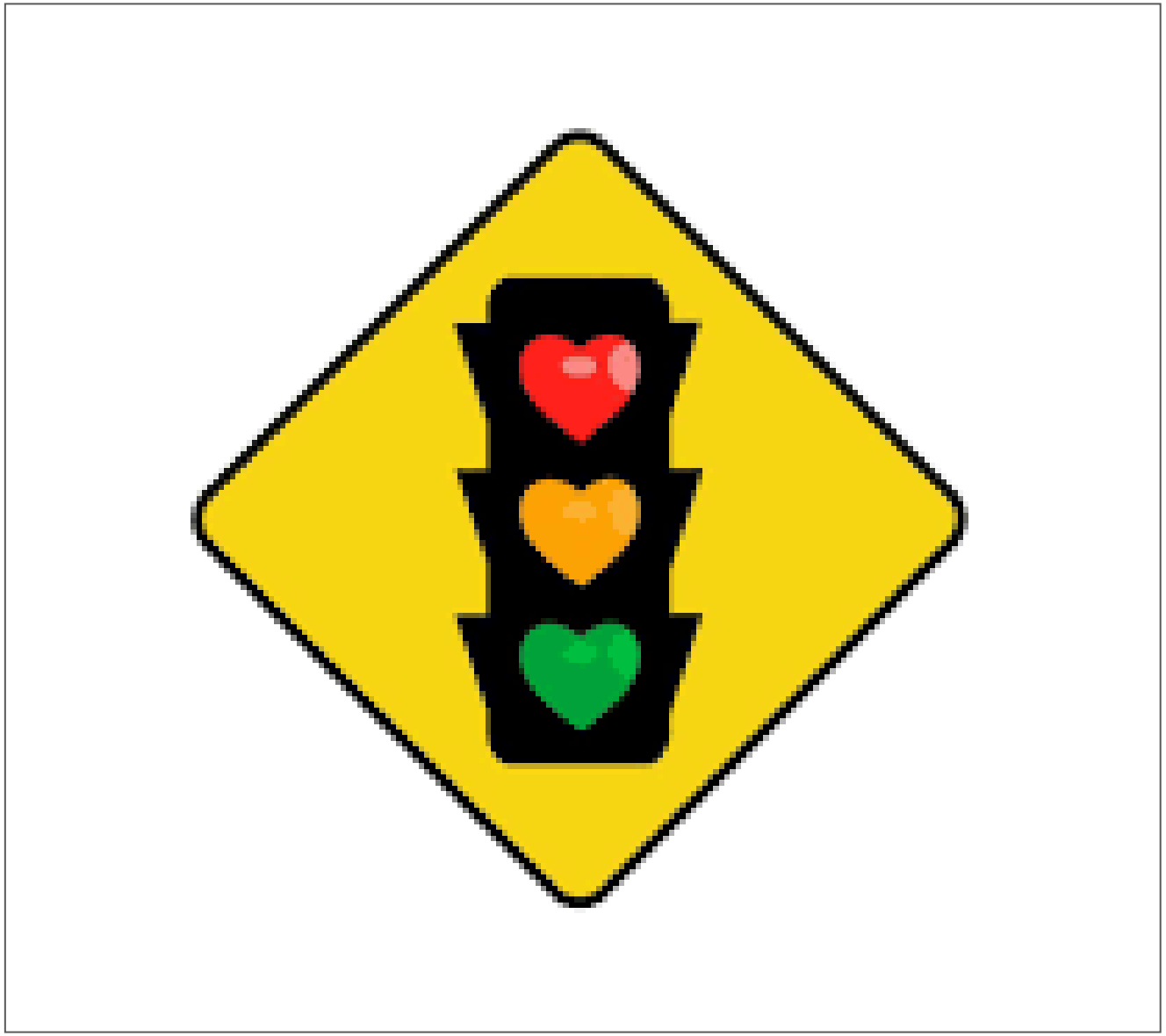


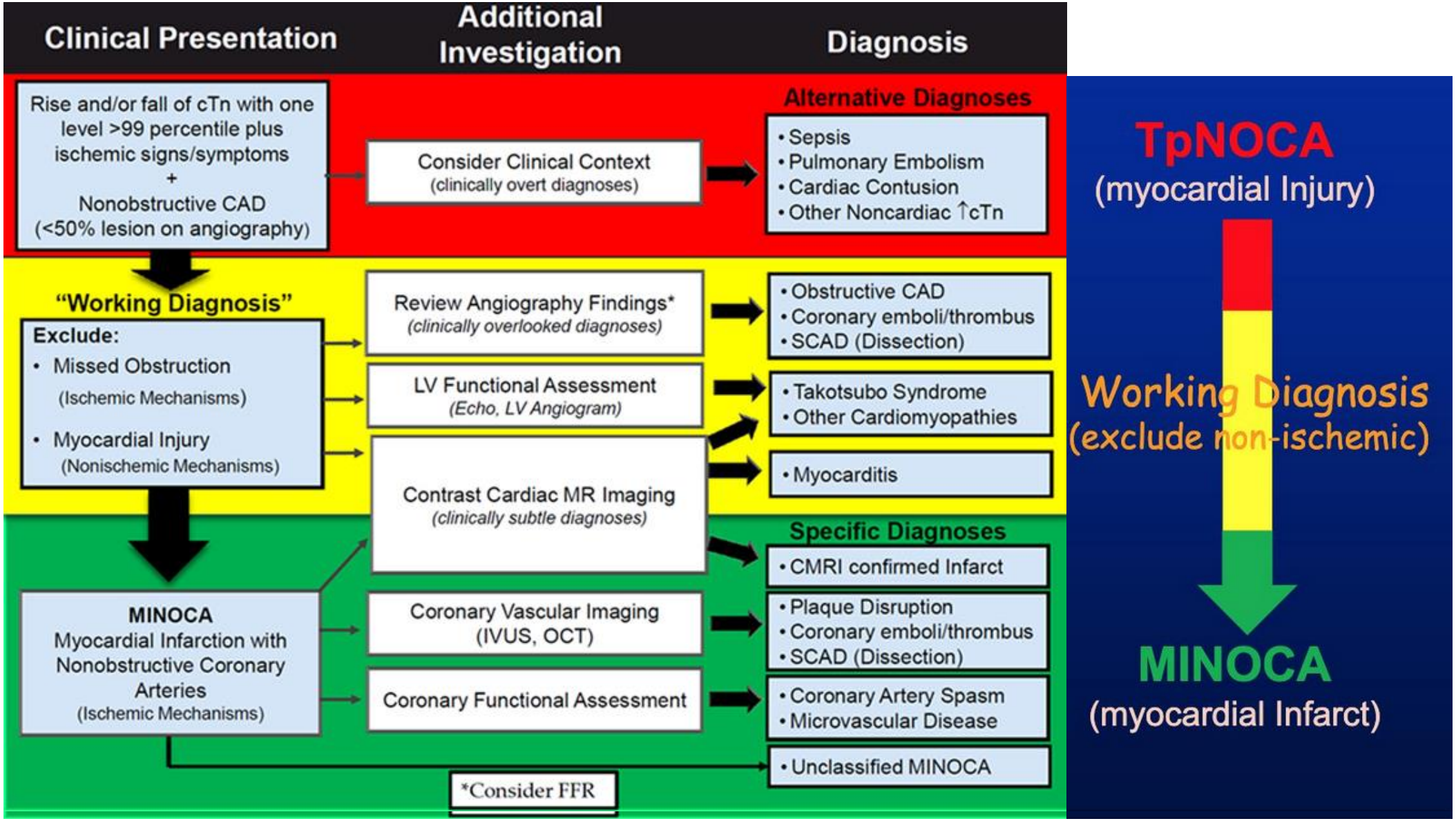
- lack of specificity of ischaemic symptoms and ischaemic ECG changes
- difficulty in measuring the exact degree of stenosis on coronary angiography

EuroIntervention 2021;17:e875-e887

Difficult to do?

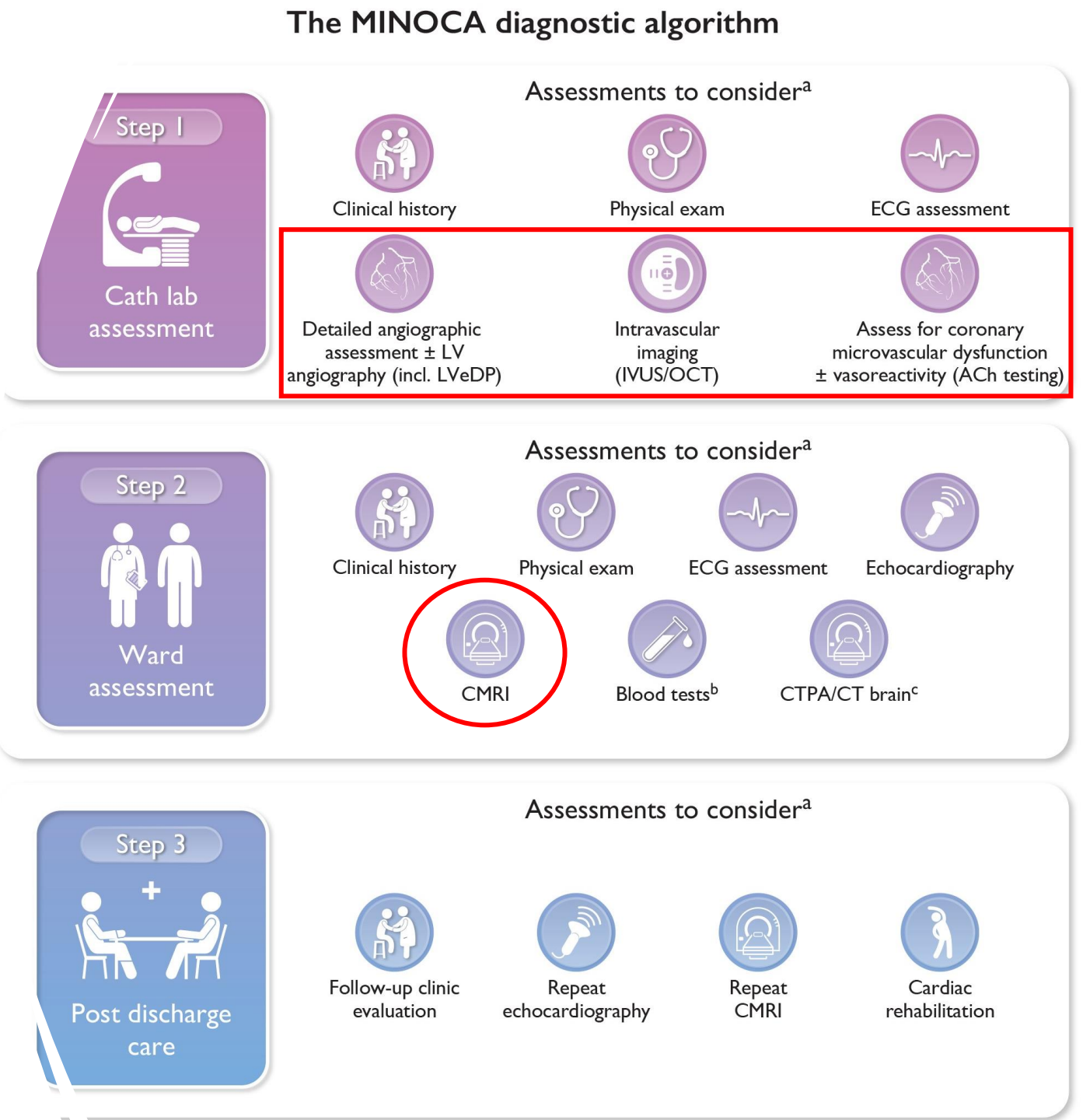
Use the traffic light approach!





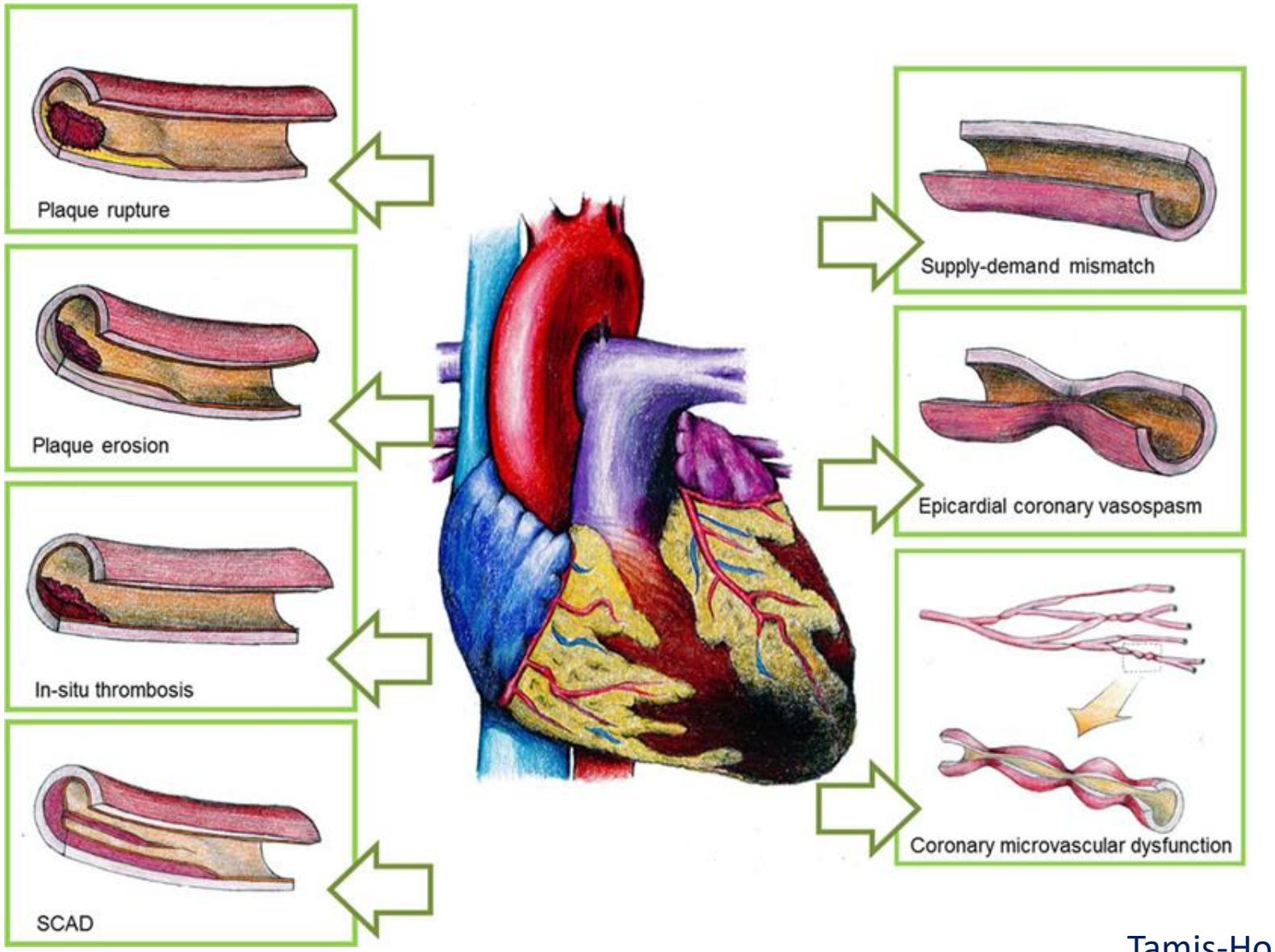
Tamis-Holland. Circulation 2019

Evaluation of patients with a working diagnosis of MINOCA



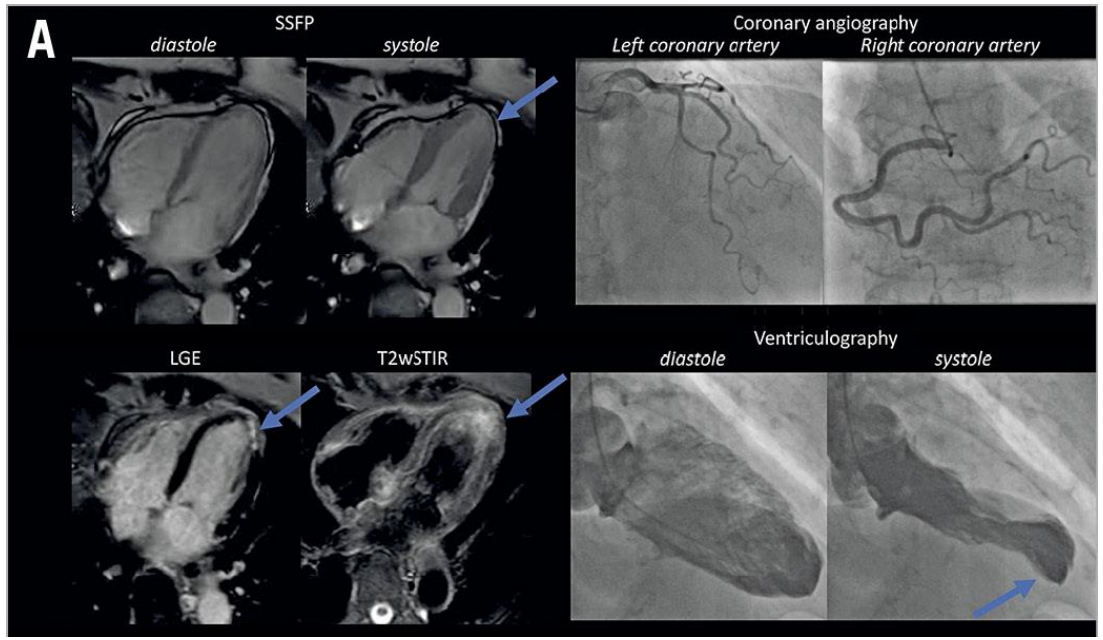
Byrne et al. EHJ, Volume 44, Issue 38, 7 October 2023

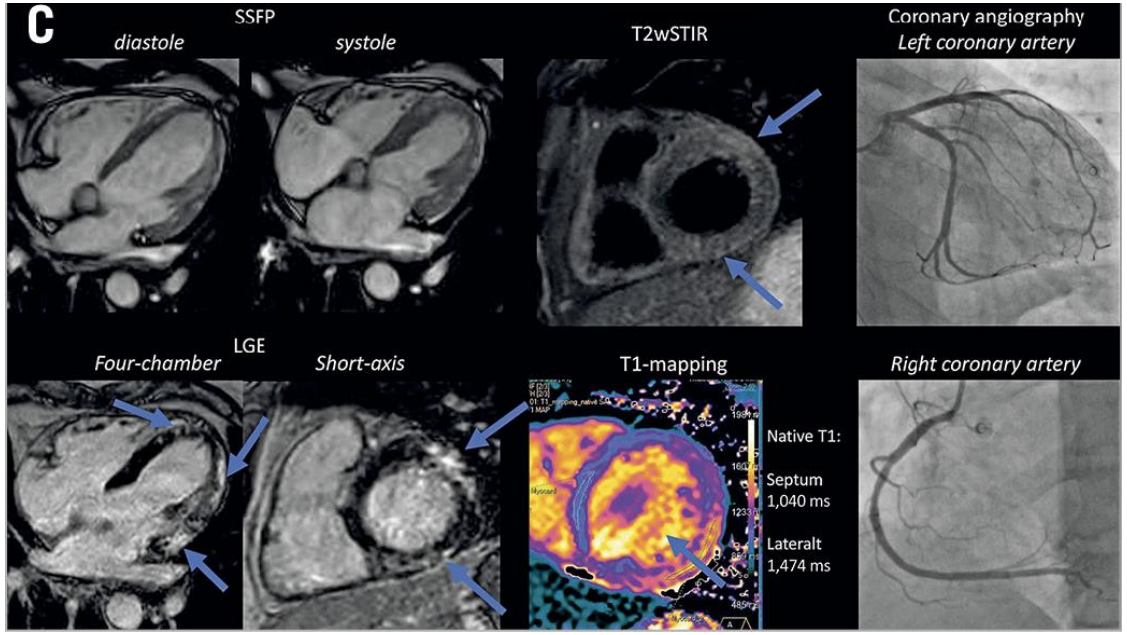
Specific Causes of MINOCA



Tamis-Holland. Circulation 2019

CMR





T2wSTIR sequence – oedema
transmural contrast enhancement in LGE sequence→ scarring→ AMI limited to a small area (embolic genesis?)

widespread subepicardial signal increase → myocarditis

EuroIntervention 2021;17:e875-e887

State of the Art
by EuroIntervention

Myocardial infarction with non-obstructive coronary artery disease

Bertil Lindahl[1]*, MD, PhD; Tomasz Baron[1], MD, PhD; Mario Albertucci[2], MD; Francesco Prati[2,3], MD

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KEYWORDS

- clinical research
- miscellaneous
- risk stratification

Abstract

As a result of the increased use of coronary angiography in acute myocardial infarction in the last two decades, myocardial infarction with non-obstructive coronary arteries (MINOCA) has received growing attention in everyday clinical practice. At the same time, research interest in MINOCA has increased significantly. MINOCA is a heterogeneous disease entity seen in 5-10% of all patients with myocardial infarction, especially in women. Clinically, MINOCA may be difficult to distinguish from other non-ischaemic conditions that can cause similar symptoms and myocardial injury. There is still some confusion around the diagnosis, investigation and management of patients with MINOCA. The present review summarises the current knowledge of MINOCA regarding epidemiology, pathophysiology, investigation, and treatment, with a special focus on imaging modalities. In addition, remaining important knowledge gaps are highlighted.

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DOI: 10.4244/EIJ-D-21-00426

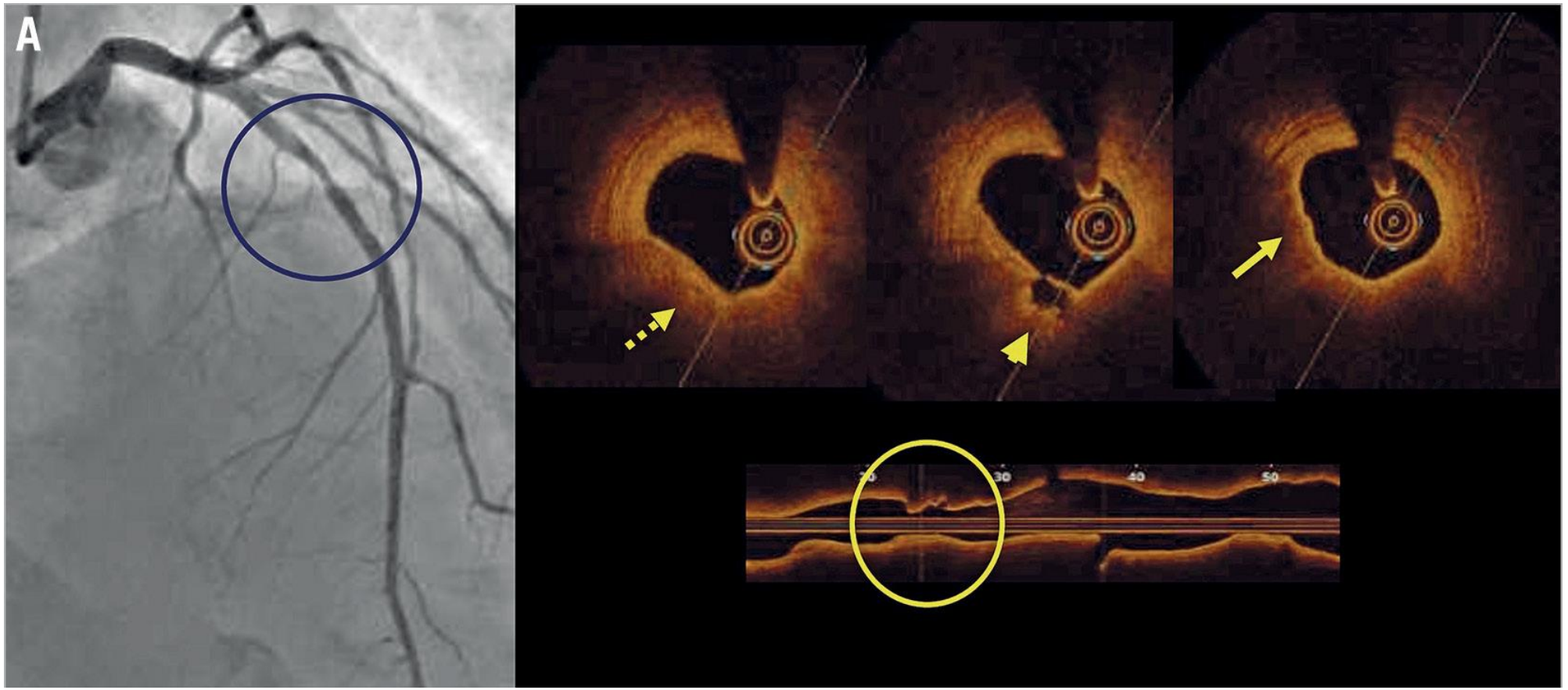
TIMING OF CMR EXAMINATION

TIMING OF CMR EXAMINATION

The diagnostic precision of CMR is increased when imaging is undertaken within 7-14 days of presentation. Delayed imaging may result in certain pathological changes, such as myocardial oedema in myocarditis no longer being apparent. Dastidar et al compared results of retrospective scans in MINOCA patients, showing that early performance of CMR (within two weeks after admission) reduces the number of non-conclusive scans from 43% to 16%, mainly due to a better detectability of Takotsubo syndrome and myocarditis[22]. In serial scans of patients with a working diagnosis of MINOCA, in whom early scans revealed myocarditis, scans more than three weeks after admission showed a complete resolution of epicardial LGE pattern in one fourth[23].

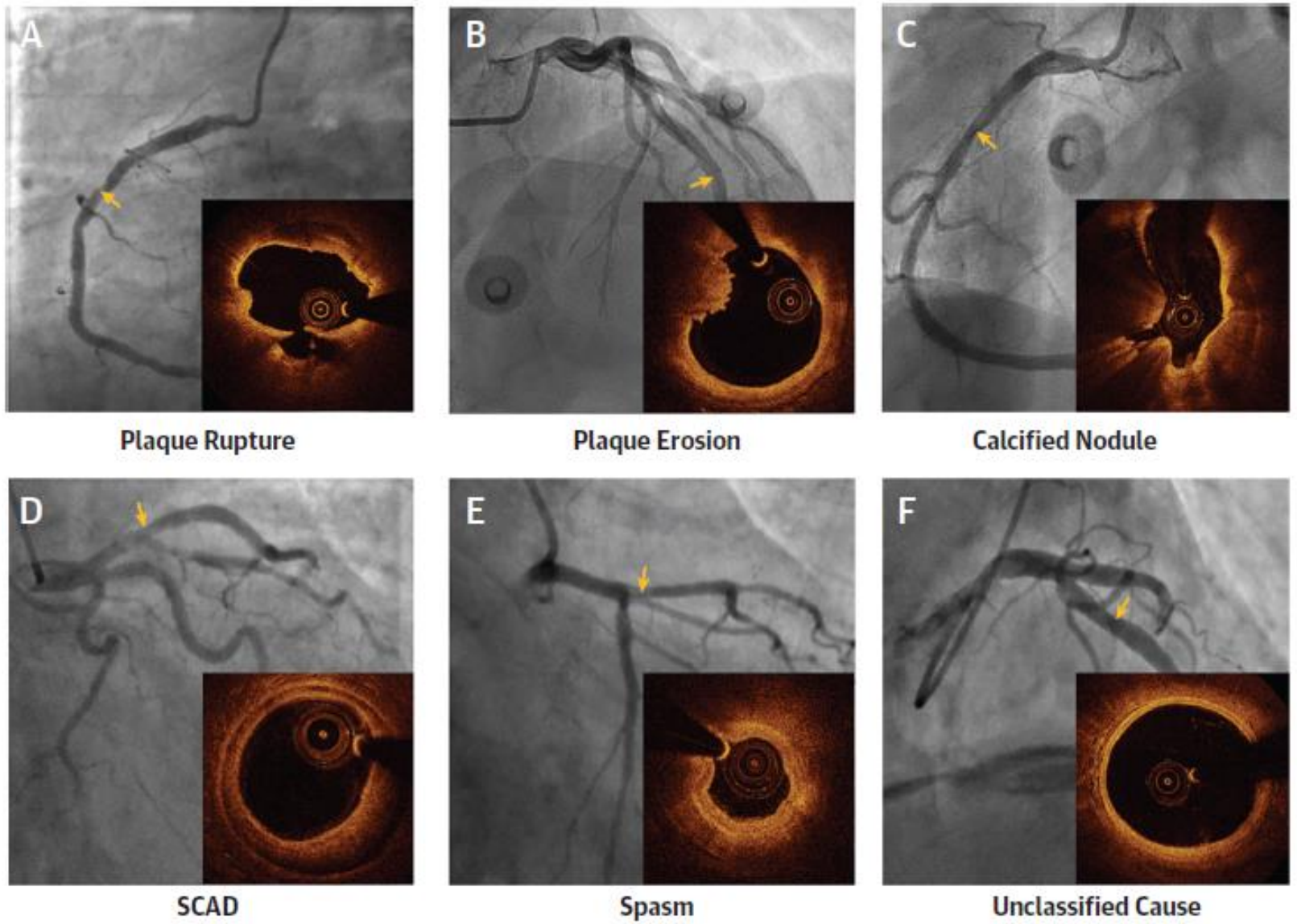
EuroIntervention 2021;17:e875-e887

OCT



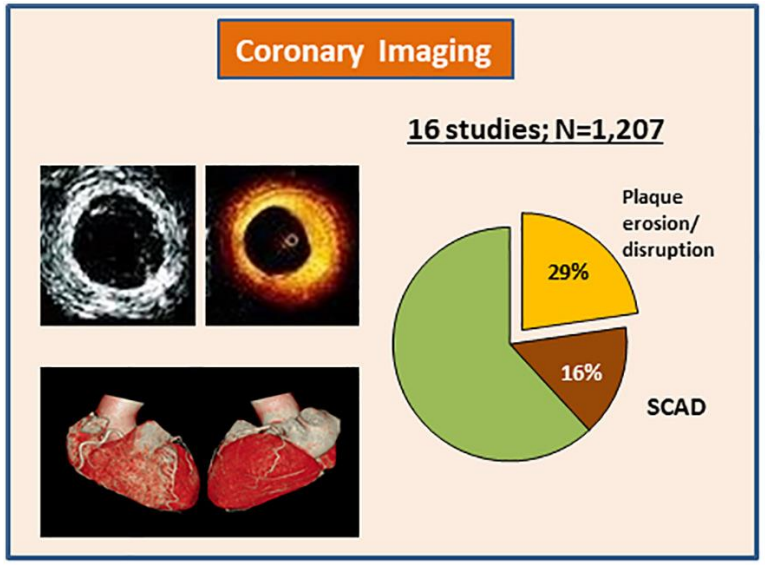
EuroIntervention 2021;17:e875-e887

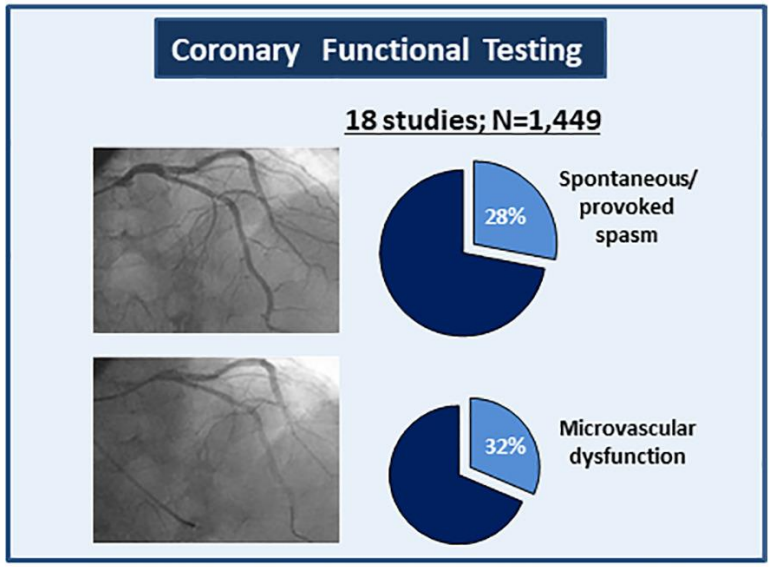
Representative OCT Images in MINOCAs

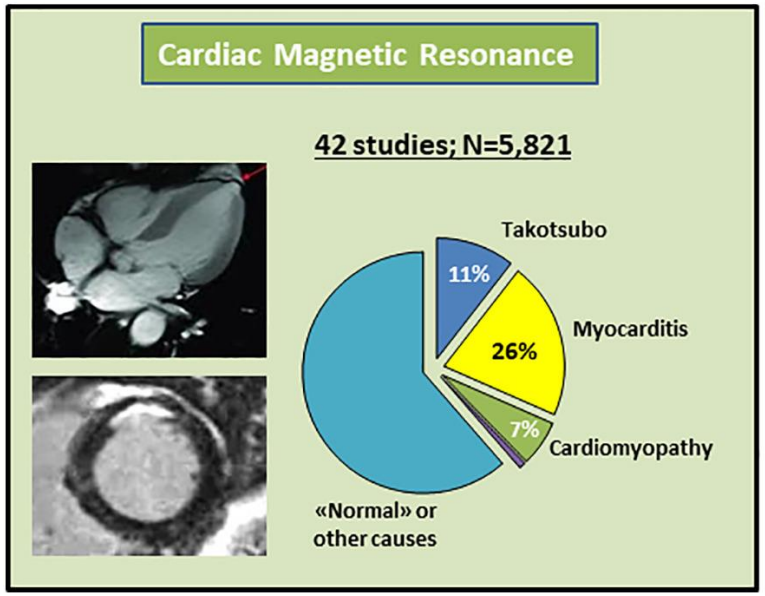


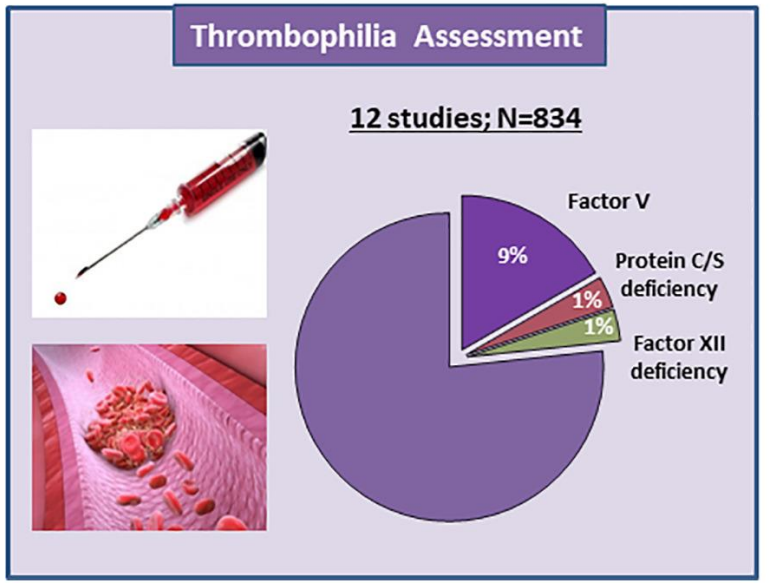
Zeng et al. JACC cardiovascular Imaging, 2023

Utility of comprehensive evaluation in MINOCA









Pelliccia et al International Journal of Cardiology, 2021

Circulation

ORIGINAL RESEARCH ARTICLE

Coronary Optical Coherence Tomography and Cardiac Magnetic Resonance Imaging to Determine Underlying Causes of Myocardial Infarction With Nonobstructive Coronary Arteries in Women

Harmony R. Reynolds, MD
Judith S. Hochman, MD

BACKGROUND: Myocardial infarction with nonobstructive coronary arteries (MINOCA) occurs in 6% to 15% of myocardial infarctions (MIs) and disproportionately affects women. Scientific statements recommend multimodality imaging in MINOCA to define the underlying cause. We performed coronary optical coherence tomography (OCT) and cardiac magnetic resonance (CMR) imaging to assess mechanisms of MINOCA.

METHODS: In this prospective, multicenter, international, observational study, we enrolled women with a clinical diagnosis of myocardial infarction. If invasive coronary angiography revealed <50% stenosis in all major arteries, multivessel OCT was performed, followed by CMR (cine imaging, late gadolinium enhancement, and T2-weighted imaging and T1 mapping). Angiography, OCT, and CMR were evaluated at blinded, independent core laboratories. Culprit lesions identified by OCT were classified as definite or possible. The CMR core laboratory identified ischemia-related and nonischemic myocardial injury. Imaging results were combined to determine the mechanism of MINOCA, when possible.

RESULTS: Among 301 women enrolled at 16 sites, 170 were diagnosed with MINOCA, of whom 145 had adequate OCT image quality for analysis; 116 of these underwent CMR. A definite or possible culprit lesion was identified by OCT in 46.2% (67/145) of participants, most commonly plaque rupture, intraplaque cavity, or layered plaque. CMR was abnormal in 74.1% (86/116) of participants. An ischemic pattern of CMR abnormalities (infarction or myocardial edema in a coronary territory) was present in 53.4% (62/116) of participants undergoing CMR. A nonischemic pattern of CMR abnormalities (myocarditis, takotsubo syndrome, or nonischemic cardiomyopathy) was present in 20.7% (24/116). A cause of MINOCA was identified in 84.5% (98/116) of the women with multimodality imaging, higher than with OCT alone ($P<0.001$) or CMR alone ($P=0.001$). An ischemic cause was identified in 63.8% of women with MINOCA (74/116), a nonischemic cause was identified in 20.7% (24/116) of the women, and no mechanism was identified in 15.5% (18/116).

CONCLUSIONS: Multimodality imaging with coronary OCT and CMR identified potential mechanisms in 84.5% of women with a diagnosis of MINOCA, 75.5% of which were ischemic and 24.5% of which were nonischemic, alternate diagnoses to myocardial infarction. Identification of the cause of MINOCA is feasible and has the potential to guide medical therapy for secondary prevention.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02905357.

The full author list is available on page 638.

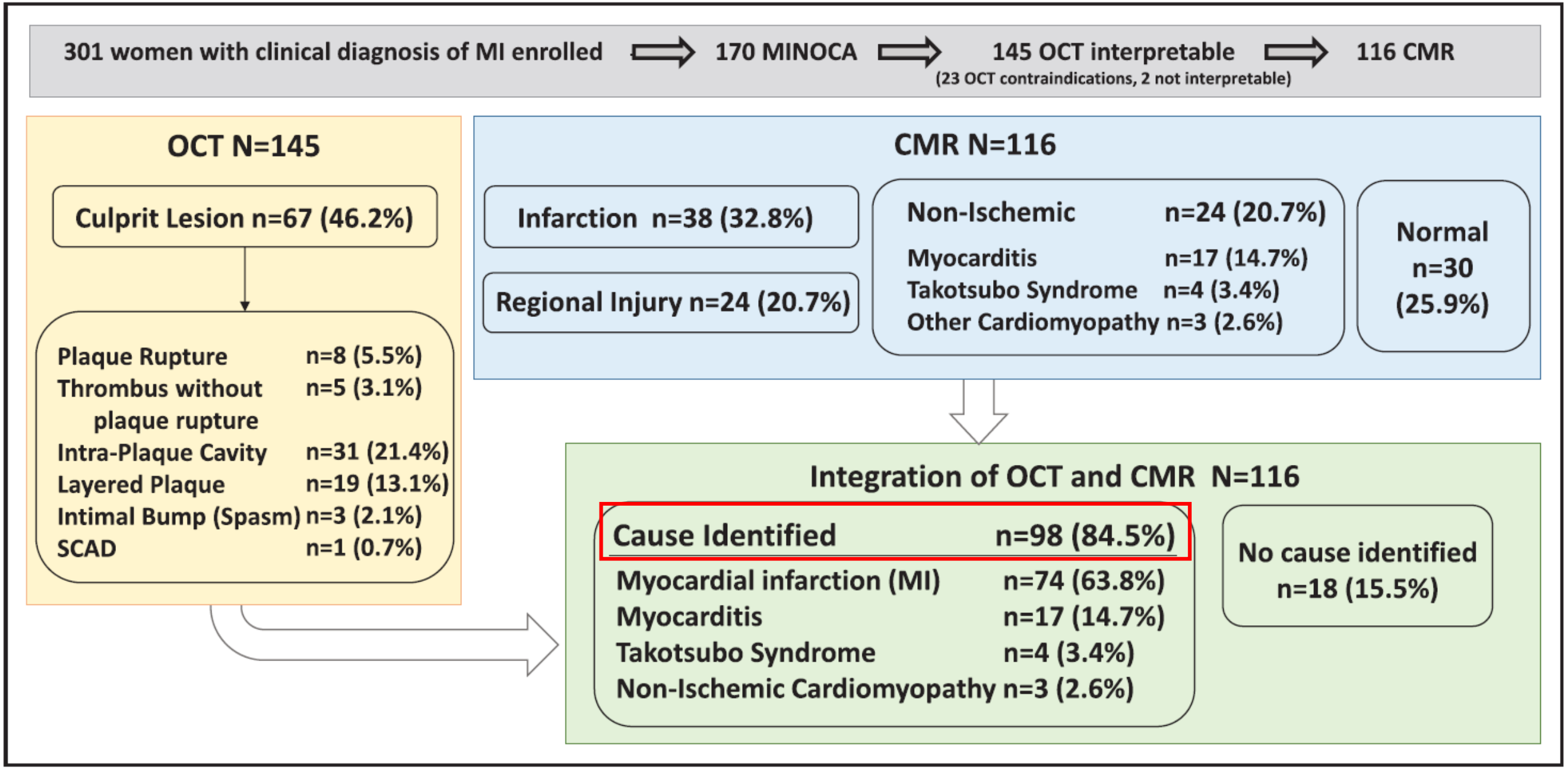
Key Words: coronary vessels ▪ magnetic resonance imaging ▪ myocardial infarction ▪ tomography, optical coherence ▪ women

Sources of Funding, see page 638

https://www.ahajournals.org/journal/circ

OCT +CMR

- 301 women enrolled at 16 sites
- Mean age 60
- OCT acquisition 2 days
- CMR acquisition 6 days


301 women with clinical diagnosis of MI enrolled
170 MINOCA
145 OCT interpretable
(23 OCT contraindications, 2 not interpretable)
116 CMR
OCT N=145
Culprit Lesion n=67 (46.2%)
Plaque Rupture n=8 (5.5%)
Thrombus without plaque rupture n=5 (3.1%)
Intra-Plaque Cavity n=31 (21.4%)
Layered Plaque n=19 (13.1%)
Intimal Bump (Spasm) n=3 (2.1%)
SCAD n=1 (0.7%)
CMR N=116
Infarction n=38 (32.8%)
Regional Injury n=24 (20.7%)
Non-Ischemic n=24 (20.7%)
Myocarditis n=17 (14.7%)
Takotsubo Syndrome n=4 (3.4%)
Other Cardiomyopathy n=3 (2.6%)
Normal n=30 (25.9%)
Integration of OCT and CMR N=116
Cause Identified n=98 (84.5%)
Myocardial infarction (MI) n=74 (63.8%)
Myocarditis n=17 (14.7%)
Takotsubo Syndrome n=4 (3.4%)
Non-Ischemic Cardiomyopathy n=3 (2.6%)
No cause identified n=18 (15.5%)

ESC European Society of Cardiology
European Heart Journal (2018) 39, 91–98
doi:10.1093/eurheartj/ehx667

CLINICAL RESEARCH
Acute coronary syndromes

Patients with acute myocardial infarction and non-obstructive coronary arteries: safety and prognostic relevance of invasive coronary provocative tests

Rocco A. Montone, Giampaolo Niccoli*, Francesco Fracassi, Michele Russo, Filippo Gurgoglione, Giulia Cammà, Gaetano A. Lanza, and Filippo Crea

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Received 16 May 2017; revised 21 August 2017; editorial decision 27 October 2017; accepted 20 November 2017; online publish-ahead-of-print 8 December 2017

See page 99 for the editorial comment on this article (doi: 10.1093/eurheartj/ehx737)

Aims Functional alterations of epicardial coronary arteries or coronary microcirculation represent a frequent cause of myocardial infarction and non-obstructive coronary arteries (MINOCA). We aimed at assessing the prognostic value of intracoronary provocative tests in patients presenting with MINOCA and in which other causes of MINOCA have been excluded.

Methods and results We prospectively evaluated patients with a diagnosis of MINOCA, excluding patients with aetiologies other than suspected coronary vasomotor abnormalities. Immediately after coronary angiography, an invasive provocative test using acetylcholine or ergonovine was performed. The incidence of death from any cause, cardiac death, and recurrence of acute coronary syndrome (ACS) was assessed at follow-up. We also assessed angina status using Seattle Angina Questionnaires (SAQ). We enrolled 80 consecutive patients [mean age 63.0 ± 10.7 years, 40 (50%) male]. Provocative test was positive in 37 (46.2%) patients without any complication. Among patients with a positive test, epicardial spasm was detected in 24 (64.9%) patients and microvascular spasm in 13 (35.1%) patients. After a median follow-up of 36.0 (range 12.0–60.0) months, patients with a positive test had a significantly higher occurrence of death from any cause [12 (32.4%) vs. 2 (4.7%); $P = 0.002$], cardiac death [7 (18.9%) vs. 0 (0.0%); $P = 0.005$], and readmission for ACS [10 (27.0%) vs. 3 (7.0%); $P = 0.015$] as well as a worse angina status as assessed by SAQ [Seattle score: 88.0 (33.0–100.0) vs. 100.0 (44.0–100.0); $P = 0.001$] when compared with patients with a negative test.

Conclusions We demonstrate that in patients presenting with MINOCA and suspected coronary vasomotor abnormalities, a positive provocative test for spasm is safe and identifies a high-risk subset of patients.

Keywords MINOCA • Invasive provocative test • Vasospasm • Prognosis

Introduction

Myocardial infarction (MI) and non-obstructive coronary arteries (MINOCA) is a syndrome with different causes, characterized by clinical evidence of MI with normal or near-normal coronary arteries on angiography.[1,2] Data from large MI registries suggest a prevalence between 5% and 25%,[2–4] but the most recent study, in a contemporary cohort of patients, reported a prevalence of 8.8%,[5] which appears to reflect daily clinical experience. Of importance, the prognosis of MINOCA is not as benign as reported by early cohort studies and as commonly assumed by physicians.[4,6,7] Moreover, a recent retrospective analysis of patients enrolled in the ACUITY trial[5] showed that, compared with non-ST elevation MI patients and obstructive coronary arteries, patients with MINOCA had a higher

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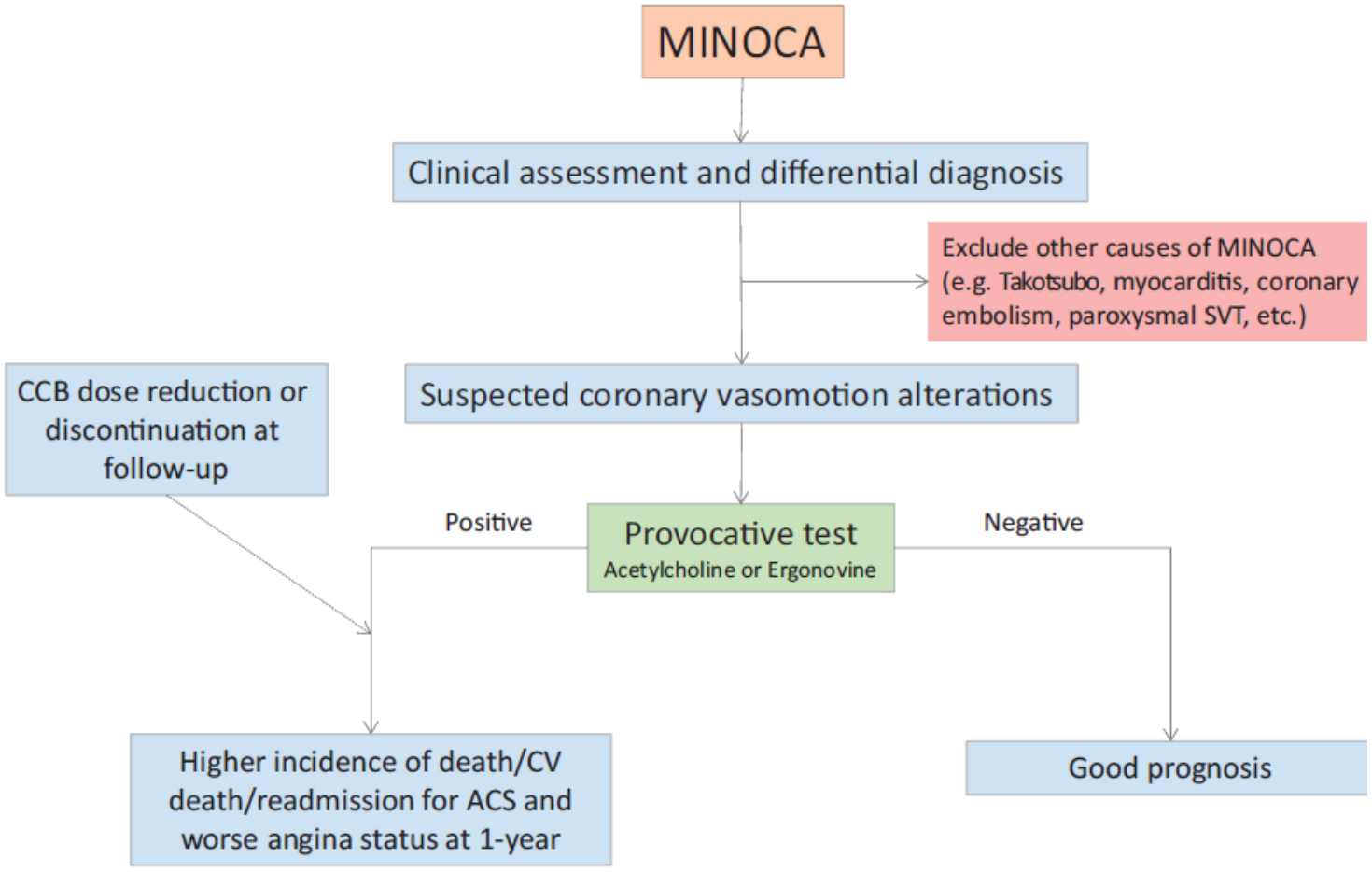
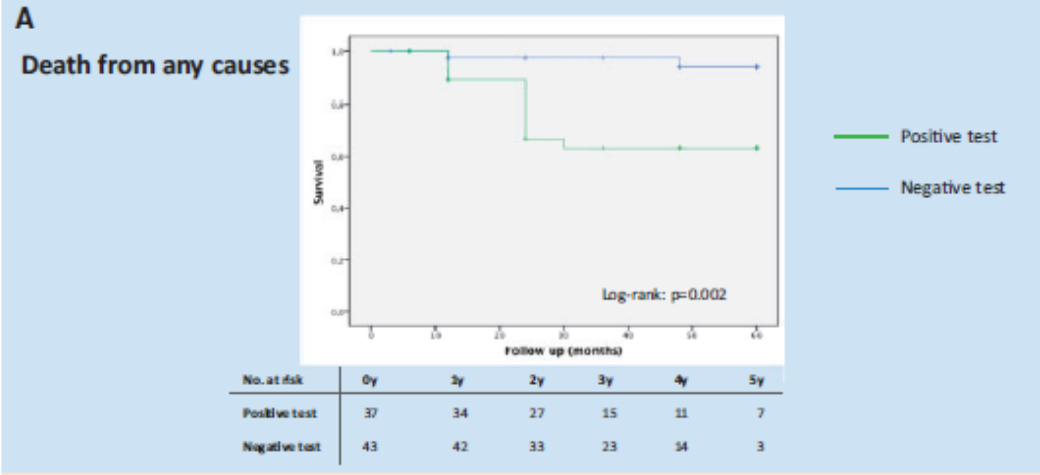
Safety and prognostic relevance of invasive coronary provocative tests

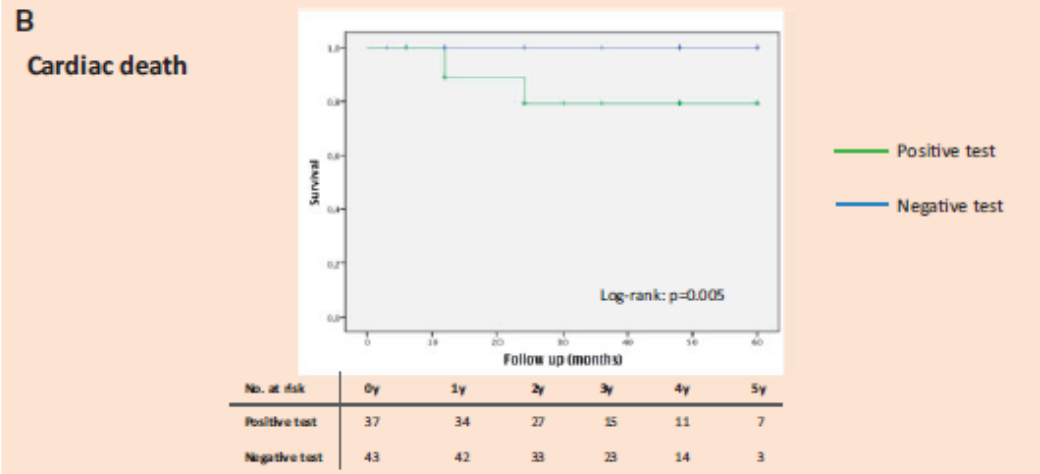
- 80 consecutive patients
- mean age 63.0± 10.7 years
- 40 (50%) male

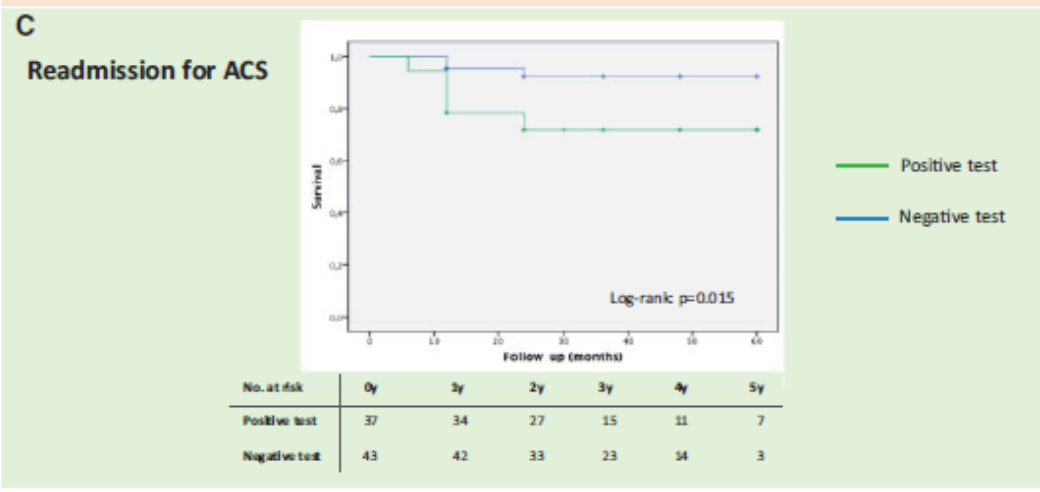
Montone et al European Heart Journal (2018) 39, 91–98

A positive provocative test for spasm is safe and identifies a high-risk subset of patients









MINOCA BAT

Randomized Evaluation of Beta Blocker and ACEI/ARB Treatment in MINOCA Patients - MINOCA-BAT (MINOCA-BAT)

ClinicalTrials.gov Identifier: NCT03686696

Recruitment Status : Terminated (Low inclusion rate.)
First Posted : September 27, 2018
Last Update Posted : November 27, 2023

Sponsor:
Uppsala University

Collaborators:
Karolinska Institutet
Göteborg University
University of Leeds
University of Adelaide
Oslo University Hospital
New York University

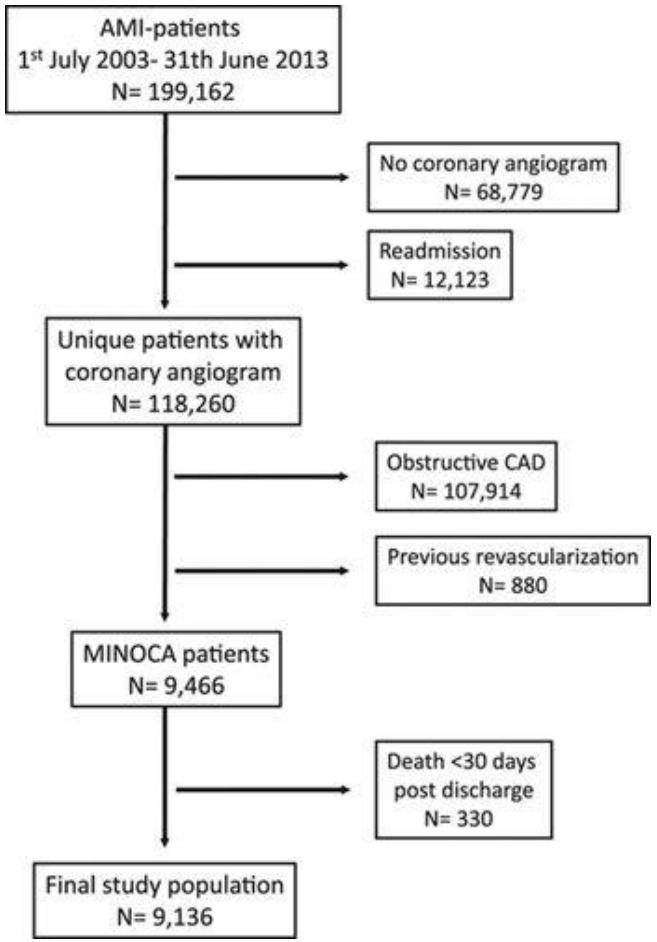
Information provided by (Responsible Party):
Uppsala University

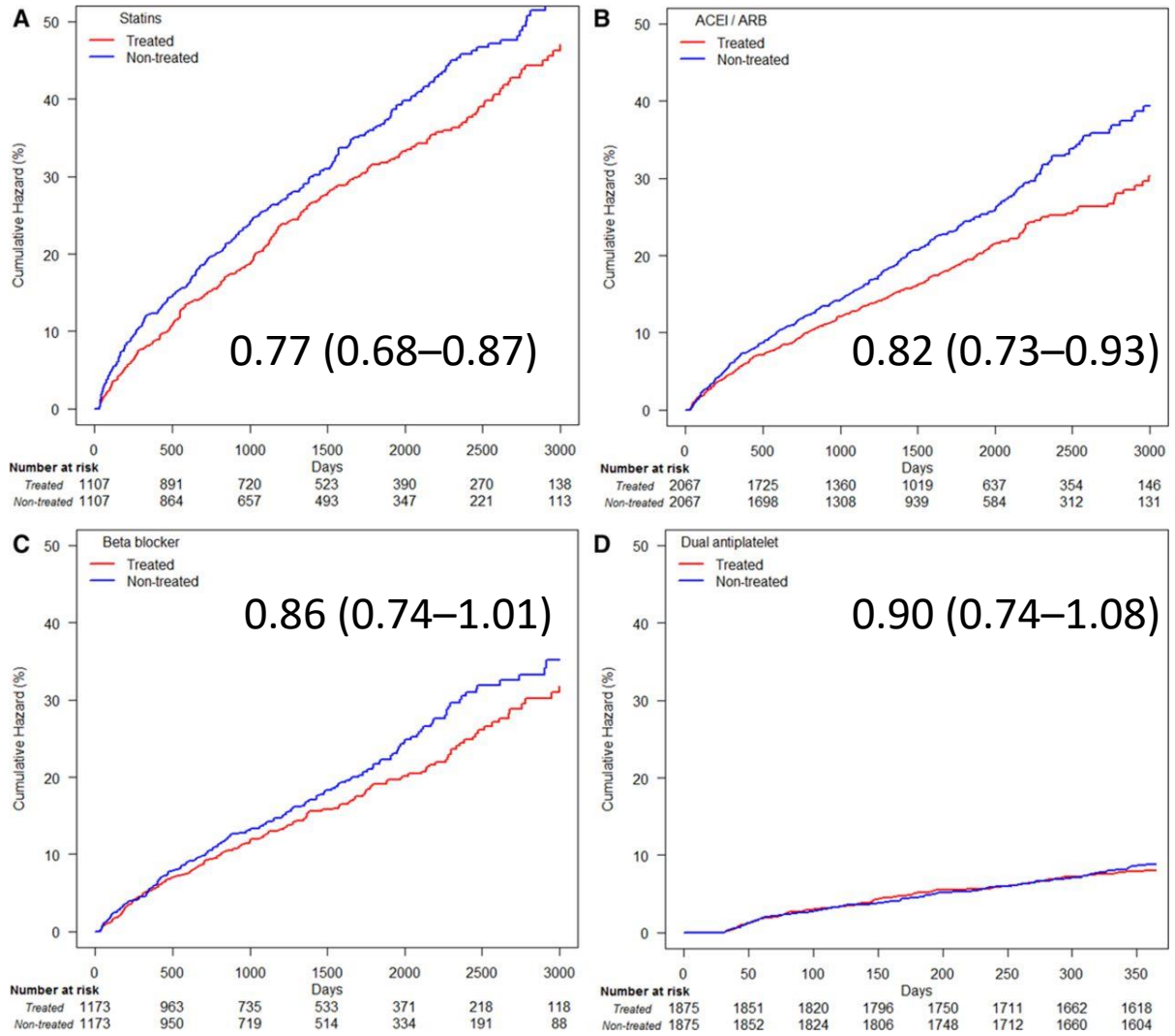
MINOCA BAT aims to randomize at least **3500 MINOCA patients** to treatment with **ACE inhibitors/ARBs and β-blockers or matching placebo**.

- all-cause mortality and cardiovascular events at 1 year
- explore the benefits of routine cardioprotective therapies in MINOCA patients.

Medical Treatment

SWEDEHEART registry





Circulation. 2017;135:1481–1489

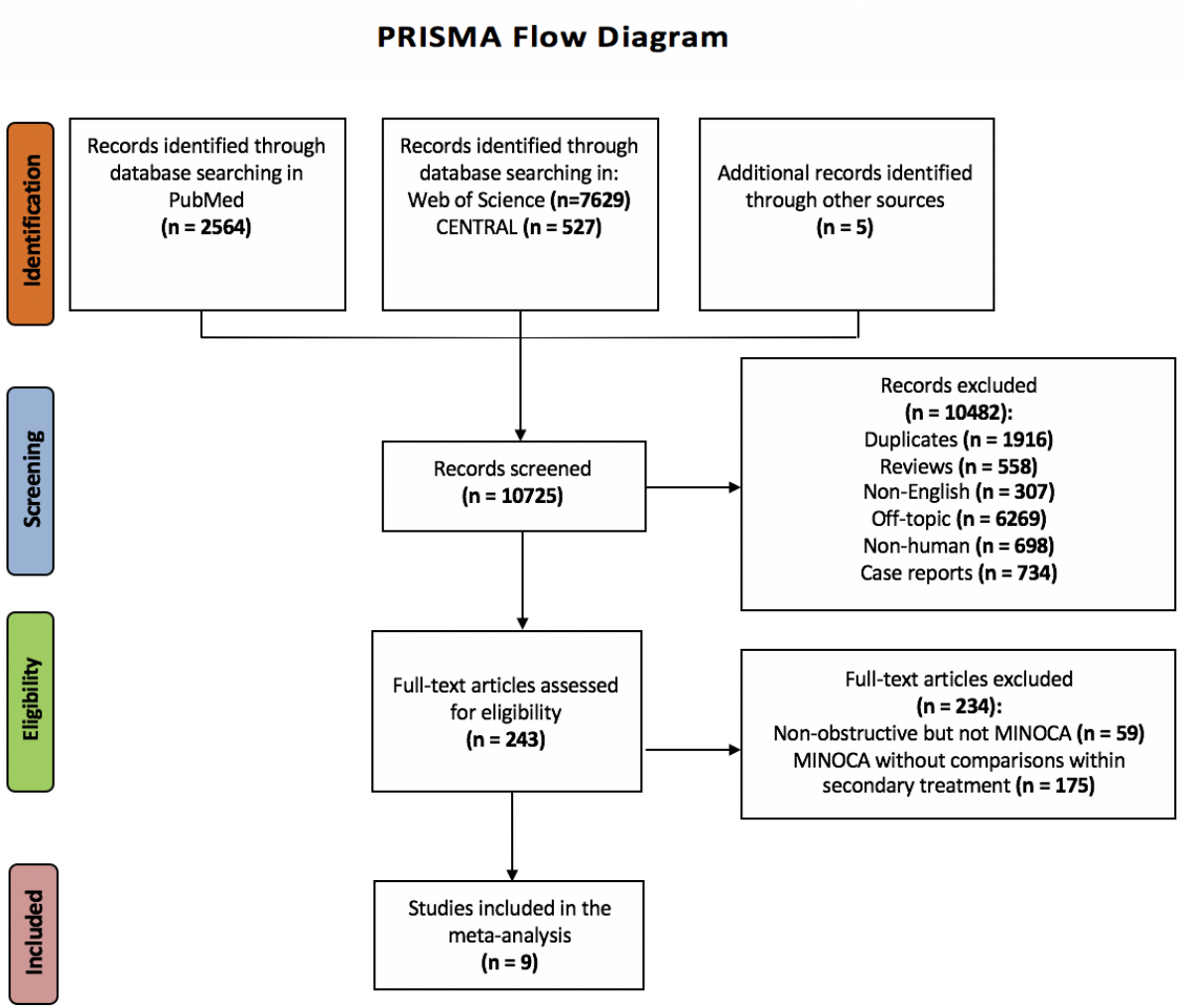
Finding from observational studies regarding benefit of secondary prevention treatment

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		

EuroIntervention 2021;17:e875-e887

Prognostic impact of secondary prevention treatment following myocardial infarction with non-obstructive coronary arteries (MINOCA):

Bayesian versus frequentist meta-analysis



Samaras et al. Eur Heart J Open. 2022 Nov 23;2(6):oeac077.

Β' ΠΑΝΕΠΙΣΤΗΜΙΑΚΗ ΚΑΡΔΙΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ Α.Π.Θ.

Prognostic impact of secondary prevention treatment following myocardial infarction with non-obstructive coronary arteries (MINOCA):

Prognostic Impact of Secondary Prevention Medical Therapy following Myocardial Infarction with Non-Obstructive Coronary Arteries:
A Bayesian and Frequentist Meta-Analysis

12,663 MINOCA patients
Meta-analysis of 5 observational studies
Medications analyzed RAAS inhibitors, statins, DAPT, β-blockers
Outcomes of interest • all-cause mortality • major adverse cardiovascular events (MACE)
Statistical methodologies • Frequentist (classical) • Bayesian (probabilistic)
Metric used: Adjusted Hazard Ratio
Mean follow-up: 12 to 90 months

	All-cause mortality		MACE
	β-blockers	Statins	RAAS inhibitors
aHR (Frequentist)	0.81 (0.67-0.97)	0.53 (0.37-0.76)	0.69 (0.53-0.90)
aHR (Bayesian)	0.83 (0.64-1.11)	0.61 (0.47-0.82)	0.74 (0.57-0.93)
Bayes Factor	1.15 (anecdotal)	32.20 (strong)	8.98 (moderate)

Prognostic benefit

- **Statins** for **all-cause mortality**
- **RAAS inhibitors** for **MACE**

Neutral effect

- **β-blockers**
- **DAPT**

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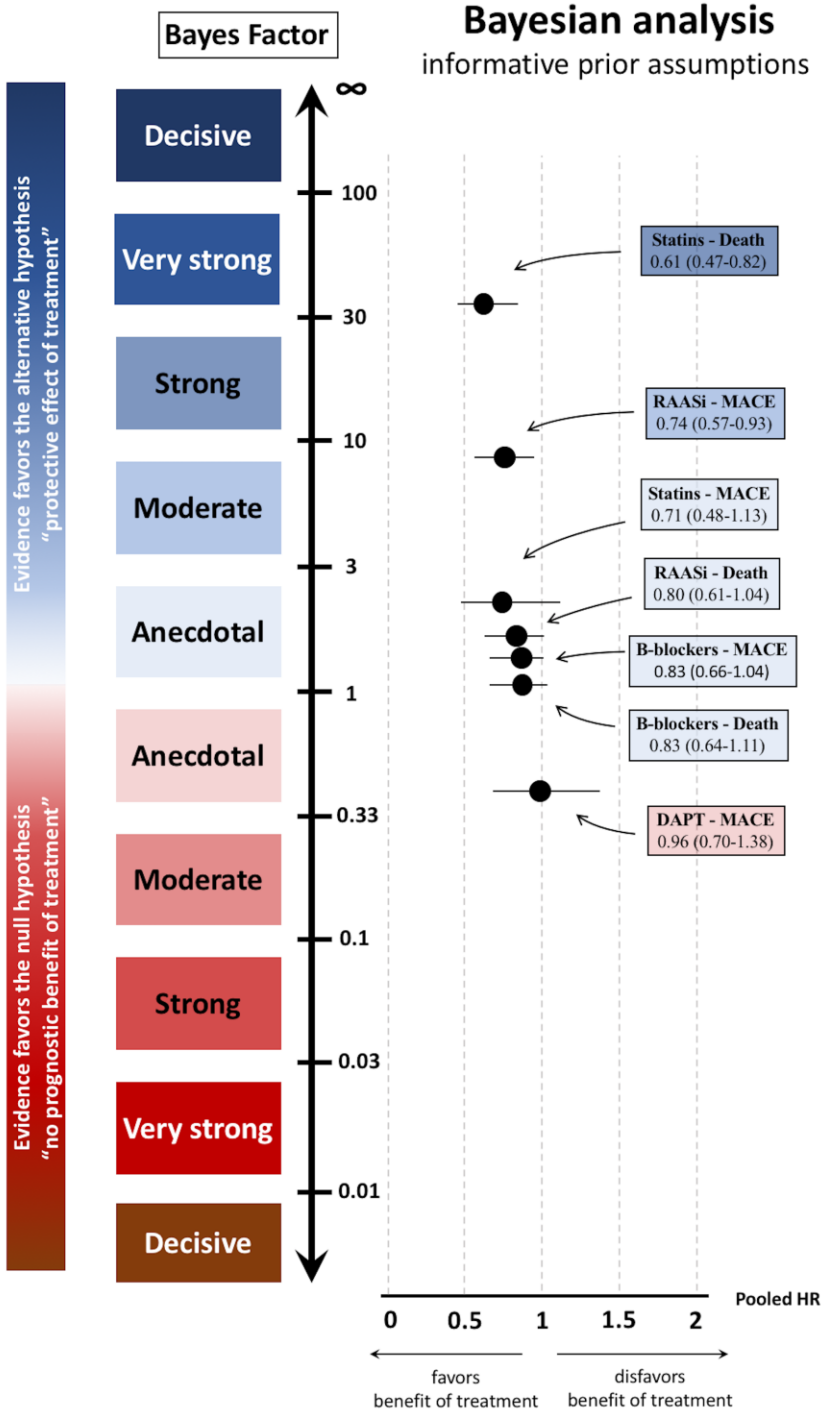
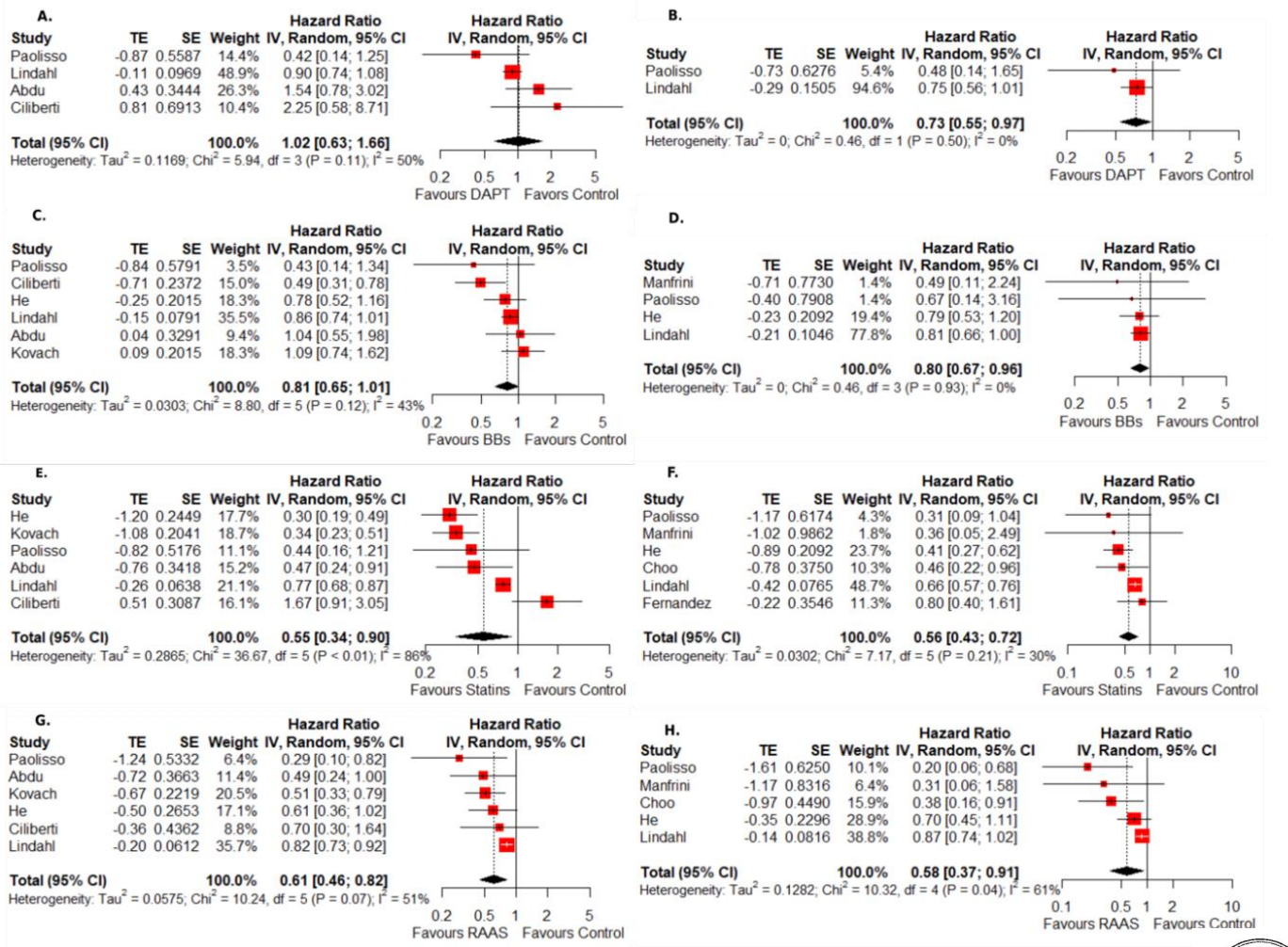
Samaras et al. Eur Heart J Open. 2022 Nov 23;2(6):oeac077.



Prognostic impact of secondary prevention treatment following myocardial infarction with non-obstructive coronary arteries (MINOCA):

Bayesian versus frequentist meta-analysis



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MINOCA challenges

- True prevalence and prognosis unknown
- Multiple diagnostic work-ups
  - ✓Cost
  - ✓Expertise
  - ✓Lack of clear sequence
- Treatment ?

Conclusions

- TpNOCA

Diagnosed at the time of angiography

Requires further investigations to delineate:

- ✓ Extra cardiac causes (eg d-dimers, CTPA)
- ✓ Non-ischemic cardiac causes (CMR imaging)

- MINOCA

Diagnosed after exclusion of non-ischemic causes

Requires further investigation for specific cause → Don't give up!

- **Underlying-cause targeted therapy**:
  - plaque disruption → SAPT
  - +thrombus → DAPT
  - Spasm (positive Ach test)→ calcium channel blockers
  - SCAD→ revascularization vs medical management

Thank you for your attention!