Test provocativi in Sala di Emodinamica: come, quando e perché -

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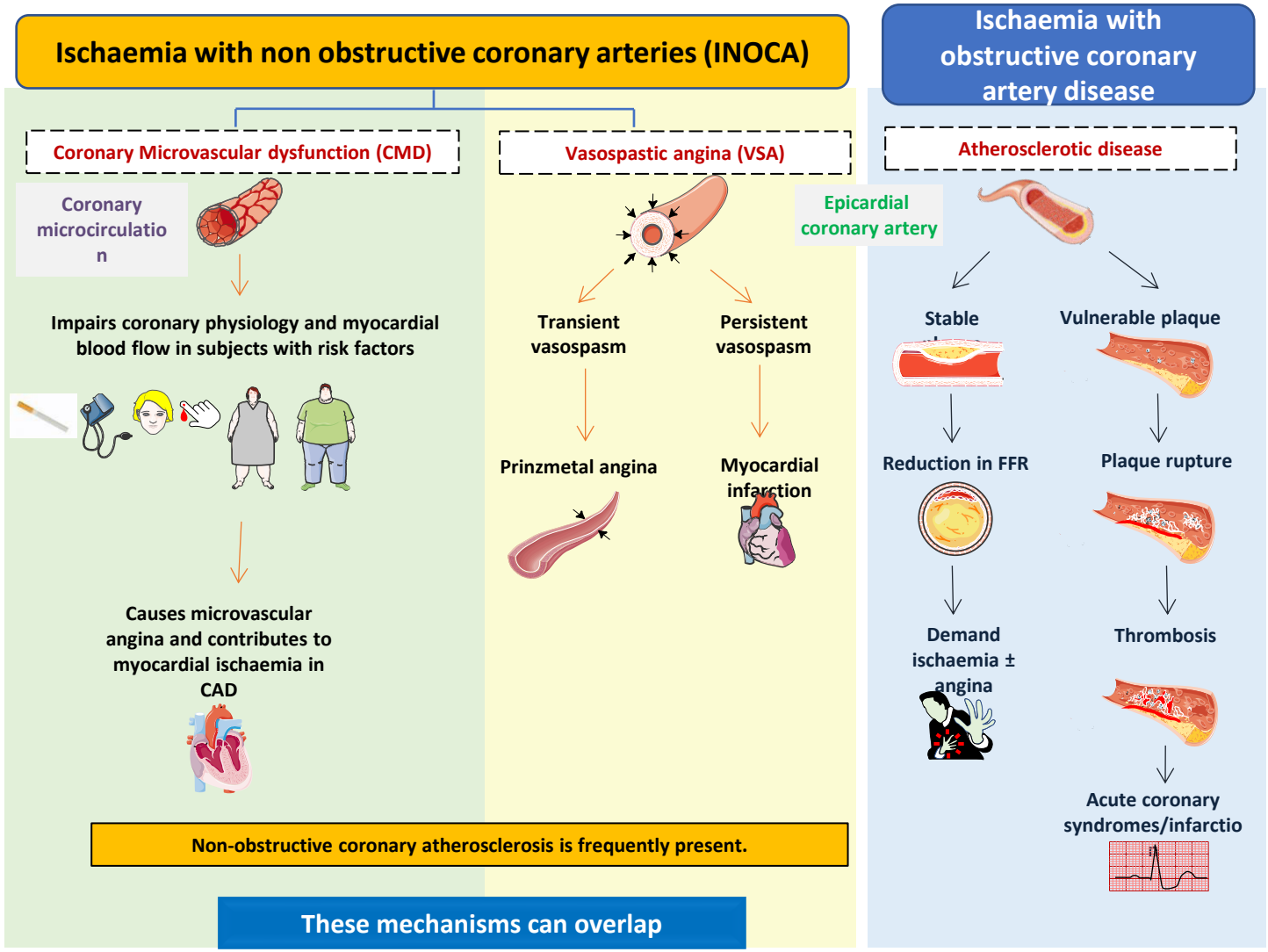
Milano



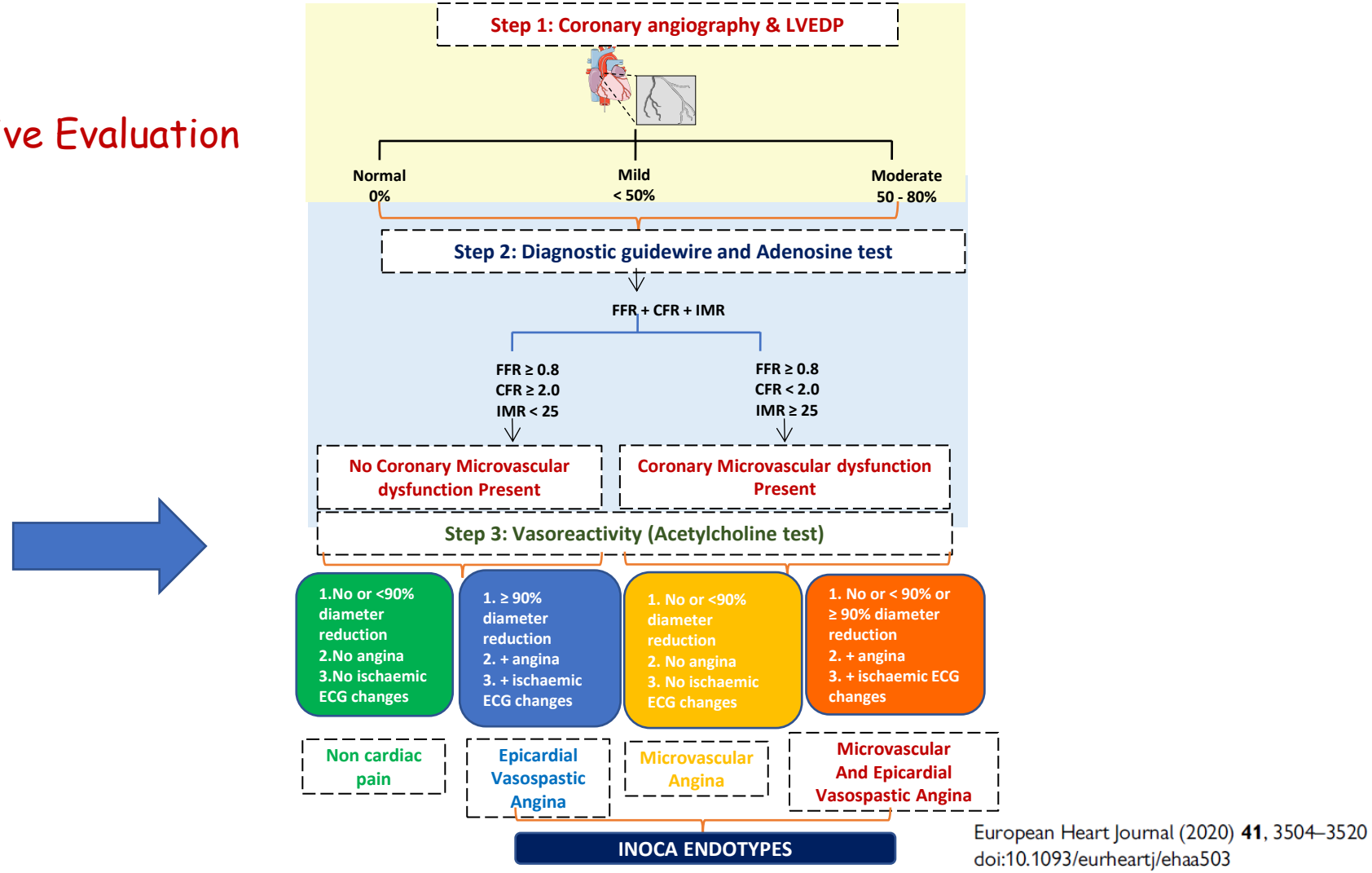
European Heart Journal (2020) **41**, 3504–3520
doi:10.1093/eurheartj/ehaa503

Invasive Assessment

Recommendations	Class[a]	Level[b]
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.[412,413]	IIa	B
Intracoronary acetylcholine with ECG monitoring may be considered during angiography, if coronary arteries are either angiographically normal or have moderate stenoses with preserved iwFR/FFR, to assess microvascular vasospasm.[412,438–440]	IIb	B
Transthoracic Doppler of the LAD, CMR, and PET may be considered for non-invasive assessment of CFR.[430–432,441]	IIb	B

Knuuti j, Wijns W et al. European Heart Journal (2020)

Invasive Evaluation



European Heart Journal (2020) **41**, 3504–3520
doi:10.1093/eurheartj/ehaa503

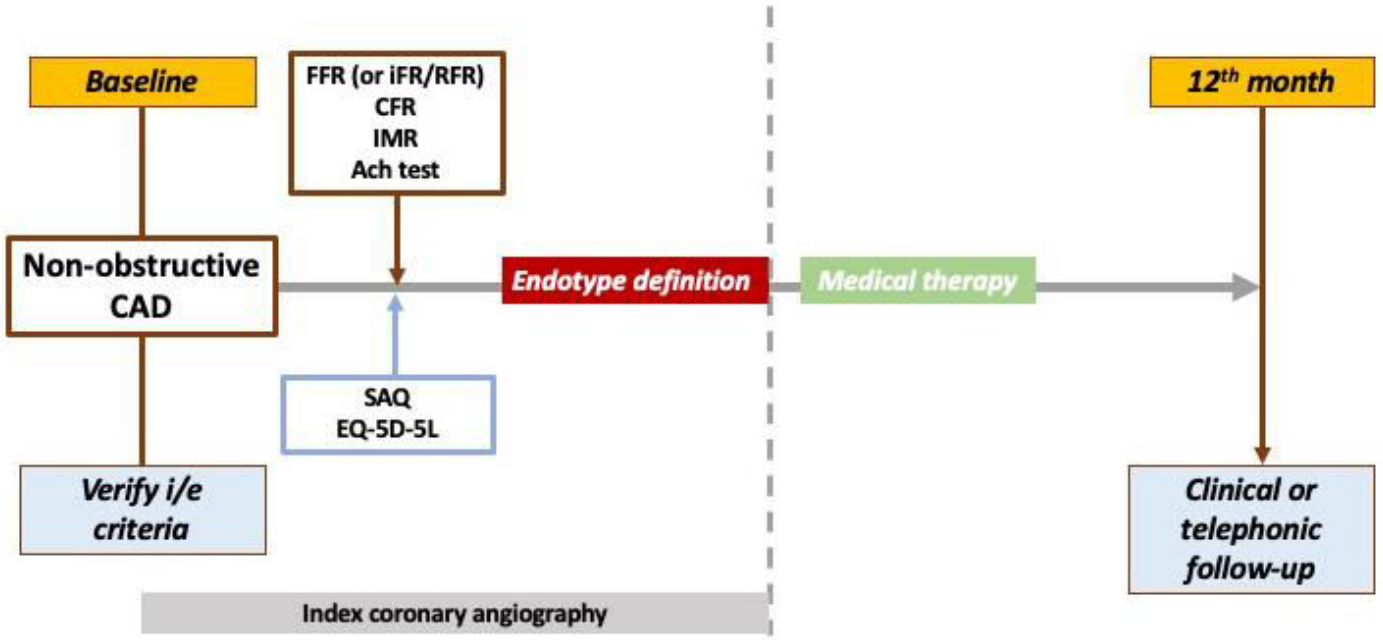
Ischemia in patients with non-obstructive disease (INOCA) in Italy: INOCA IT Multicenter Registry (RF-2019-12369486)

- Interventional Cardiology Unit IRCCS San Raffaele Hospital, Milano
- Dipartimento di Scienze Cardiovascolari e Toraciche Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma
- Dipartimento Assistenziale Integrato di Emergenze Cardiovascolari, Medicina Clinica e dell'Invecchiamento Azienda Ospedaliera Universitaria Federico II, Napoli

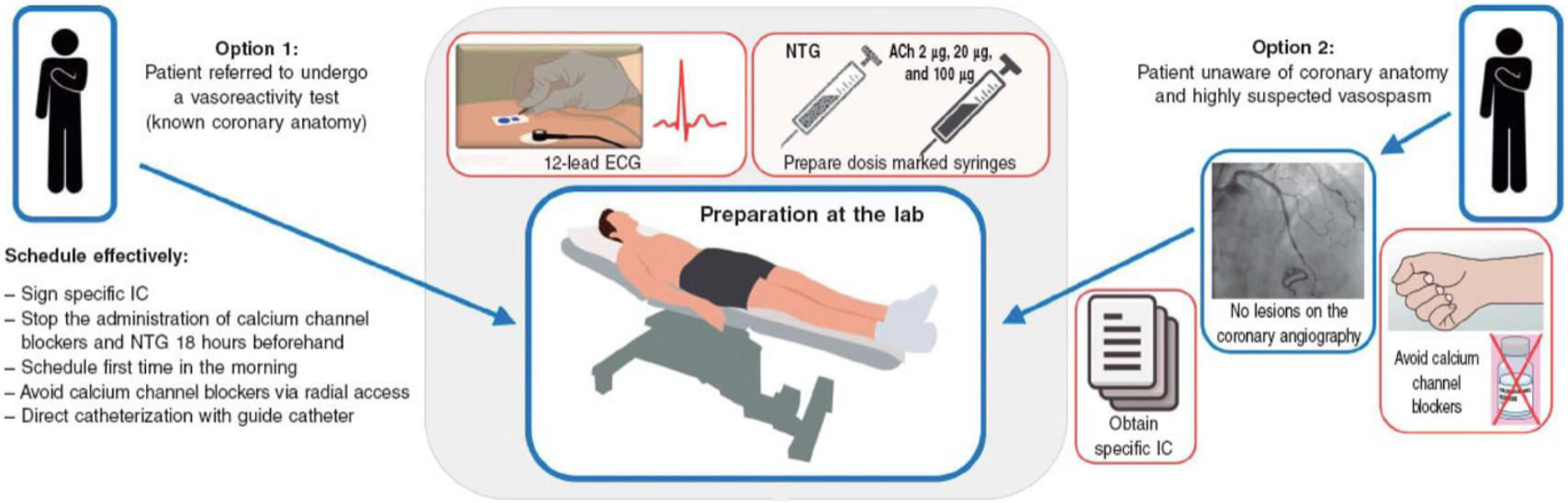
INOCA IT Multicenter Registry

Trial Flow-chart

N=200 pts



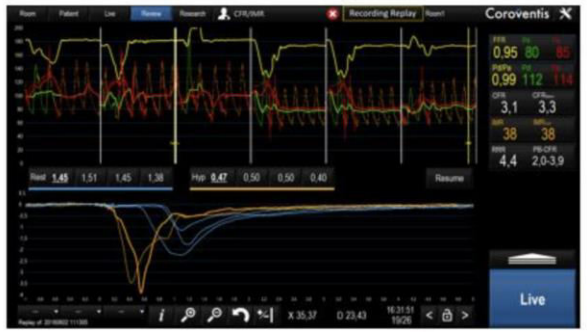
1. Invasive Testing



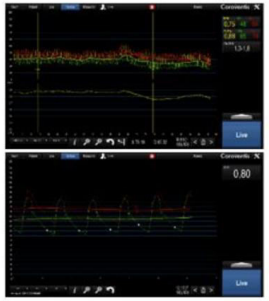
REC Interv Cardiol. 2021; 3(4):286-296. doi.org/10.24875/RECICE.M21000215

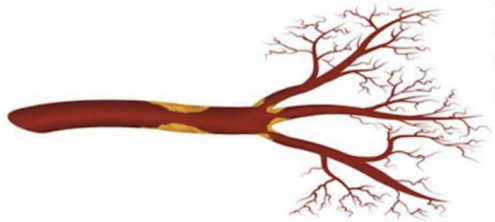
2. Coronary function testing: Diagnostic guidewire and Adenosine test

- Intravenous Adenosine (140 mcg/kg/min) to inducing steady-state hyperaemia and achieve endothelium-independent vasodilation



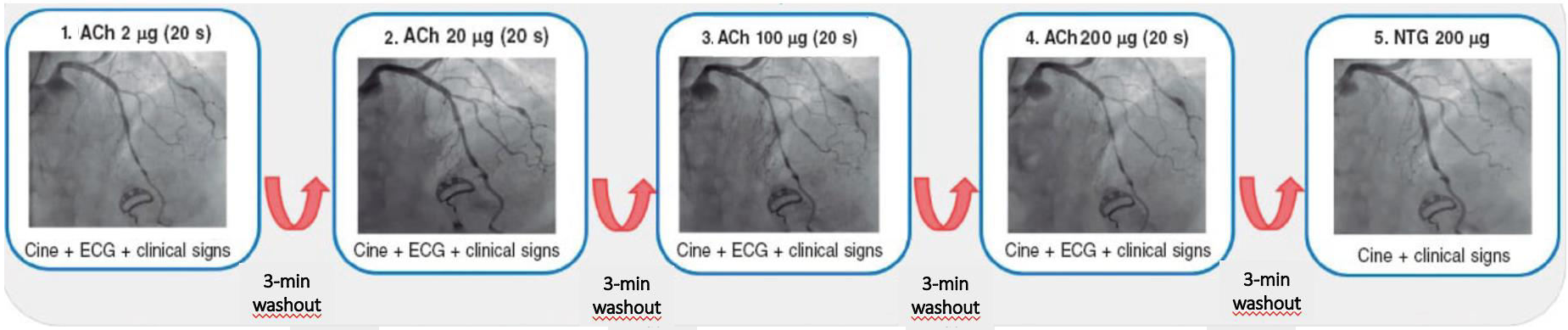
Epicardial assessment
- FFR, RFR, Pd/Pa
- Pullback





Microvascular assessment
- IMR, RRR
- CFR, PB-CFR
- Absolute Flow/Resistance

3. Vasoreactivity (Ach test) to detect epicardial or microvascular spasm



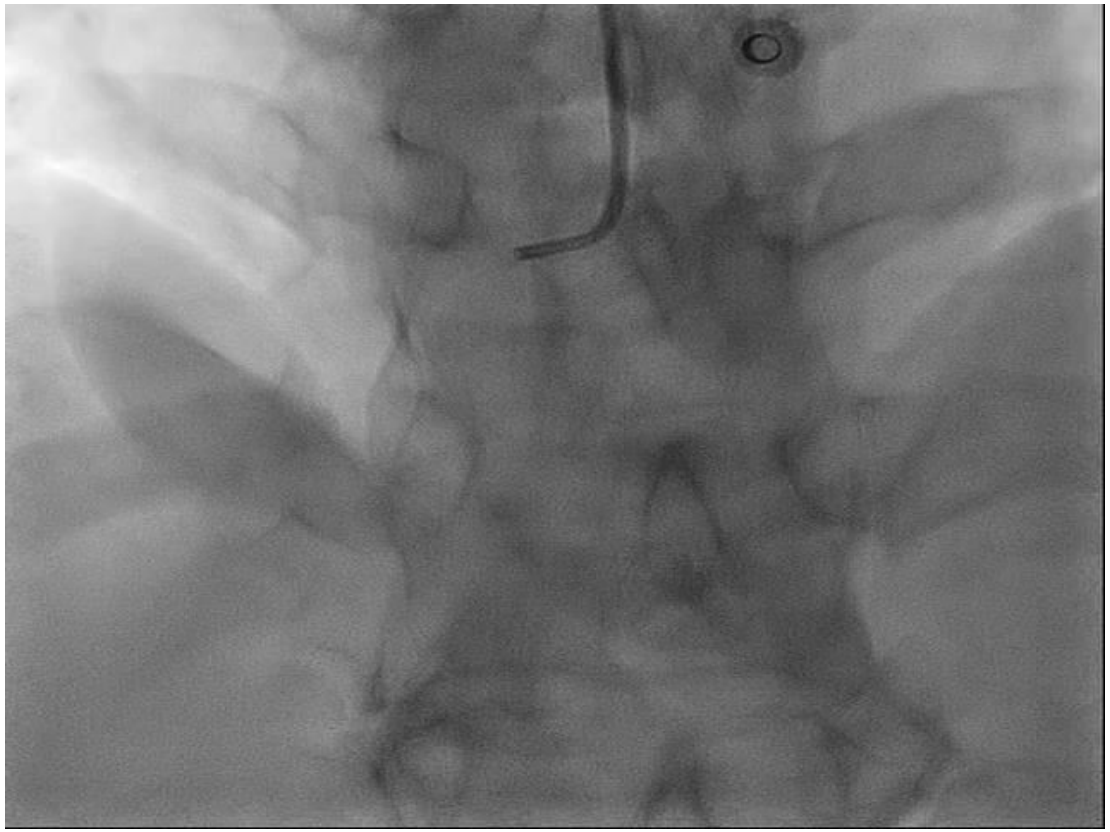
- Vasospastic Angina: anginal symptoms, ischemic ECG shifts, epicardial spasm during ACh testing
- Microvascular spasm: anginal symptoms, ischemic ECG shifts, but no epicardial spasm during ACh testing

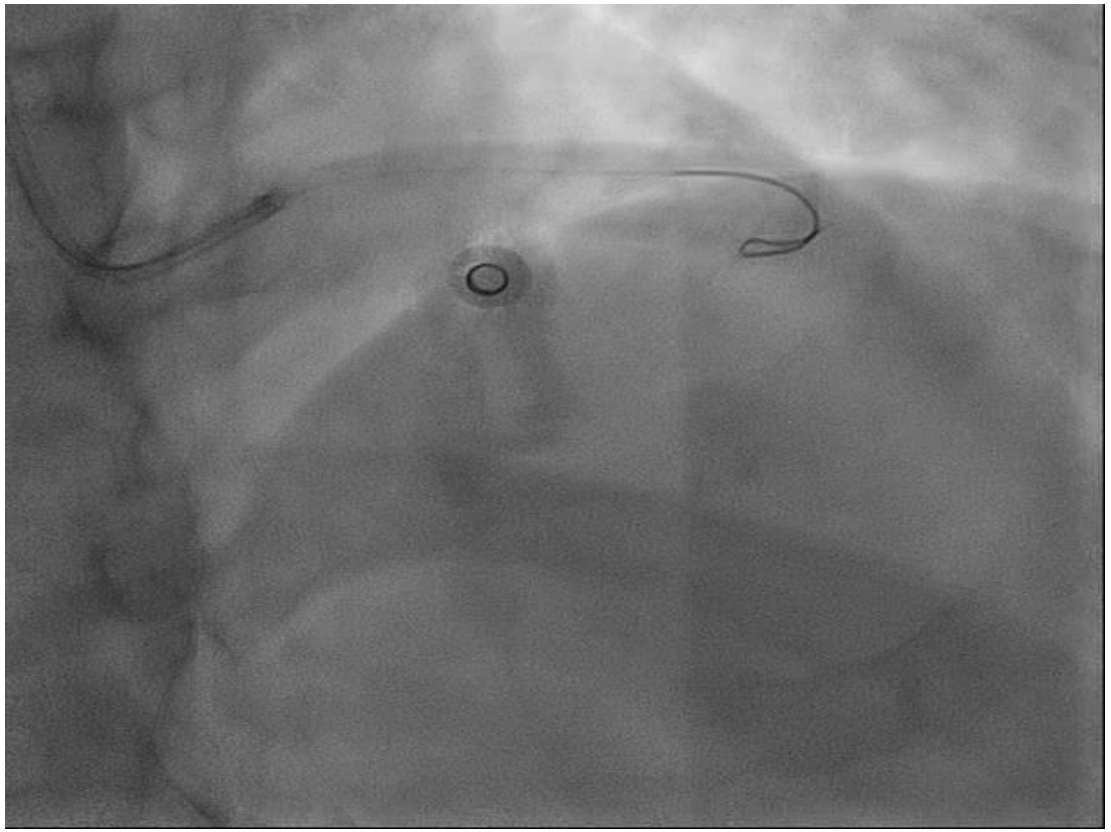
Readapted from Interv Cardiol. 2021; 3(4):286-296. doi.org/10.24875/RECICE.M21000215

CLINICAL PRESENTATION

- ♀, 51 years old
- **Risk factors for Cardiovascular Disease:** Hypertension, Dyslipidaemia, Family History for CAD
- **Comorbidities:** none
- **Cardiovascular History:**
  - Exertional Angina Pectoris since 2020
  - Episodes of Angina Pectoris at rest in 2021
  - Normal echocardiographic findings
- **Baseline Medication**: Diltiazem 60 mg x3/die, Olmesartan 20 mg/die
- December 2021: recruited to **INOCA- IT Registry**

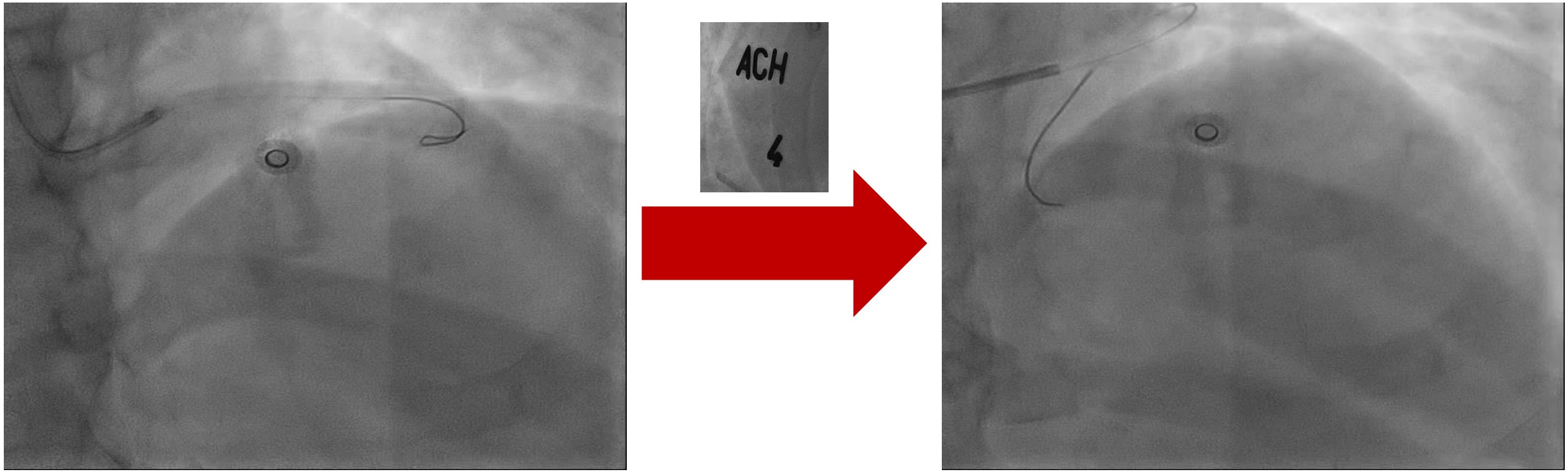
CORONARY ANGIOGRAPHY



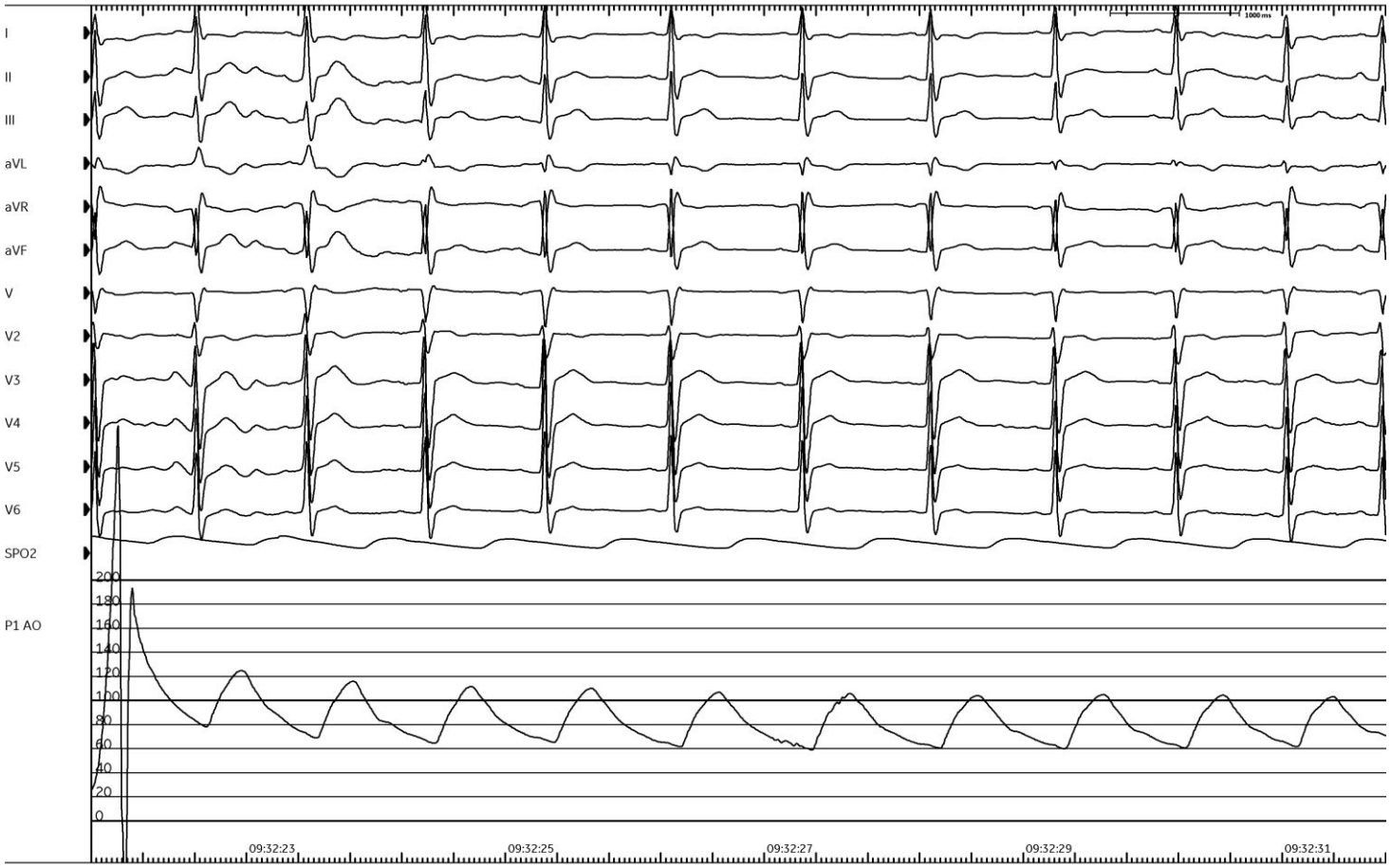


CORONARY FUNCTION TESTING: CMD

ACETYLCHOLINE PROVOCATION TEST: NEGATIVE



ACETYLCHOLINE PROVOCATION TEST: NEGATIVE



MANAGEMENT

- **Diagnosis:** Coronary Microvascular Dysfunction
- **Changes to Medication:**

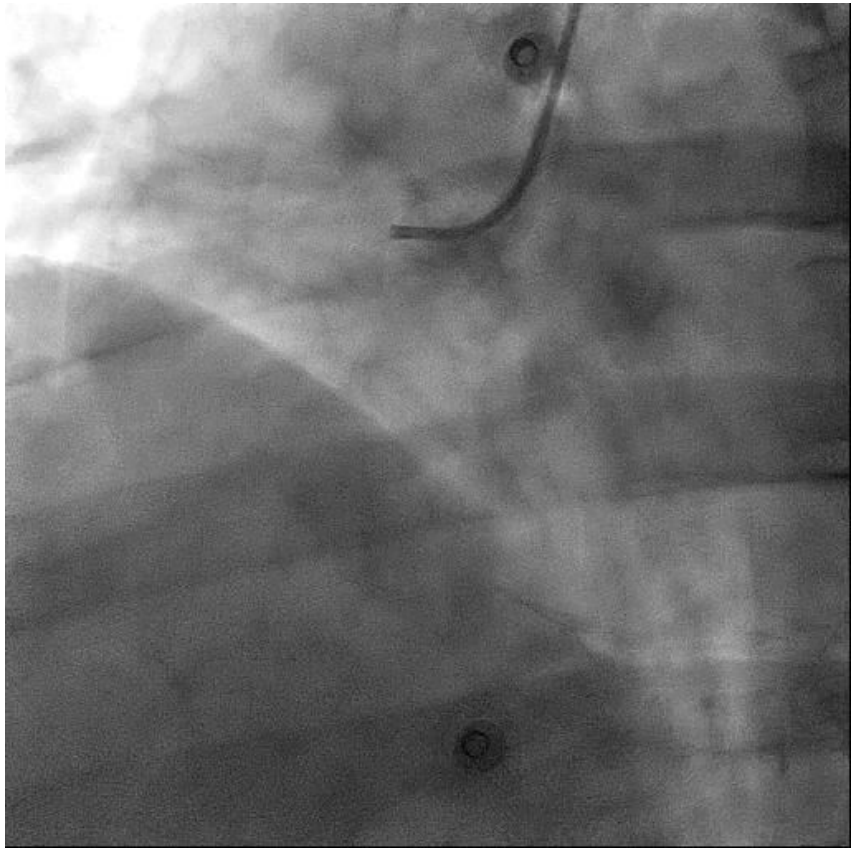
Diltiazem

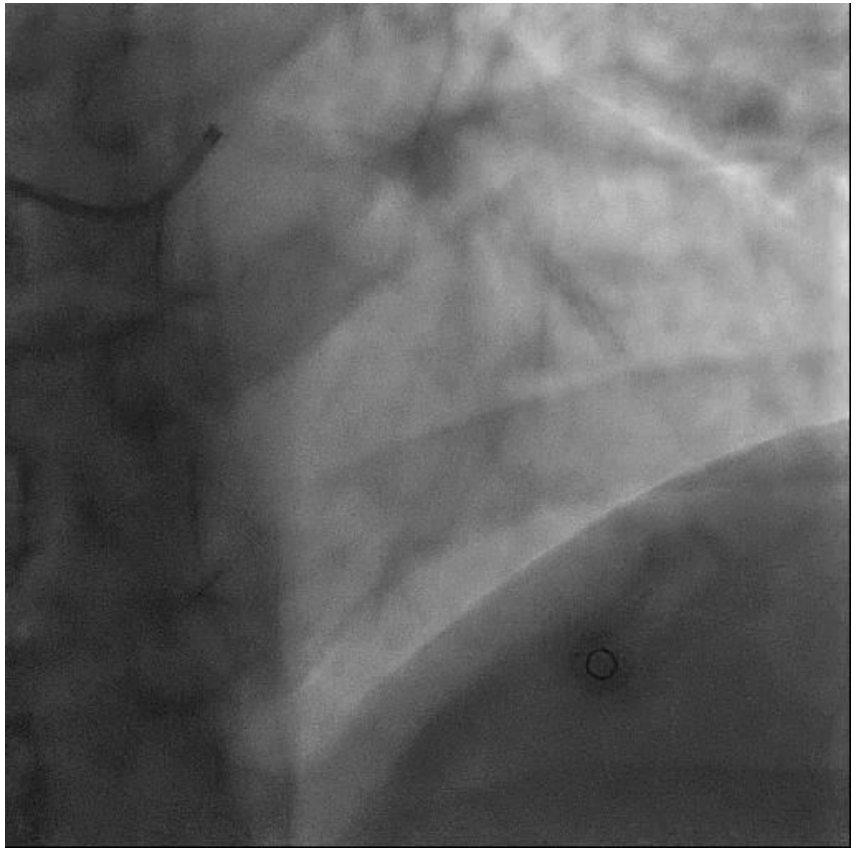
Nebivolol 5 mg/die

CLINICAL PRESENTATION

- ♂, 36 years old
- **Risk factors for Cardiovascular Disease:** Overweight, Dyslipidaemia, Family History of CAD, former Smoker
- **Cardiovascular History:**
  - Chronic Ischemic Heart Disease:
    - LAD PCI in April 2022 for ASC-NSTE
    - D2 PCI in May 2022 for recurrence of episodes of angina at rest
  - Normal echocardiographic findings
- **Baseline Medication:** Acetylsalicylic Acid 100 mg, Ticagrelor 90 mg BID, Rosuvastatin+Ezetimibe 20+10 mg, Olmesartan 20 mg, Bisoprolol 2.5 mg
- **December 2022:** recruited to INOCA- IT (RF-2019-12369486) for recurrence of angina (CCS IV)

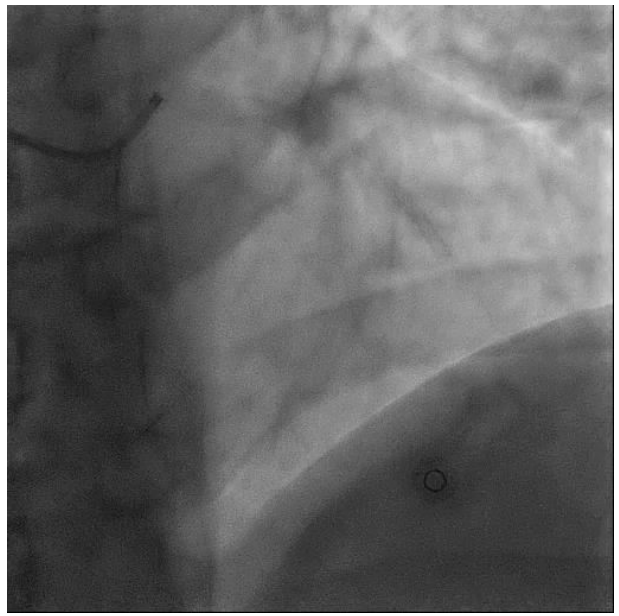
CORONARY ANGIOGRAPHY



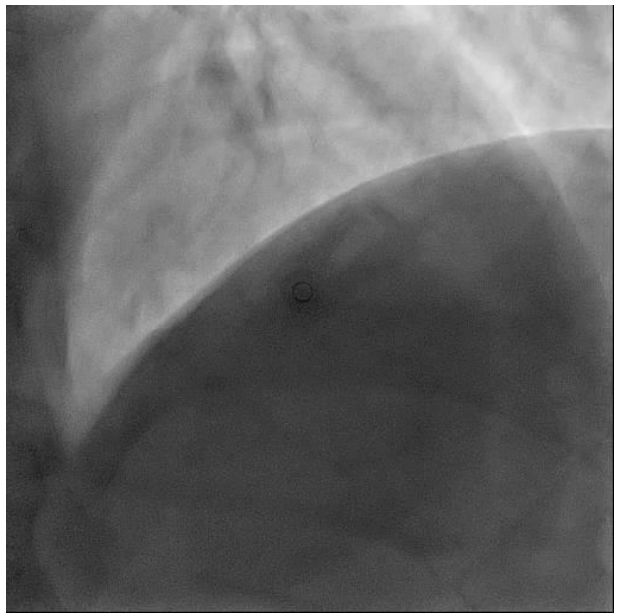


CORONARY FUNCTIONAL TEST: NEGATIVE

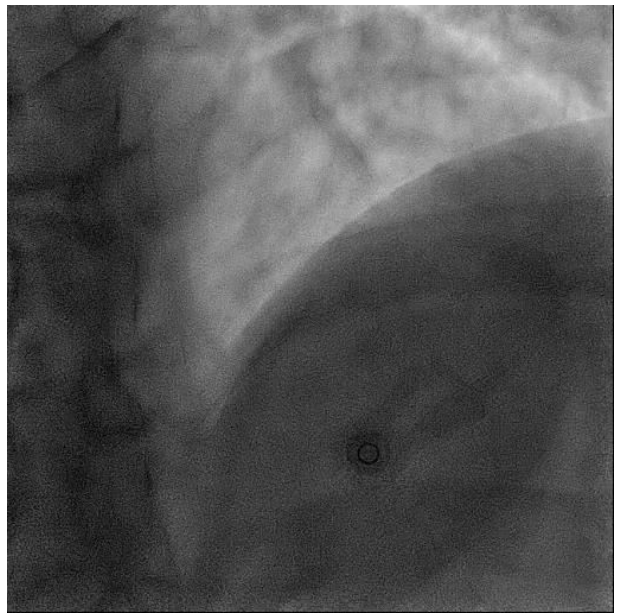
ACETYLCHOLINE PROVOCATION TEST: POSITIVE



Basal angiography

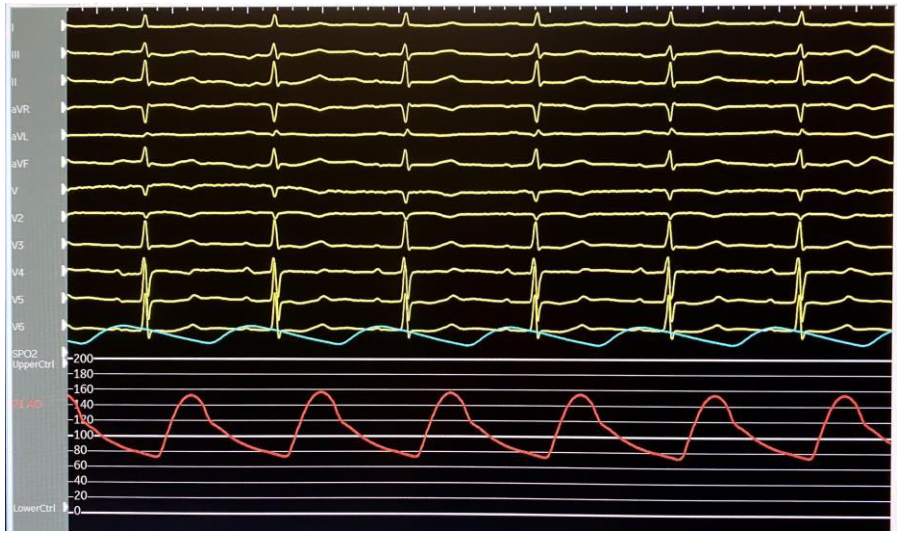


ACh 200 mcg

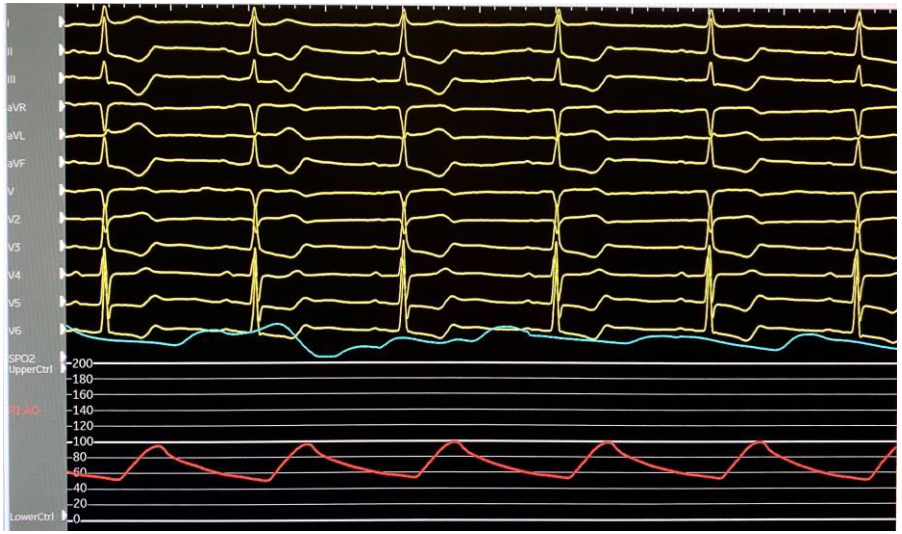


NTG 200 mcg

ACETYLCHOLINE PROVOCATION TEST: POSITIVE

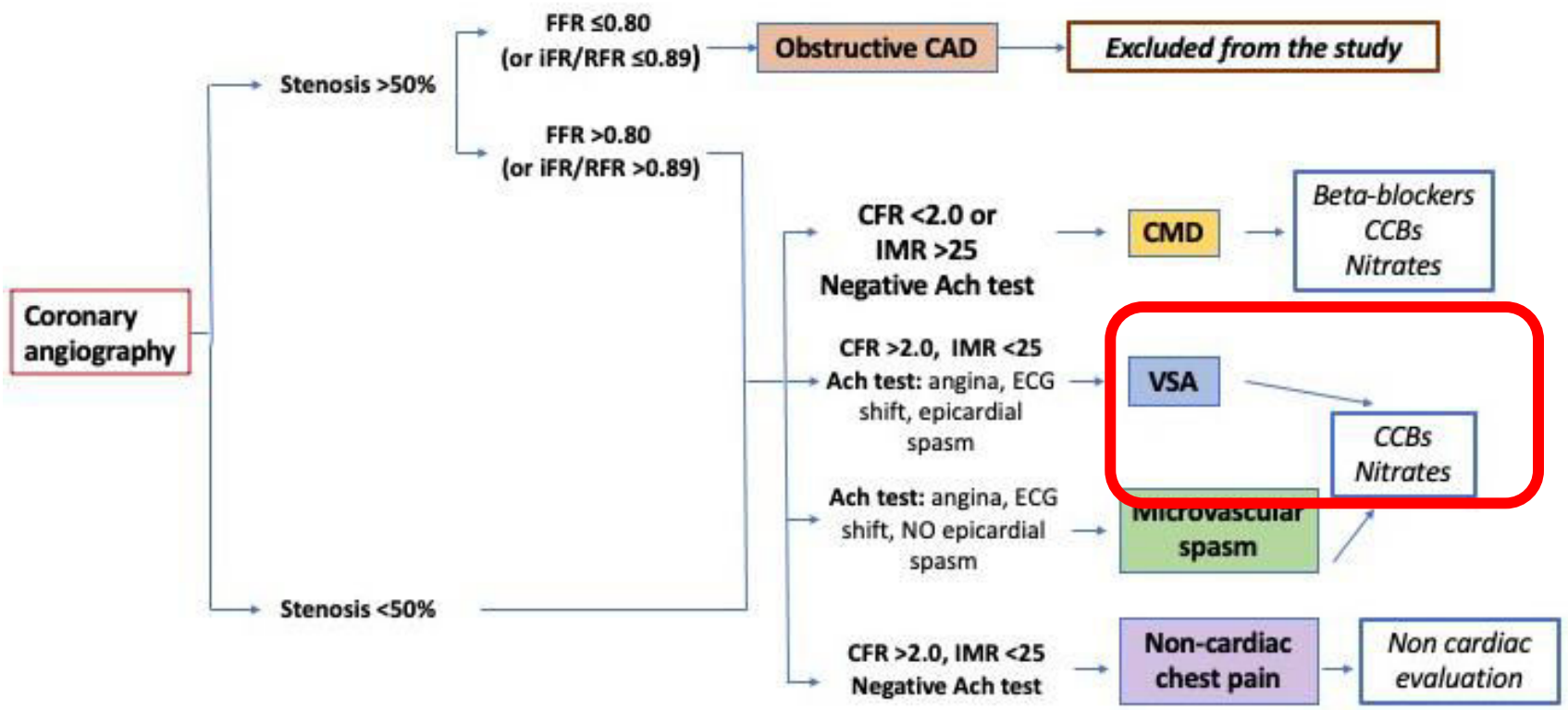


Basal ECG



ECG after Ach 200 mcg

MANAGEMENT


Coronary angiography
Stenosis >50%
FFR ≤0.80 (or iFR/RFR ≤0.89)
Obstructive CAD
Excluded from the study
FFR >0.80 (or iFR/RFR >0.89)
Stenosis <50%
CFR <2.0 or IMR >25 Negative Ach test
CMD
Beta-blockers CCBs Nitrates
CFR >2.0, IMR <25 Ach test: angina, ECG shift, epicardial spasm
VSA
CCBs Nitrates
Ach test: angina, ECG shift, NO epicardial spasm
Microvascular spasm
CFR >2.0, IMR <25 Negative Ach test
Non-cardiac chest pain
Non cardiac evaluation

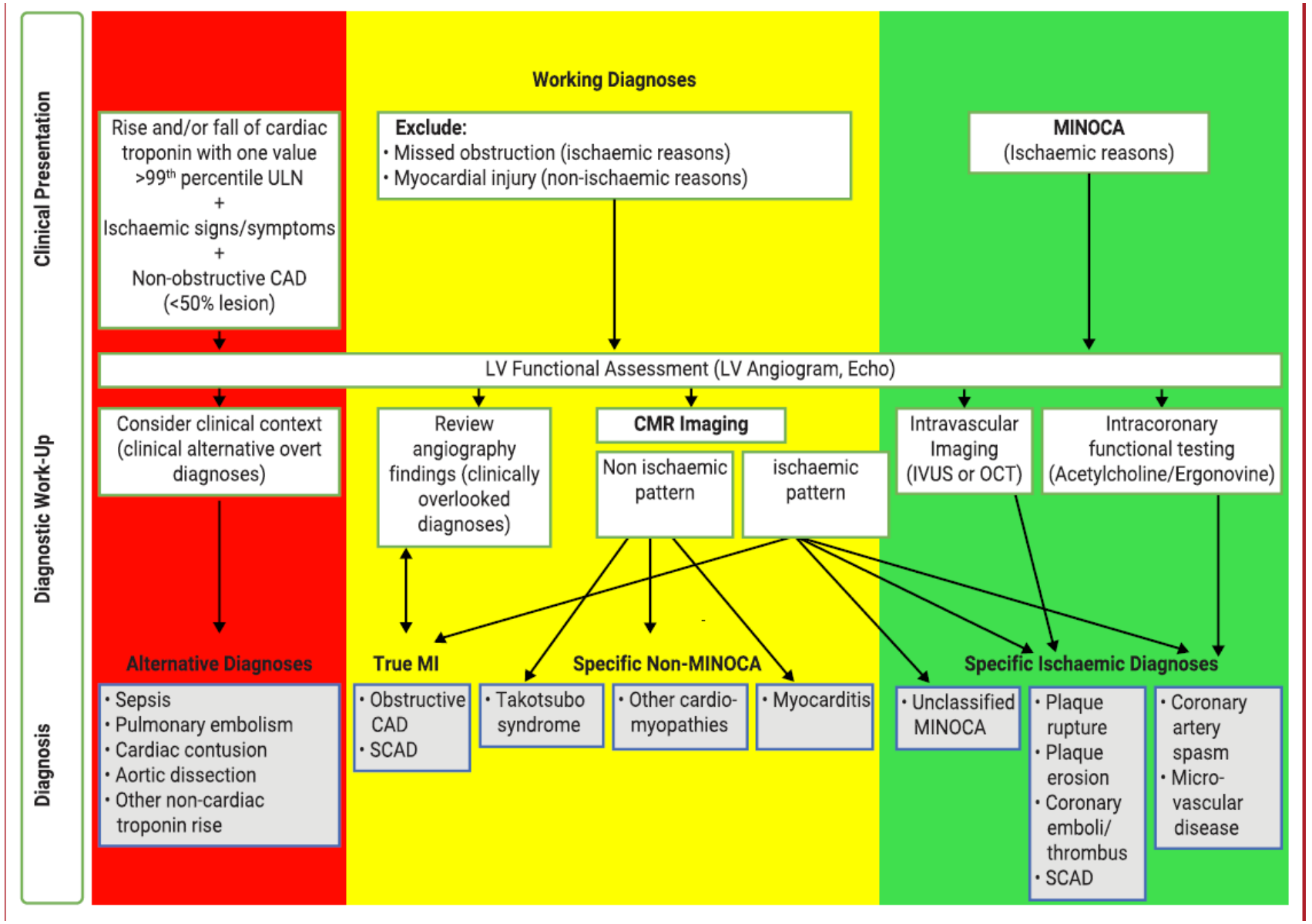
MANAGEMENT

- Diagnosis: VSA
- Changes to Medication:

Bisoprolol

Diltiazem 120 mg BID

Diagnostic Algorytm for MINOCA



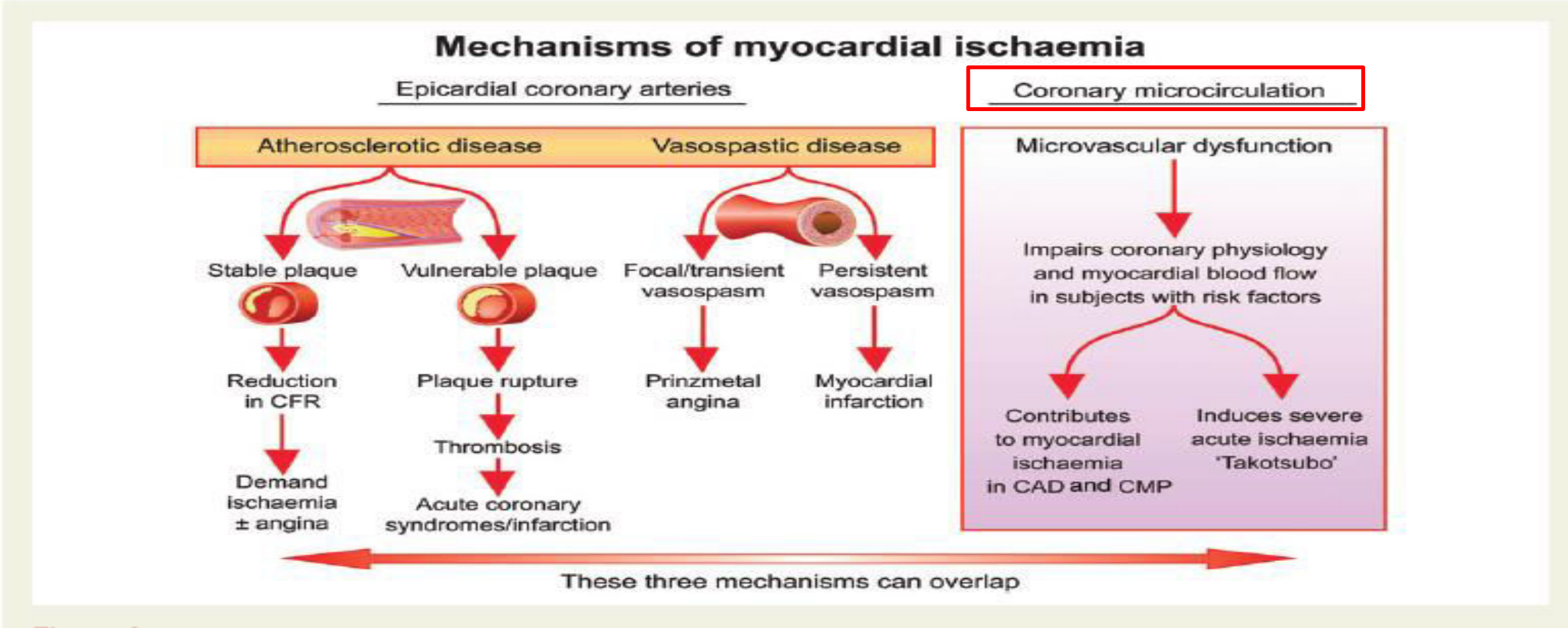
European Heart Journal (2021) **42**, 1289–1367
doi:10.1093/eurheartj/ehaa575

ESC Recommendations - MINOCA

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

CMR = cardiac magnetic resonance; MINOCA = myocardial infarction with non-obstructive coronary arteries.
[a]Class of recommendation.
[b]Level of evidence.

European Heart Journal (2021) **42**, 1289–1367
doi:10.1093/eurheartj/ehaa575



Crea, Camici, Merz. Eur Heart J. 2014;35:1101–1111

Epicardic cause: Coronary vasospasm

Systematic Review of Patients Presenting With Suspected Myocardial Infarction and Nonobstructive Coronary Arteries

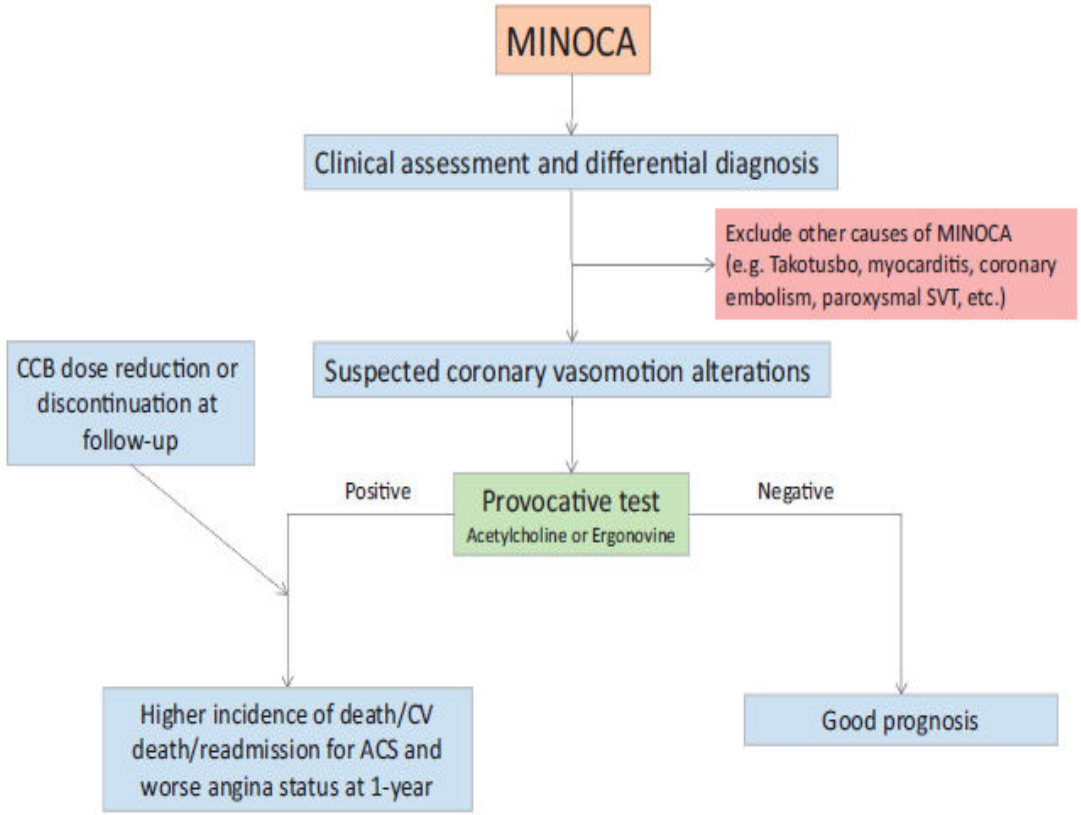
Provocative Spasm Testing in Patients With MINOCA

Publications	No. of Patients in the Study	Provocation Test	Spasm Definition	Provoked/ Spontaneous Spasm, n (%)
Early provocative spasm testing (within 6 wk of acute myocardial infarction)				
Bory, 1988	59	iv ergot	≥50% constriction on angio	2/59 (3%)
Fukai, 1993	21	iv ergot	≥75% constriction on angio	13/16 (81%)
Dacosta, 2001	91	iv ergot	≥70% constriction on angio	11/71 (15%)
Wang, 2002	23	ic ergot	≥90% constriction on angio	17/23 (74%)
Hung, 2003	19	ic ergot	≥70% constriction on angio	18/19 (95%)
Dacosta, 2004	82	iv ergot	≥70% constriction on angio	13/82 (16%)
Abid, 2012	21	iv ergot	≥70% constriction on angio	5/21 (24%)
Ong, 2008	7	ic acetylcholine	≥75% constriction on angio	4/7 (57%)
Total (provocative spasm testing <6 wks)				(83/298) 28%
Late provocative spasm testing (≥6 wk after myocardial infarction)				
Legrand, 1982	18	iv ergot	Chest pain & ST elevation	6/18 (33%)
Raymond, 1988	74	iv ergot	≥75% constriction on angio	5/16 (31%)
Ammann, 2000	23	Hyperventilate	ST elevation	0/23 (0%)
Kim, 2005	33	iv ergot	RWMA on echocardiography	20/33 (61%)
Total (provocative spasm testing ≥6 wks)				(31/90) 34%
Undefined timing for provocative spasm testing (relative to myocardial infarction)				
Salem, 1985	10	iv ergot	Chest pain & ST elevation	0/7 (0%)
Verheugt, 1987	21	iv ergot	NR	0/7 (0%)
Provocative spasm testing in cocaine induced MINOCA patients				
*Kossowsky, 1989	5	cold pressor	NR	0%
Overall pooled spasm				114/402 (28%)

Pasupathy et al. Circulation. 2015;131:861-870

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



Montone et al. Eur Heart J 2017; 1:1-9

Treatment

Mechanism	Diagnosis	Therapy
Epicardic causes		
Coronary artery disease	Intravascular imaging	PCI; antiplatelet therapy, statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, beta-blocker treatment
Coronary dissection	Intravascular imaging	Conservative treatment (beta-blocker and single antiplatelet therapy)
Coronary artery spasm	Intracoronary ergonovine or Ach test	Calcium antagonist, nitrates, rho-kinase inhibitors
Microvascular causes		
Microvascular coronary spasm	Intracoronary Ach test	Rho-kinase inhibitors?
Takotsubo syndrome	Ventriculography, echocardiography with adenosine, CMR	Heart failure treatment

Scalone G et al. European Heart Journal: Acute Cardiovascular Care 2018

CONCLUSIONS

- **Invasive strategies** using coronary angiography and interventional diagnostic procedure (IDP) should be implemented to differentiate between vasospastic angina, microvascular angina and non-cardiac pain.
  - Diagnostic guidewire, pressure and flow measurements
  - Pharmacological coronary reactivity testing

- ***A stratified approach*** to the management of INOCA and MINOCA to address the short and long-term well-being and prognosis is warranted.

- Given the lack of in-depth knowledge, **further research is urgently needed**.
  - To increase our mechanistic understanding
  - To develop innovative therapies to better manage this serious condition

THANK YOU!

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