

Microvascular disorders

A diagnostic and therapeutic challenge

Suzette Elias-Smale, Cardiologist
April, 5 2019



Radboudumc

Female, 46 yrs old



Medical history:

2000: migraine

2004: spontaneous abortion (13 weeks)

Patient history

Since 4 weeks: Retrosternal chest pain during exercise radiating to left arm and throat, nausea and dyspnea

CVRF: Never smoked, no diabetes or dyslipidemia, hypertension during last pregnancy, Fam: P: myocardial infarction at 60 yrs, PAD

Med: none

Physical: L 174 cm, W 78 kg, BMI 25.8 kg/m². RR 139/67 mmHg, HR 65/min, normal physical exam

Diagnostic tests

ECG: normal

Treatmill test: ischemia at maximal intensity and in recovery

CT scan coronary arteries:

Negative calcium score.

Minimal wall irregularities in mid and distal LAD.

No significant stenoses

So: angina, positive treatmill test and no obstructive CAD

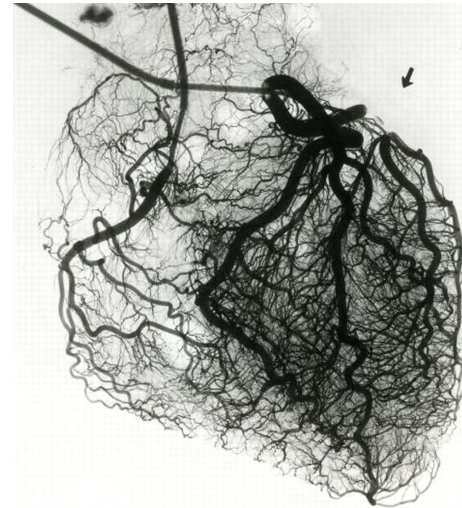
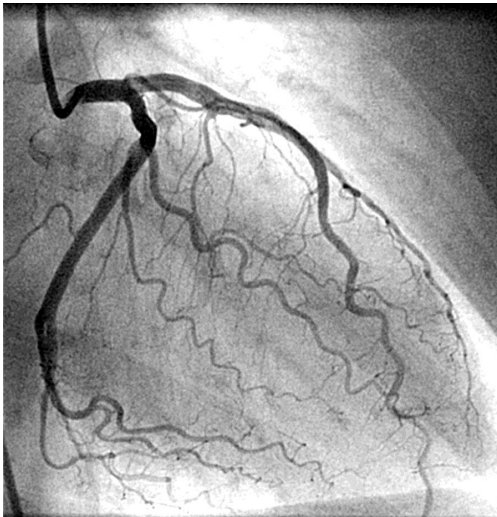


Diagnosis?



Ischemia but no obstructive CAD

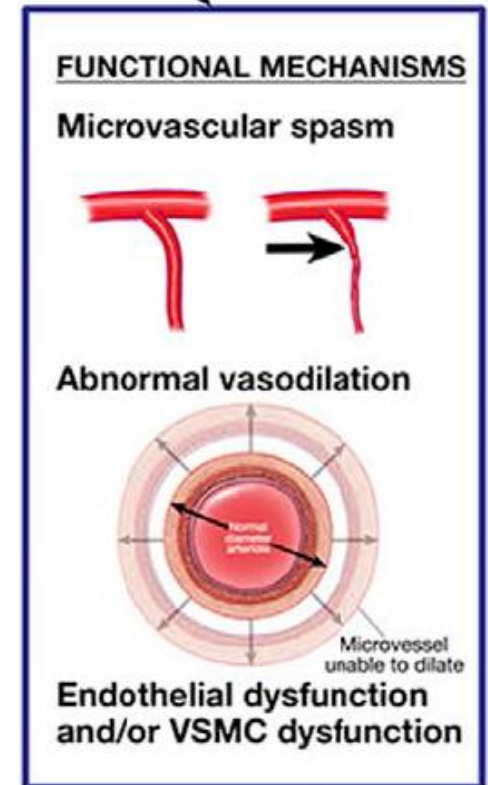
- **INOCA** (Ischemia and No Obstructive Coronary Artery disease):
Patients with **stable** symptoms and signs of ischemic heart disease without obstructed coronary arteries (<50% stenosis, FFR > 0.8)
- **INOCA is a new term incorporating coronary microvascular dysfunction / microvascular angina**



INOCA / CMD

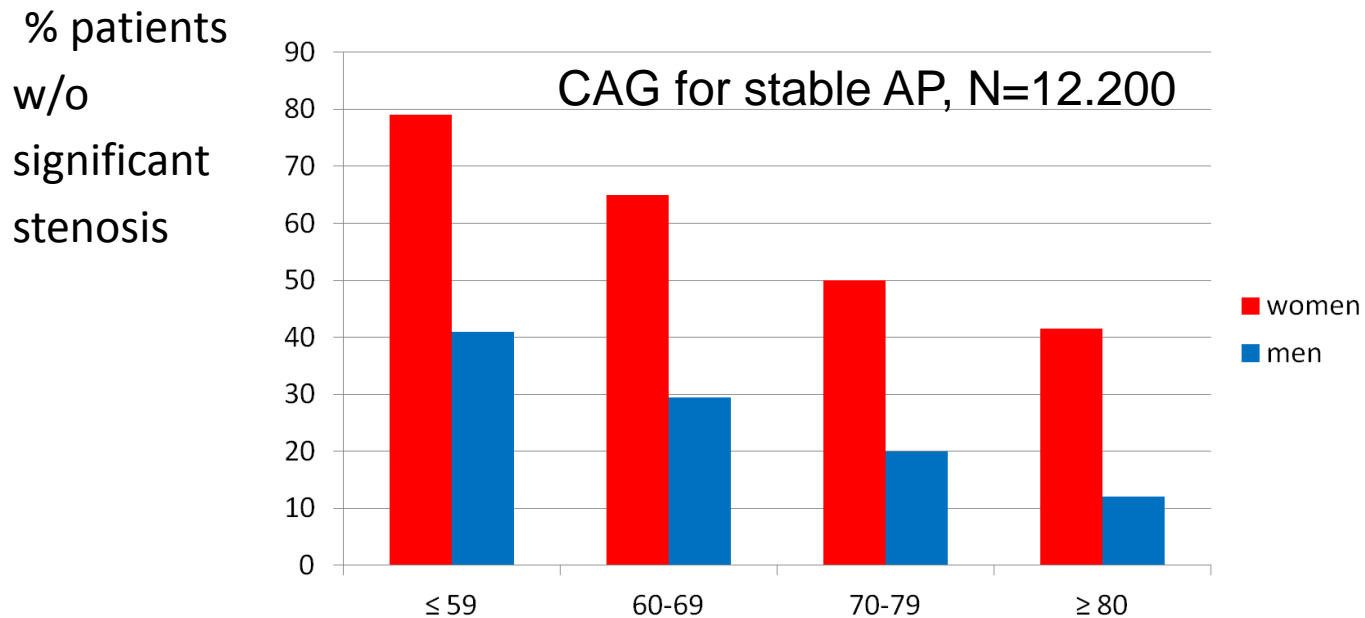
Various pathophysiological mechanisms, oa:

- Diffuse atherosclerosis in large coronary arteries
 - Macrovascular coronary artery spasms
 - Dysfunction of the microvasculature
 - Structural abnormalities of the microvasculature
- ➔
- Prognosis not benign: 2-3 times higher risk on myocardial infarction, stroke or heart failure
 - Therapeutic options (medication and lifestyle)
 - So: adequate diagnosis is clinically important



How common?

Overall, about 40% of patients undergoing CAG for signs and symptoms of ischemia have normal coronary arteries or non-obstructive CAD (<50% stenosis), **more women than men**



CMD Classification

Type of CMD	Description
Primary CMD: CMD in the absence of obstructive CAD and myocardial disease	This type is related to traditional cardiovascular risk factors. Both endothelial dependent and non-endothelial dependent vasoreactivity plays a role
CMD in myocardial disease	This type is sustained by adverse remodeling of intramural coronary arterioles and found in primary and secondary cardiomyopathies
CMD in obstructive CAD	This type accompanies stable CAD or ACS
Iatrogenic CMD	This type occurs after PCI and seems to be caused by distal embolization and or vasoconstriction

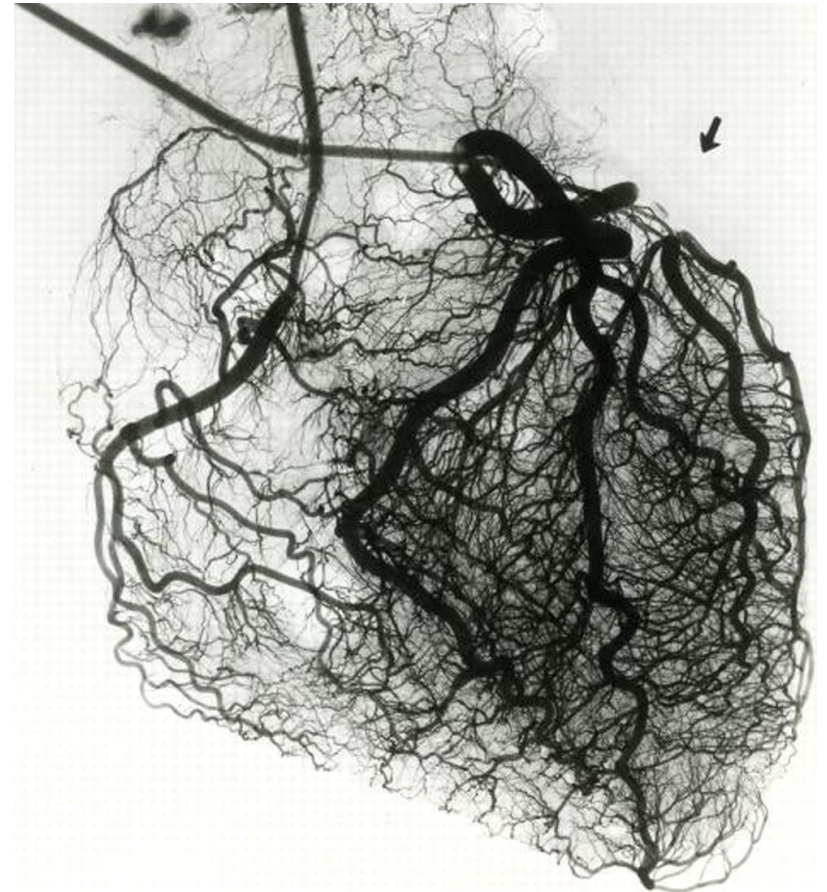
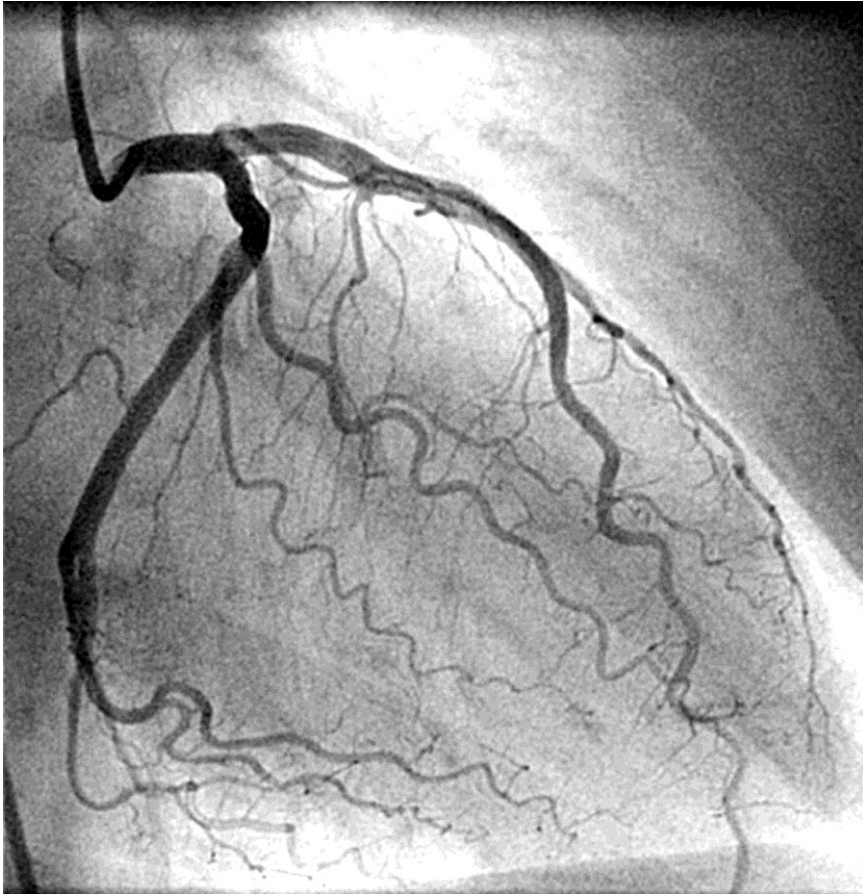
Symptoms

- Angina which is provoked by:
 - a variable threshold of physical activity
 - low heart rate activities such as mental arousal, or palpitations
- Angina typically persists for hours after interrupting activity and/or shows poor response to short-acting nitrates.
- Exertional dyspnea
- Fatigue (especially the day after a busy day)

Risk factors

- Traditional CV risk factors, especially obesity
- Female specific risk factors:
 - Gestational hypertension/HELLP
 - Gestational diabetes
 - Early menopause (<45 yrs)
 - Miscarriages
 - Polycystic ovarium syndrome
 - Reduced fertility
 - Migraine (with aura)
 - Auto-immune disease

Diagnosis often missed



Left: coronary arteries as visible on CAG; Right: entire coronary circulation

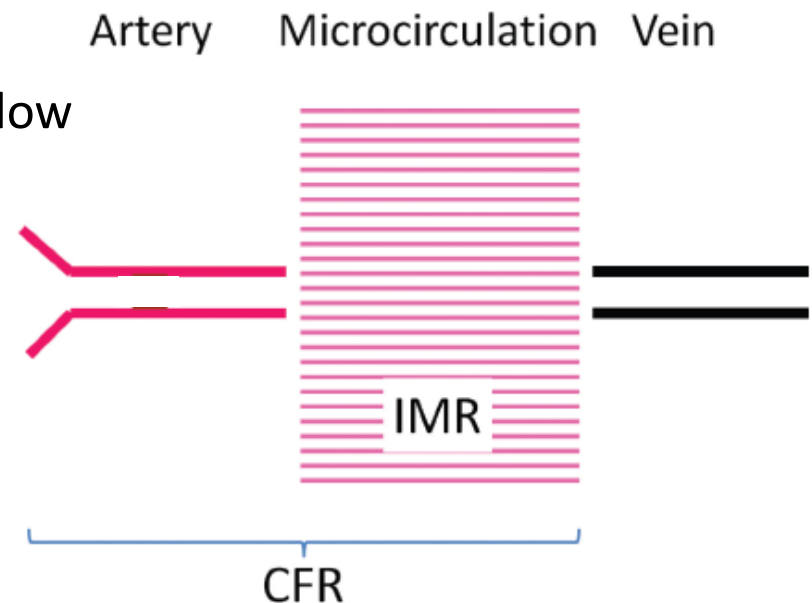
Diagnostic criteria for INOCA / CMD

1. Symptoms of cardiac ischemia: (a)typical angina, exertional dyspnea
2. No obstructive CAD (<50% stenosis on CTA or CAG, FFR > 0.80)
3. Objective evidence of ischemia (ischemic ECG changes during chest pain, positive ischemia detection tests)
4. Evidence of (micro)vascular coronary dysfunction:
 1. Abnormal coronary flow reserve (CFR < 2-2.5)
 2. Abnormal coronary microvascular resistance (IMR >25 U)
 3. Macro-or microvascular coronary spasms (acetylcholine test)

¾ criteria: possible INOCA. Note: classical stress tests: often no ischemia

CFR measurement

- CFR: the ability of the cardiac circulation to increase myocardial blood supply in response to increased oxygen requirements (**dilatation**)
- Info on large coronary arteries and microcirculation
- CFR is measured as the ratio of hyperemic blood flow/resting blood flow (adenosine)
- Normal CFR: 3-5
- INOCA/CMD: CFR < 2-2.5



Diagnostic options for CFR measurement

- Non-invasive:
 - PET/CT (Gold standard)
 - Cardiac MR (Myocardial perfusion reserve index)
 - Trans thoracic Doppler echocardiography
- Invasive:

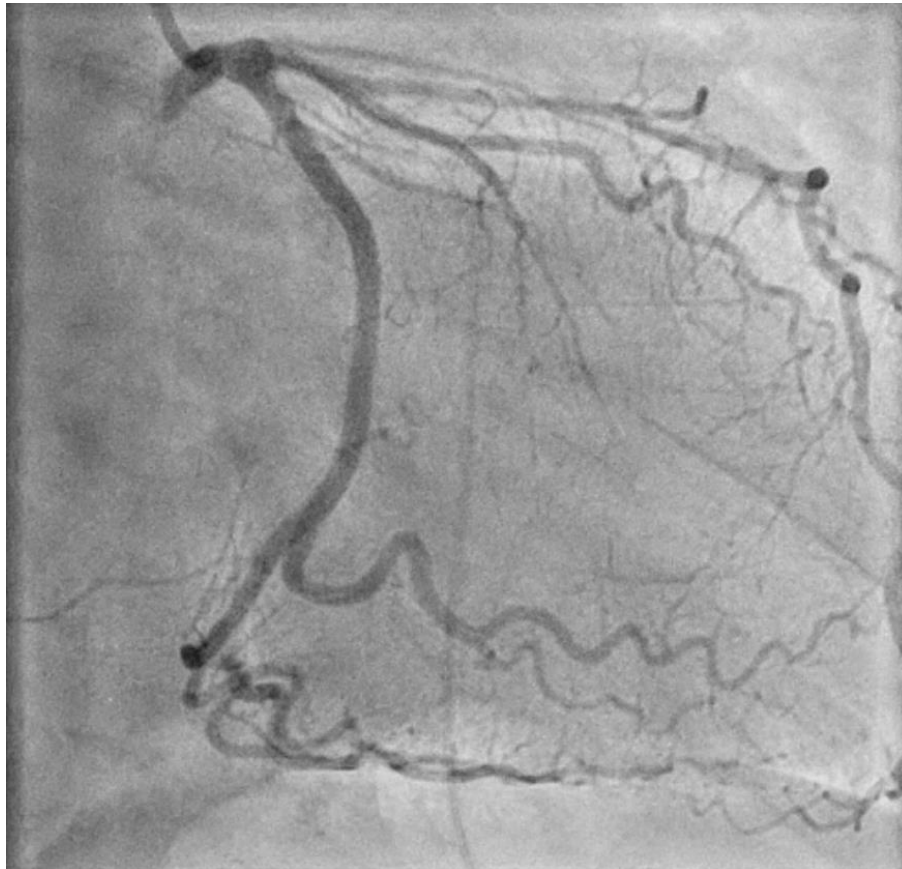
As part of “coronary reactivity testing”:

 - CFR
 - IMR: microvascular resistance
 - Acetylcholine testing: macro- or microvascular spasms

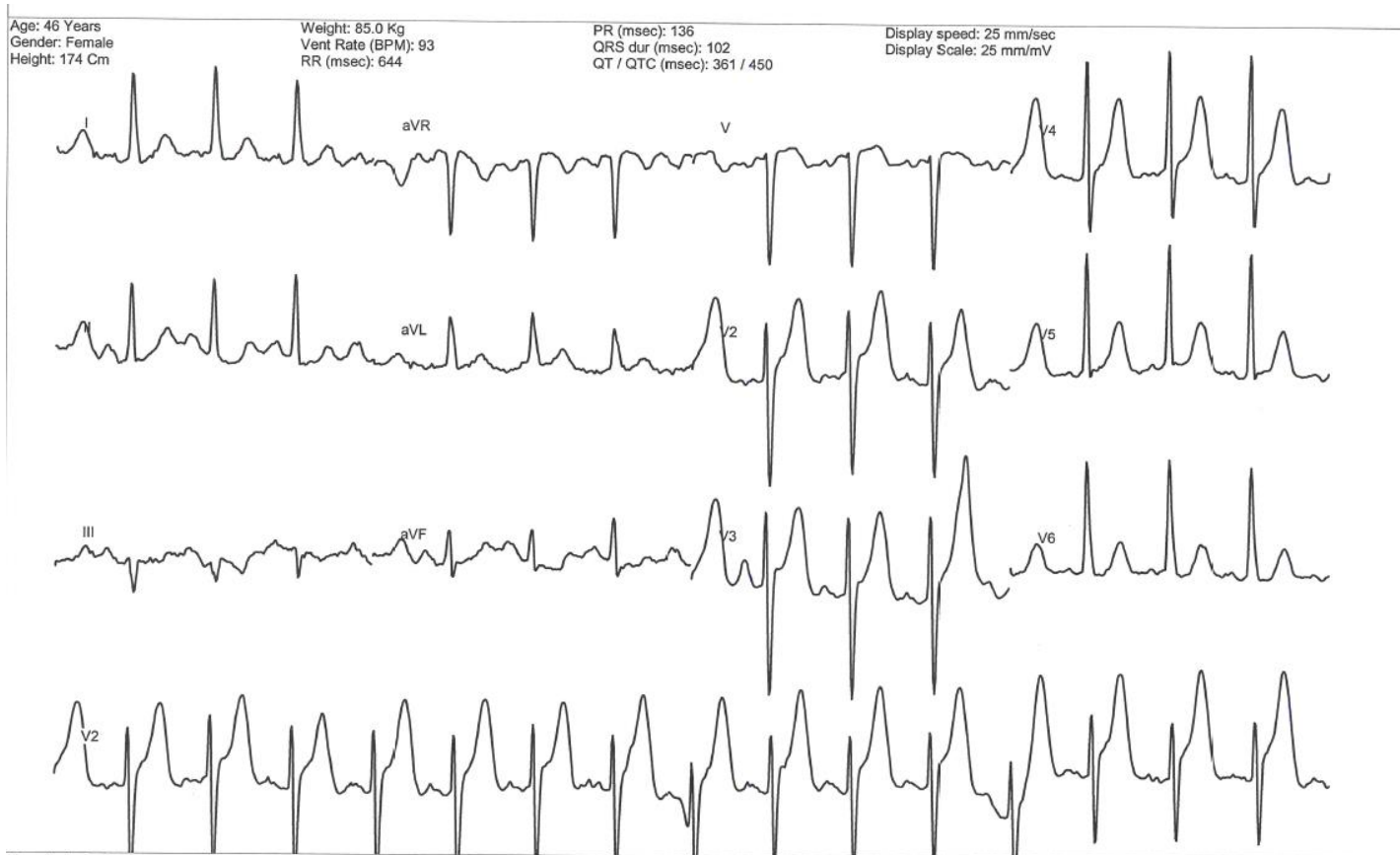
Diagnosics in our patient

- Invasive coronary reactivity testing:
- Acetylcholine test:
- 2-20-110-200 mcg
- Angina + ischemic ECG changes + diameter reduction >90%
= **epicardial** spasm
- Angina + ischemic ECG changes + diameter reduction <90%
= **microvascular** spasm

LAD baseline



Acetylcholine test – 2mcg



LAD-2 mcg acetylcholine



Acetylcholine test – 2mcg

Age: 46 Years
Gender: Female
Height: 174 Cm

Weight: 85.0 Kg
Vent Rate (BPM): 170
RR (msec): 351

PR (msec): 1426
QRS dur (msec): 133
QT / QTC (msec): 274 / 462

Display speed: 25 mm/sec
Display Scale: 25 mm/mV



LAD-2 mcg acetylcholine



Acetylcholine test – NTG

Age: 46 Years
Gender: Female
Height: 174 Cm

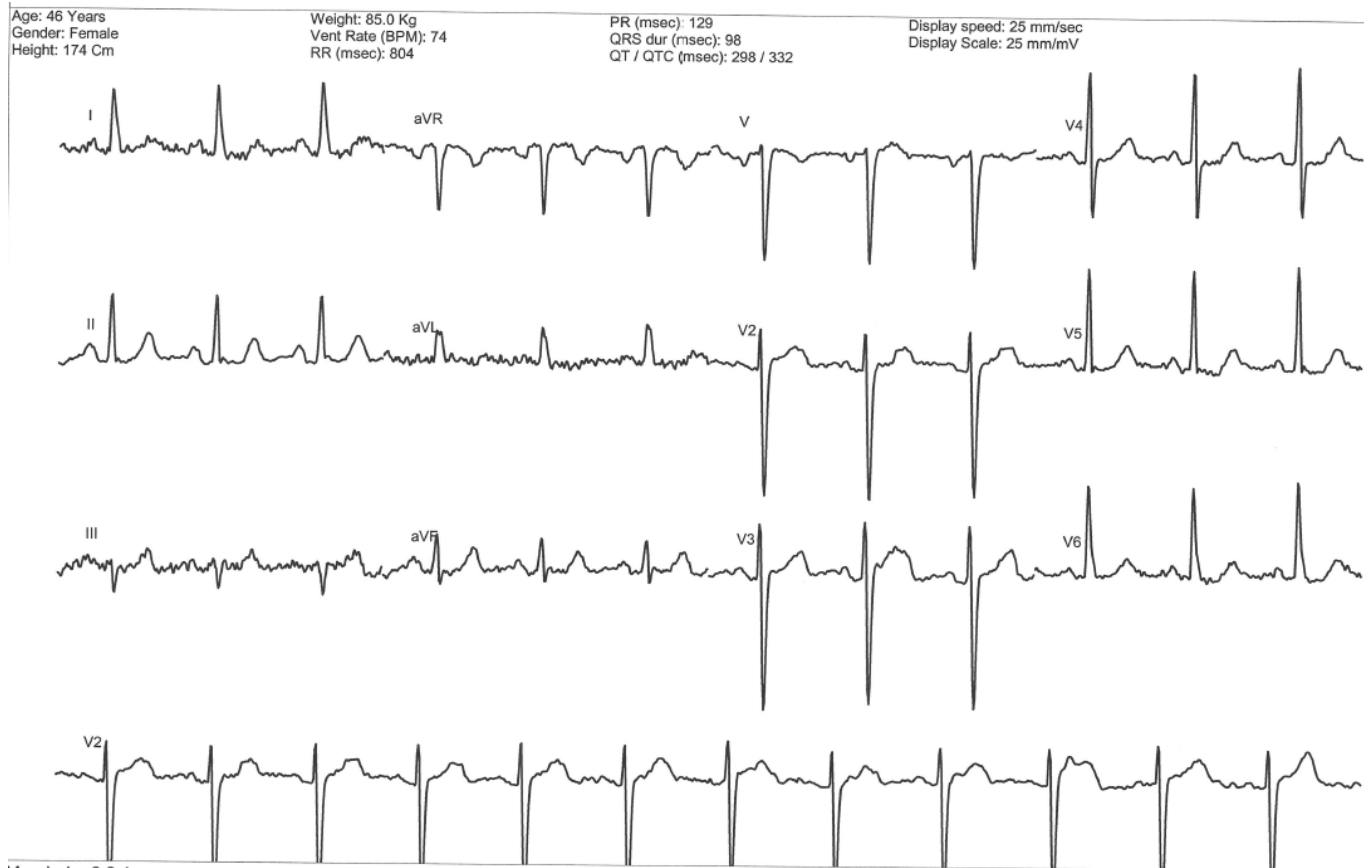
Weight: 85.0 Kg
Vent Rate (BPM): 68
RR (msec): 879

PR (msec): 134
QRS dur (msec): 95
QT / QTC (msec): 355 / 379

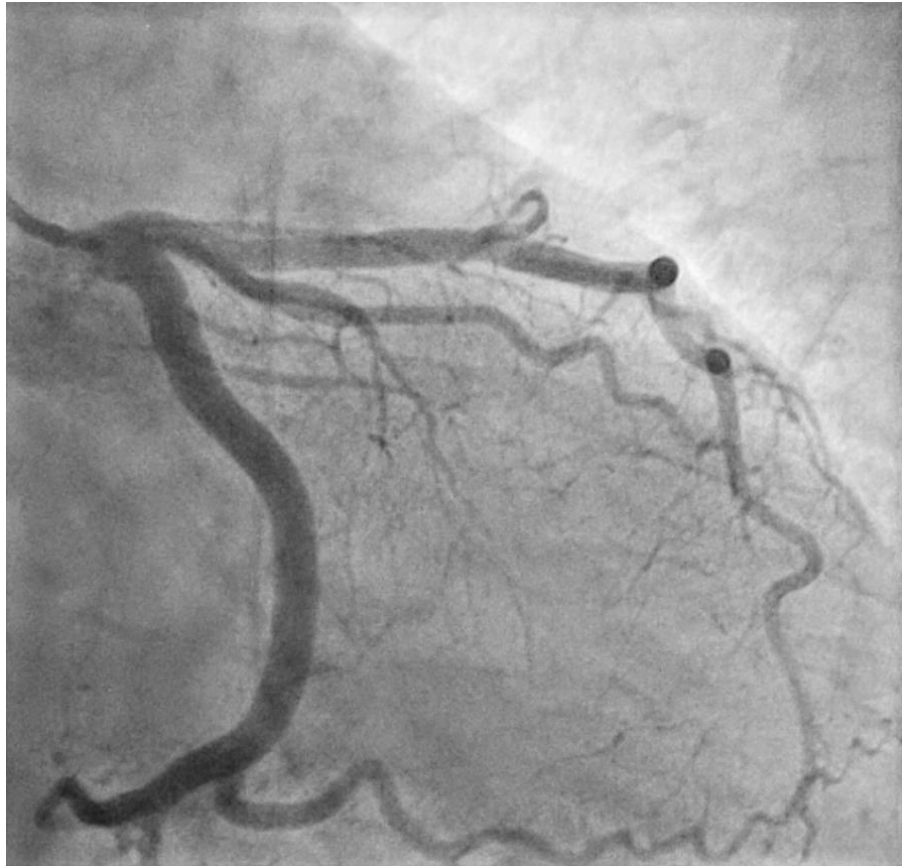
Display speed: 25 mm/sec
Display Scale: 25 mm/mV



Acetylcholine test – end of test



LAD – end of test



CFR and IMR

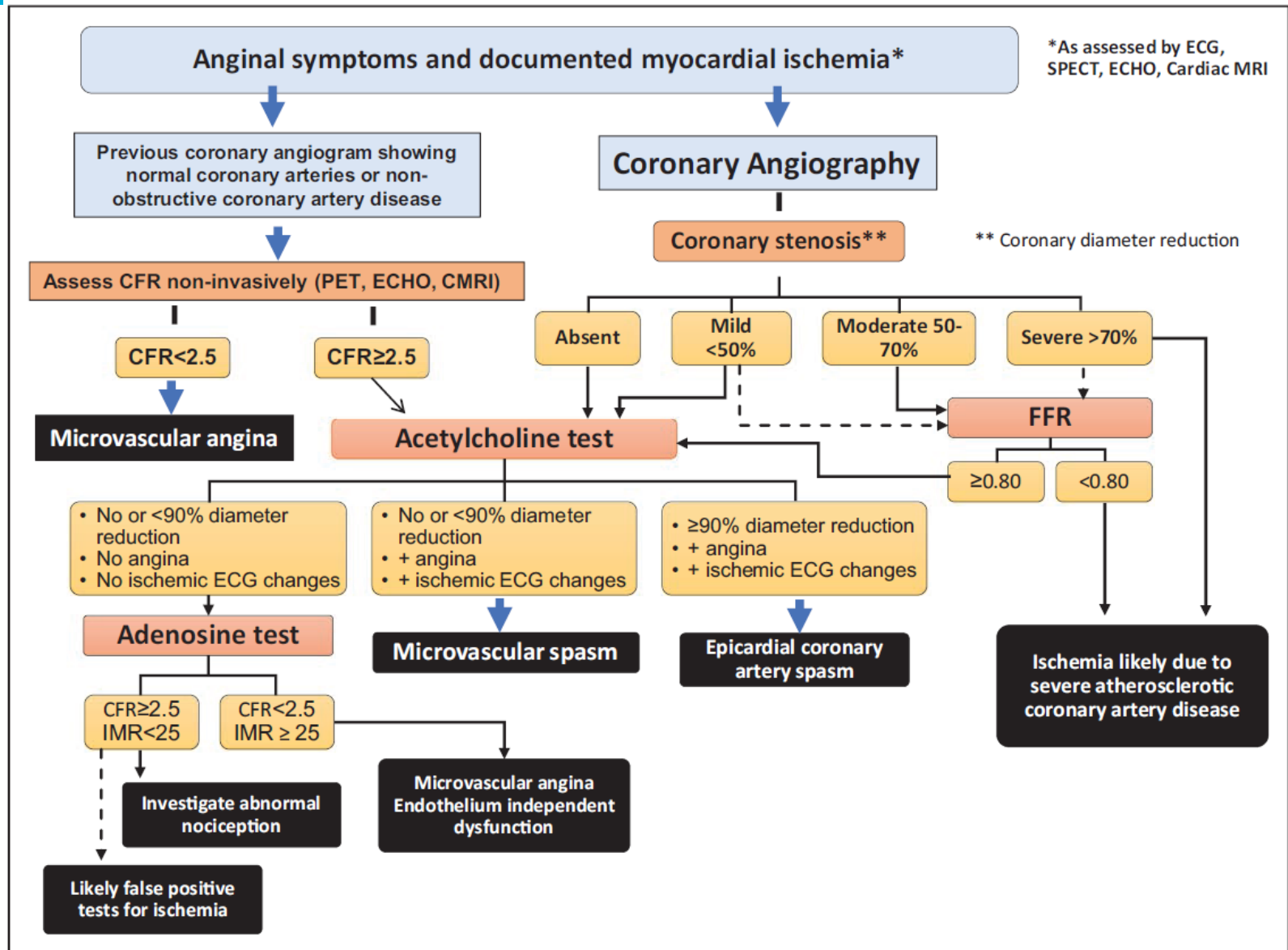


Definite diagnosis

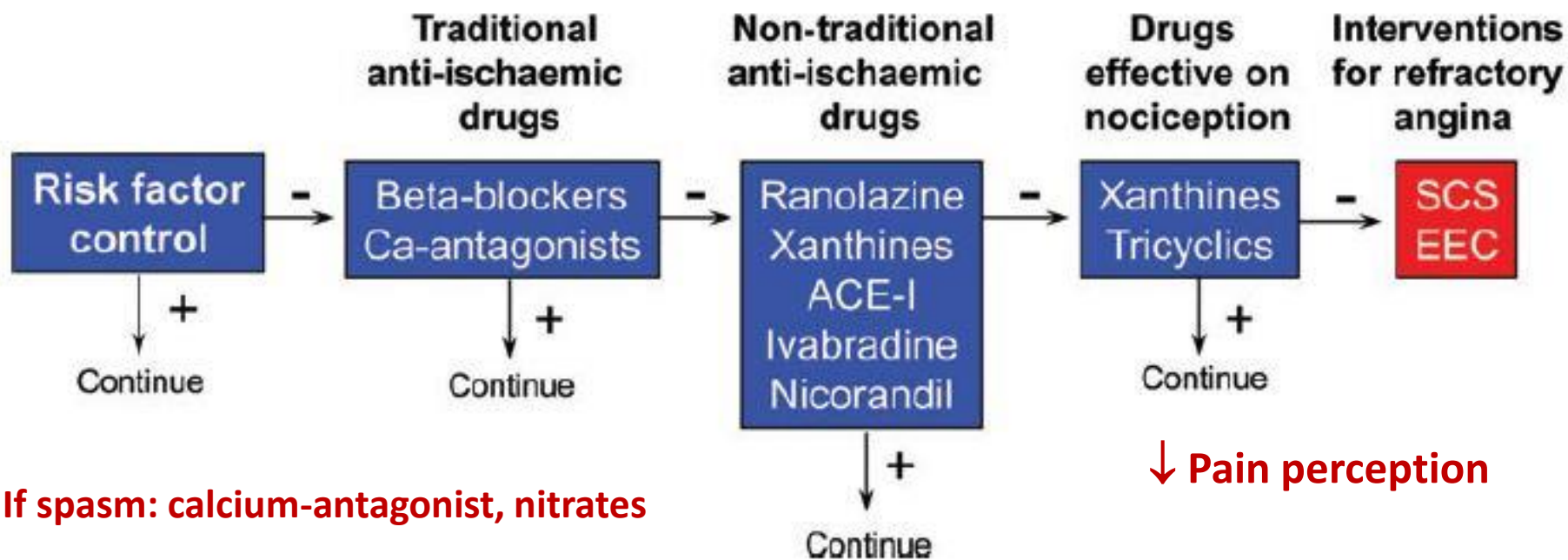
Severe epicardial coronary spasm of the LAD

- Treatment:
- Calcium-antagonist (tildiem)
- Nitrates (monocedocard and nicorandil)

Diagnostic work-up INOCA



Treatment for CMD



SCS: spinal cord stimulation; EEC: enhanced external counterpulsation

ESC guidelines stable CAD; EHJ 2013

Take home messages

- INOCA is a common ischemic heart disease
- Under-diagnosed due to use of traditional diagnostic tests designed to reveal obstructive CAD
- Diagnosis is important: for patients and prognosis
- Various non-invasive (and invasive) diagnostic test can reveal INOCA



Thank you for your attention





Radboudumc