

# Van Heberden tot ANOCA

250 jaar Angina Pectoris



Universiteit Antwerpen  
Faculteit Geneeskunde en  
Gezondheidswetenschappen

UZA'



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Volume 45, Issue 36  
21 September 2024

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JOURNAL ARTICLE GUIDELINES

## 2024 ESC Guidelines for the management of chronic coronary syndromes: Developed by the task force for the management of chronic coronary syndromes of the European Society of Cardiology (ESC) Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) FREE

Christiaan Vrints ✉, Felicita Andreotti ✉, Konstantinos C Koskinas, Xavier Rossello, Marianna Adamo, James Ainslie, Adrian Paul Banning, Andrzej Budaj, Ronny R Buechel, Giovanni Alfonso Chiariello ... [Show more](#)

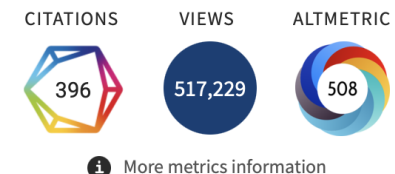
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<https://doi.org/10.1093/eurheartj/ehae177>

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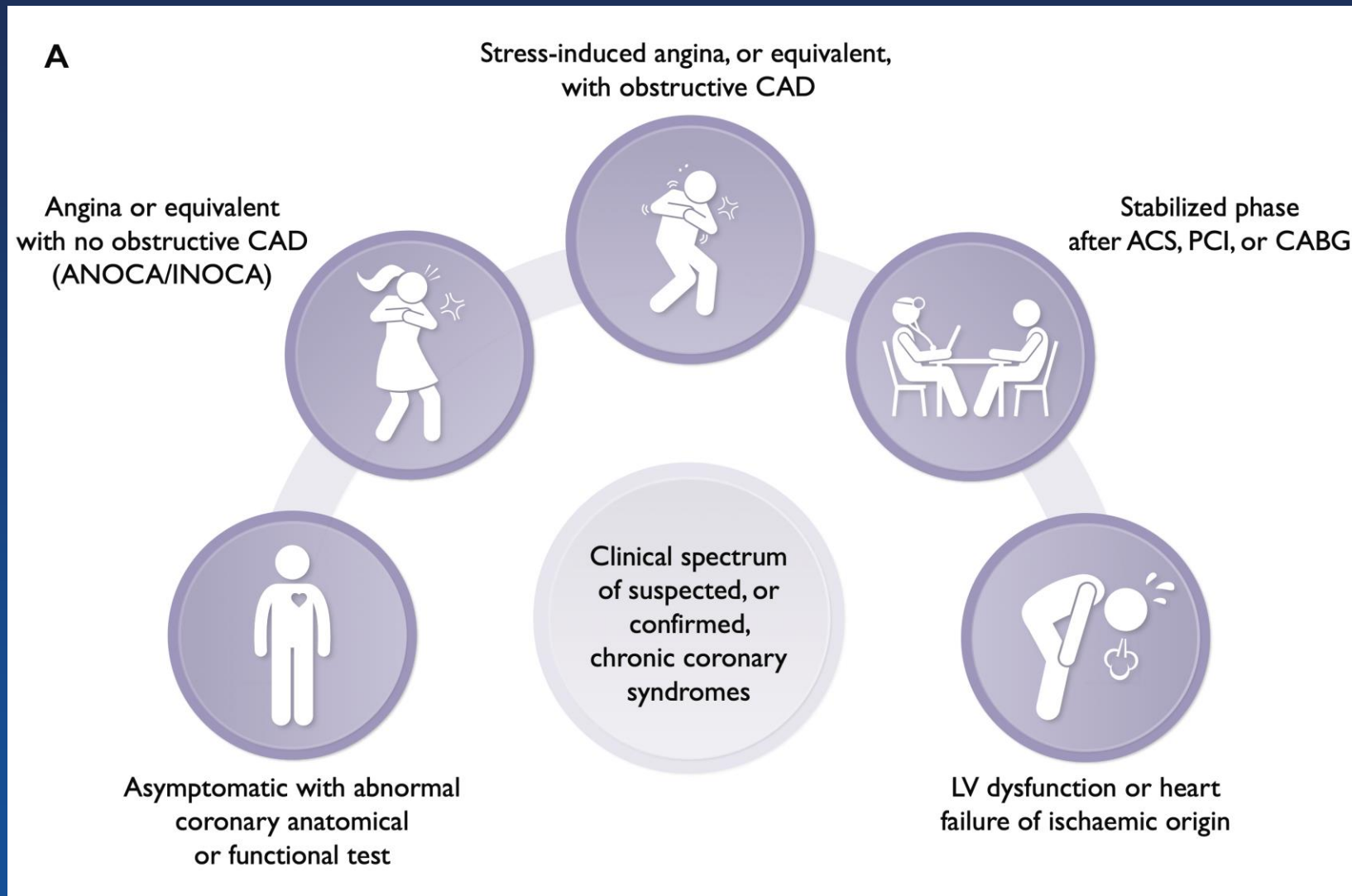
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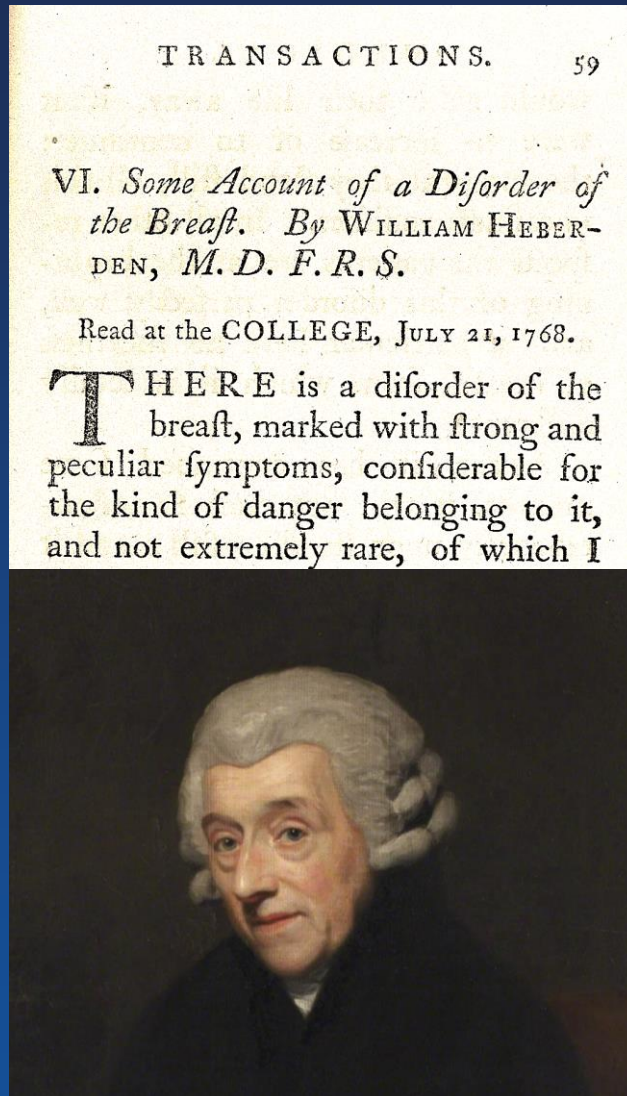
## Recommended

2023 ESC Guidelines for the management of endocarditis: Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC...  
Victoria Delgado, *European Heart Journal*, 2023

# Chronische coronaire syndromen



# Some account of a disorder of the breast: angina pectoris



*There is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, which deserves to be mentioned more at length.*

*The seat of it and the sense of strangling and anxiety with which it is attended, may make it not improperly be called **angina pectoris**.*

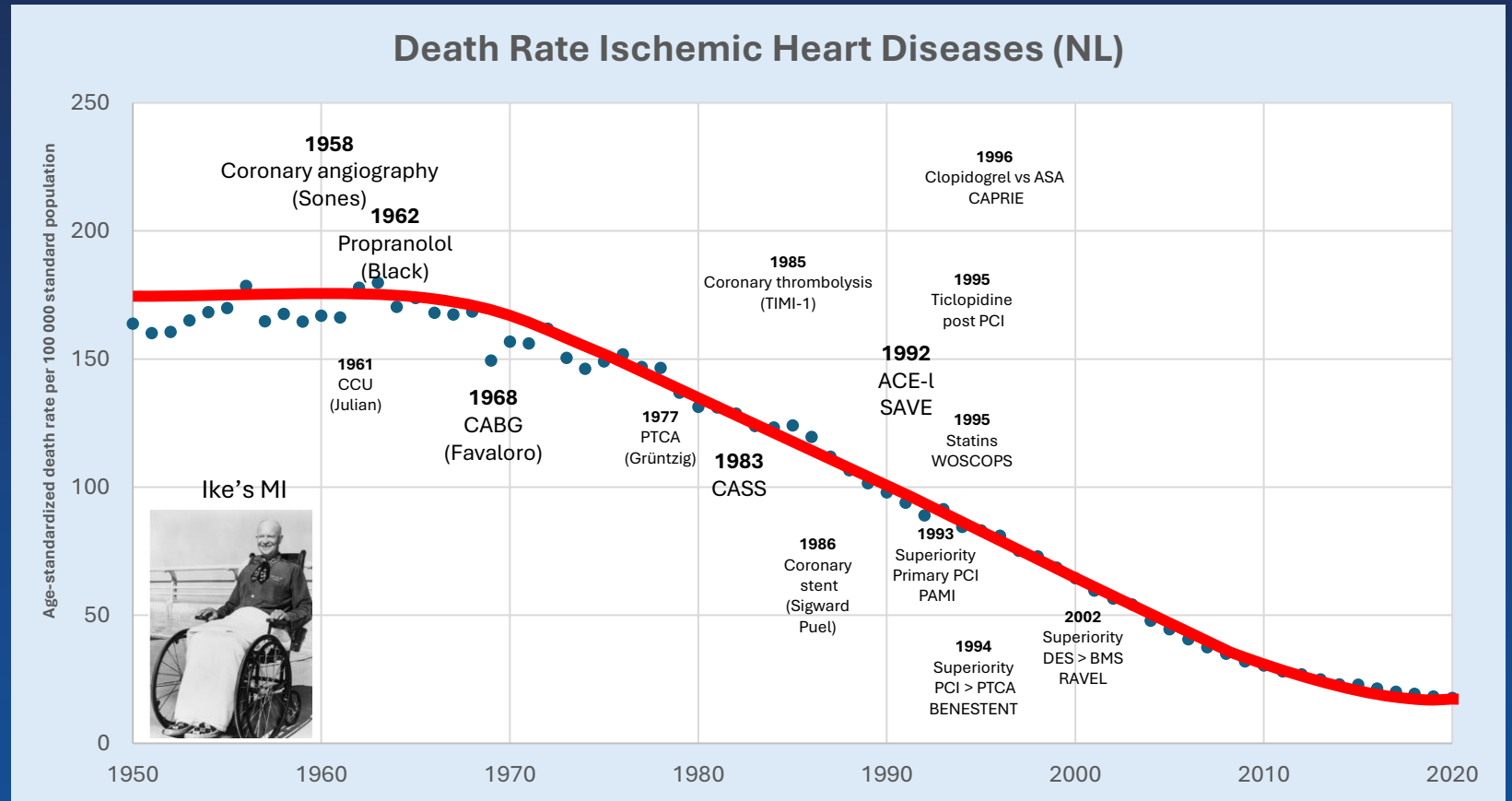
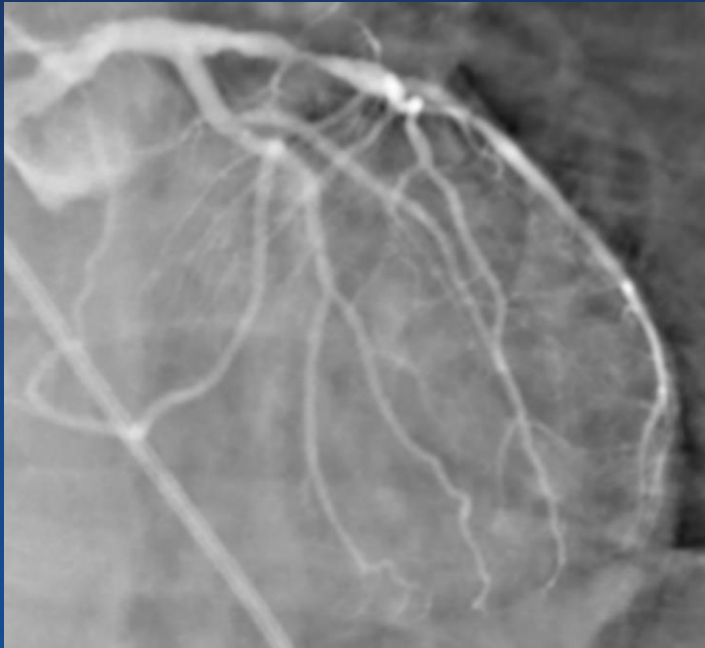
*Those who are afflicted with it, are seized while they are walking (more especially if it be uphill, and soon after eating) with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life if it were to increase or to continue; but the moment they stand still, all this uneasiness vanishes.*

*In all other respects, the patients are, at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different.*

*It likewise very frequently extends from the breast to the middle of the left arm.*

# 20ste eeuw concept:

Epicardiale coronaire stenose/occlusie  $\Rightarrow$  myocardische



WHO data



Universiteit Antwerpen  
Faculteit Geneeskunde en  
Gezondheidswetenschappen



# Klinische waarschijnlijkheid op obstructief coronair lijden?



- 55 jarige man met
  - wringende, drukkende retrosternale pijn
  - bij inspanning
  - die snel overgaat in rust
- Risicofactoren:
  - roken,
  - hoge cholesterol

Wat is de waarschijnlijkheid dat er een coronaire stenose wordt gevonden ?

A. 90%

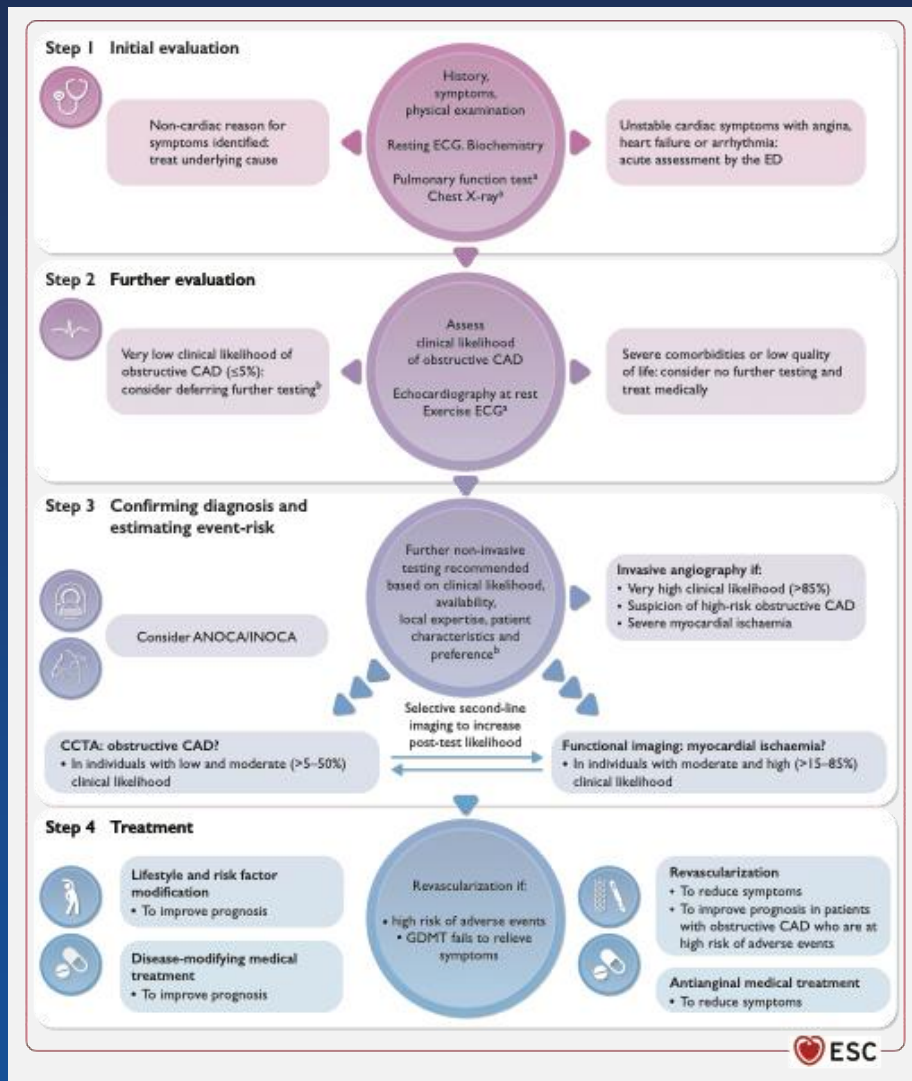
B. 70%

C. 50%

D. 30%



# Stapsgewijze aanpak



**1 Symptom score (0-3 points)**

Chest pain characteristics		Symptom score
Type and location	Constricting discomfort located retrosternally or in neck, jaw, shoulder or arm (1 point)	Main symptom either: Chest pain (0-3 points) or Dyspnoea (2 points)
Aggravated by	Physical or emotional stress (1 point)	
Relieved by	Rest or nitrates within 5 min (1 point)	
Dyspnoea characteristics		
Shortness of breath and/or trouble catching breath aggravated by physical exertion (2 points)		

**2 Number of risk factors for CAD (0-5):**  
Family history, smoking, dyslipidaemia, hypertension and diabetes

**3 Estimate the Risk Factor-weighted Clinical Likelihood (RF-CL) of obstructive CAD**

Number of risk factors	Symptom score					
	0-1 point		2 points		3 points	
	Women	Men	Women	Men	Women	Men
Age 30-39	0 1 2	1 2 5	0 1 3	2 4 8	2 5 10	9 14 22
Age 40-49	1 1 3	2 4 8	1 2 5	3 6 12	4 7 12	14 20 27
Age 50-59	1 2 5	4 7 12	2 3 7	6 11 17	6 10 15	21 27 33
Age 60-69	2 4 7	8 12 17	3 6 11	12 17 25	10 14 19	32 35 39
Age 70-80	4 7 11	15 19 24	6 10 16	22 27 34	16 19 23	44 44 45

Clinical likelihood: ● Very low ● Low ● Moderate

ESC

# Risicofactor-gewogen predictiemodel obstructief coronair lijden

1

## Symptom score (0–3 points)

### Chest pain characteristics

Type and location

Constricting discomfort located retrosternally or in neck, jaw, shoulder or arm (1 point)

Aggravated by

Physical or emotional stress (1 point)

Relieved by

Rest or nitrates within 5 min (1 point)

### Dyspnoea characteristics

Shortness of breath and/or trouble catching breath aggravated by physical exertion (2 points)

### Symptom score

Main symptom either:

Chest pain  
(0–3 points)

or

Dyspnoea  
(2 points)

2

## Number of risk factors for CAD (0–5):

Family history, smoking, dyslipidaemia, hypertension and diabetes



# Risico factor-gewogen klinische waarschijnlijkheidmodel

3

Estimate the Risk Factor-weighted Clinical Likelihood (RF-CL) of obstructive CAD

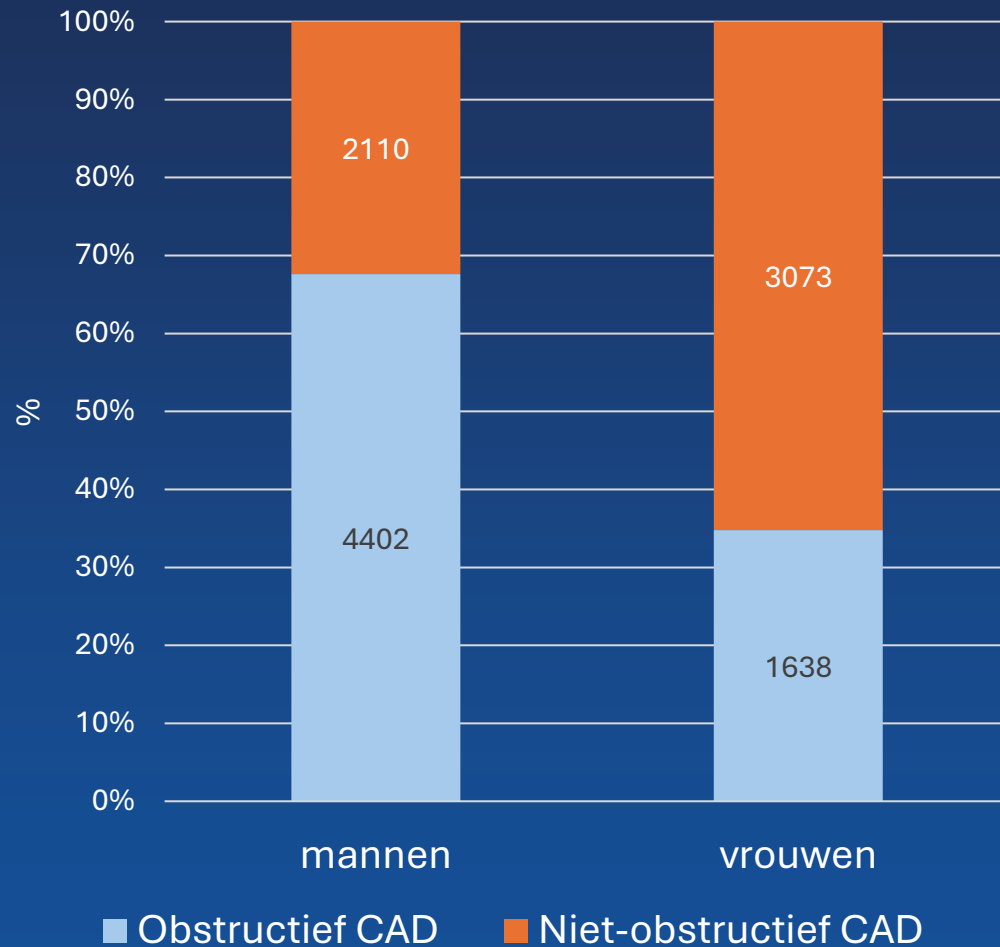
Number of risk factors	Symptom score																	
	0-1 point		2 points		3 points													
	Women	Men	Women	Men	Women	Men												
	0-1	2-3	4-5	0-1	2-3	4-5	0-1	2-3	4-5									
Age 30-39	0	1	2	1	2	5	0	1	3	2	5	10	9	14	22			
Age 40-49	1	1	3	2	4	8	1	2	5	3	6	12	4	7	12	14	20	27
Age 50-59	1	2	5	4	7	12	2	3	7	6	11	17	6	10	15	21	27	33
Age 60-69	2	4	7	8	12	17	3	6	11	12	17	25	10	14	19	32	35	39
Age 70-80	4	7	11	15	19	24	6	10	16	22	27	34	16	19	23	44	44	45

Clinical likelihood: ● Very low ● Low ● Moderate

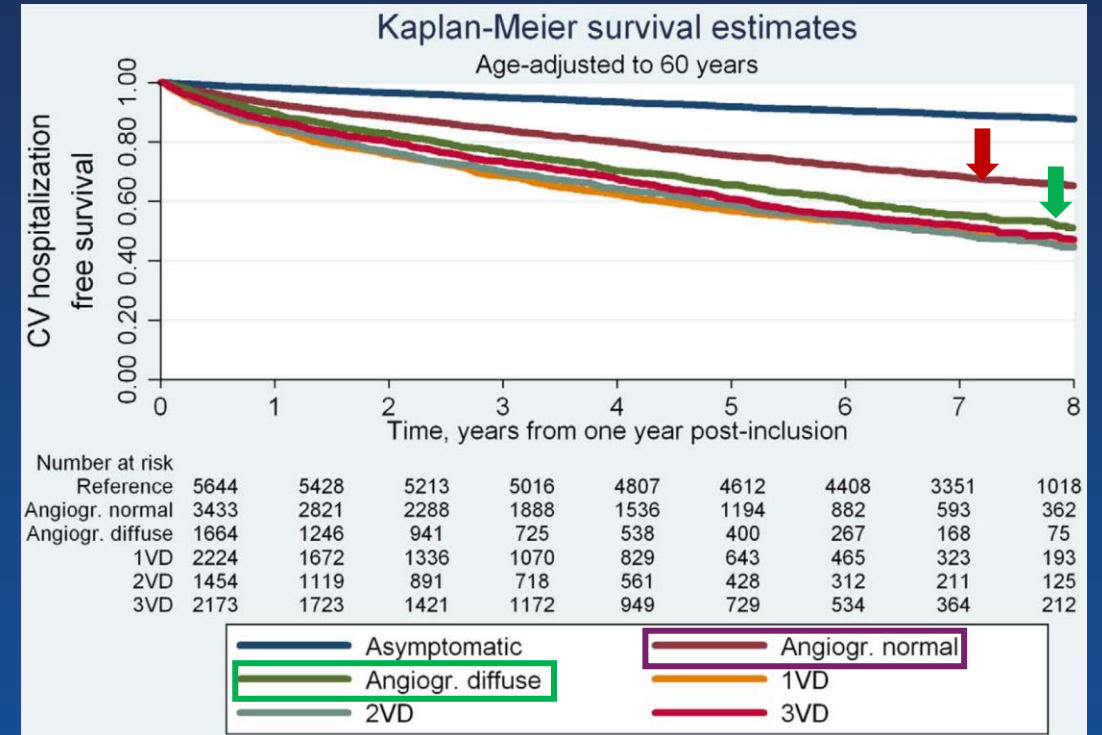


# Bevindingen bij coronarografie en klinische evolutie

## Bevindingen bij coronarografie



## Nieuwe hospitalisatie voor CV reden

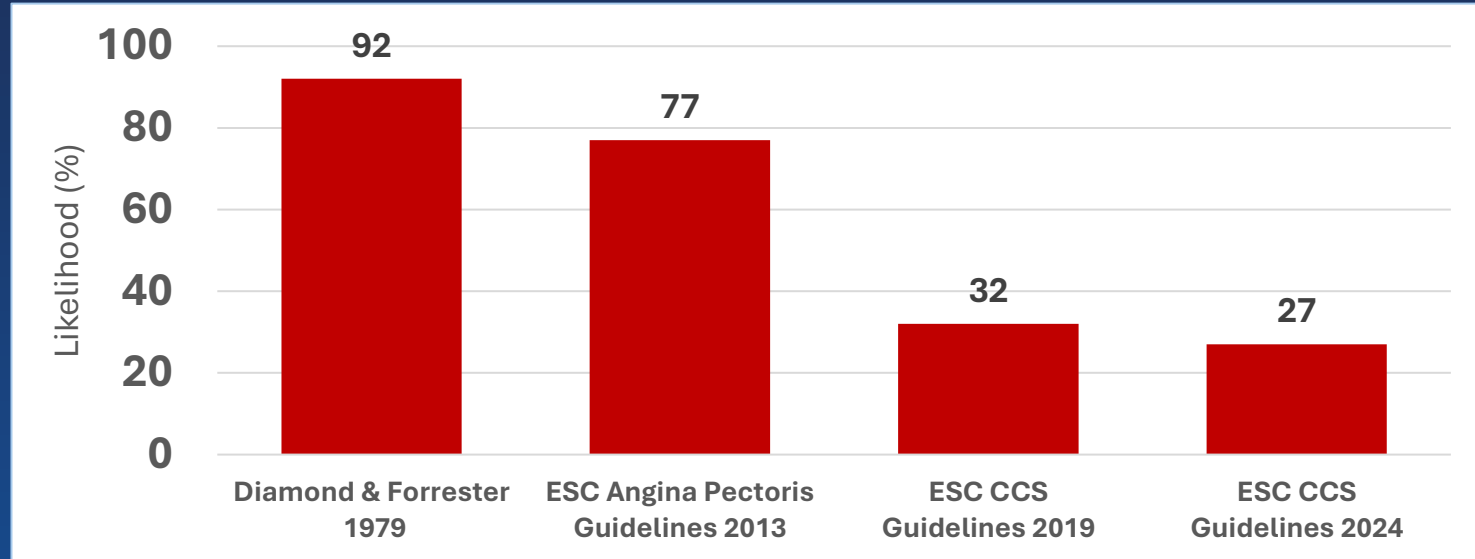


# Evolution of models to predict obstructive CAD

A 55-year-old man with two risk factors and constricting retrosternal chest pain on exertion and resolving after a five-minute rest

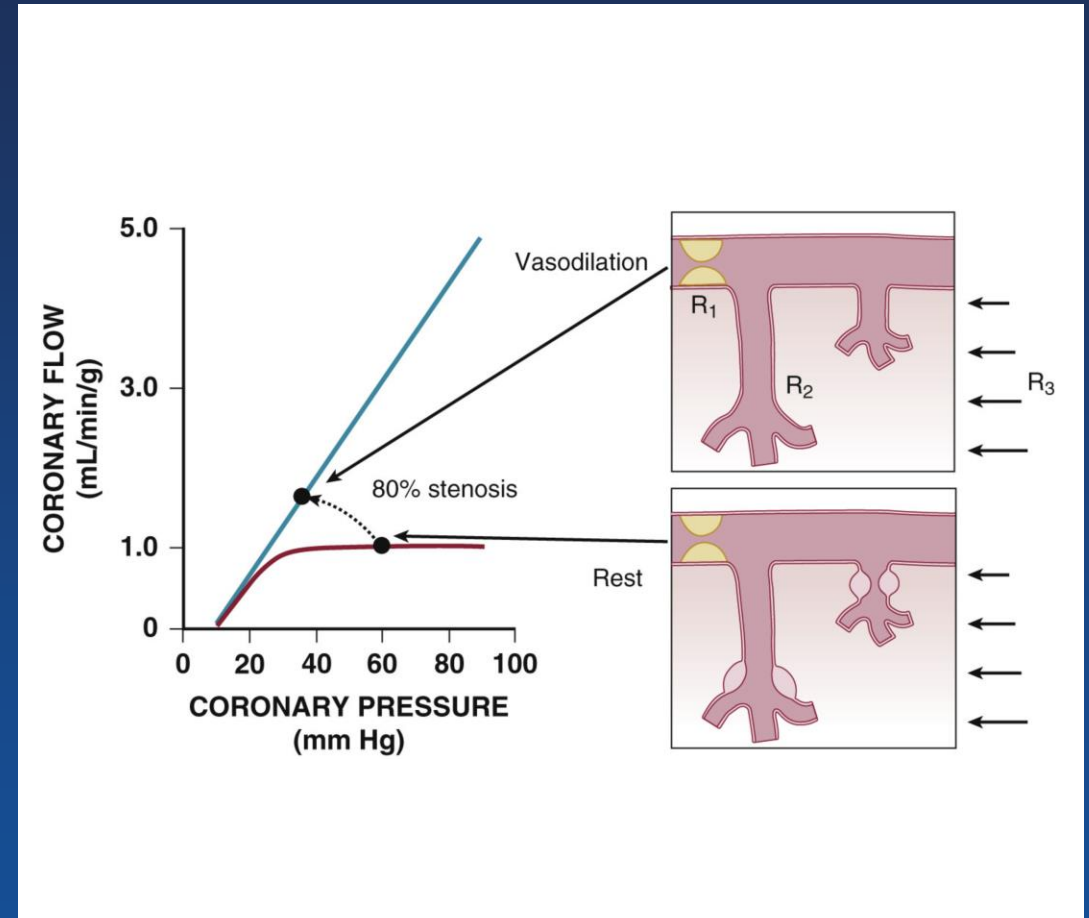
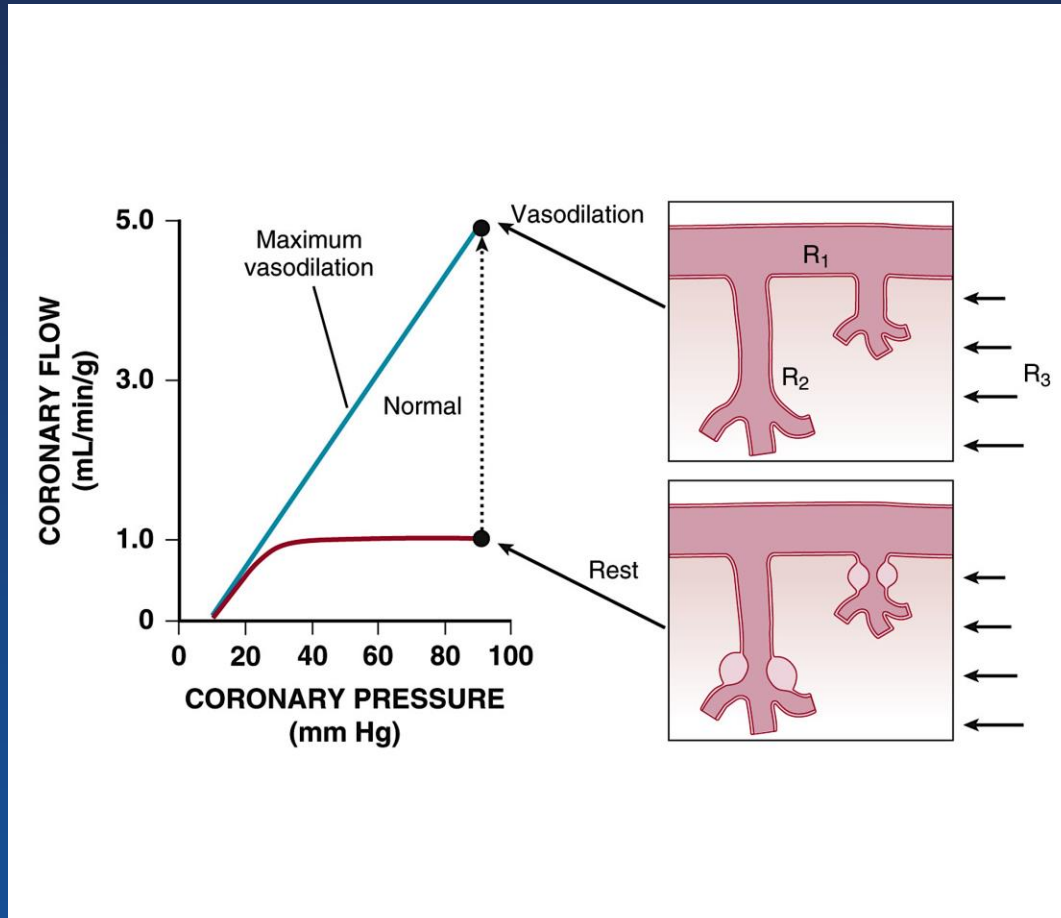
The numbers in the tables and graphs represent % likelihoods

Age	Nonanginal chest pain		Atypical angina		Typical angina	
	Men	Women	Men	Women	Men	Women
30-39	5	1	22	4	70	26
40-49	14	3	46	13	87	55
50-59	21	8	59	32	<b>92</b>	79
60-69	28	19	67	54	94	91

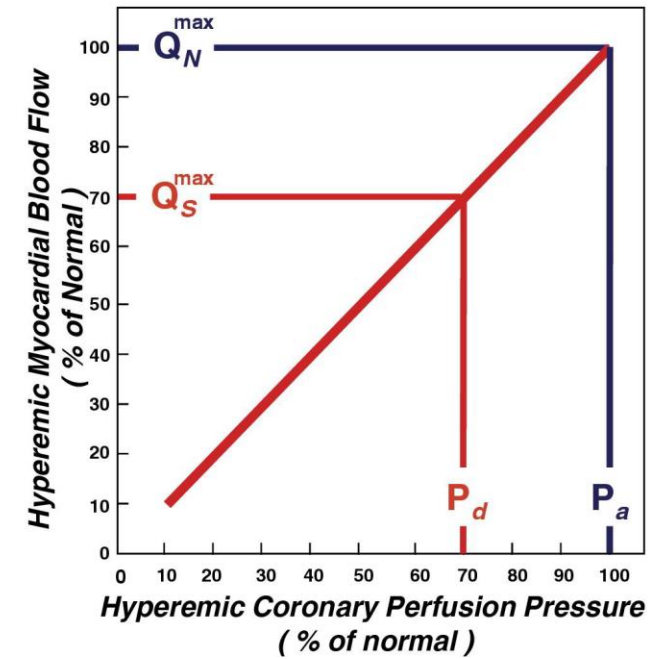
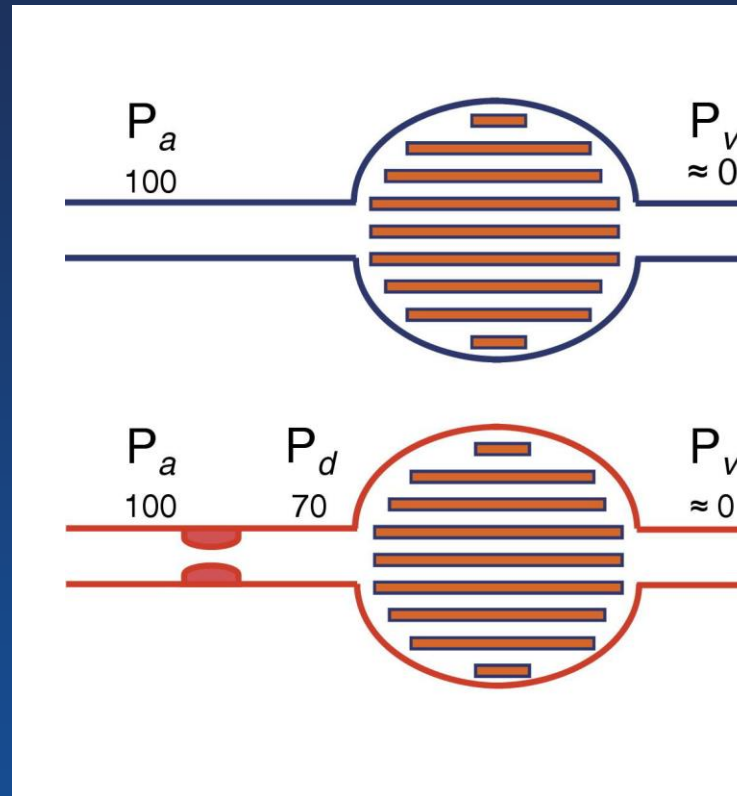
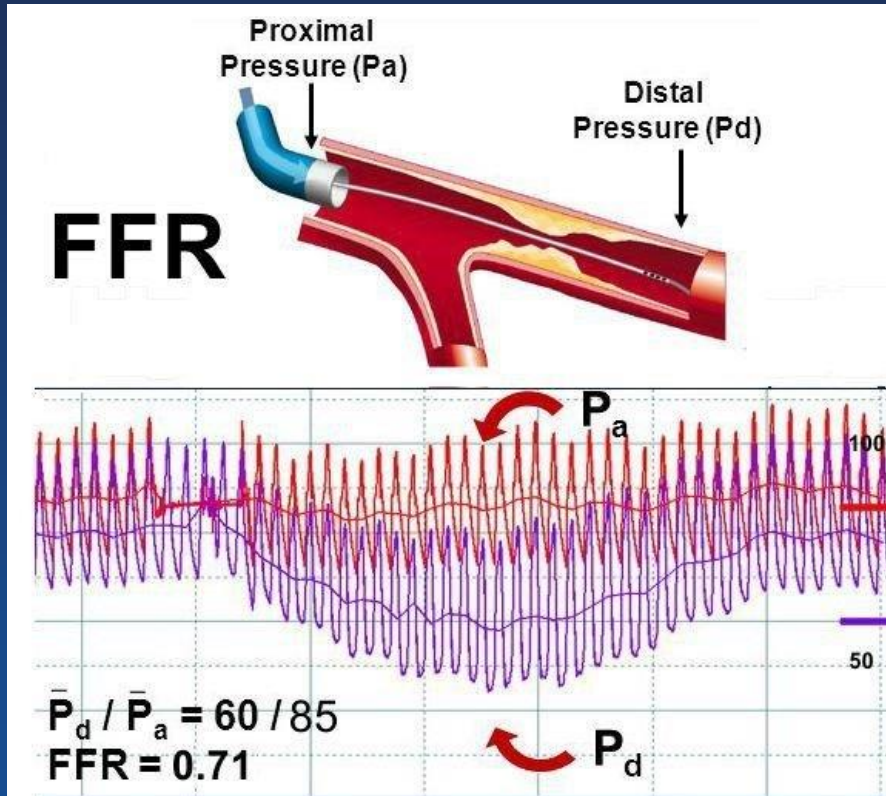


Number of risk factors	Symptom score					
	0-1 point		2 points		3 points	
	Women	Men	Women	Men	Women	Men
Age 30-39	0-1: 0, 2-3: 1, 4-5: 2	0-1: 1, 2-3: 2, 4-5: 5	0-1: 0, 2-3: 1, 4-5: 3	0-1: 2, 2-3: 4, 4-5: 8	0-1: 2, 2-3: 5, 4-5: 10	0-1: 9, 2-3: 14, 4-5: 22
Age 40-49	0-1: 1, 2-3: 1, 4-5: 3	0-1: 2, 2-3: 4, 4-5: 8	0-1: 1, 2-3: 2, 4-5: 5	0-1: 3, 2-3: 6, 4-5: 12	0-1: 4, 2-3: 7, 4-5: 12	0-1: 14, 2-3: 20, 4-5: 27
Age 50-59	0-1: 1, 2-3: 2, 4-5: 5	0-1: 4, 2-3: 7, 4-5: 12	0-1: 2, 2-3: 3, 4-5: 7	0-1: 6, 2-3: 11, 4-5: 17	0-1: 6, 2-3: 10, 4-5: 15	0-1: 21, 2-3: <b>27</b> , 4-5: 33
Age 60-69	0-1: 2, 2-3: 4, 4-5: 7	0-1: 8, 2-3: 12, 4-5: 17	0-1: 3, 2-3: 6, 4-5: 11	0-1: 12, 2-3: 17, 4-5: 25	0-1: 10, 2-3: 14, 4-5: 19	0-1: 32, 2-3: 35, 4-5: 39
Age 70-80	0-1: 4, 2-3: 7, 4-5: 11	0-1: 15, 2-3: 19, 4-5: 24	0-1: 6, 2-3: 10, 4-5: 16	0-1: 22, 2-3: 27, 4-5: 34	0-1: 16, 2-3: 19, 4-5: 23	0-1: 44, 2-3: 44, 4-5: 45

# Fysiopathologie van de coronaire circulatie

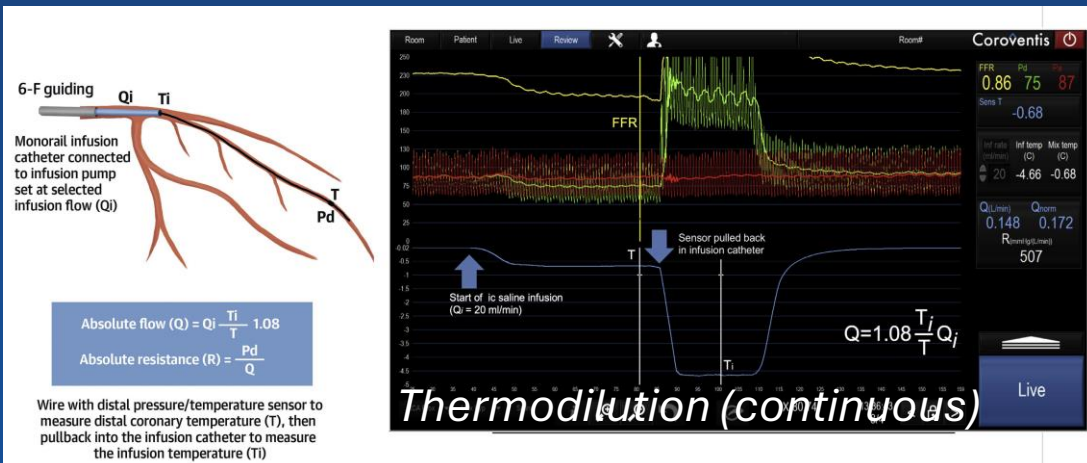
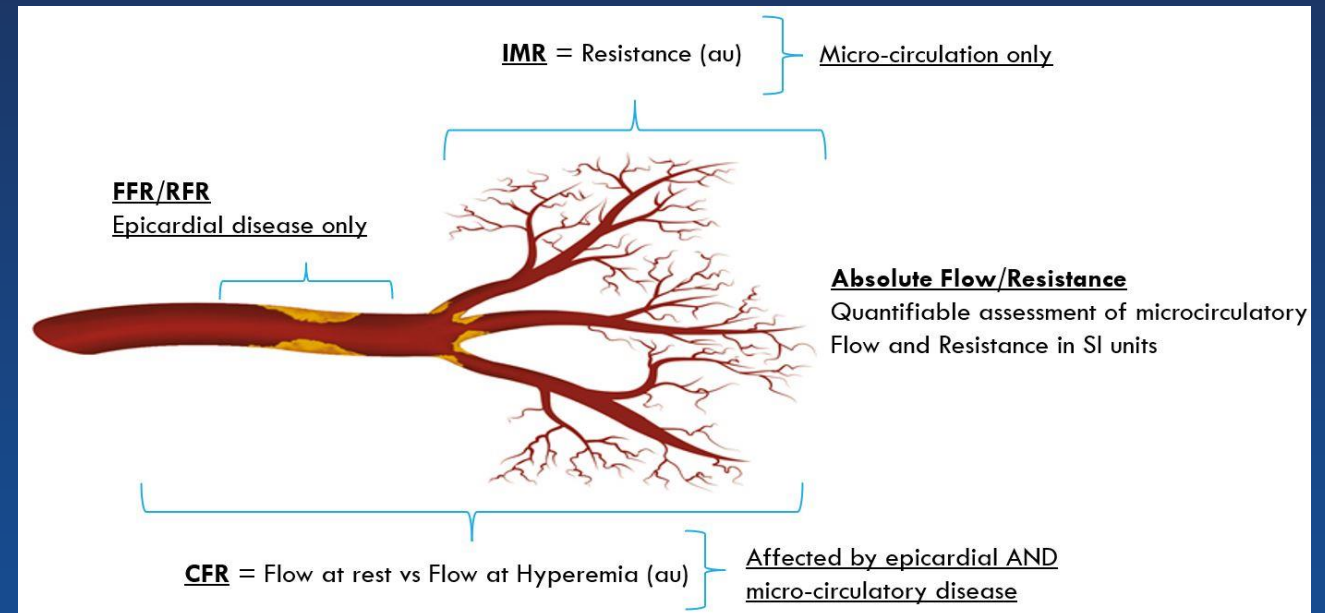
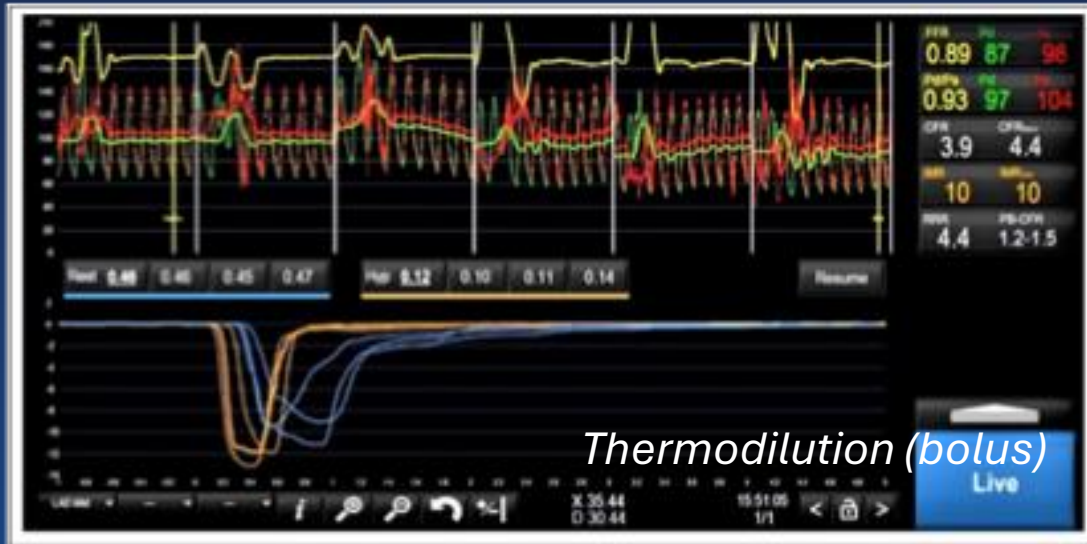


# Fractionale Flow Reserve (FFR)



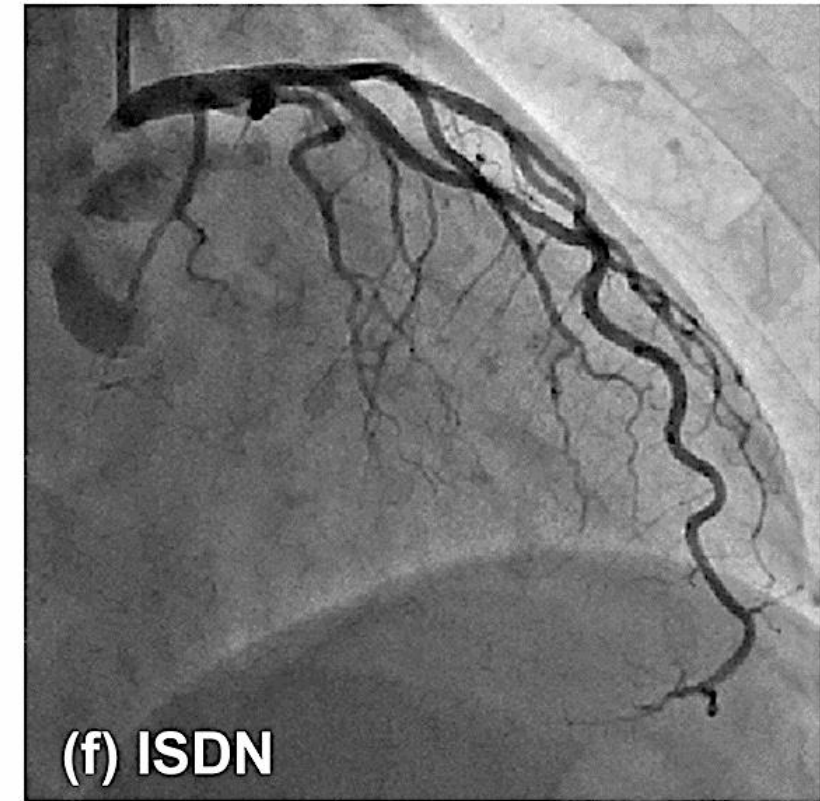
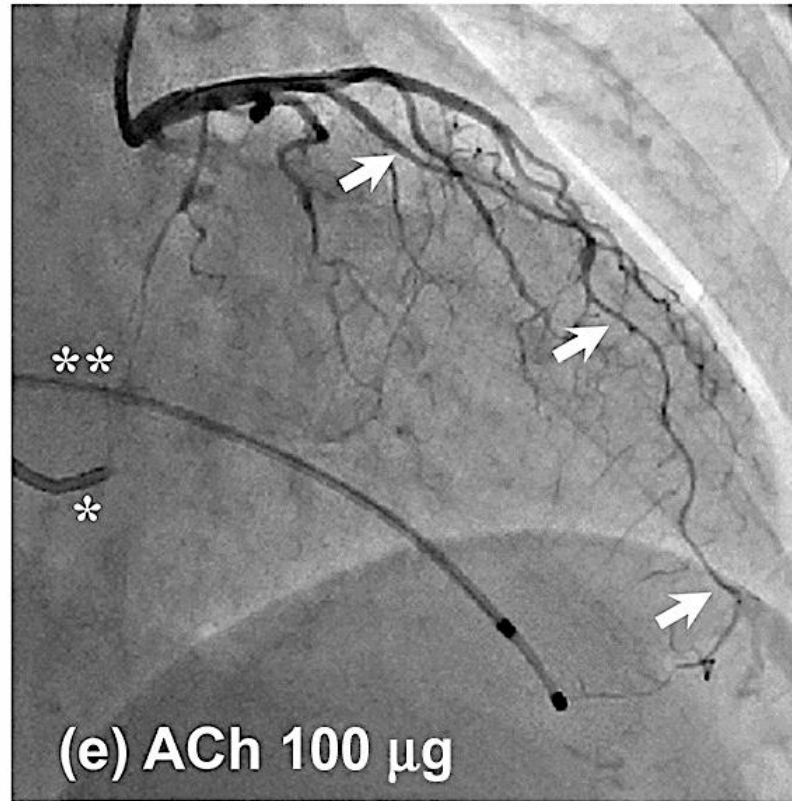
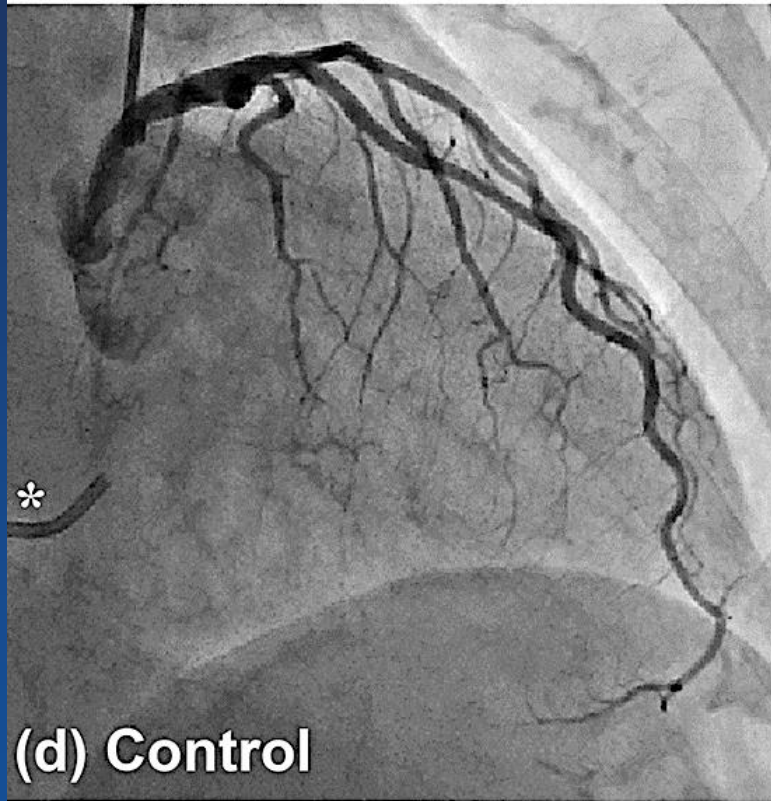
$$FFR = P_d / P_a$$

# Nieuwe methoden voor evaluatie van de coronaire circulatie

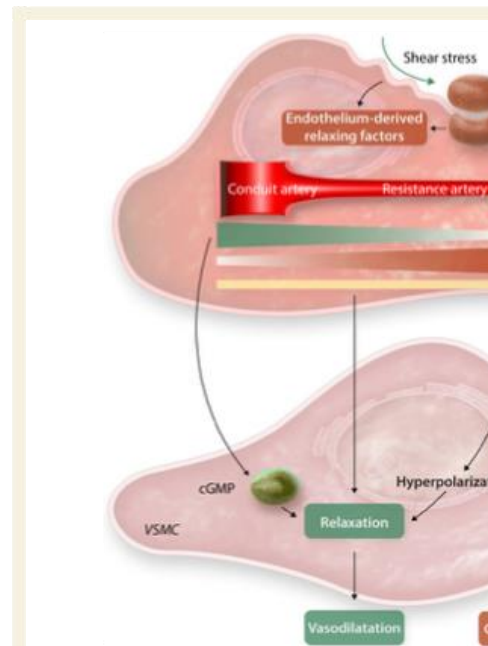
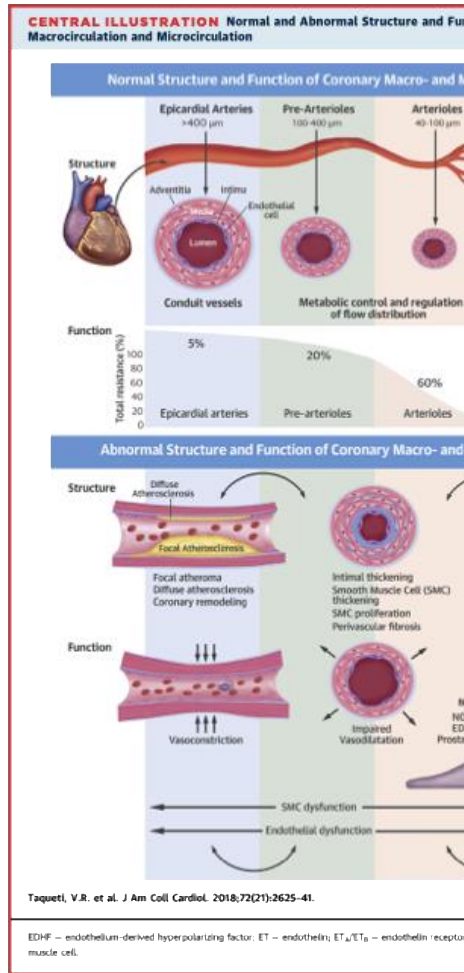


# Nieuwe methoden voor evaluatie van de coronaire circulatie

Provocatietesten voor detecteren coronaire vaatspasmen  
(epicardiaal & microcirculatoir)



# Changing concepts...



**Figure 4** Endothelial modulation of vascular tone and rho-kinase-mediated vascular smooth muscle contraction. EDHF, endothelium-derived hyperpolarizing factor(s); NO, nitric oxide; PGs, prostaglandins.

laboratory.<sup>45,46</sup> In brief, as stated above, the healthy human coronary circulation is regulated by NO and low physiological levels of H<sub>2</sub>O<sub>2</sub> as an EDHF. However, various atherosclerotic risk factors (e.g. ageing, hypertension, obesity, and smoking) can cause a switch from NO to H<sub>2</sub>O<sub>2</sub> as the mediator of endothelium-dependent vasodilatation in human coronary arteries. The resultant impaired production of NO and pathologically elevated levels of H<sub>2</sub>O<sub>2</sub>, both favour vasoconstriction, pro-inflammatory, pro-proliferative, and pro-thrombotic states, thus contributing to the development of coronary atherosclerosis.<sup>45,46</sup> Taken together, these observations may provide insight into the underlying mechanisms by which CMD contributes to the development of epicardial coronary atherosclerosis, even though these focal lesions are located upstream to the microcirculation.

### 3.2 Coronary microvascular spasm

CMD comprises both impaired coronary microvascular dilatation and enhanced coronary microvascular constriction.<sup>47</sup> Coronary artery

spasm at a wide variety of sites is a major cause of myocardial ischemia. It is a major cause of myocardial ischemia in the microcirculation. It is a major cause of myocardial ischemia in the microcirculation. It is a major cause of myocardial ischemia in the microcirculation.

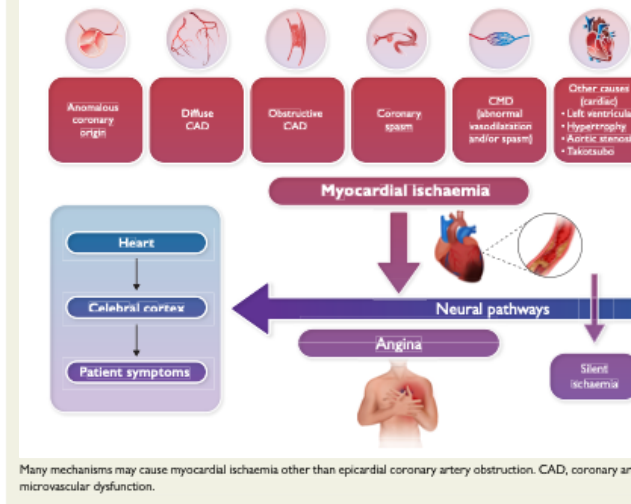
## Reprising Heberden's description of angor pectoris after 250 years

William E. Boden<sup>1\*</sup>, Juan Carlos Kaski<sup>2</sup>, and Colin Berry<sup>3</sup>

<sup>1</sup>VA Boston Healthcare System, Boston University School of Medicine and Harvard Medical School, 150 S Huntington Avenue, Boston, MA 02130, USA; <sup>2</sup>Research Institute, St. George's University of London, Cranmer Terrace, London SW17 0RE, UK; and <sup>3</sup>School of Cardiovascular and Metabolic Health, British Cardiovascular Research Centre, University of Glasgow, 124 University Place, Glasgow G12 8TA, UK

Online publish ahead of print: 14 December 2022

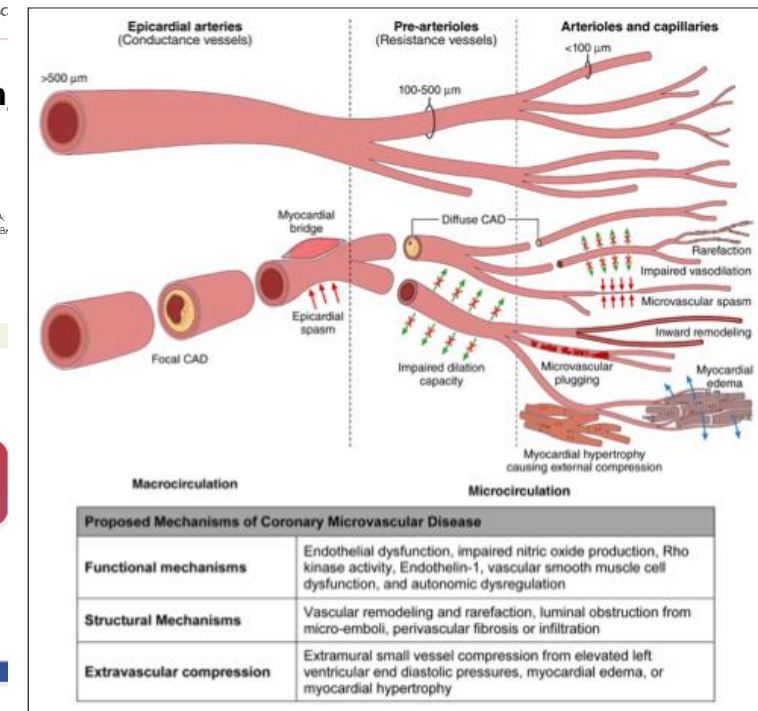
### Graphical Abstract



Many mechanisms may cause myocardial ischaemia other than epicardial coronary artery obstruction. CAD, coronary artery disease; CMD, coronary microvascular disease.

\*But there is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, which deserves to be mentioned more at length. The seat of it and the sense of strangling and anxiety with which it is attended, may be called angina pectoris. Those who are seized while they are walking (more or less and soon after eating) with a painful

\* Corresponding author. Tel: +1 857 364 5413; Email: [william.boden@va.gov](mailto:william.boden@va.gov)  
Published by Oxford University Press on behalf of the European Society of Cardiology 2022.  
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**Figure 1.** Anatomy of the coronary microcirculation and potential mechanisms of coronary microvascular dysfunction. CAD indicates coronary artery disease.

spasm. Thus, a proposed CMD classification scheme includes the following subtypes: (1) primary CMD in the absence of myocardial disease or obstructive CAD; (2) CMD in primary myocardial diseases; (3) CMD in obstructive CAD post myocardial infarction (MI), and (4) iatrogenic CMD associated with reperfusion injury and microvascular distal embolization following coronary revascularization.<sup>4</sup>

Mechanisms of CMD may be multifactorial. Functional etiologies of CMD include impaired relaxation, or in the case of microvascular spasm, transient vasoconstriction of the microcirculatory arterioles. This may be caused by endothelial dysfunction with insufficient nitric

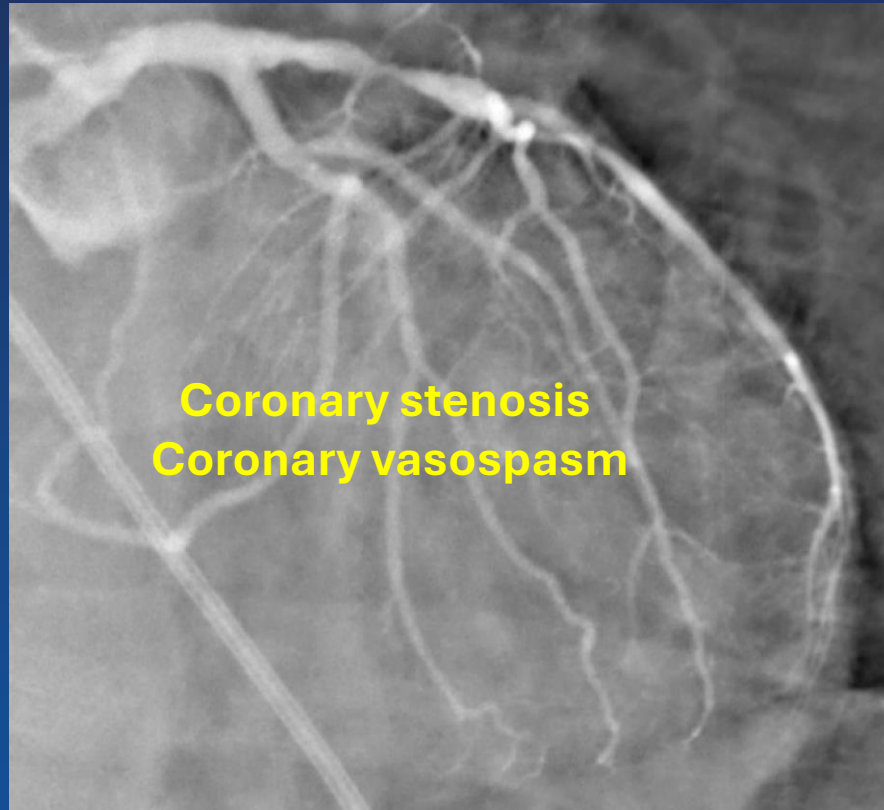
oxide production, or due to direct endothelin-kinase or rho-kinase-mediated constriction of microcirculatory vascular smooth muscle.<sup>48-51</sup> In other cases, CMD may be characterized by an abnormal loss of microcirculatory tone in resting conditions, with little capacity for further vasodilatation. Structural causes of CMD may include microvascular remodeling with narrowing of the lumen due to intimal and medial smooth muscle cell hypertrophy, fibrosis of the intramyocardial arterioles and capillaries, perivascular fibrosis (from inflammation or injury), intravascular platelet plugging, or capillary rarefaction, all of which may be associated with traditional risk factors for atherosclerosis. Inflammation, platelet dysfunction,



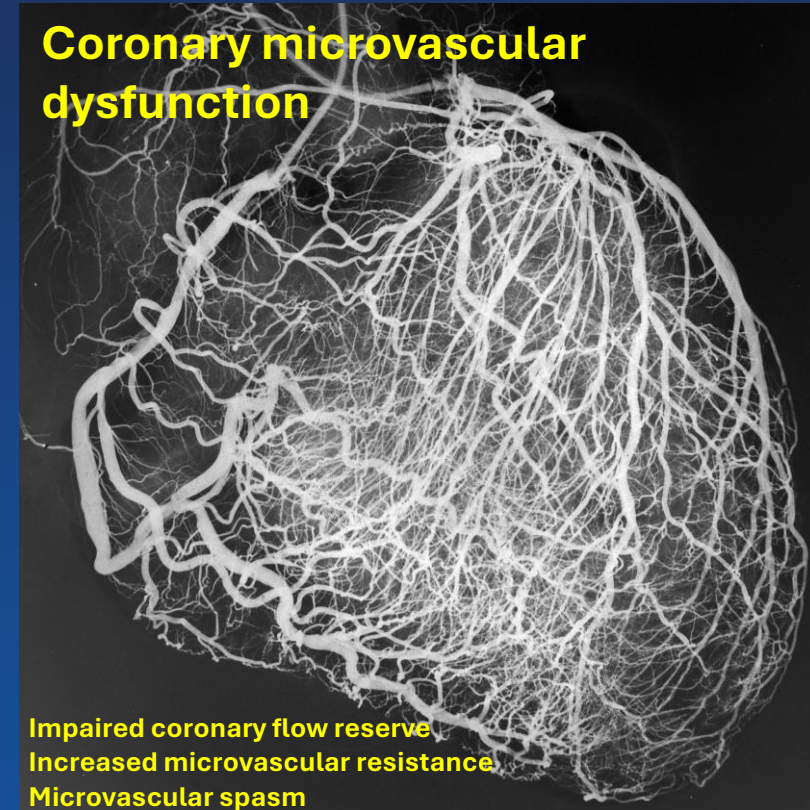
# 21st century's evolving concepts:

Myocardial ischaemia results from structural and/or functional changes in the epicardial coronary arteries and/or microcirculation.

## Epicardial coronary arteries

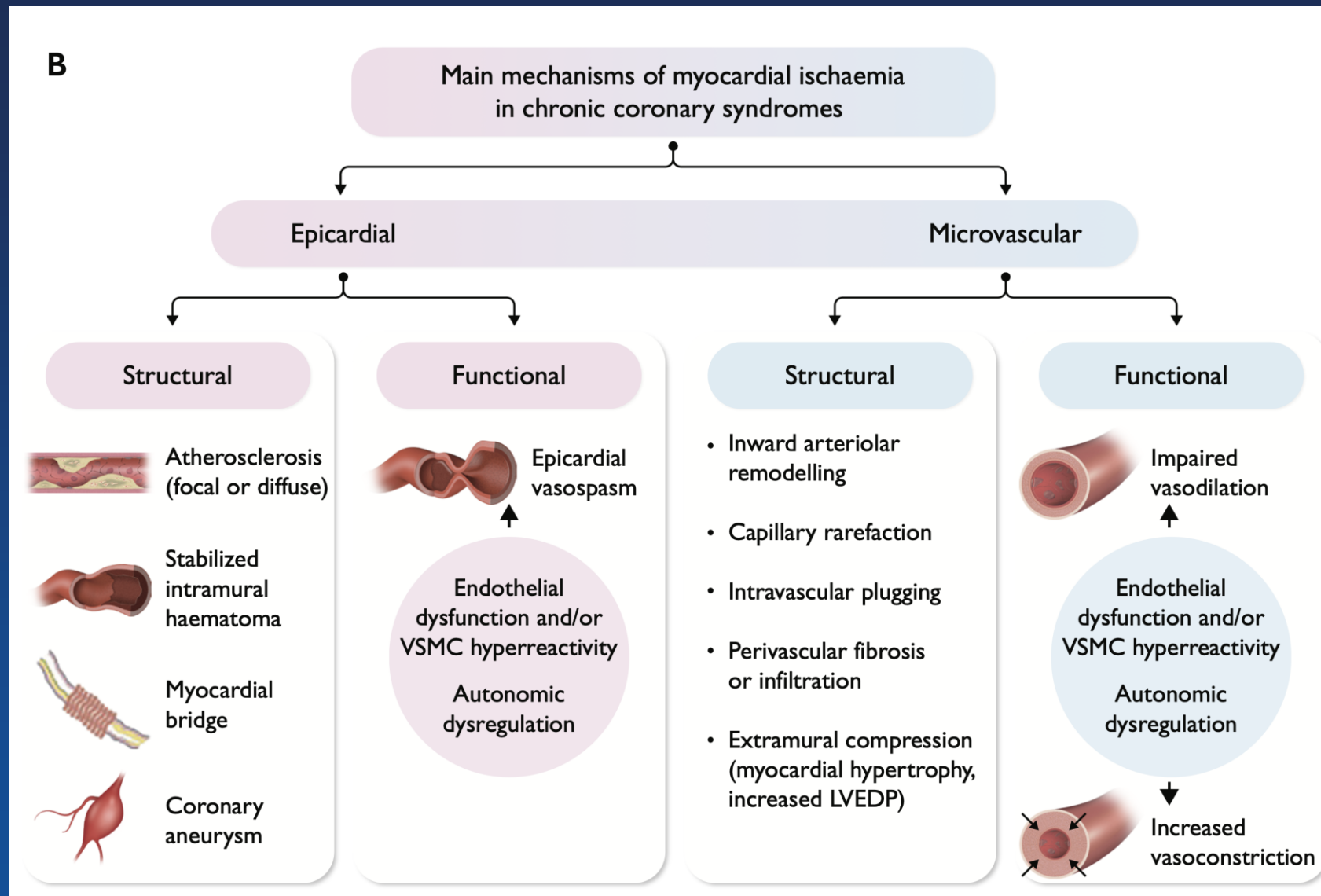


## Coronary microcirculation

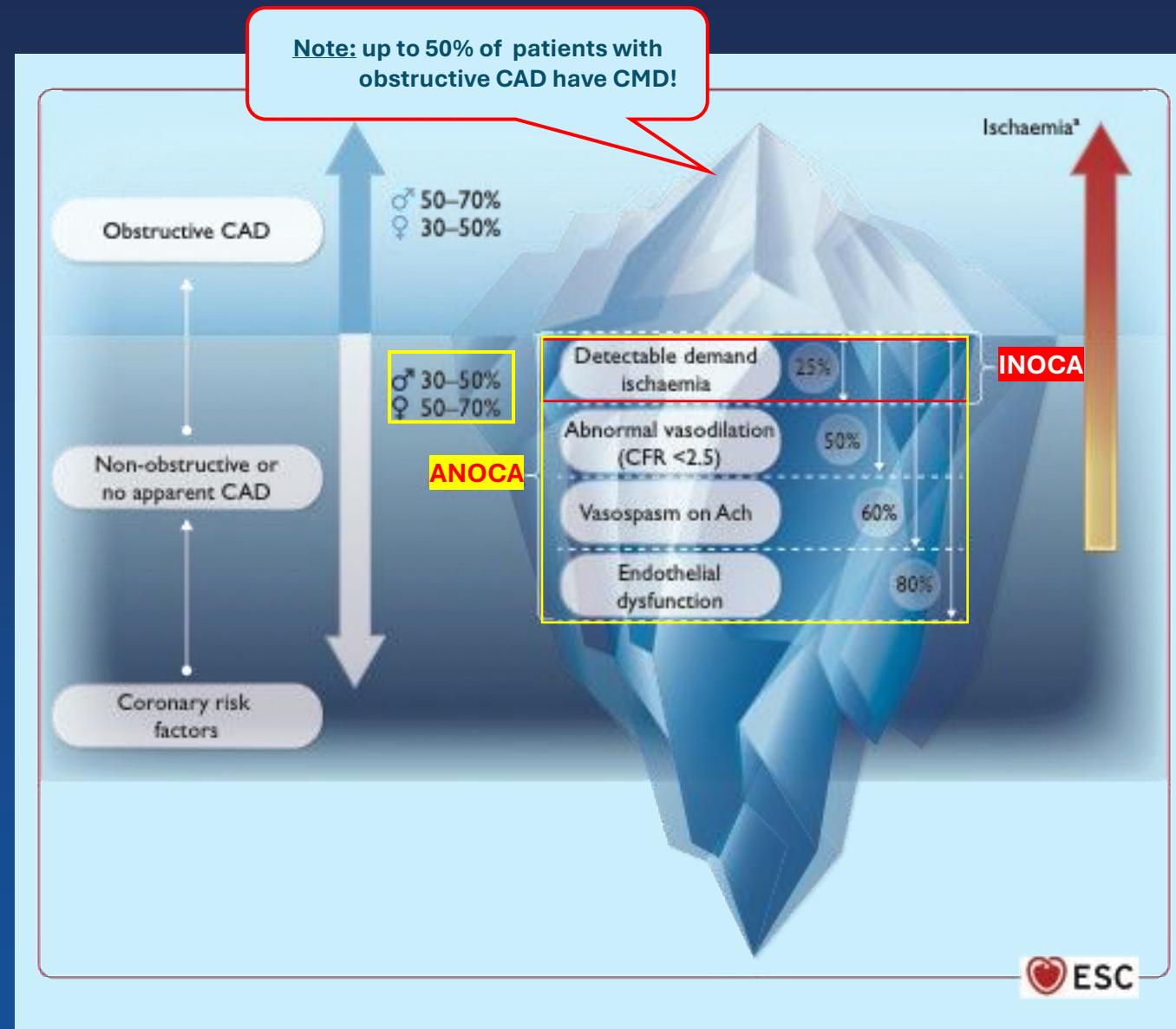


William Fulton, MD Thesis Univ Glasgow (1963); courtesy C Berry

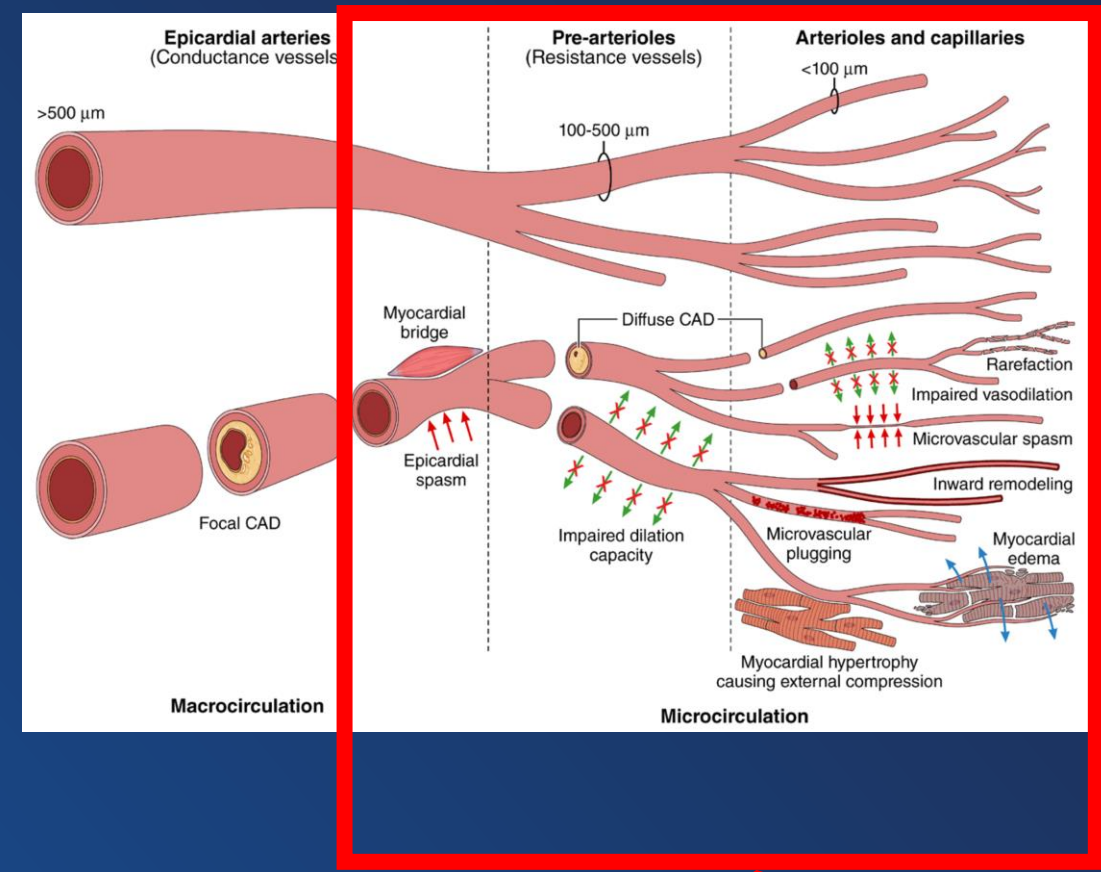
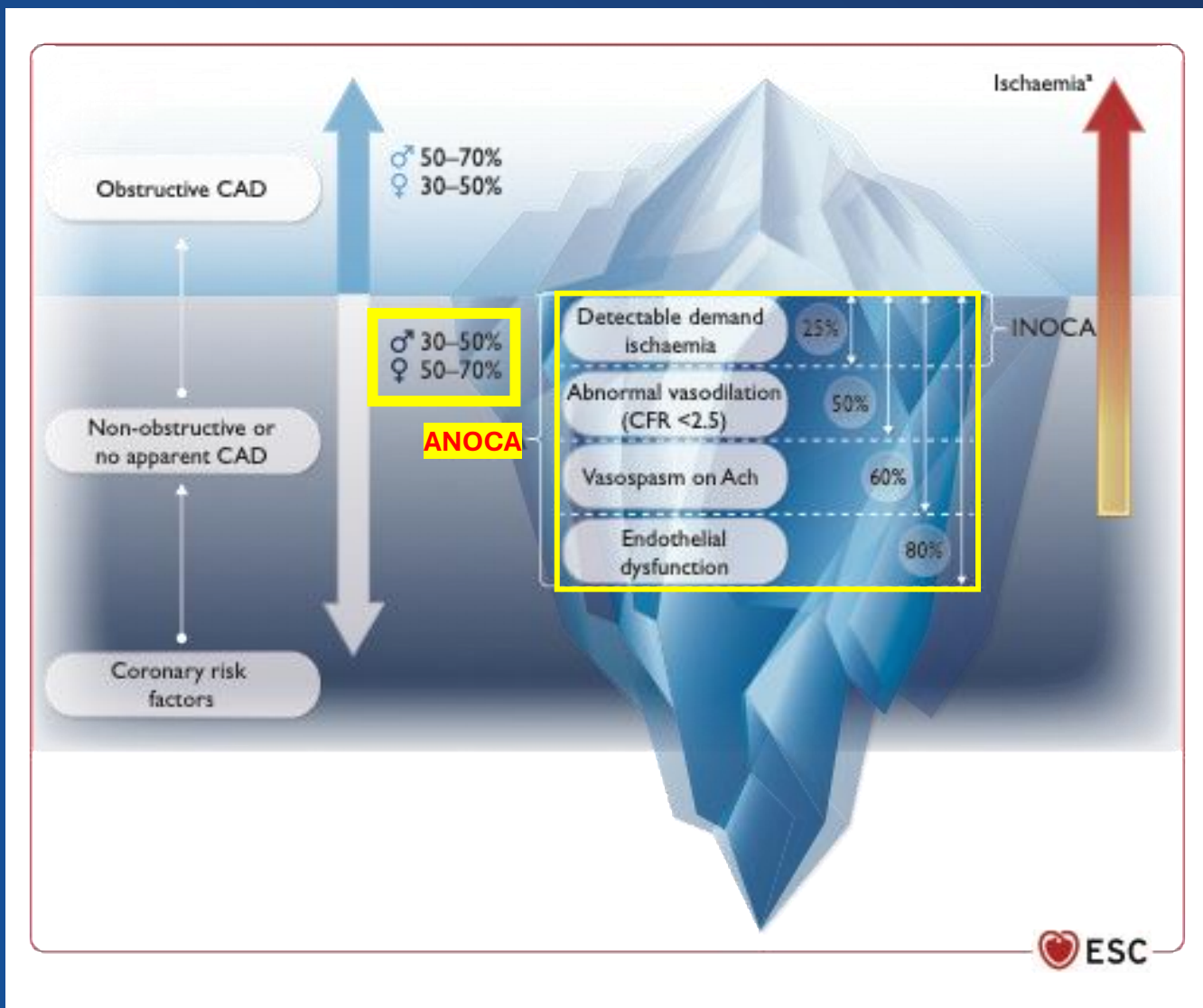
# Pathofysiologie myocardischemie



# Prevalentie obstructief coronair lijden/microvasculaire disfunctie



# ANOCA / INOCA: Angina / Ischemia with nonobstructive coronary arteries



In 50 à 70% van de patiënten met angina pectoris ligt de oorzaak hier!

# ANOCA-INOCA

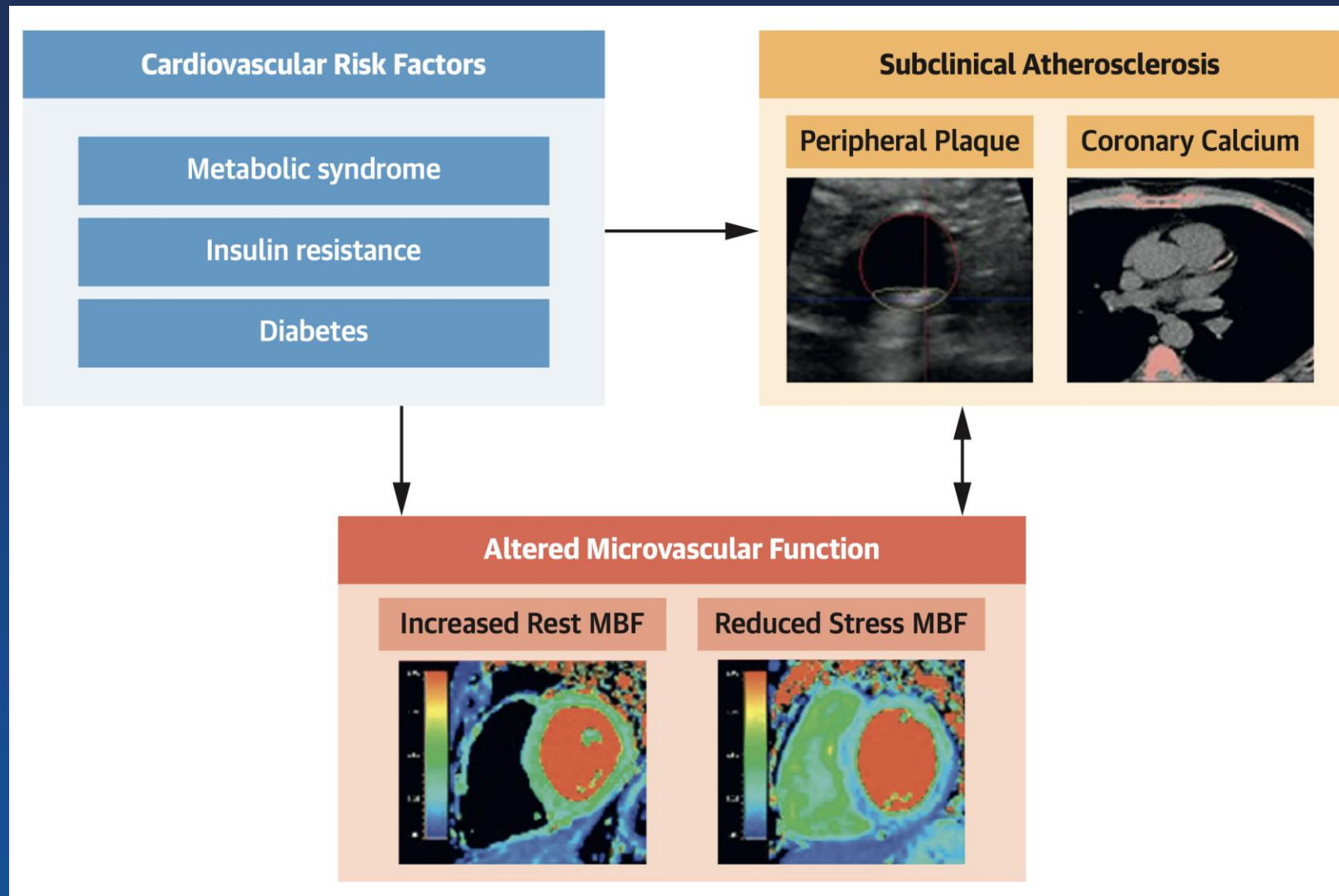
ANOCA: Angina with Non - Obstructive Coronary Arteries

INOCA : Ischaemia with Non-Obstructive Coronary Arteries

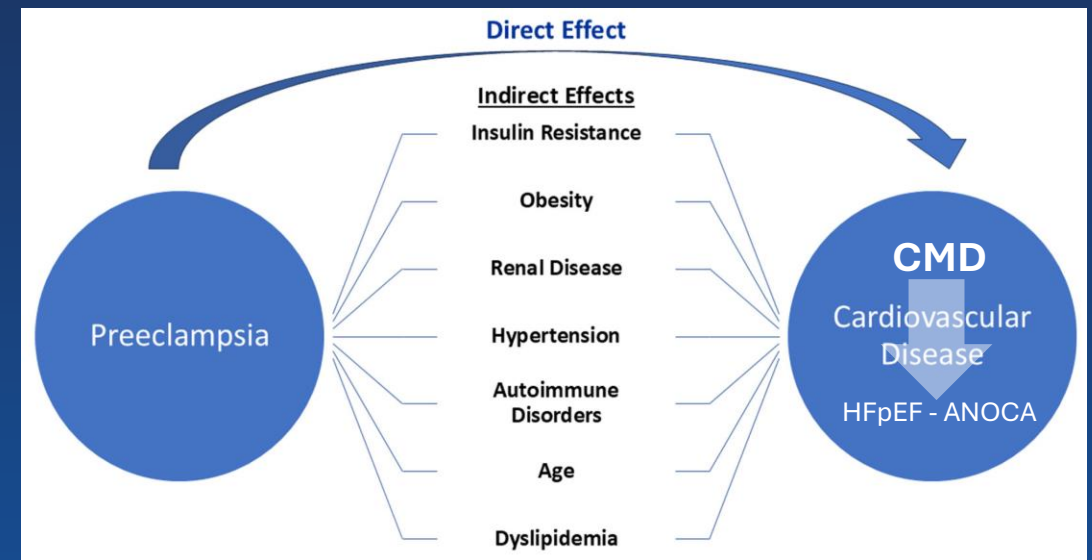
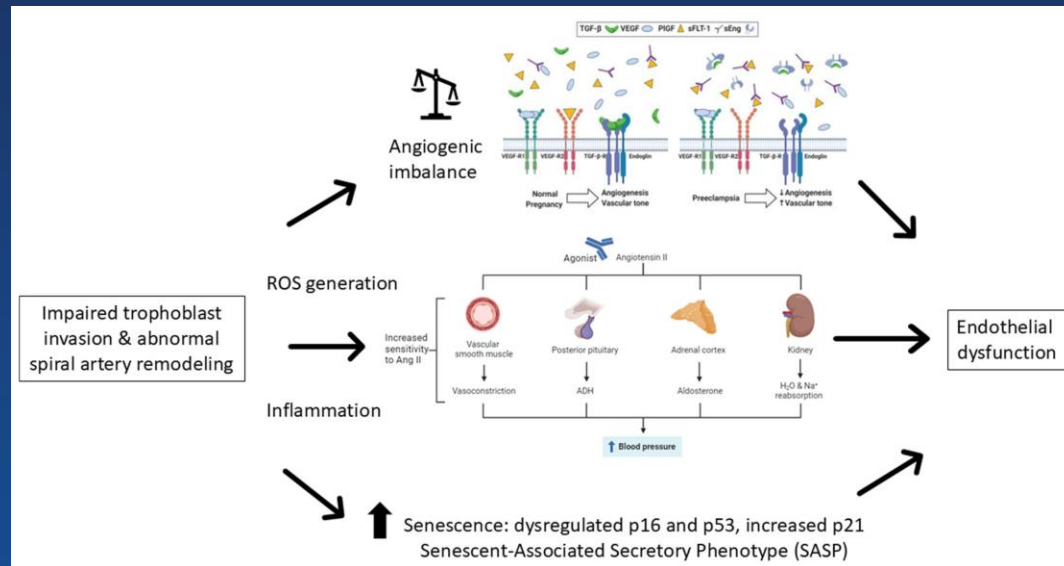
? Wanneer er aan denken:

- Erg verdachte klachten voor angina pectoris – dyspnoe d’effort\*
- V é é l coronaire risicofactoren
- Vrouw met:
  - Pre-eclampsie voorgeschiedenis
  - Meerdere miskramen
  - Vroegtijdige menopauze

# Cardiovasculaire Risicofactoren → ANOCA

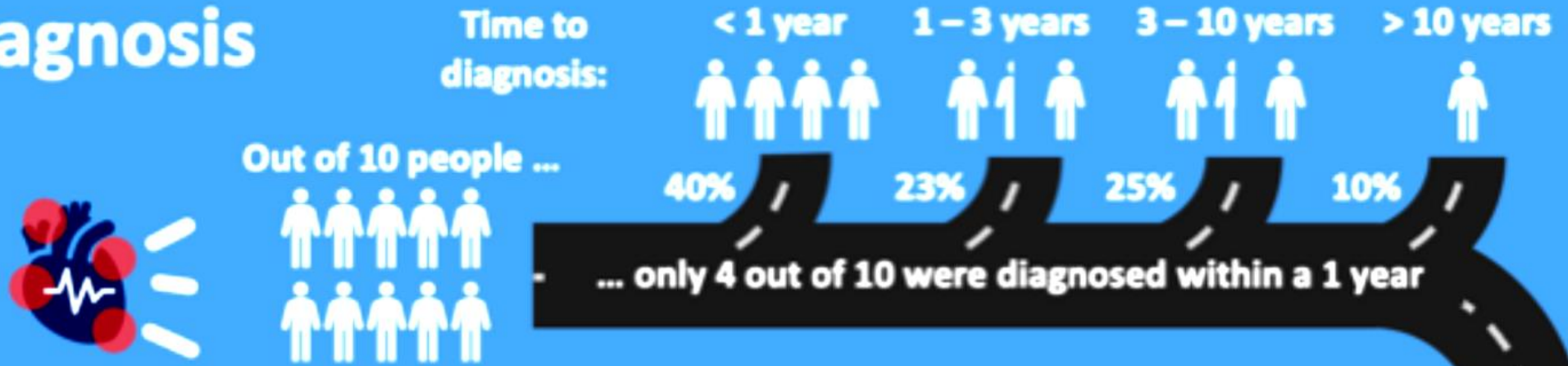


# Late gevolgen van preeclampsie...



*CMD: coronaire microvasculaire disfunctie*

# A typical journey from the onset of symptoms to diagnosis



3 in 4 were told their symptoms weren't cardiac



2 in 3 were discharged without treatment from A&E



Over half (59%) of respondents called an ambulance due to symptoms of INOCA



## Misdiagnoses

Only 8 out 100 ambulance crews understood INOCA





Only 8 out of 100 ambulance crews understood INOCA

## Misdiagnoses

1 in 4 respondents were prescribed antidepressants



1 in 3 respondents were referred to a Psychiatrist



1 in 2 respondents were told that symptoms were GERD



6 % were diagnosed on first consultation

29% had 2 – 3 consultations

Consultations prior to diagnosis

35% had 4 – 6 consultations

25% had over 6 consultations

Number of cardiologists consulted



# Prognose ANOCA

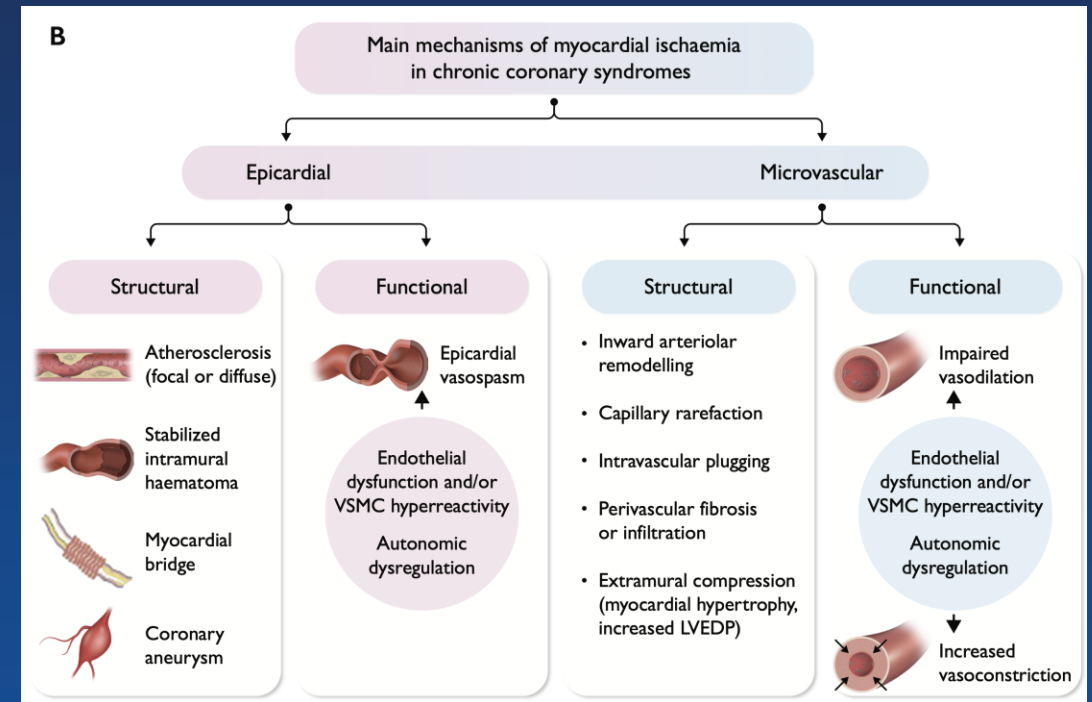
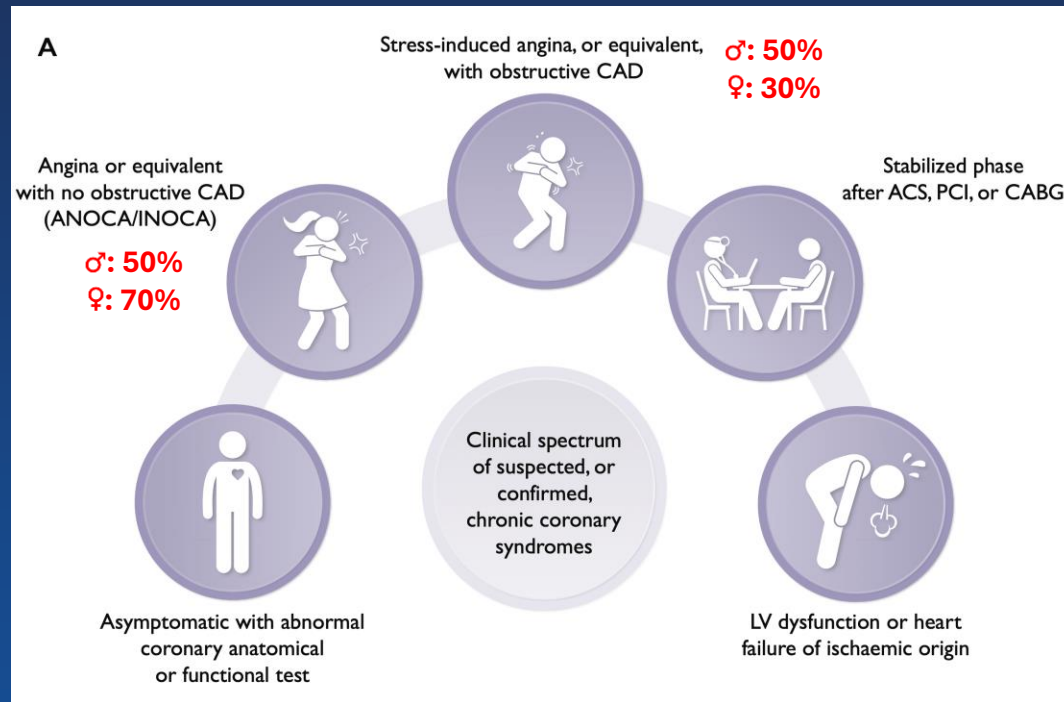
ANOCA met gedaalde CFR gaat gepaard met een 4 à 5 maal hoger risico op overlijden en MACE

	Meta-analyse	N patiënten	HR	95% CI
<b>Mortaliteit</b>	Gdowski et al.	6631	<b>3,93</b>	2,91-5,30
	Kelshiker et al.	4481	<b>5,44</b>	3,78-7,83
<b>MACE</b>	Gdowski et al.	5189	<b>5,16</b>	2,81-9,47
	Kelshiker et al.	6367	<b>3,56</b>	2,14-5,90

M. A. Gdowski, V. L. Murthy, M. Doering, A. G. Monroy-Gonzalez, R. Slart & D.L Brown.  
J Am Heart Assoc 2020 Vol. 9 Issue 9 Pages e014954 PMID: 32345133

M. A. Kelshiker, H. Seligman, J. P. Howard, H. Rahman, M. Foley, A. N. Nowbar, et al.  
Eur Heart J 2022 Vol. 43 Issue 16 Pages 1582-1593 PMID: 34849697

# Spectrum van chronische coronaire syndromen



# Nieuw diagnostisch algoritme

Indien geen of niet-obstructieve coronaire atherosclerose: behandel als ANOCA indien verdachte symptomen!

