Odessa National Medical University
Internal Medicine Department 2 with postgraduate education

Lecture for 4th years students

Topic:

CHRONIC ISCHEMIC HEART DISEASE

2024-2025 ed.y.

Lecturer:
Tykhonova Susanna,
MD, PhD, Professor

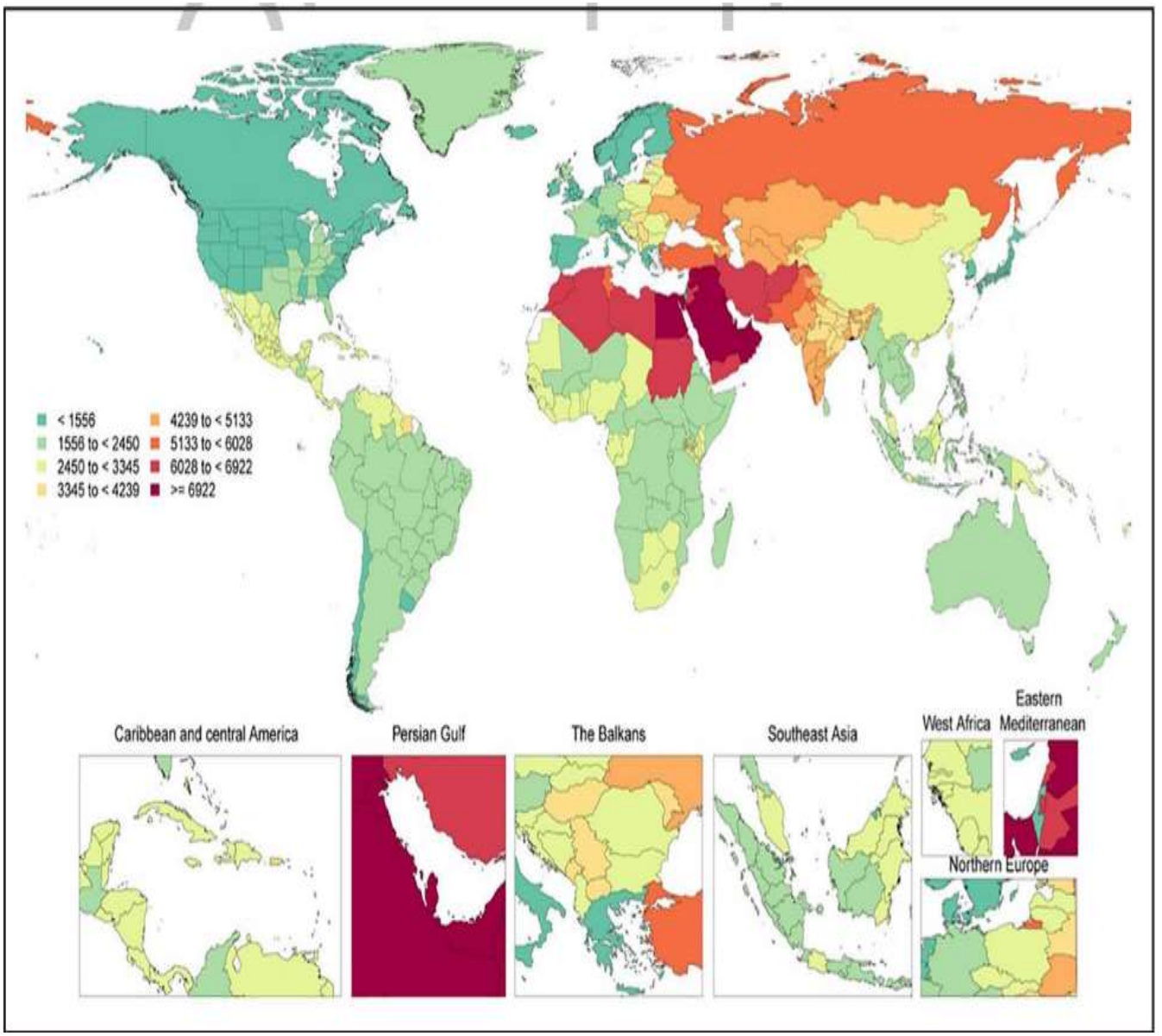
Topic for consideration

Definition
Epidemiology
Etiology, Pathphysiology

General Principles of Evaluation,
Diagnosis, and Risk Stratification,
Treatment Selection

Guideline-Directed Management and Therapy

Global Age-Adjusted Prevalence of CCD per 100000, by Sex, 2020



Globally, it was estimated that **197.2 million people had IHD in 2019, and it was more prevalent in men (113.7 million) than in women (83.6 million).**

Despite a male predominance and roughly 10-year lag in incidence in women, IHD is the leading cause of mortality for women worldwide.

Prevalence of IHD varies widely both between and within countries

Source: Data courtesy of the Global Burden of Disease Study 2020, Institute for Health Metrics and Evaluation. Used with permission. All rights reserved.

CLINICAL PRACTICE GUIDELINE

2023 AHA/ACC/ACCP/ASPC/NLA/PCNA

Guideline for the Management of Patients With Chronic Coronary Disease:

A Report of the American Heart Association / American College of Cardiology Joint Committee on Clinical Practice Guidelines

Circulation. 2023;148:e00–e00. DOI: 10.1161/CIR.0000000000001168

Chronic coronary disease (CCD)

CCD is a heterogeneous group of conditions that includes obstructive and nonobstructive coronary arteries disease (CAD) with or without previ ous myocardial infarction (MI) or revascularization, isch emic heart disease (IHD) diagnosed only by noninvasive testing, and chronic angina syndromes with varying underlying causes

(AHA / ACC, 2023)

ESC
European Society of Cardiology
European Heart Journal (2024) **00**, 1–123
https://doi.org/10.1093/eurheartj/ehae177

ESC 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)

Based on expanded pathophysiological concepts, a new, more comprehensive definition of CCS is introduced by ESC 2024:

‘CCS are a range of clinical presentations or syndromes that arise due to structural and/or functional alterations related to chronic diseases of the coronary arteries and/or microcircula tion.

These alterations can lead to transient, reversible, myocar dial demand vs. blood supply mismatch resulting in hypoperfusion (*ischaemia*), usually provoked by exertion, emotion or other stress, and may manifest as angina, other chest discomfort, or dyspnoea, or be asymptomatic.

Although stable for long periods, chronic coronary diseases are frequently progressive and may destabilize at any moment with the development of an ACS.’

Etiology

Ischemic heart disease (IHD) is primarily caused by atherosclerosis.

Less common, nonatherosclerotic causes include:
- vasospasm,
- endothelial and microvascular dysfunction,
- spontaneous thrombosis or embolism,
- coronary artery dissection,
- extrinsic compression,
- systemic vasculitis/arteritis,
- damage from radiation.

These etiologies are more common in younger patients,women, and those without traditional IHD risk factors.

Pathophysiological concepts of chronic coronary syndromes (ESC, 2024):

Structural and functional abnormalities in both the macro- and microvascular compartments of the coronary tree that may lead to transient myocardial ischaemia.

At the macrovascular level:

- not only fixed, flow-limiting stenoses but also diffuse atheroscler otic lesions without identifiable luminal narrowing may cause ischaemia under stress;
- structural abnormalities such as myocardial bridging and congenital arterial anomalies or dynamic epicardial vasospasm may be responsible for transient ischaemia.

Pathophysiological concepts of chronic coronary syndromes (ESC, 2024):

At the microvascular level, ***coronary microvascular dysfunction (CMD)*** is increasingly acknowl edged as a prevalent factor characterizing the entire spectrum of CCS; functional and structural microcirculatory abnormalities may cause angina and ischaemia even in patients with non-obstructive disease of the large or medium coronary arteries [***angina with non-obstructive coronary arteries (ANOCA); ischaemia with non obstructive coronary arteries (INOCA)***].

Finally, **systemic or extracor onary condition**s, such as anaemia, tachycardia, blood pressure (BP) changes, myocardial hypertrophy, and fibrosis, may contribute to the complex pathophysiology of non-acute myocardial ischaemia.

Pathophysiology

A traditional model suggests two means of plaque progression:

- ***Large thick-walled plaques*** are thought to slowly obstruct the lumen of coronary arteries, thereby causing decreased perfusion and chronic intermittent exertional symptoms when they reach 70% to 80% stenosis.

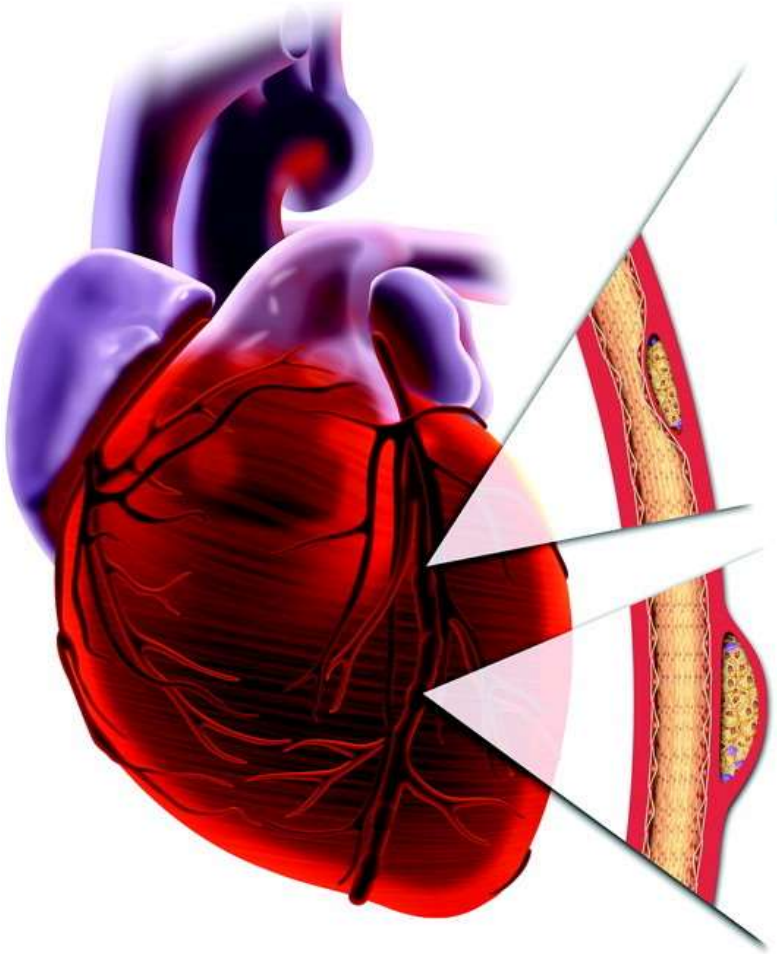
- ***Thin-walled "vulnerable plaques"*** may not cause meaningful obstruction until the wall is disrupted, at which point acute hematoma and thrombus formation cause sudden myocardial infarction by occluding the arterial lumen locally or embolizing distally into the coronary circulation.

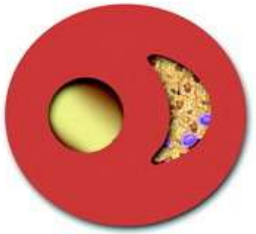
This model explains two clinically important phenomena:

1) myocardial infarction may occur in patients at anatomic sites without baseline flow limitation;
2) therapies that reduce chronic intermittent angina (improve flow) may be different from those that reduce ischemic heart disease mortality (stabilize plaque, prevent thrombosis).

Additionally, plaque development is not linear; plaques may move repeatedly through development, regression, and erosion/rupture.

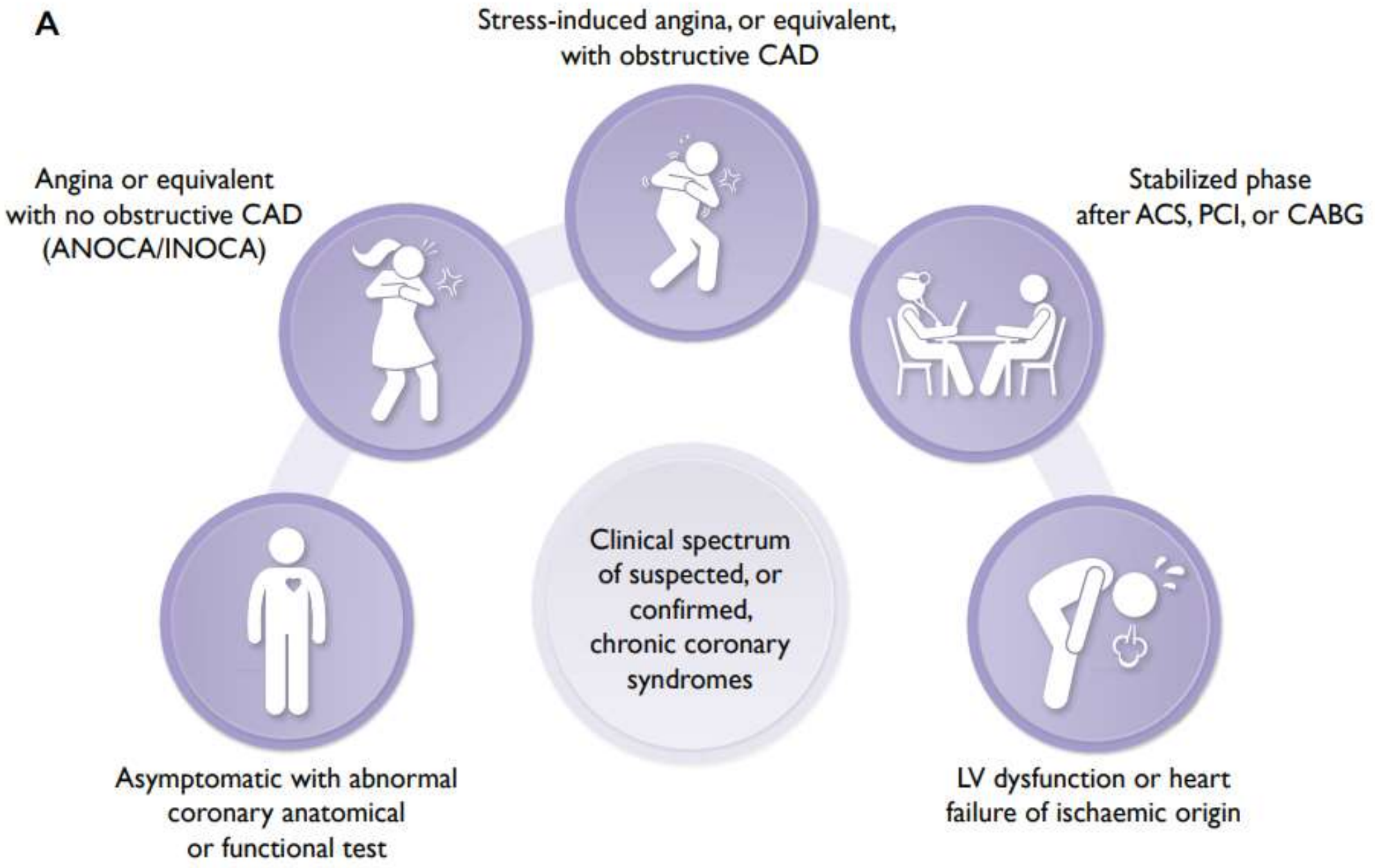
Simplified schema of diversity of lesions in human coronary atherosclerosis



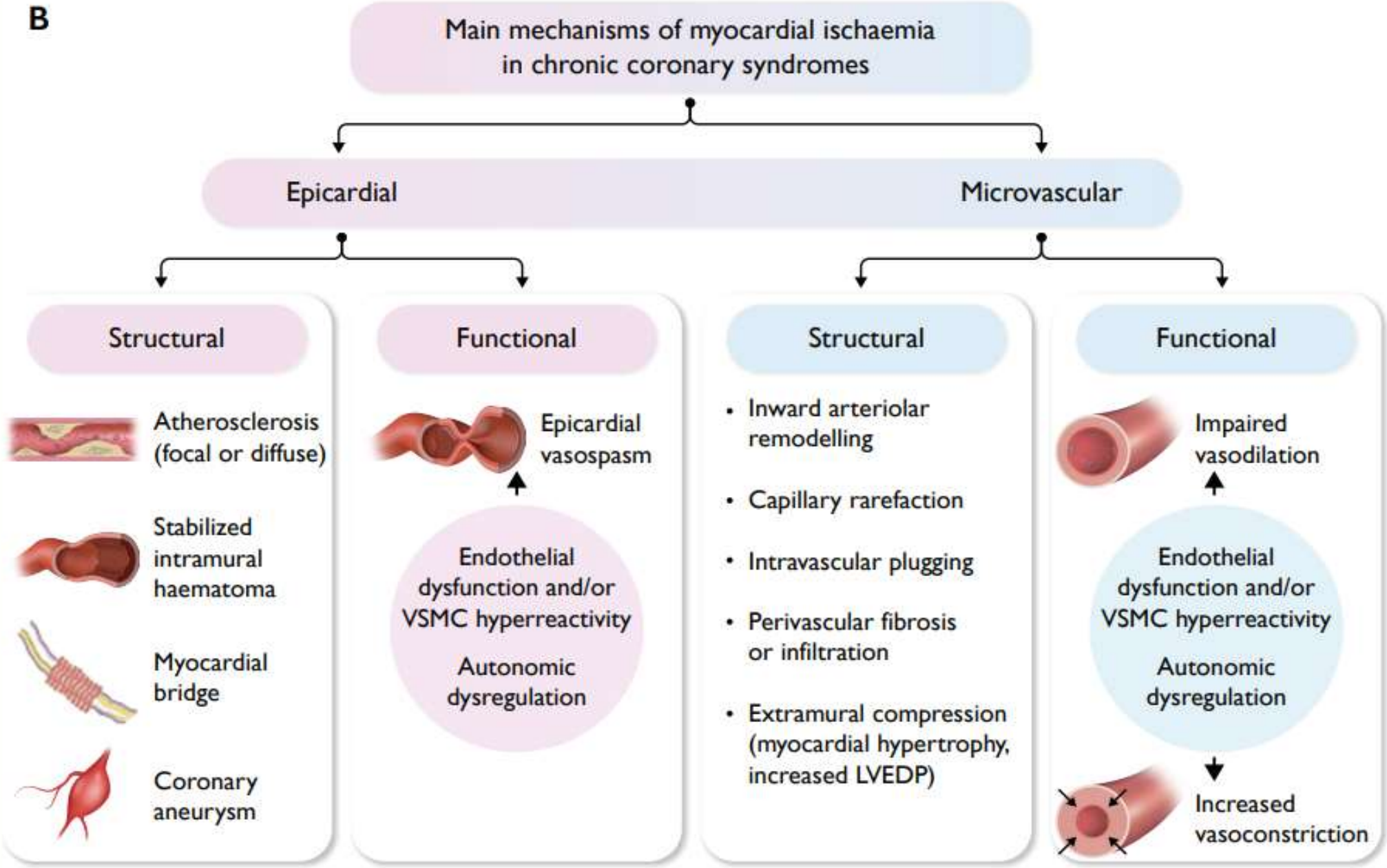
Type of Lesion	Clinical Manifestation	Management
 **Stenotic** • Few • Fibrotic • Thick Cap • Less Compensatory Enlargement	 **Ischemia** • Angina Pectoris • Positive Exercise Test • Perfusion Defect	**Local Therapy/ Revascularization** • **PTCA** • **Stent** • **CABG**
 **Non-Stenotic** • Many • Lipid-Rich • Thin Cap • Compensatory Enlargement	 **Infarction**	**Systemic Therapy** • **Lifestyle Modification** • **Drug Therapy**

Peter Libby. Circulation. Pathophysiology of Coronary Artery Disease, Volume: 111, Issue: 25, Pages: 3481-3488, DOI: (10.1161/CIRCULATIONAHA.105.537878)

Clinical presentations of chronic coronary syndrome and mechanisms of myocardial ischaemia



Clinical presentations of chronic coronary syndrome and mechanisms of myocardial ischaemia



Stepwise approach to the initial management of individuals with suspected chronic coronary syndrome

STEP 1. General clinical evaluation that focuses on as sessing symptoms and signs of CCS, differentiating non-cardiac causes of chest pain and ruling out ACS.

This initial clinical evaluation requires recording a 12-lead resting electrocardiogram (ECG), basic blood tests, and in selected individuals, chest X-ray imaging and pul monary function testing. ***This evaluation can be done by the general practitioner.***

Stepwise approach to the initial management of individuals with suspected chronic coronary syndrome

STEP 2. Further cardiac examination, including ***echocardiography at rest to rule out left ventricular (LV) dysfunc tion and valvular heart disease***. After that, it is recommended to ***es timate the clinical likelihood of obstructive CAD*** to guide deferral or referral to further non-invasive and invasive testing.

STEP 3. Diagnostic testing to establish the diag nosis of CCS and determine the patient's risk of future events

Stepwise approach to the initial management of individuals with suspected chronic coronary syndrome

STEP 4. The final step includes lifestyle and risk-factor modification combined with disease-modifying medications.

A combination of antianginal medications is frequently needed, and coronary revascu larization is considered if symptoms are refractory to medical treat ment or if high-risk CAD is present.

If symptoms persist after obstructive CAD is ruled out, coronary microvascular disease and vasospasm should be considered.

STEP 1. History, differential diagnosis, and physical examination

Anginal pain symptoms have been traditionally classified as: ***typical,***

atypical,

or non-anginal/non-cardiac”

based on the location of the pain, as well as precipitating and relieving factors.

Typical angina meets all three characteristics, with retrosternal chest discomfort provoked by exertion or emotional stress and relieved by rest or nitro glycerine (highly suggestive of ischaemia caused by obstructive CAD)

Main CCS symptoms: angina and exertional dyspnoea

Chest discomfort

Symptom characteristics	Decreasing likelihood of CCS	Increasing likelihood of CCS
Quality	• Burning • Sharp • Tearing - Ripping • Pleuritic • Aching	• Strangling • Constricting • Squeezing • Pressure • Heaviness
Location and size	• Right • Shifting • Large area or fine spot	• Retrosternal • Extending to left arm, or to jugular or intrascapular region • "Fist"-size
Duration	• Lasting	• Short: up to 5–10 min if triggered by physical exertion or emotion
Trigger	• At rest • On deep inspiration or when coughing • When pressing on ribs or sternum	• On effort • More frequent in cold weather, strong winds or after a heavy meal • Emotional distress (anxiety, anger, excitation or nightmare)
Relief	• By antacids, drinking milk	• Subsiding within 1–5 min after effort discontinuation • Relief accelerated by sublingual nitroglycerin

Main CCS symptoms: angina and exertional dyspnoea

Dyspnoea

Quality	• Difficulty to exhale • With wheezing	• Difficulty catching breath
Trigger	• Both at rest and on effort • While coughing	• On effort
Relief	• Slowly subsiding at rest or after inhalation of bronchodilators	• Rapidly subsiding after effort discontinuation

ESC

Classification

The Canadian Cardiovascular Society grades angina by the extent of limitation of physical activity

Grade I: Ordinary physical activity (walking, climbing stairs) does not cause angina. Angina occurs with strenuous or rapid or prolonged exertion at work or recreation.

Grade II: Slight limitation of ordinary activity. Angina may occur with moderate exertion, such as walking or climbing stairs rapidly, walking uphill, walking or climbing stairs after meals, in cold or wind, under emotional stress, or during the few hours after awakening, or walking more than two blocks on level ground, or climbing more than one flight of ordinary stairs at a normal pace and in normal conditions.

Grade III: Marked limitation of ordinary physical activity. Angina occurs with mild exertion, such as walking one or two blocks on level ground and climbing one flight of stairs in normal conditions and at normal pace.

Grade IV: Inability to carry on any physical activity without discomfort, anginal syndrome may be present at rest.

Recommendations for ba sic ECG, biochemistry in the initial diagnostic management of individuals with suspected chronic coronary syndrome

12-lead Electrocardiogram

detecting **repolarization abnormalities**, mainly in the form of ST-segment depressions or T wave abnormalities.

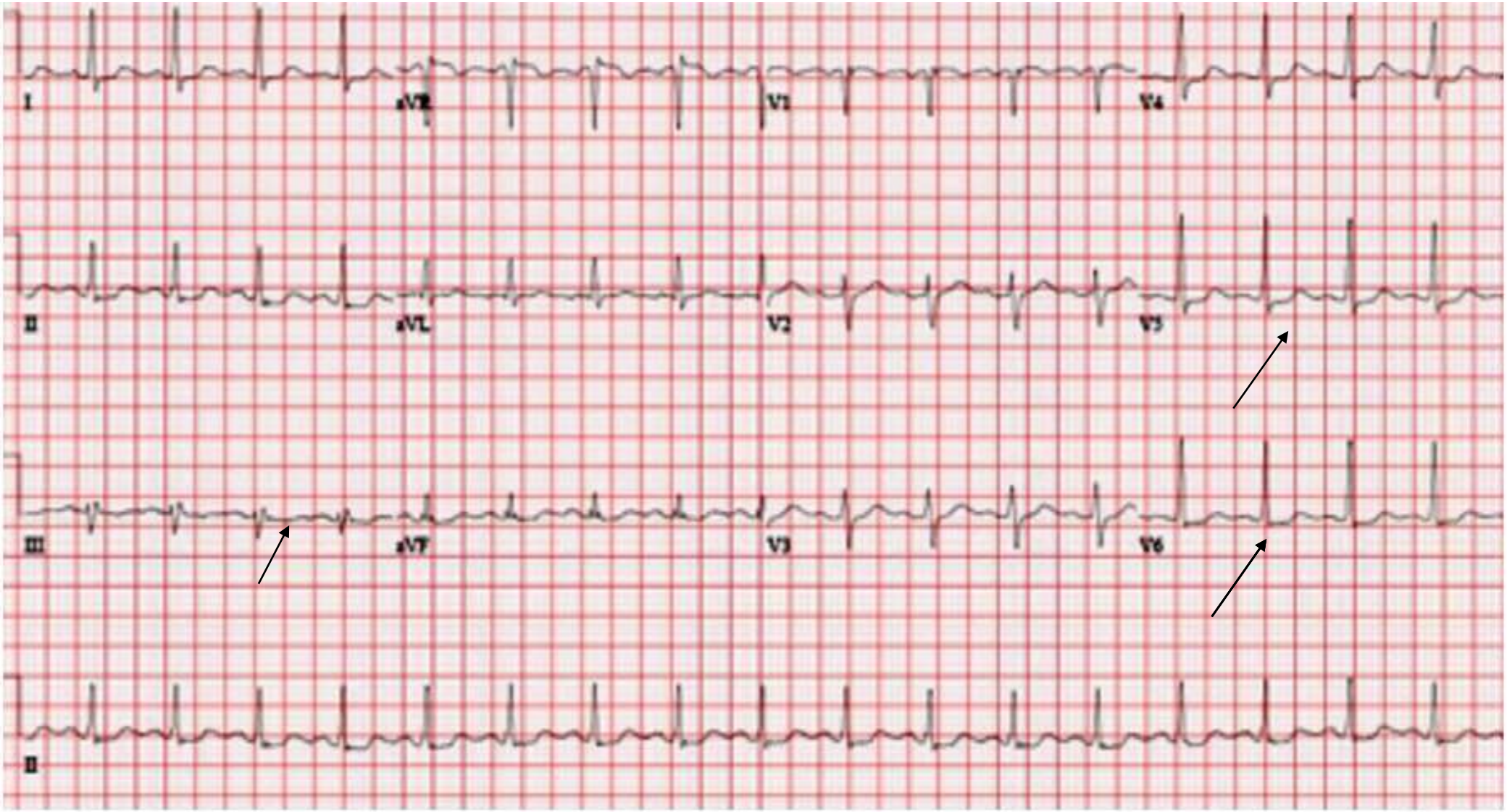
normal resting ECG is frequently recorded after an anginal attack. However, even in the absence of repolarization abnormalities, the ECG at rest may suggest CCS indirectly, through signs of previous MI (patho logical Q or R waves) or conduction abnormalities [mainly lebranch block (LBBB) and impaired atrioventricular conduction].

Atrial fibrillation (AF) is not rarely associated with CCS.

The ECG can be crucial for diagnosing transient myocardial **ischae mia by recording dynamic ST-segment changes during ongoing angina.**

Vasospastic angina (VSA) should be suspected when observing typical **transient ST-segment elevations or depressions with U-wave changes during an angina attack at rest**

ECG showing nonspecific ST depressions in V5 and V6, which may indicate ischemia. There are nonspecific ST-segment changes in III and aVF



Recommendations for ba sic ECG? biochemistry in the initial diagnostic management of individuals with suspected chronic coronary syndrome

Long-term ambulatory ECG monitoring can be considered in se lected patients to detect ischaemia during anginal episodes unrelated to physical activities.

ECG changes suggesting ischaemia on ambulatory ECG monitoring are frequent in women but do not correlate with find ings during stress testing.

Ambulatory ECG monitoring may also re veal ‘silent’ ischaemia in patients with CCS

Resting echocardiography (Echo-CG)

Resting Echo-CG can identify:

- prior myocardial infarction (MI)
- suggest alternative myocardial, valvular, or pericardial causes of chest symptoms
- provide prognostic information in patients with SIHD
- signs of heart failure,
- undiagnosed murmur.

European guidelines endorse EchoCG in all cases of suspected SIHD and consideration of adding carotid ultrasound to identify peripheral atherosclerosis.

Recommendations for ba sic ECG? biochemistry in the initial diagnostic management of individuals with suspected chronic coronary syndrome

Recommendations	Class[a]	Level[b]
The following blood tests are recommended in all individuals to refine risk stratification, diagnose comorbidities, and guide treatment:		
• lipid profile including LDL-C;[64,128]	I	A
• full blood count (including haemoglobin);[129–133]	I	B
• creatinine with estimation of renal function;[134]	I	B
• glycaemic status with HbA1c and/or fasting plasma glucose.[16,86,135,136]	I	B
In patients with suspected CCS, it is recommended to assess thyroid function at least once.[137,138]	I	B
Additionally, hs-CRP and/or fibrinogen plasma levels should be considered.[109–118,121,125]	IIa	B

STEP 2: Further evaluation
Pre-test clinical likelihood of obstructive atherosclerotic coronary artery disease

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

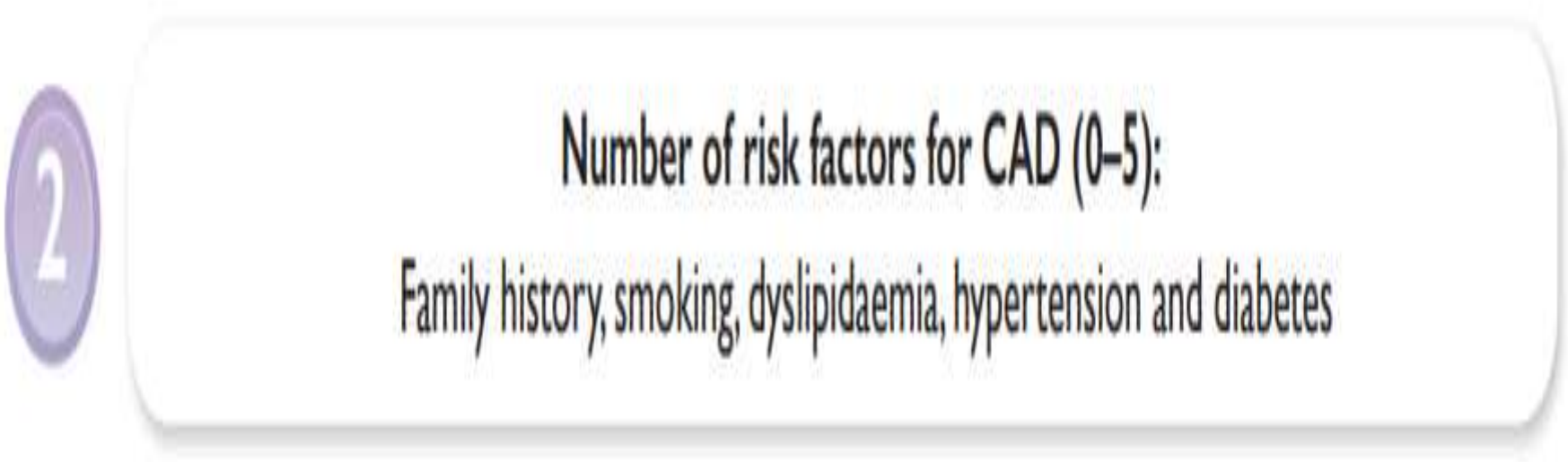
Main symptom either:

Chest pain (0–3 points)

or

Dyspnoea (2 points)

STEP 2: Further evaluation
Pre-test clinical likelihood of obstructive atherosclerotic coronary artery disease



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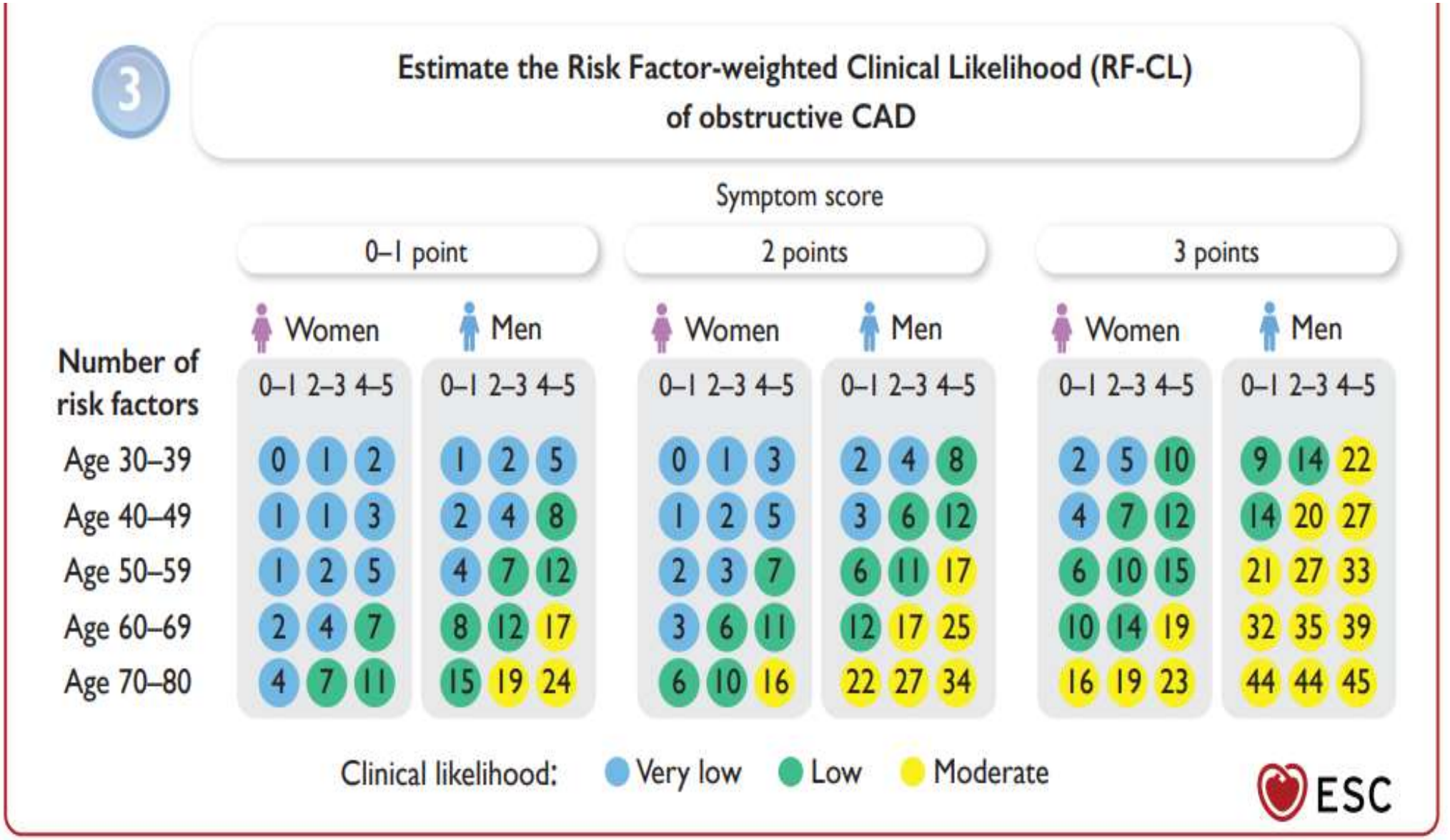


Stress tests

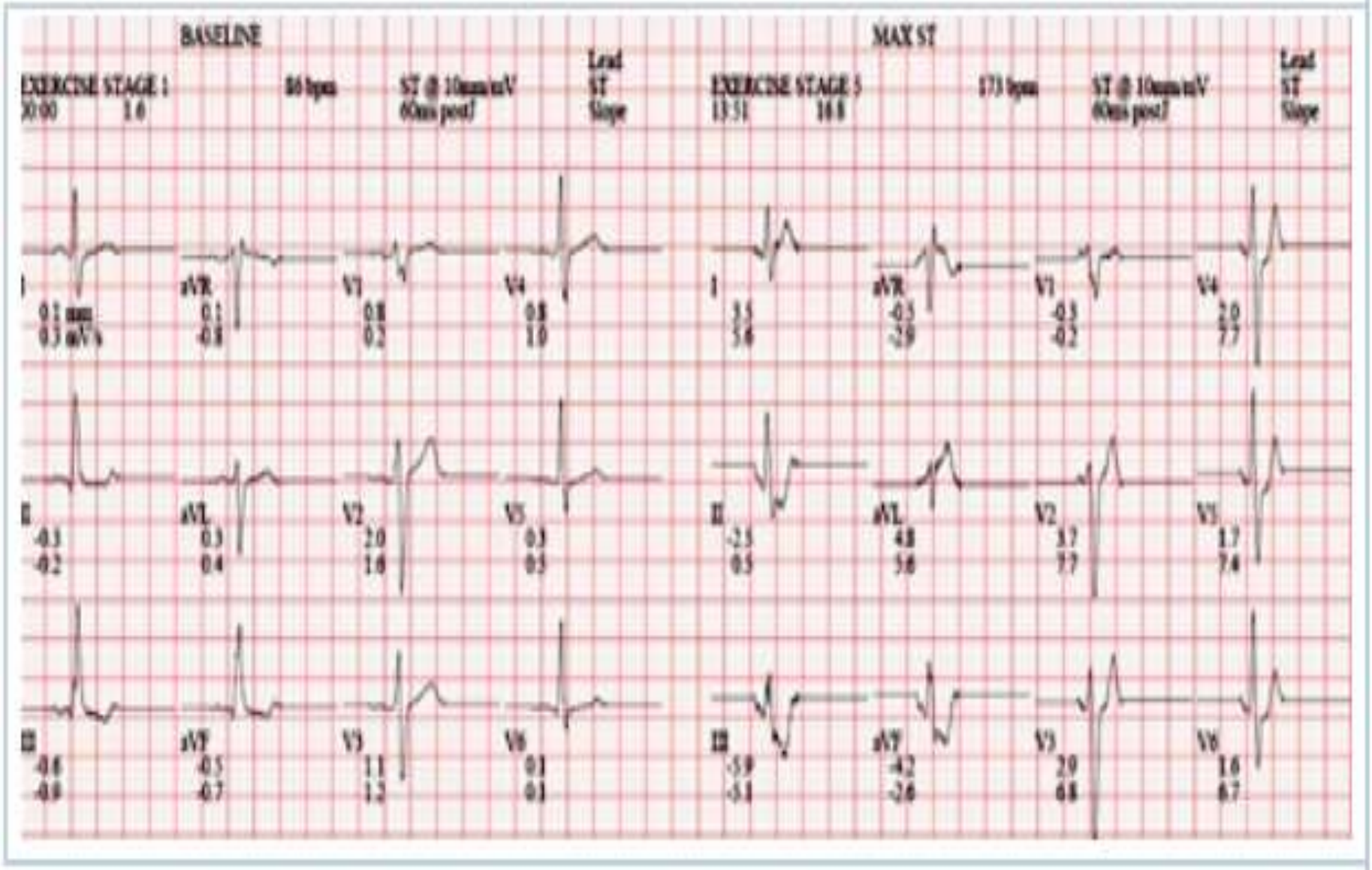
Exercise is generally preferred as a means of stress because it can provide higher levels of physiologic stress as well as prognostically valuable information about patients' functional status.

Use of **pharmacologic stress rather than exercise is typically reserved for patients unable to perform moderate exercise** due to orthopedic, pulmonary, or other comorbidities. Options for pharmacologic stress testing include vasodilators (adenosine, dipyridamole, or regadenoson) or a beta-agonist (dobutamine).

Stress tests

In addition to predicting the likelihood of obstructive lesions on angiogram, functional testing can stratify patients in relation to risk of cardiovascular mortality.

The Duke treadmill score is a well-validated model derived from the duration of exercise, ST-segment changes, and angina on a standard treadmill exercise ECG. Models with additional variables may improve the ability to identify patients at low risk.



Computerized summary of exercise ECG in a 55-year-old man with a 1-month history of angina on exertion

Duke treadmill score

Duke treadmill score = (Exercise duration [minutes]) – (5 × ST deviation [mm]) – (4 × angina index)

Angina index:
0 = no angina,
1 = nonlimiting angina,
2 = exercise limiting angina.

Duke treadmill score:
≥ 5 indicates **low risk** for cardiovascular events,
≤ −11 indicates **high risk** for cardiovascular events,
between 4 and − 10 indicates **intermediate risk**

Coronary computed tomography angiography (CCTA)

CCTA - a contrast-enhanced computed tomography (CT) study, can identify coronary plaque and stenosis.

CCTA has advanced to achieve high concordance with invasive angiography in identifying significant stenoses and thus offers a noninvasive anatomic test.

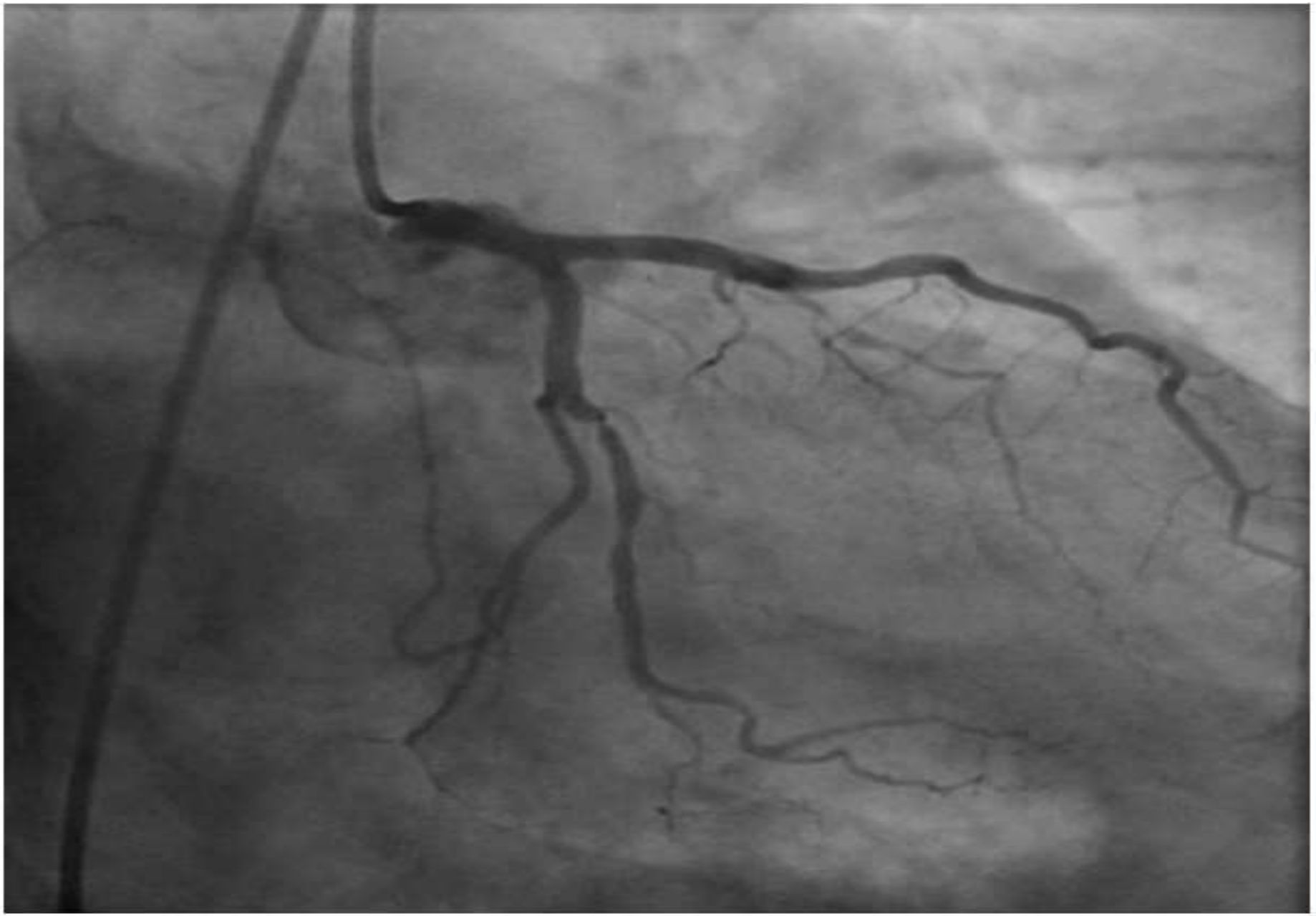
Like invasive angiography, CCTA can also identify lesser, nonobstructive atherosclerotic lesions.

Coronary angiography

Coronary angiography uses catheters to inject contrast directly into epicardial coronary arteries, providing visualization of the artery lumen and degree of stenosis.

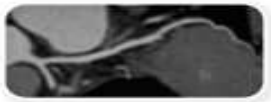
Risks of invasive angiography include those from contrast and radiation, thrombosis or hemorrhage related to vascular access, arrhythmia, and atheroembolism.

Traditionally, **lesions causing stenosis greater than 50% to 70% are considered significant**, although the presence of lesser degrees of stenosis are also associated with worse cardiac outcomes.



Angiogram (right anterior oblique caudal projection) in a 55-year-old man with a 1-month history of angina on exertion. A 90% proximal stenosis of obtuse marginal 1 is present, explaining the patient's lateral ischemia

Appropriate first-line testing in symptomatic individuals with suspected chronic coronary syndrome

Risk factor-weighted clinical likelihood of obstructive CAD	Appropriate first-line test for suspected CCS
Very high >85%	Invasive coronary angiography 
High >50–85%	Functional imaging  PET/SPECT CMR Stress ECHO
Moderate >15–50%	CCTA  OR Functional imaging  PET/SPECT CMR Stress ECHO
Low >5–15%	Adjust the clinical likelihood  OR CCTA 
Very low ≤5%	Defer further testing

ESC

STEP 4: Initial therapy

- The main goals of treating CCS are to improve both QoL and life expectancy.

  This involves vari ous interventions to reduce the risk of

  (i) cardiac mortality,

  (ii) non-fatal ischaemic events,

  (iii) progression of epicardial and/or microvascular chronic coronary disease,

  (iv) symptoms and limitations caused by CCS.

Education and lifestyle modification

Physical activity

• The patient should be encouraged to participate in 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, at least 5 days and preferably 7 days per week.
This should be supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, using the stairs, gardening, household work) to improve cardiorespiratory fitness.

Diet

- Dietary therapy for all patients should include reduced intake of saturated fats (to <7% of total calories) and trans-fatty acids (to <1% of total calories), and/or fiber (>10 g/day) may be reasonable dietary interventions.

Weight management

- Specifically patients should demonstrate understanding of weight control goals with maintenance of a body mass index of 18.5 kg/m² to 24.9 kg/m² and a waist circumference less than 40 inches for men and less than 35 inches for women (less for certain racial groups).

Smoking cessation

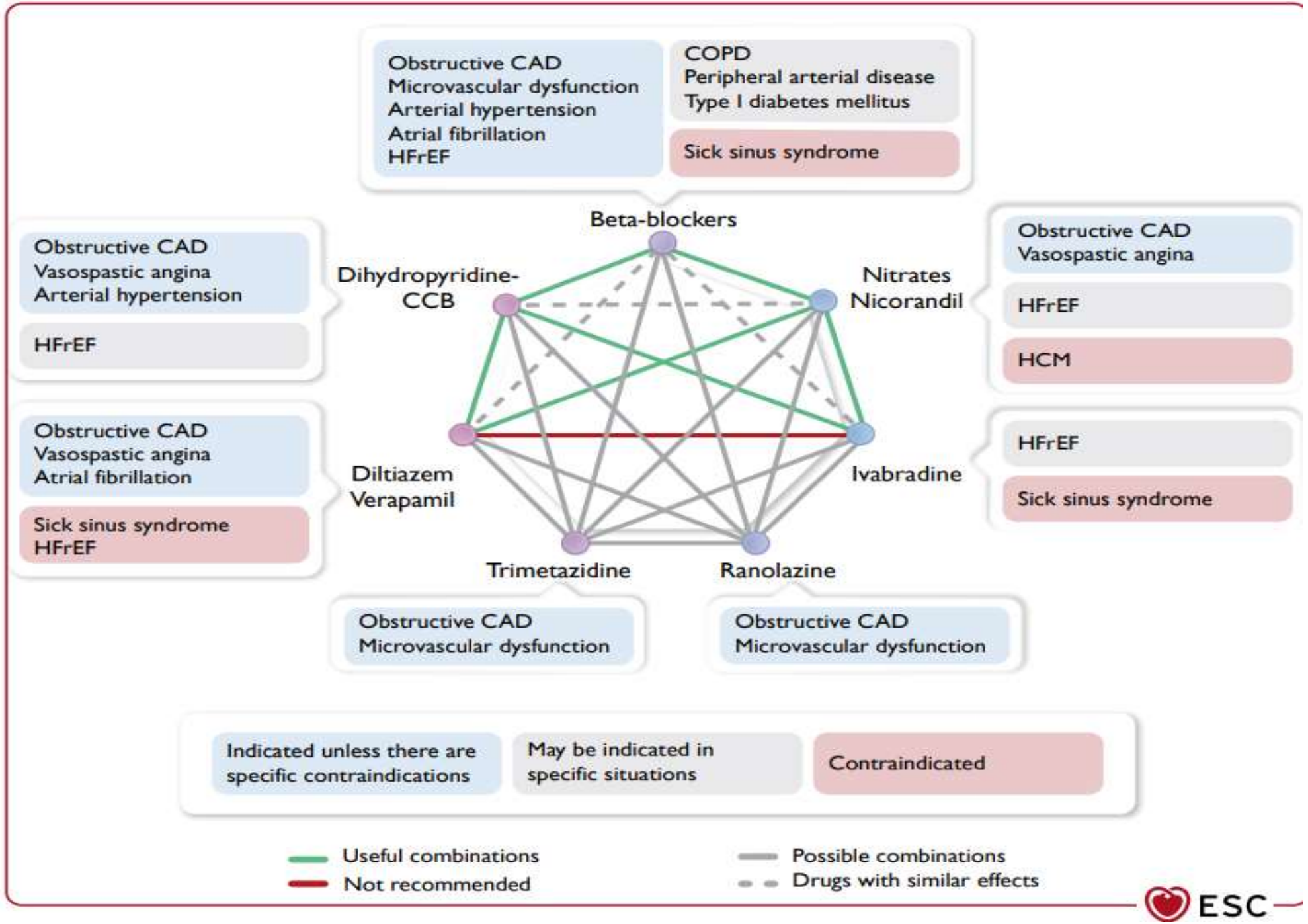
Antianginal/anti-ischaemic medication
General strategy

For many patients with CCS, initial drug therapy should include a beta- blocker and/or a CCB.

Other antianginal drugs *(long-acting nitrates, ivabradine, nicorandil, ranolazine, trimetazidine*) **can be added on top of a beta-blocker and/or a CCB**, or as a part of initial combination ther apy in appropriately selected patients.

Regardless of the initial strategy, response to initial antianginal therapy should be reassessed, and treatment should be adapted if adequate an gina control is not achieved or if the initial treatment is poorly tolerated.

Possible combinations of antianginal drugs



Guideline-directed medical therapy to improve outcomes

This should be instituted in all patients and may include:

- Antiplatelet therapy
- Beta-blockers
- Renin-angiotensin-aldosterone antagonists
- Lipid management
- Blood pressure control
- Diabetes management.

Lipid-lowering drugs

Because patients with CCS are considered at very high cardiovascular risk, the treatment goal is to lower LDL-C levels to <1.4 mmol/L (<55 mg/dL) and achieve a reduction by at least 50% from baseline.

For patients who experience a second vascular event within 2 years while taking maximum tolerated statin-based therapy, an even lower LDL-C goal of <1.0 mmol/L (40 mg/dL) may be considered.

Lipid-lowering drugs

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Revascularization for chronic coronary syndromes

Invasive treatment of CAD with either CABG or PCI is historically de scribed under the term revascularization.

Although both procedures in crease CFC and prevent myocardial ischaemia during exercise or emotional stress, they do not heal coronary atherosclerosis.

Revascularization by both modalities improves angina-related health status

Prognosis

With aggressive lifestyle modification and guideline-directed medical therapy, patients can expect a reduction in anginal symptoms. With guideline-directed management, 58% of patients can expect to be angina-free within 1 year.

Ischemic heart disease is a dynamic process. Even with aggressive medical management and lifestyle changes, some patients may experience recurrence or worsening of anginal symptoms due to progression of atherosclerotic disease.

Upward titration of antianginal medications may resolve these symptoms; however,some patients may require revascularization to improve anginal symptoms and exercise tolerance.