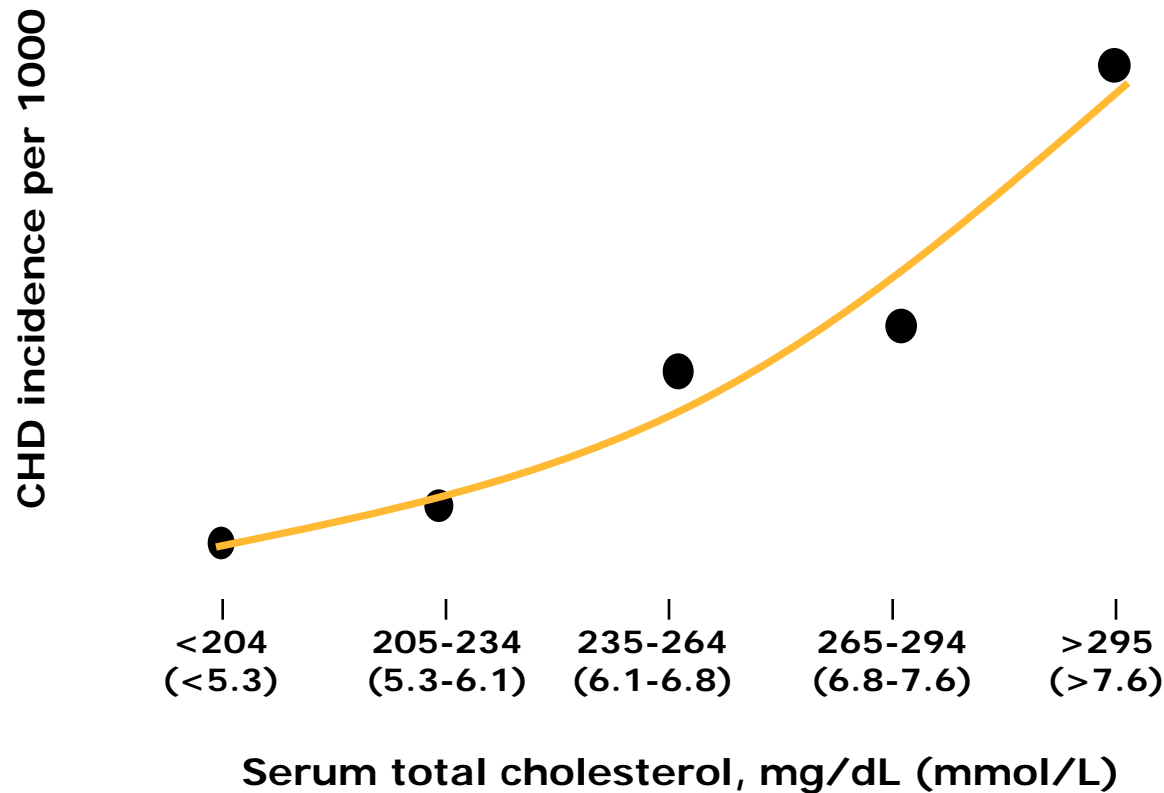


Atherosclerosis
Invasive and noninvasive
investigations

Dr. Mátyás Keltai

The Framingham Study: Relationship Between Cholesterol and CHD Risk



Cardiology 2011



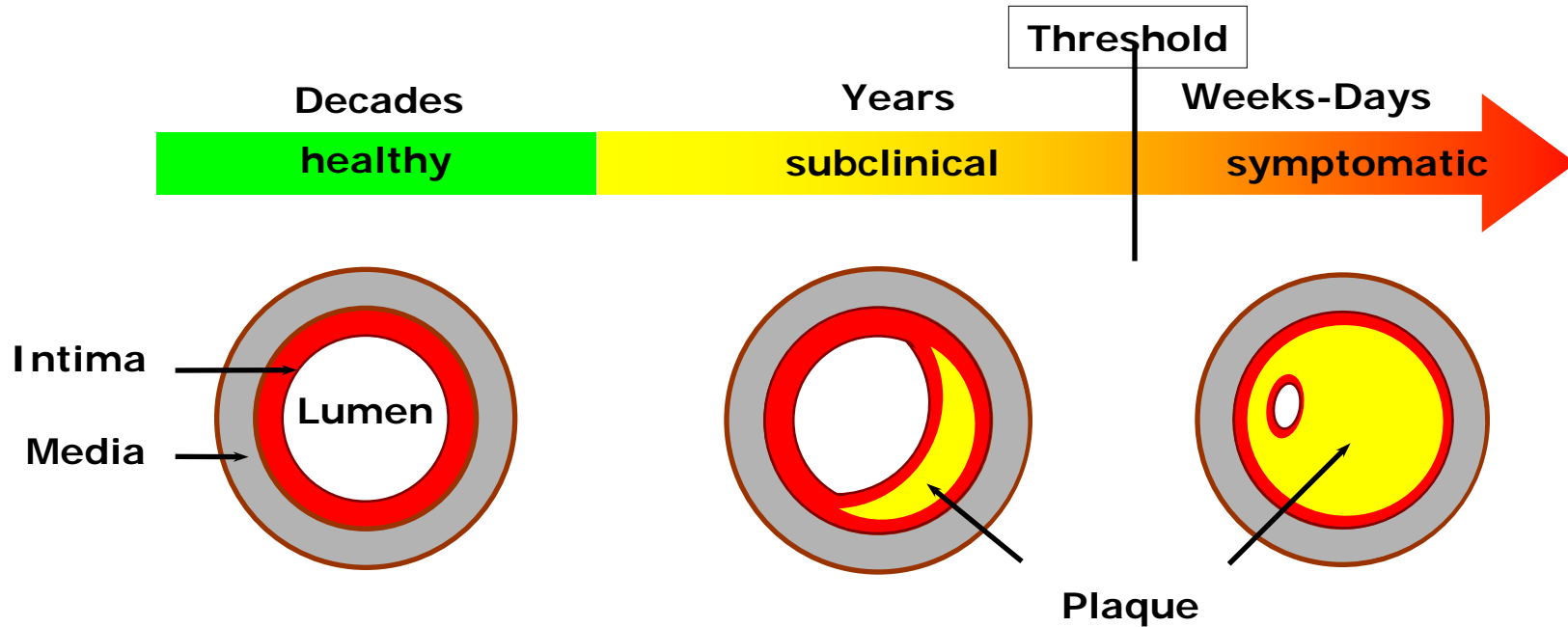
Cholesterol: A Modifiable Risk Factor

- In the USA, 51% (105 million) have elevated total cholesterol (>200 mg/dL, 5.2 mmol/L)¹
- In EUROASPIRE II, 58% of patients with established CHD had elevated total cholesterol (≥ 5 mmol/L, 190 mg/dL)²
- 10% reduction in total cholesterol results in:
 - 15% reduction in CHD mortality ($p < 0.001$)
 - 11% reduction in total mortality ($p < 0.001$)³
- LDL-C is the primary target to prevent CHD

Cardiology 2011

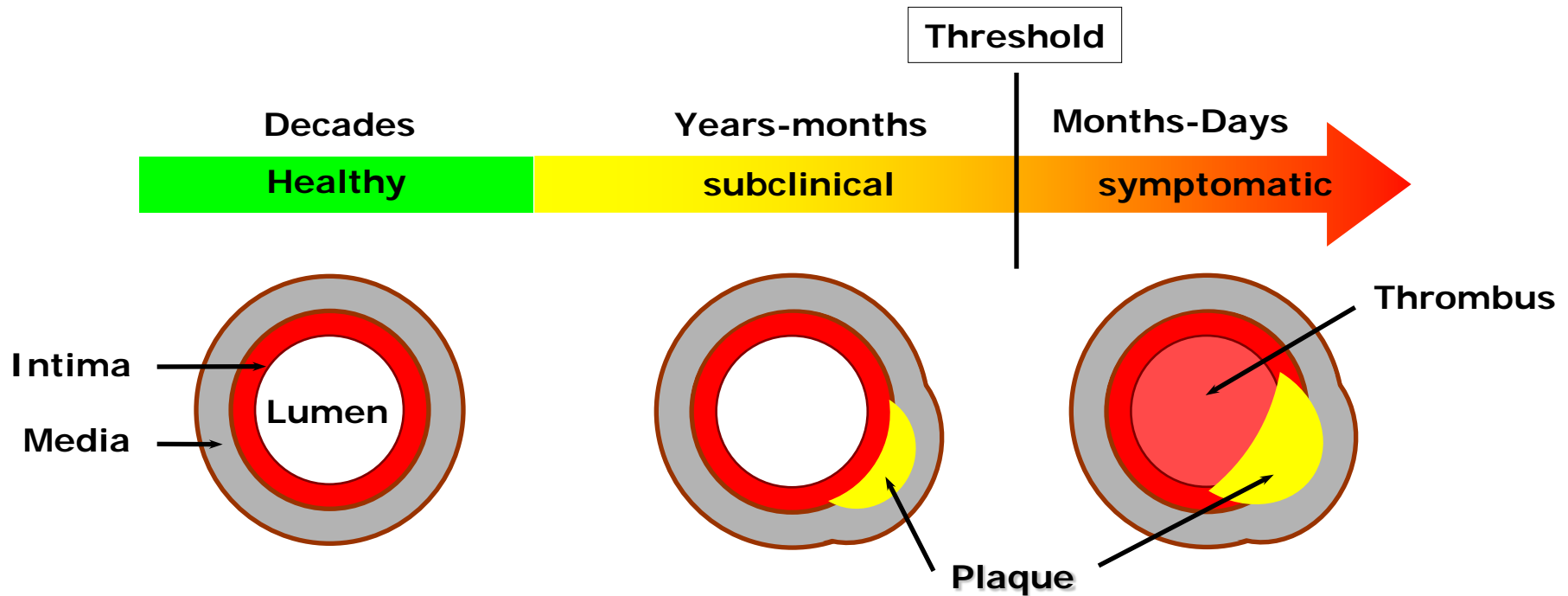
1. American Heart Association. Heart and Stroke Statistical Update; 2002; 2. EUROASPIRE II Study Group. *Eur Heart J* 2001; **22**:554-572; 3. Gould AL *et al.* *Circulation* 1998; **97**:946–952.

Old paradigm about the progression of atherosclerosis



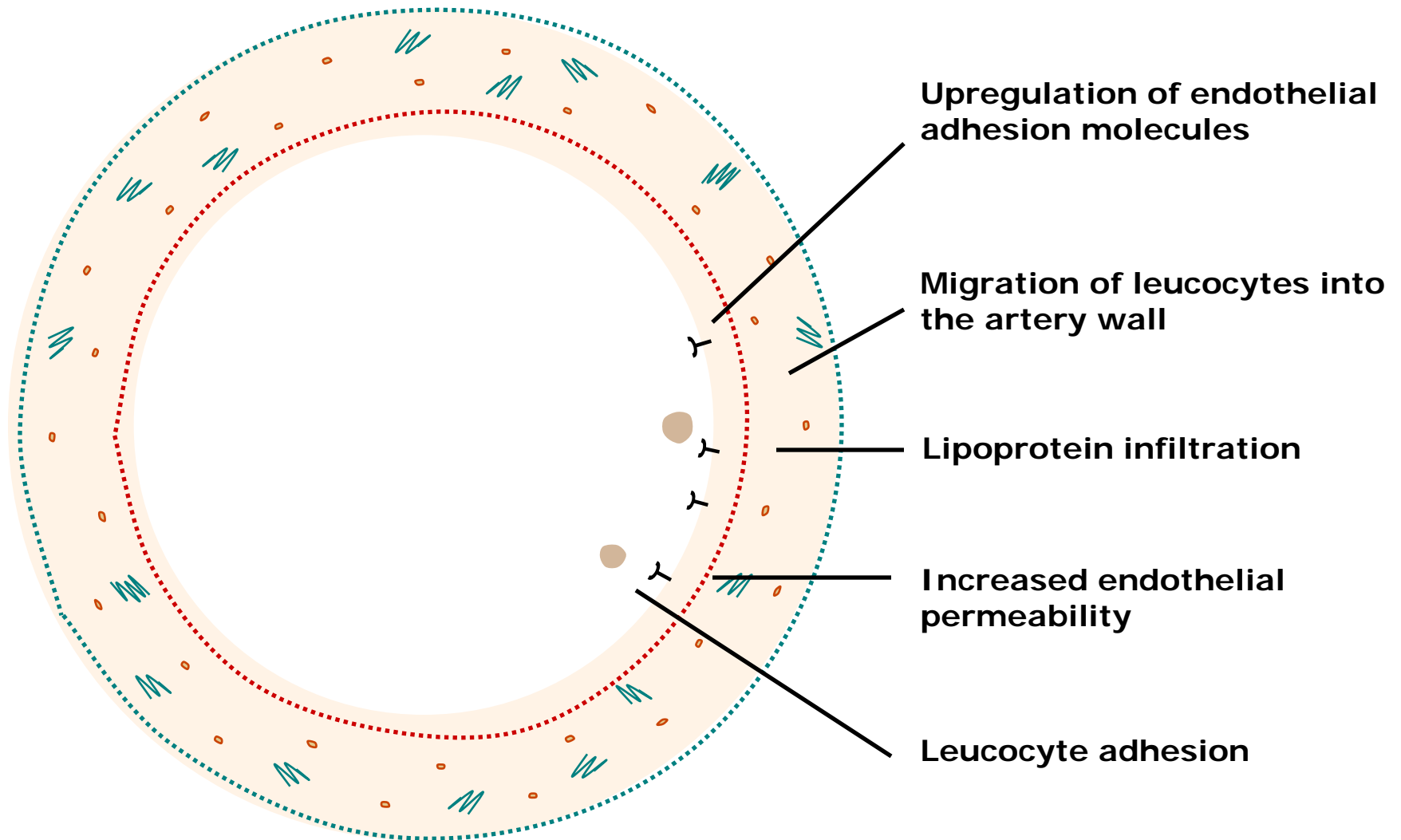
- Stable angina
- Stable angina with narrowing
- Easy diagnostics (ECG, angiography)
- MI rear
- Treatment simple

New paradigm

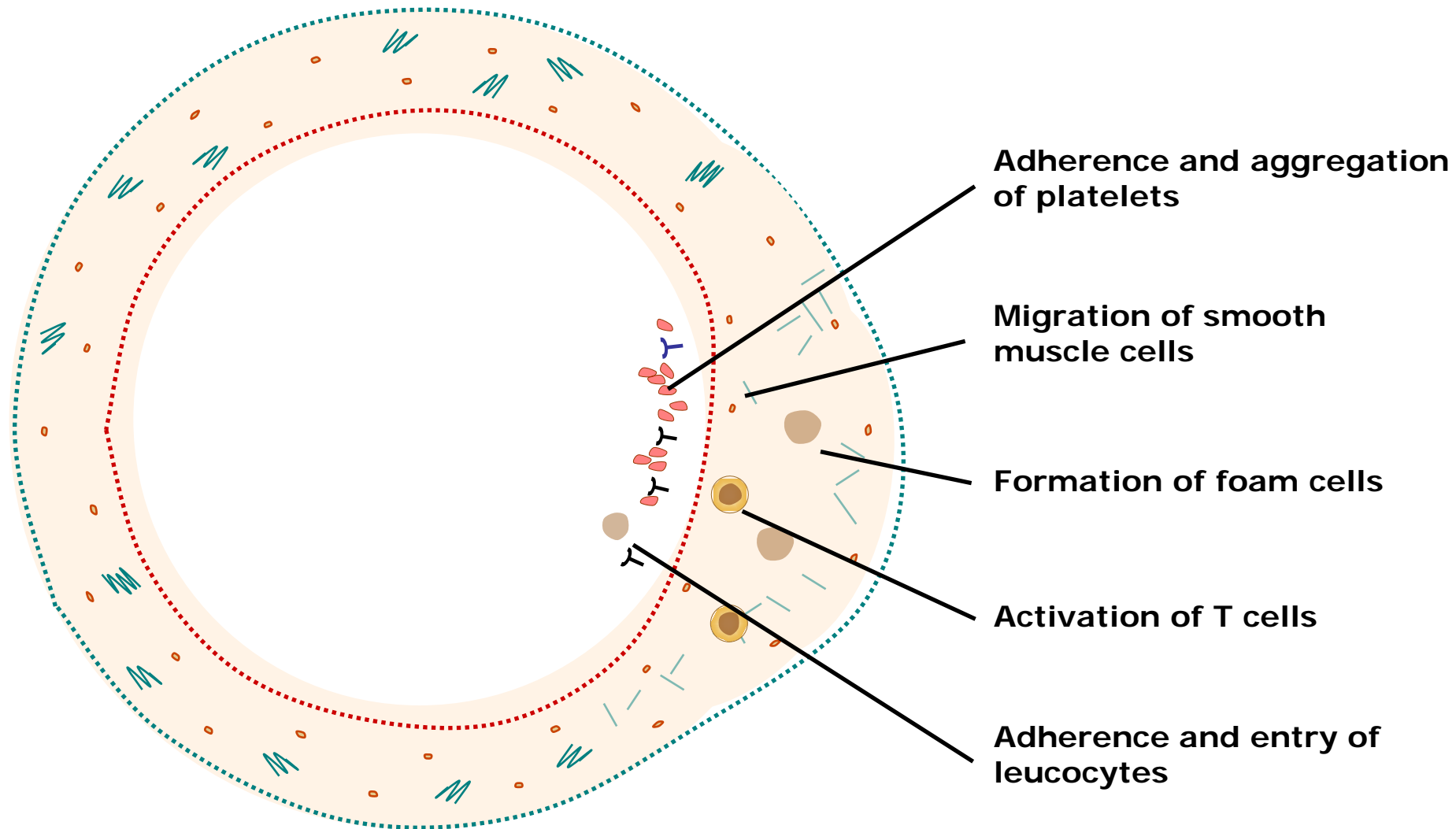


- Unstable angina (Acute coronary syndrome)
- Unstable angina with narrowing
- Difficult diagnosis (MR, IVUS, OCT)
- Frequent MI
- Prevention is simple

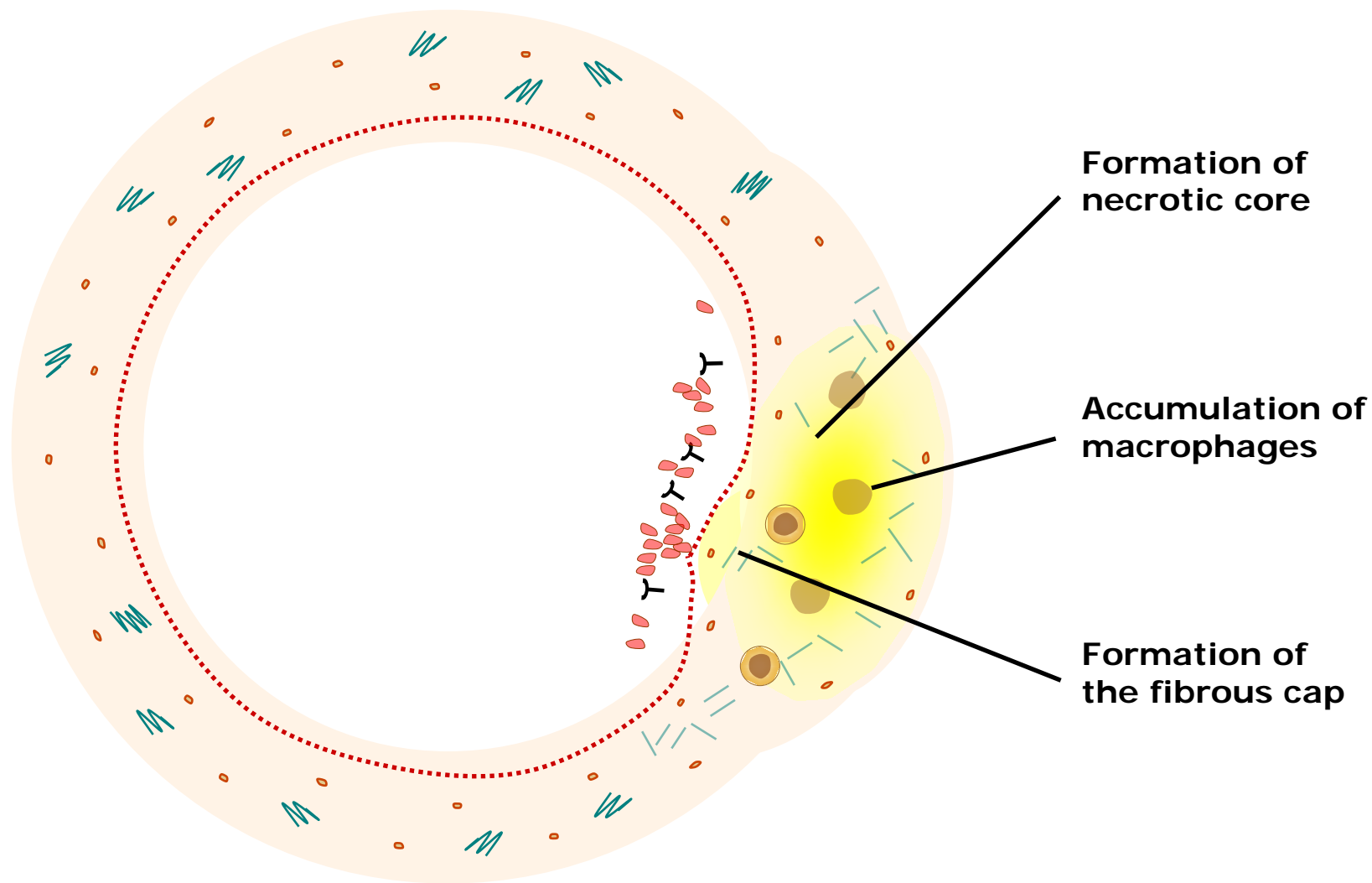
Endothel dysfunction



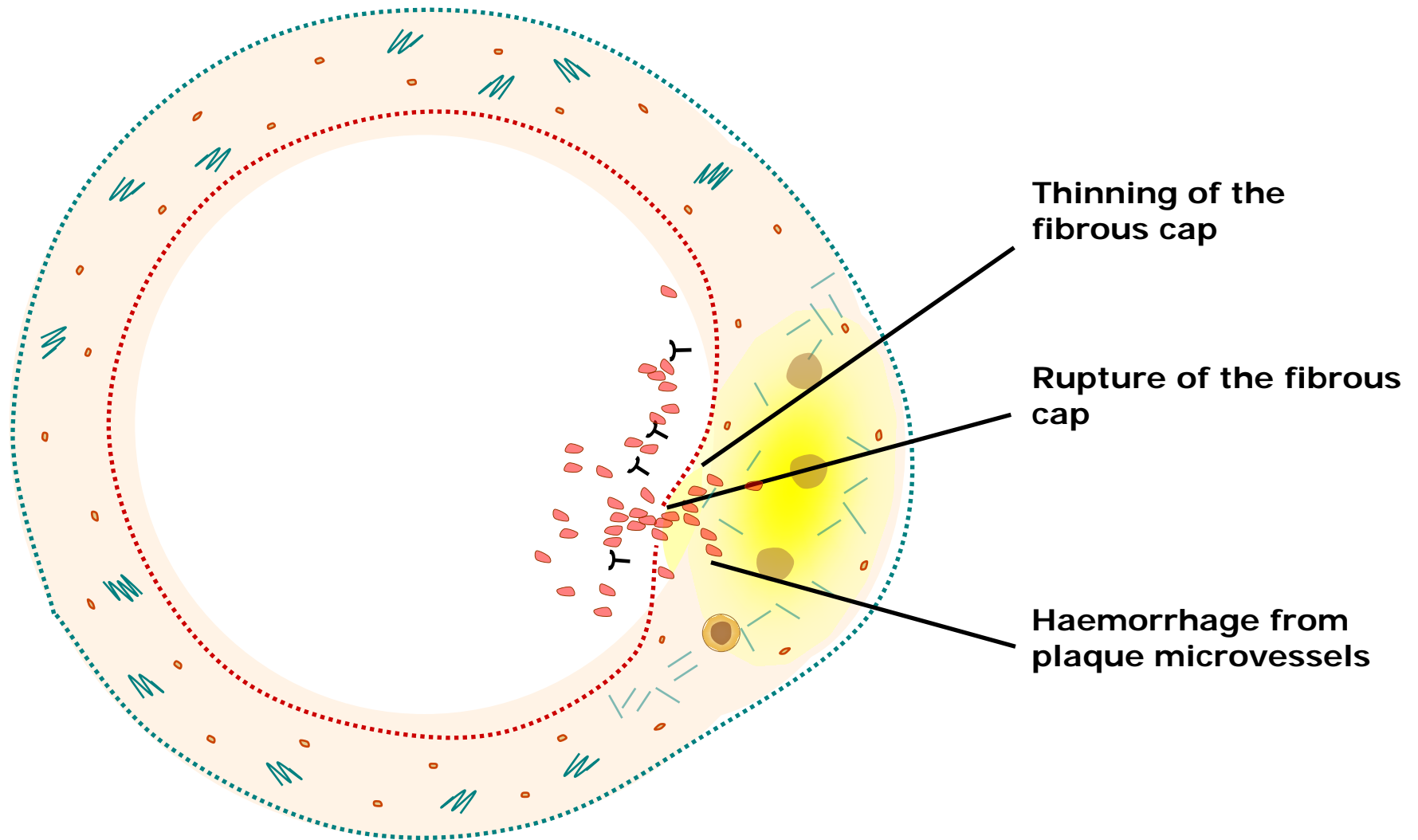
Fatty Streak Formation in Atherosclerosis



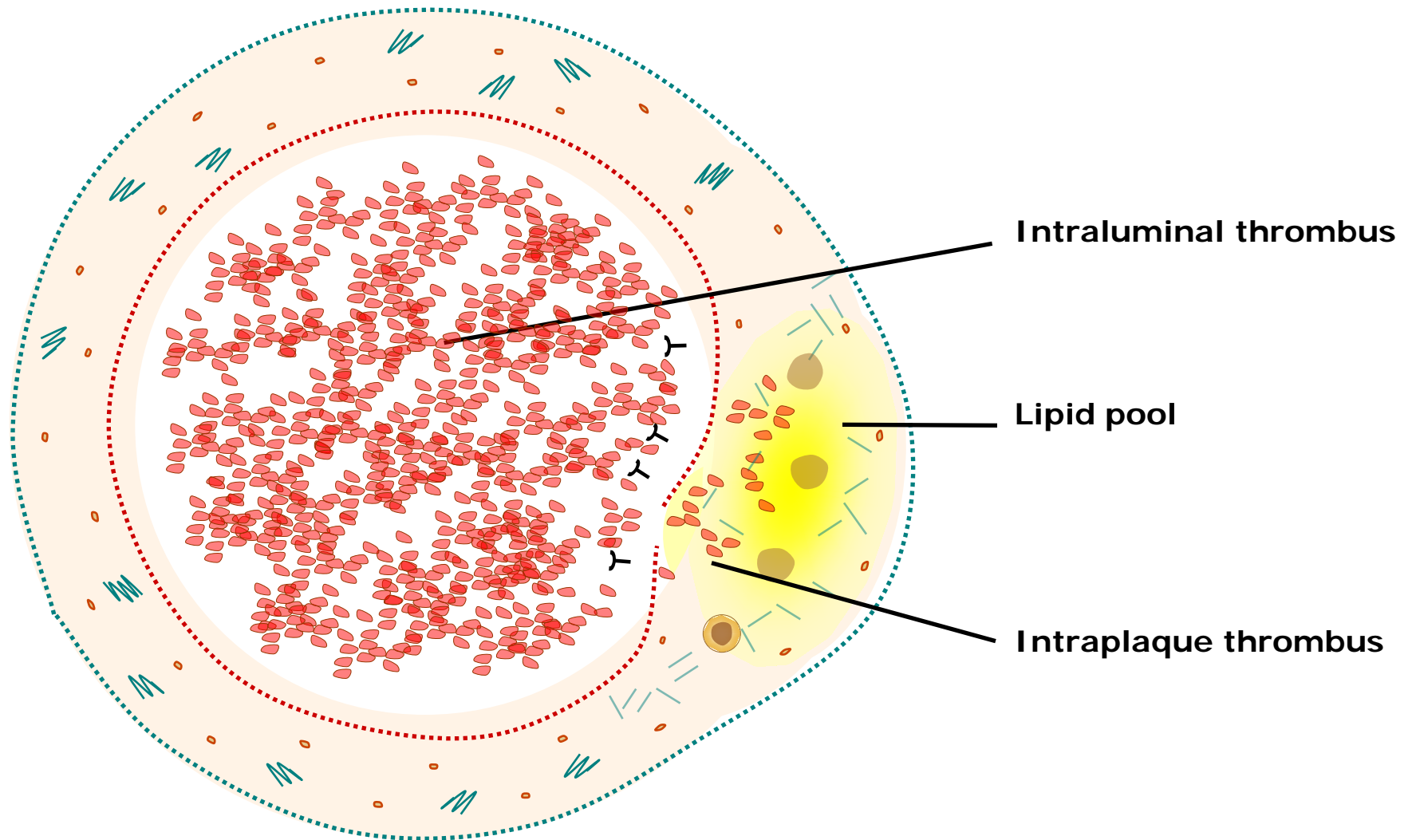
Formation of the Complicated Atherosclerotic Plaque



The Unstable Atherosclerotic Plaque



Atherosclerotic Plaque Rupture and Thrombus Formation



Clinical evaluation of heart diseases

- **History**
- **Physical**
- **Clinical chemistry**
- **ECG**
- **Echocardiography**
- **Nuclearcardiology**
- **Computed Tomography**
- **Invasive investigations**

IHD is a benign disorder

- **Fatty streak appears already in teenagers**
- **Coronary lesion of less than 50 % diameter, or 70 % area stenosis don't cause symptoms**
- **Long intervals with or without medical treatment are symptomfree.**
- **Problems arise only, when the intracoronary plaque becomes unstable**

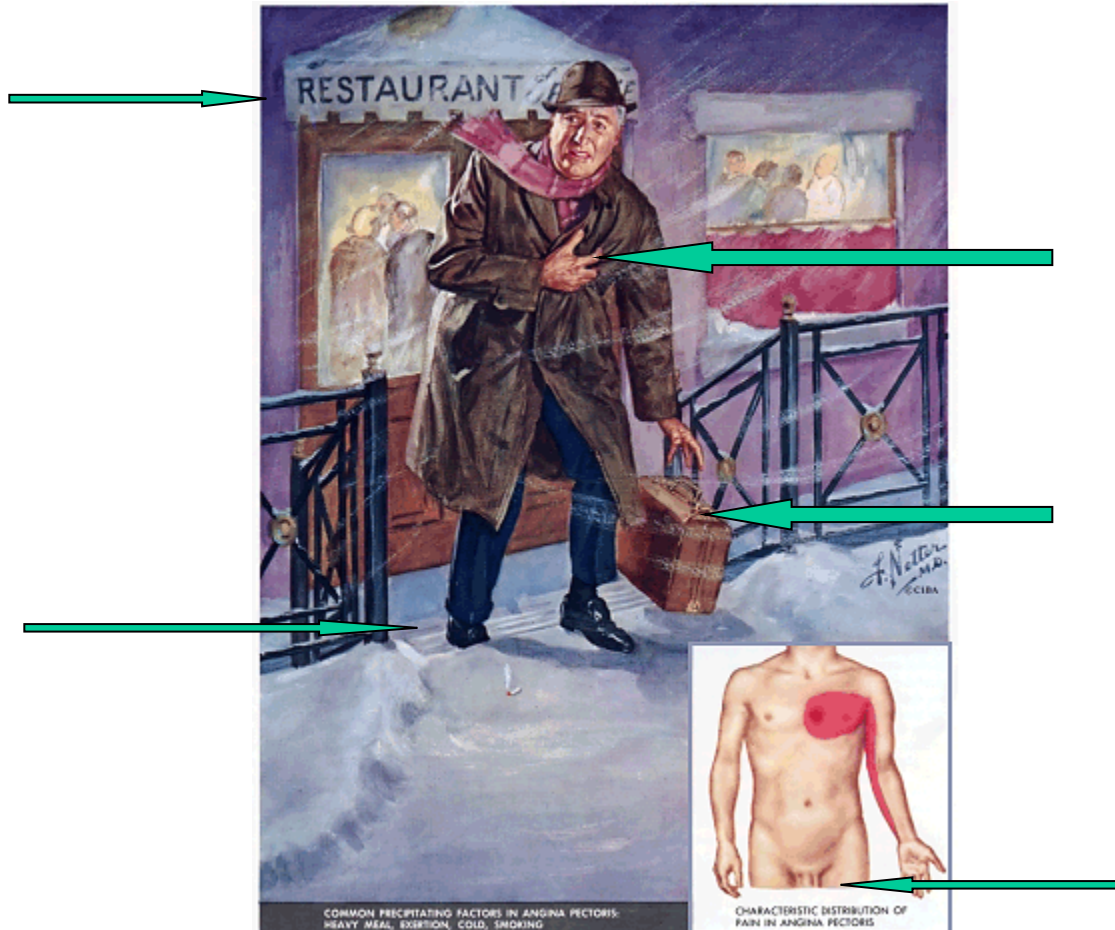
Patients' history (Hx)

- **Based on thorough Hx, focused on physical exercise-related symptoms, and also physical exam reveal sufficient information for the physician to estimate the probability of IHD.**
- **Use diagnostic algorithms to construct your work-up**

The definition of stable angina

- **Angina is a clinical syndrome characterized by dyscomfort in the chest, jaw, or shoulder, irradiating into the back or the arm (left).**
- **It is typically aggravated by exertion or emotional stress**
- **It is usually relieved by sublingual NG**
- **All the three criteria must be present**

The patient with AP



Angina usually means coronary artery disease (CAD)

- **Angina usually develops in pts with CAD in >1 epicardial coronary artery**
- **Angina may develop in patients without significant CAD (hypertension, HOCM, valvular heart disease) especially in those who prone to coronary spasm (because of endothelial dysfunction).**
- **Differentiate from esophageal, and chest wall-disorders-caused symptoms**

Wording of typical anginal pain

- **Usual words : Squeezing, griplike, pressure, suffocating - angina, heaviness**
- **Sometimes not pain - only discomfort**
- **Almost never sharp, stabbing**
- **Typical gesture - closed fist on the chest**
- **No changes with posture or inspiration, lasts few minutes, ceases with rest or NG**

The CCS Classification of AP

- **I. Only strenuous, prolonged exercise results in angina, but normal daily activities don't**
- **II. Normal daily activity is slightly limited (morning, cold, 2 blocks, or flights)**
- **III. Marked limitation of normal daily activity**
- **IV. Inability to carry on any physical activity without discomfort. Angina may be present at rest.**

New York Heart Association classification of HF

- **I. Usual daily activity does not cause symptoms**
- **II. More strenuous, than usual activity (> 2 blocks, or flights) causes dyspnea**
- **III. Moderate physical activity (<2 blocks, or flights) causes dyspnea**
- **IV. Dyspnea at rest**

Physical investigation

- **General impression**
- **Edema, cyanosis, dystended neck veins**
- **Blood pressure. Body weight, height, BMI**
- **Heart enlargement, apical impulse**
- **Murmurs, thrills (Heart, carotids, femorals)**
- **Pulmonary percussion, rales,**
- **Hepatic enlargement**
- **Peripheral pulses**

Loudness of murmurs

- 1. Very faint**
- 2. Faint**
- 3. Audible**
- 4. Loud**
- 5. Very loud – with thrills**
- 6. Maybe heard with distant stethoscop**

EKG methods

- **12 lead EKG**
- **Rhythm strip**
- **Holter monitoring (PM memory)**
- **Event monitoring**
- **Signal averaged EKG**
- **Intracardial EKG (electrophysiology)**
 - **Transtelephonic EKG**
 - **Vectorcardiography**

Clinical chemistry 1.

- **Risk factors**
 - **Diabetes (IGT,IFG)**
 - Fasting, 120 postprandial, HgbA1C
 - **Hyperlipoproteinaemia**
 - Total cholesterol, HDL, LDL, TG
- **Inflammatory markers (Wgr.,CRP, adhesion molecules, antibodies)**
- **Necrosis markers (CK-MB, troponin)**
- **BNP in heart failure**

Clinical chemistry 2.

- **Hypertension:**
 - **Renal function: urine analysis, BUN, Se kreatinin, Kreatinine clearance, albuminuria (micro- < 300 µg)**
 - **Endocrinology: renin, TSH, T₄,**
- **Treatment optimisation:**
 - **Electrolyte measurements: Se Na, K, Haematology, Se digoxin, serum level of antibiotics**
- **Side effect disclosure: ASAT, ALAT, CPK, GGT, haematology, TSH, T₄, renal function**

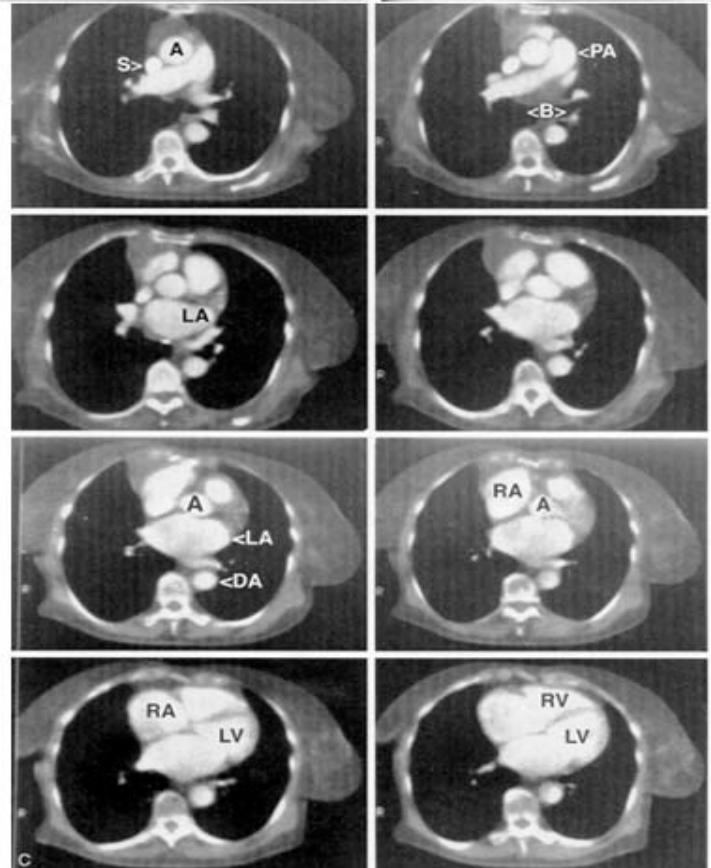
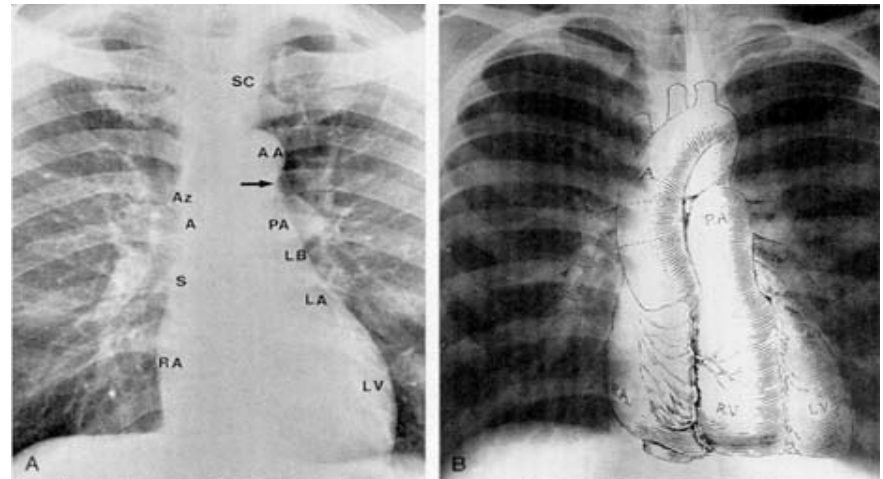
Imaging modalities

- **Chest x-ray**
- **Chest CT**
- **Echocardiography**
 - **Transthoracic (TTE)**
 - **Transesophageale (TEE)**
- **MR**
- **Multislice CTA,**

Chest x-ray

- **Anteroposterior and lateral exposures**
- **Contours, heart enlargement, heart volume measureable**
- **Pulmonary vascularisation (pulmonary hypertension, pulmonary venous pressure)**
- **Comparable**

Chest x-ray and CT



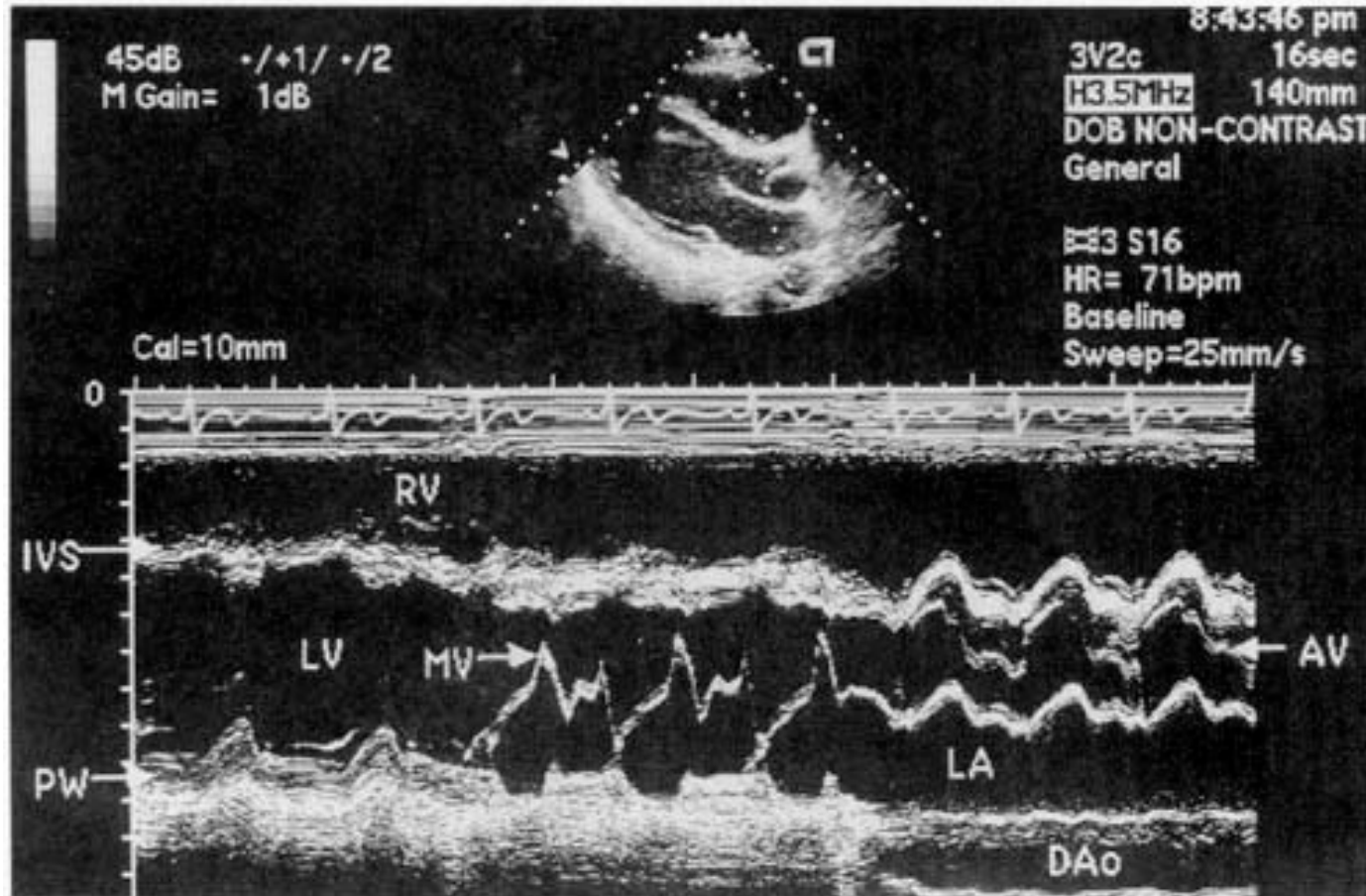
Cardiology

Echocardiography

- **Non-invasive diameters, wall thickness, valve movements**
- **Non-invasive hemodynamic evaluation by Doppler ultrasound flow measurements**
 - **Pressure gradients**
 - **Pathologic flow (qualitative, quantitative)**

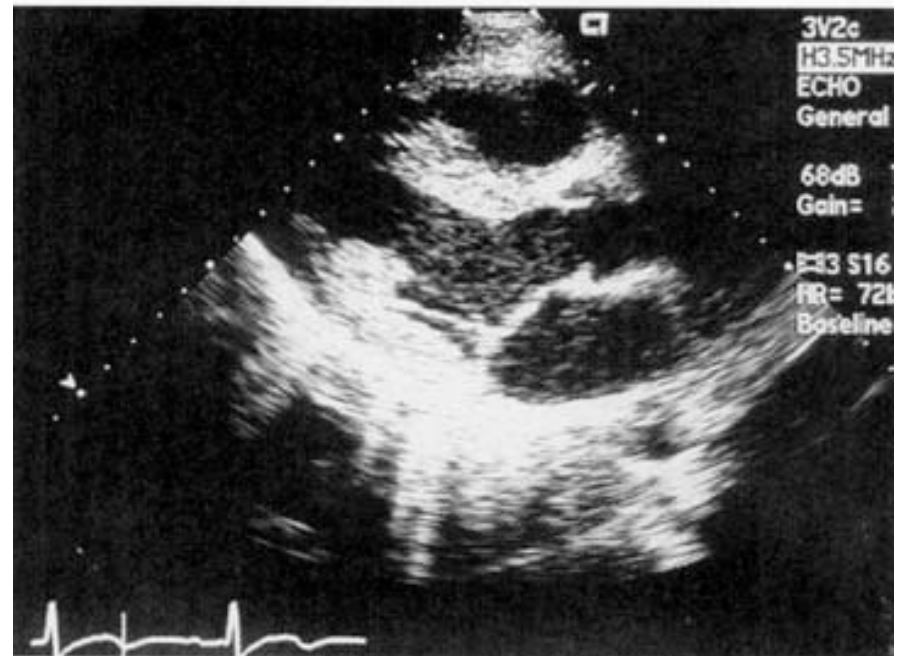
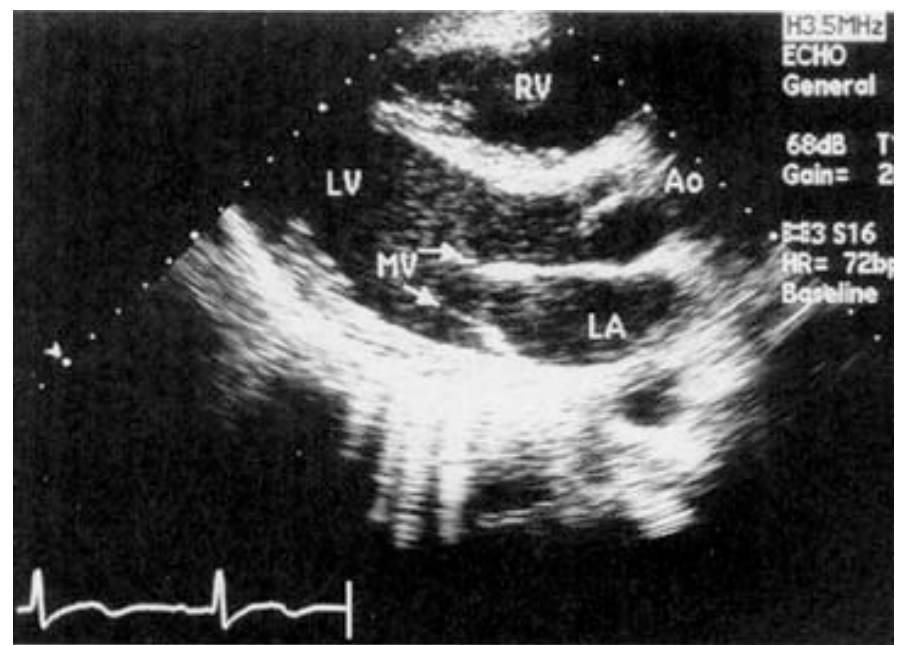
Echocardiography

M-mode registration



Echocardiography

2-D registration



Echocardiography in CAD

- **Class I. indication:**
 - **patients with systolic murmur (AS, HOCM)**
 - **Evaluation of the severity of ischemia (segmental wall motion abnormality) during pain, or within 30 minutes after pain**
- **Class II. indication:**
 - **Patients with a click, or murmur suggestive MVP**

Nuclear, Imaging

- **Many possibilities**
 - **Cardiac index - J_{125} red blood cells**
 - **Perfusion (Technetium, Thallium)**
 - **Viability**
- **Imaging time is long**
- *Linear, or single photon SPECT*
- **CTA**
- **MRI**

Exercise ECG

- **Exercise ECG is a well established procedure used for decades.**
- **Safe (MI or death 1/2500)**
- **20-30 % of patients are unable to perform ETT because of contraindication**
- **Bicycle and treadmill are both useful.**
- **Use standard, comparable protocols**

ETT standards

- **Supervised by a physician (personally?)**
- **1 MET = 3,5 ml/kg/min oxygen uptake**
- **Continuous monitoring for heart rate, blood pressure, ST segment shift, arrhythmias**
- **Target 85 % of maximal HR, or angina, or >2mm ST depression (horizontal, or downsloping)**
- **Maximal HR= 220 - age**

Costs of ETT

- **ECG ETT is cheap**
- **Stress echocardiography twofold**
- **SPECT scintigraphy fivefold**
- **Coronarography twentyfold**

Interpretation of ETT

- **Lead selection - more leads-more information**
- **Upsloping ST segment depression**
- **ST segment elevation – rare, great likelihood of arrhythmias, probable transmural ischemia**
- **R wave changes are not reliable**

Class I indication for ETT

- **Patients with an intermediate probability of CAD (based on age, gender, symptoms) including patients with RBBB or < 1 mm ST depression at rest**
- **Excluding patients with WpW sy., PM rhythm. More than 1 mm ST depression at rest, LBBB.**
- **Established CAD -functional capacity, prognosis**

Exercise imaging tests

- **Myocardial scintigraphy (specificity: 70-85 %, sensitivity: 85-90 %)**
 - MIBI, or Thallium
 - SPECT, or planar
 - Physical exercise, or pharmacological stress
- **Stress echocardiography: (specificity: 60-90 %, sensitivity: 85-94 %)**
 - low-dose dobutamine infusion stress

Invasive investigations

- **Essentials are pressure measurement, *flow measurement, angiocardiology, coronarography***
- **Coronarography**
- **Pressure measurement**
 - **Direct or indirect (fluid column)**
 - **Pressure difference**
 - **Gradients (peak or mean)**

Technique of coronary arteriography

- **Percutaneous insertion of catheter**
 - femoral - preformed catheter (Judkins)
 - brachial – Sones
 - **radial**
- **Fluoroscopy**
- **Contrast dye injection**
- **Pressure measurement**
- **Digital or x-ray cinefilm recording**

Risks of coronary arteriography

- **Vascular, Arrhythmias, Allergic reactions, Bleeding, Thrombosis, Stroke, AMI**
- **Morbidity <1 %**
- **Mortality < 1 ‰**

Value of coronary arteriography

- **Most accurate diagnostic tool for obstructive atherosclerotic and non-atherosclerotic (Kawasaki, spasm, dissection) coronary disease.**
- **The most accurate method to disclose coronary anatomy**

Medical therapy of angina

- **A: Aspirin (antiplatelet) and Antianginal (nitrate), ACEI**
- **B: Beta receptor blocker and Blood pressure control**
- **C: Cigarette smoking and Cholesterol lowering**
- **D: Diet and Diabetes control**
- **E: Education and Exercise**

ACC/AHA Classification

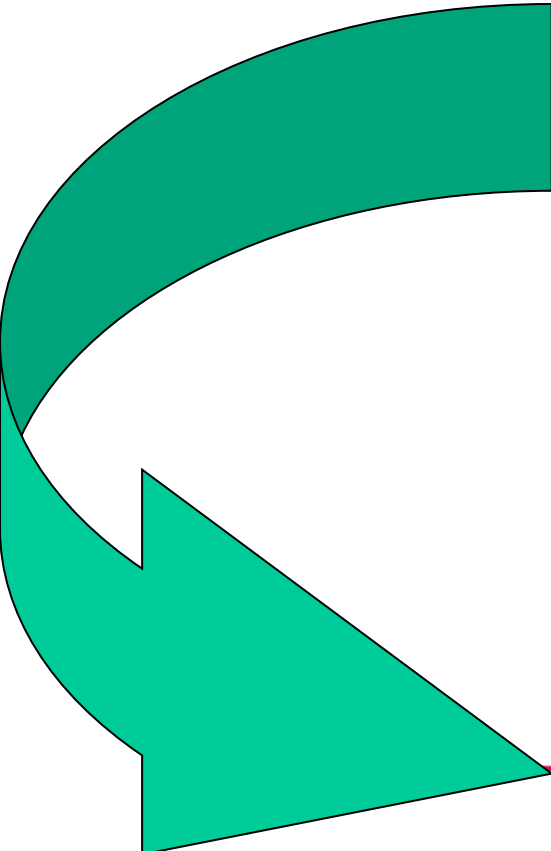
- **Class I.: Conditions for which there is evidence or general agreement to be useful - SHOULD**
- **Class IIa.: Conflicting evidence, diverging opinions, but in favour of efficacy – MAY BE**
- **Class IIb.: Conflicting evidence, diverging opinions, less well established efficacy – CAN BE**
- **Class III.: There is evidence, or general agreement to be ineffective, not useful, can be even harmful –DO NOT**

Ranking of evidences in ACC/AHA guidelines

- **A level evidence**: Multiple randomized, clinical trials, with large number of patients
- **B level evidence** : Small randomized trials, or careful analysis of nonrandomized trials, or registries
- **C level evidence**: No randomized trials, based on expert consensus

When to perform ad hoc PCI ?

Decision of the Heart Team



Ad hoc PCI
Haemodynamically unstable patients (including cardiogenic shock).
Culprit lesion in STEMI and NSTEMI-ACS.
Stable low-risk patients with single or double vessel disease (proximal LAD excluded) and favourable morphology (RCA, non-ostial LCx, mid- or distal LAD).
Non-recurrent restenotic lesions.
Revascularization at an interval
Lesions with high-risk morphology.
Chronic heart failure.
Renal failure (creatinine clearance <60 mL/min), if total contrast volume required >4 mL/kg.
Stable patients with MVD including LAD involvement.
Stable patients with ostial or complex proximal LAD lesion.
Any clinical or angiographic evidence of higher periprocedural risk with <i>ad hoc</i> PCI.

ESC guideline

Revascularisation in stable angina

	Subset of CAD by anatomy	Class ^a	Level ^b	Ref. ^c
For prognosis	Left main >50% ^d	I	A	30, 31, 54
	Any proximal LAD >50% ^d	I	A	30–37
	2VD or 3VD with impaired LV function ^d	I	B	30–37
	Proven large area of ischaemia (>10% LV)	I	B	13, 14, 38
	Single remaining patent vessel >50% stenosis ^d	I	C	—
	IVD without proximal LAD and without >10% ischaemia	III	A	39, 40, 53
For symptoms	Any stenosis >50% with limiting angina or angina equivalent, unresponsive to OMT	I	A	30, 31, 39–43
	Dyspnoea/CHF and >10% LV ischaemia/viability supplied by >50% stenotic artery	IIa	B	—
	No limiting symptoms with OMT	III	C	—

Method of revascularisation

Subset of CAD by anatomy	Favours CABG	Favours PCI	Ref.
IVD or 2VD - non-proximal LAD	IIb C	I C	—
IVD or 2VD - proximal LAD	IA	IIa B	30, 31, 50, 51
3VD simple lesions, full functional revascularization achievable with PCI, SYNTAX score ≤ 22	IA	IIa B	4, 30–37, 53
3VD complex lesions, Incomplete revascularization achievable with PCI, SYNTAX score > 22	IA	III A	4, 30–37, 53
Left main (isolated or IVD, ostium/shaft)	IA	IIa B	4, 54
Left main (isolated or IVD, distal bifurcation)	IA	IIb B	4, 54
Left main + 2VD or 3VD, SYNTAX score ≤ 32	IA	IIb B	4, 54
Left main + 2VD or 3VD, SYNTAX score ≥ 33	IA	III B	4, 54

Long-term care of revascularised patient

Long-term management is based on risk stratification that should include: <ul style="list-style-type: none"> • full clinical and physical evaluation • ECG • laboratory testing • HbA1c • physical activity level by history and exercise testing • echocardiogram prior to and after CABG. 	I	C
	I	B
	I	B
	I	A
	I	B
	I	C
Echocardiography should be considered pre- or post-PCI.	IIa	C
<ul style="list-style-type: none"> • Counselling on physical activity and exercise training should include a minimum of 30–60 min/day of moderately intense aerobic activity. • Medically supervised programmes are advisable for high-risk patients (e.g. recent revascularization, heart failure). 	I	A
	I	B
Resistance training 2 days/week may be considered	IIb	C
<ul style="list-style-type: none"> • Diet and weight control management should aim at BMI <25 kg/m² and waist circumferences <94 cm in men and <80 cm in women. • It is recommended to assess BMI and/or waist circumferences on each visit and consistently encourage weight maintenance/reduction. • The initial goal of weight-loss therapy is the reduction of body weight by ~10% from baseline. • Healthy food choices are recommended. 	I	B
	I	B
	I	B
	I	B
• Dietary therapy and lifestyle changes are recommended.	I	B

Long term care... continued

• It is recommended to reach LDL-cholesterol <100 mg/dL (2.5 mmol/L).	I	A
• In high-risk patients, it is recommended to reach LDL-cholesterol <70 mg/dl (2.0 mmol/L).	I	B
Increased consumption of omega-3 fatty acids in the form of fish oil may be considered.	IIb	B
• It is recommended to implement lifestyle changes and pharmacotherapy in order to achieve blood pressure <130/80 mmHg.	I	A
• β -Blockers and/or ACE inhibitors are indicated as first-line therapy.	I	A
It is recommended to assess, at each visit, smoking status, to insist on smoking cessation, and to advise avoiding passive smoking.	I	B
In patients with diabetes, the following is recommended:		
• Lifestyle changes and pharmacotherapy to achieve HbA1c <6.5%.	I	B
• Vigorous modification of other risk factors.	I	B
• Coordination of diabetic care with a specialized physician.	I	C
Screening for psychological distress is indicated.	I	C
Annual influenza vaccination is indicated.	I	B

Drug treatment after revascularisation

	Class ^a	Level ^b
• ACE inhibitors should be started and continued indefinitely in all patients with LVEF \leq 40% and for those with hypertension, diabetes, or CKD, unless contraindicated.	I	A
• ACE inhibitors should be considered in all patients, unless contraindicated.	IIa	A
• Angiotensin receptor blockers are indicated in patients who are intolerant of ACE inhibitors and have HF or MI with LVEF \leq 40%.	I	A
• Angiotensin receptor blockers should be considered in all ACE-inhibitor intolerant patients.	IIa	A
• It is indicated to start and continue β -blocker therapy in all patients after MI or ACS or LV dysfunction, unless contraindicated.	I	A
• High-dose lipid lowering drugs are indicated in all patients regardless of lipid levels, unless contraindicated.	I	A
• Fibrates and omega-3 fatty acids (1 g/day) should be considered in combination with statins and in patients intolerant of statins.	IIa	B
• Niacin may be considered to increase HDL cholesterol.	IIb	B

ACE inhibitor

ARB

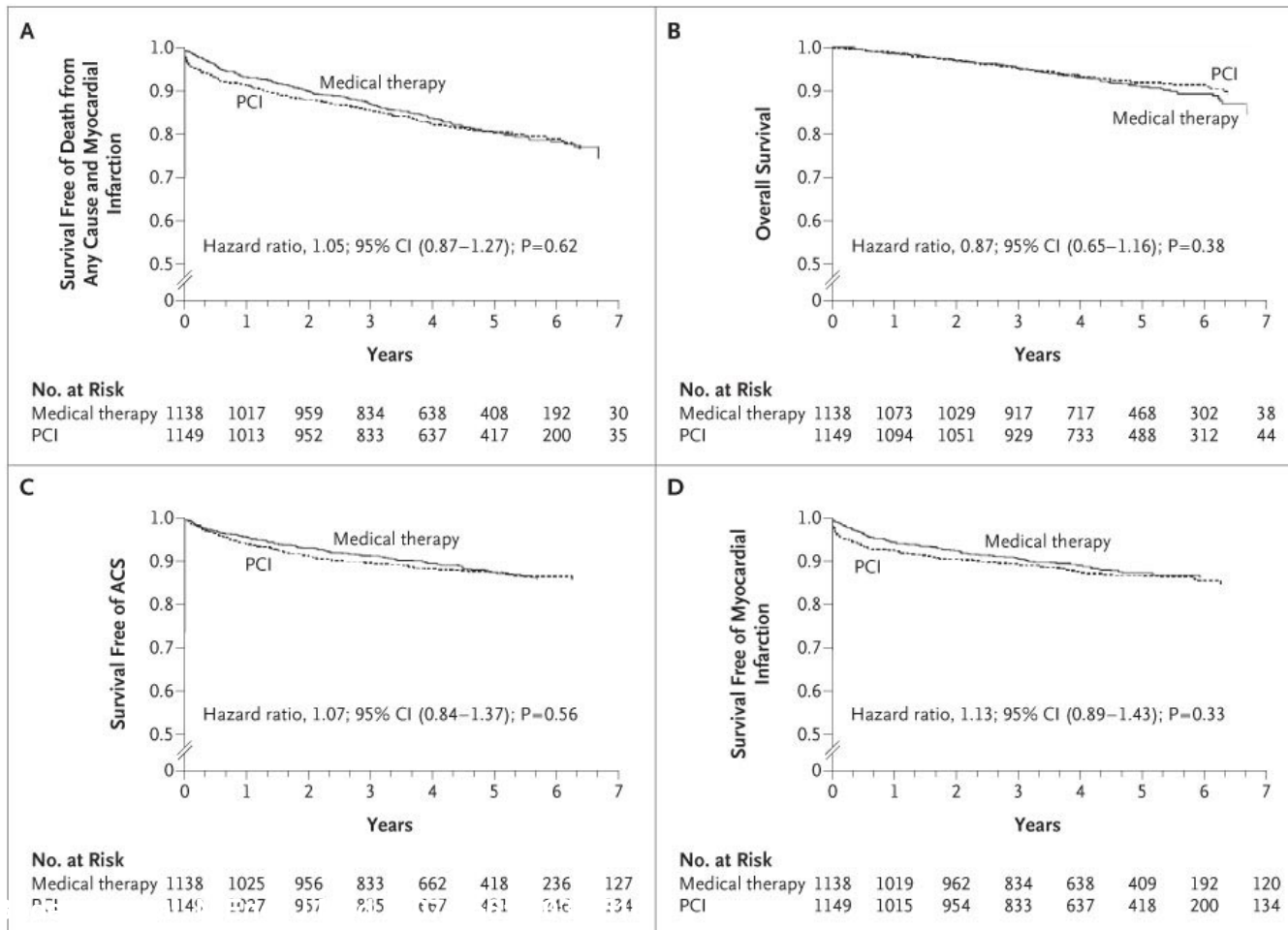
Beta receptor blocker

Antilipemic

Imaging need in revascularised patients

symptomfree	Class ^a	Level ^b	With symptoms	Class ^a	Level ^b
Stress Imaging (stress echo or MPS) should be used rather than stress ECG.	I	A	Stress Imaging (stress echo or MPS) should be used rather than stress ECG.	I	A
<ul style="list-style-type: none"> • With low-risk findings (+) at stress testing, it is recommended to reinforce OMT and lifestyle changes. • With high- to intermediate-risk findings (++) at stress testing, coronary angiography is recommended. 	IIa	C	It is recommended to reinforce OMT and life style changes in patients with low-risk findings (+) at stress testing.	I	B
Early imaging testing should be considered in specific patient subsets. ^d	IIa	C	With intermediate- to high-risk findings (++) at stress testing, coronary angiography is recommended.	I	C
Routine stress testing may be considered ≥ 2 years after PCI and ≥ 5 years after CABG.	IIb	C	Emergent coronary angiography is recommended in patients with STEMI.	I	A
			Early Invasive strategy is indicated in high-risk NSTEMI-ACS patients.	I	A
			Elective coronary angiography is indicated in low-risk NSTEMI-ACS patients.	I	C

COURAGE trial 2007



Optimal medical therapy of angina

- **A: Aspirin (Antiplatelet) and Antianginal (nitrate), ACEI (ARB)**
- **B: Beta receptor blocker and Blood pressure control**
- **C: Cigarette smoking and Cholesterol lowering**
- **D: Diet and Diabetes control**
- **E: Education and Exercise**