

2013 ESC guidelines on the management of stable coronary artery disease

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The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

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Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/ is indicated.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
<i>Class IIa</i>	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>	<i>Should be considered.</i>
<i>Class IIb</i>	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>	<i>May be considered.</i>
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended.

Levels of evidence

Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Main features of SCAD

Pathogenesis

Stable anatomical atherosclerotic and/or functional alterations of epicardial vessels and/or microcirculation

Natural history

Stable symptomatic or asymptomatic phases which may be interrupted by ACS

Mechanisms of myocardial ischaemia

Fixed or dynamic stenoses of epicardial coronary arteries

Microvascular dysfunction

Focal or diffuse epicardial coronary spasm

The above mechanisms may overlap in the same patient and change over time

Clinical presentations

Effort induced angina caused by:

- epicardial stenoses • microvascular dysfunction • vasoconstriction at the site of dynamic stenosis
- combination of the above

Rest angina caused by:

- Vasospasm (focal or diffuse):
 - epicardial focal • epicardial diffuse • microvascular • combination of the above

Asymptomatic:

- because of lack of ischaemia and/or of LV dysfunction • despite ischaemia and/or LV dysfunction

Ischaemic cardiomyopathy

ACS = acute coronary syndrome; LV = left ventricular; SCAD = stable coronary artery disease.
This slide corresponds to Table 3 in the full text.

Traditional clinical classification of chest pain

Typical angina (definite)	Meets all three of the following characteristics: <ul style="list-style-type: none">• substernal chest discomfort of characteristic quality and duration;• provoked by exertion or emotional stress;• relieved by rest and/or nitrates within minutes.
Atypical angina (probable)	Meets two of these characteristics.
Non-anginal chest pain	Lacks or meets only one or none of the characteristics.

This slide corresponds to Table 4 in the full text.

Classification of angina severity according to the Canadian Cardiovascular Society

Class I	Ordinary activity does not cause angina such as walking and climbing stairs. Angina with strenuous or rapid or prolonged exertion at work or recreation.
Class II	Slight limitation of ordinary activity. Angina on walking or climbing stairs rapidly, walking or stair climbing after meals, or in cold, wind or under emotional stress, or only during the first few hours after awakening. Walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal conditions.
Class III	Marked limitation of ordinary physical activity. Angina on walking one to two blocks ^a on the level or one flight of stairs in normal conditions and at a normal pace.
Class IV	Inability to carry on any physical activity without discomfort, angina syndrome may be present at rest.

^aEquivalent to 100–200 m.

This slide corresponds to Table 5 in the full text.

Blood tests in assessment of patients with known or suspected SCAD in order to optimize medical therapy

Recommendations	Class	Level
If evaluation suggests clinical instability or ACS, repeated measurements of troponin preferably using high sensitivity or ultrasensitive assays are recommended to rule out myocardial necrosis associated with ACS.	I	A
Full blood count including haemoglobin and white cell count is recommended in all patients.	I	B
It is recommended that screening for potential T2DM in patients with suspected and established SCAD is initiated with HbA _{1c} and fasting plasma glucose and that an OGTT is added if HbA _{1c} and fasting plasma glucose are inconclusive.	I	B
Creatinine measurement and estimation of renal function (creatinine clearance) are recommended in all patients.	I	B
A fasting lipid profile (including LDL) is recommended in all patients.	I	C
If indicated by clinical suspicion of thyroid disorder assessment of thyroid function is recommended.	I	C
Liver function tests are recommended in patients early after beginning statin therapy.	I	C
Creatine kinase measurements are recommended in patients taking statins and complaining of symptoms suggestive of myopathy.	I	C
BNP/NT-proBNP measurements should be considered in patients with suspected heart failure.	IIa	C

ACS = acute coronary syndrome; BNP = B-type natriuretic peptide; HbA_{1c} = glycated haemoglobin; LDL = low-density lipoprotein; NT-proBNP = N-terminal pro B-type natriuretic peptide; SCAD = stable coronary artery disease; T2DM = type 2 diabetes mellitus. This slide corresponds to Table 6 in the full text.

Blood tests for routine reassessment in patients with chronic SCAD

Recommendation	Class	Level
Annual control of lipids, glucose metabolism and creatinine is recommended in all patients with known SCAD.	I	C

SCAD = stable coronary artery disease.

This slide corresponds to Table 7 in the full text.

Resting ECG for initial diagnostic assessment of SCAD

Recommendations	Class	Level
A resting ECG is recommended in all patients at presentation.	I	C
A resting ECG is recommended in all patients during or immediately after an episode of chest pain suspected to indicate clinical instability of CAD.	I	C

CAD = coronary artery disease; ECG = electrocardiogram; SCAD = stable coronary artery disease.
This slide corresponds to Table 8 in the full text.

Echocardiography

Recommendations	Class	Level
A resting transthoracic echocardiogram is recommended in all patients for: a) exclusion of alternative causes of angina; b) identification of regional wall motion abnormalities suggestive of CAD; c) measurement of LVEF for risk stratification purpose; d) evaluation of diastolic function.	I	B
Ultrasound of the carotid arteries should be considered to be performed by adequately trained clinicians to detect increased IMT and/or plaque in patients with suspected SCAD without known atherosclerotic disease.	Ila	C

CAD = coronary artery disease; IMT = intima-media thickness; LVEF = left ventricular ejection fraction; SCAD = stable coronary artery disease.

This slide corresponds to Table 9 in the full text.

Ambulatory ECG monitoring for initial diagnostic assessment of SCAD

Recommendations	Class	Level
Ambulatory ECG monitoring is recommended in patients with SCAD and suspected arrhythmia.	I	C
Ambulatory ECG monitoring should be considered in patients with suspected vasospastic angina.	Ila	C

ECG = electrocardiogram; SCAD = stable coronary artery disease.
This slide corresponds to Table 10 in the full text.

CXR for initial diagnostic assessment of SCAD

Recommendations	Class	Level
CXR is recommended in patients with atypical presentation or suspicion of pulmonary disease.	I	C
CXR should be considered in patients with suspected heart failure.	Ila	C

CXR = chest X-ray.

This slide corresponds to Table 11 in the full text.

Characteristics of tests commonly used to diagnose the presence of CAD

	Diagnosis of CAD	
	Sensitivity (%)	Specificity (%)
Exercise ECG ^a	45-50	85-90
Exercise stress echocardiography	80-85	80-88
Exercise stress SPECT	73-92	63-87
Dobutamine stress echocardiography	79-83	82-86
Dobutamine stress MRI ^b	79-88	81-91
Vasodilator stress echocardiography	72-79	92-95
Vasodilator stress SPECT	90-91	75-84
Vasodilator stress MRI ^b	67-94	61-85
Coronary CTA ^c	95-99	64-83
Vasodilator stress PET	81-97	74-91

CAD = coronary artery disease; CTA = computed tomography angiography; ECG = electrocardiogram; MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = single photon emission computed tomography.

^aResults without/with minimal referral bias; ^bResults obtained in populations with medium-to-high prevalence of disease without compensation for referral bias; ^cResults obtained in populations with low-to-medium prevalence of disease.

This slide corresponds to Table 12 in the full text.

Clinical pre-test probabilities^a in patients with stable chest pain symptoms

Age	Typical angina		Atypical angina		Non-anginal pain	
	Men	Women	Men	Women	Men	Women
30-39	59	28	29	10	18	5
40-49	69	37	38	14	25	8
50-59	77	47	49	20	34	12
60-69	84	58	59	28	44	17
70-79	89	68	69	37	54	24
>80	93	76	78	47	65	32

^a Probabilities of obstructive coronary disease shown reflect the estimates for patients aged 35, 45, 55, 65, 75, and 85 years. This slide corresponds to Table 13 in the full text.

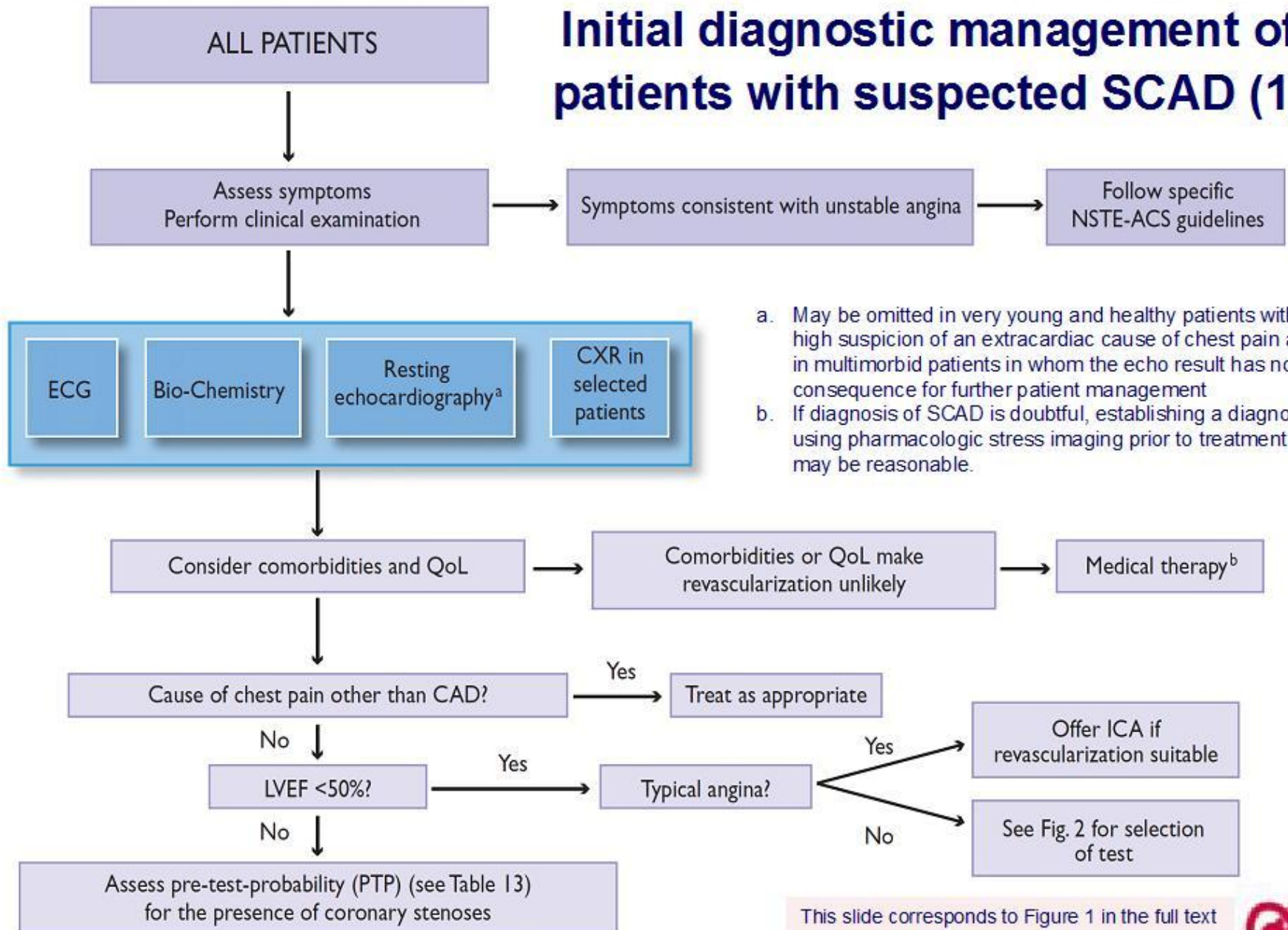
From: Genders TS, et al. Eur Heart J 2011;32:1316–1330.

Performing an exercise ECG for initial diagnostic assessment of angina or evaluation of symptoms

Recommendations	Class	Level
Exercise ECG is recommended as the initial test for establishing a diagnosis of SCAD in patients with symptoms of angina and intermediate PTP of CAD, free of anti-ischaemic drugs, unless they cannot exercise or display ECG changes which make the ECG non-evaluable.	I	B
Stress imaging is recommended as the initial test option if local expertise and availability permit.	I	B
Exercise ECG should be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIa	C
Exercise ECG in patients with ≥ 0.1 mV ST-depression on resting ECG or taking digitalis is not recommended for diagnostic purposes.	III	C

CAD = coronary artery disease; ECG = electrocardiogram; PTP = pre-test probability; SCAD = stable coronary artery disease. This slide corresponds to Table 14 in the full text.

Initial diagnostic management of patients with suspected SCAD (1)



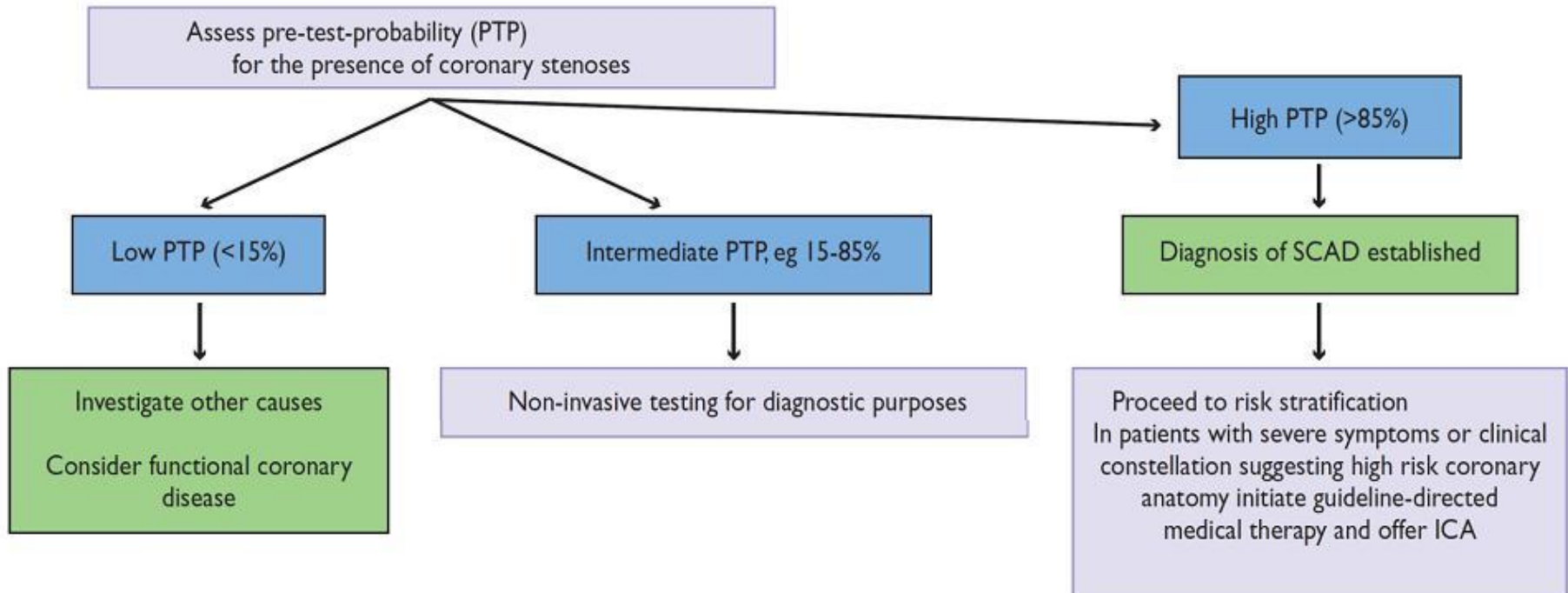
- a. May be omitted in very young and healthy patients with a high suspicion of an extracardiac cause of chest pain and in multimorbid patients in whom the echo result has no consequence for further patient management
- b. If diagnosis of SCAD is doubtful, establishing a diagnosis using pharmacologic stress imaging prior to treatment may be reasonable.

This slide corresponds to Figure 1 in the full text



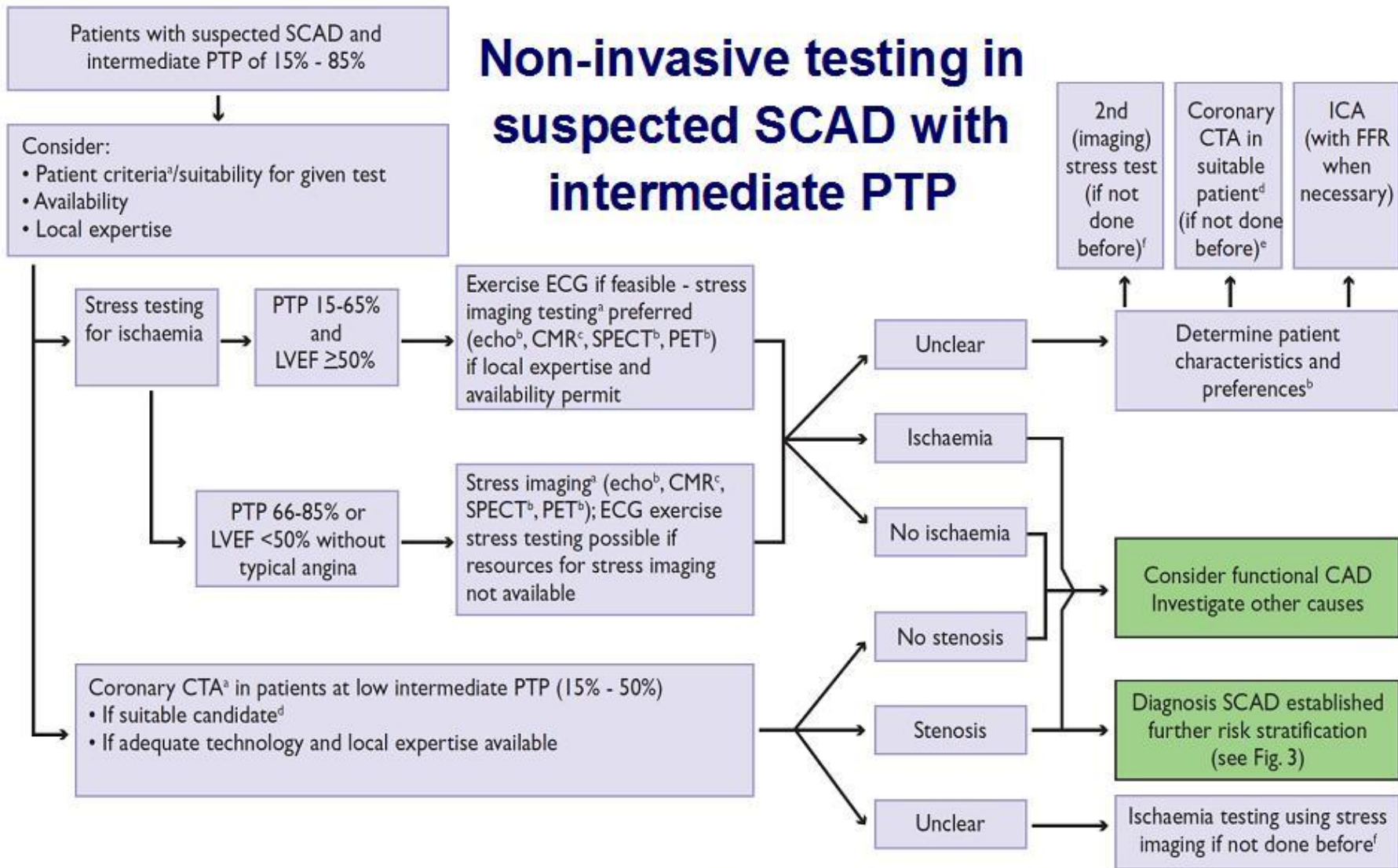
^aMay be omitted in very young and healthy patients with a high suspicion of an extracardiac cause of chest pain and in multimorbid patients in whom the echo result has no consequence for further patient management. ^bIf diagnosis of SCAD is doubtful, establishing a diagnosis using pharmacological stress imaging prior to treatment may be reasonable.

Initial diagnostic management of patients with suspected SCAD (2)



This slide corresponds to Figure 1 in the full text
ICA = invasive coronary angiography.

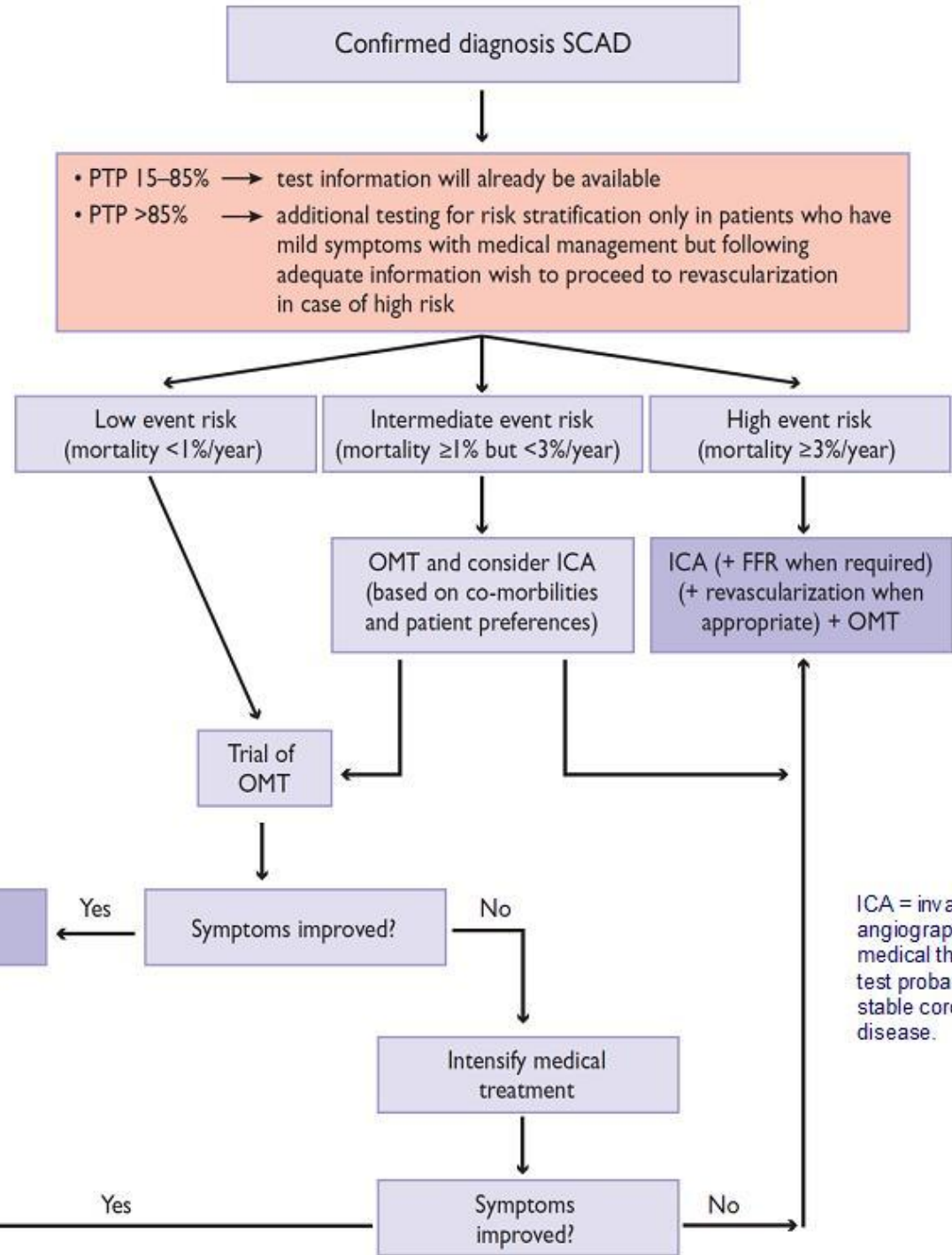
Non-invasive testing in suspected SCAD with intermediate PTP



- Consider age of patient versus radiation exposure.
- In patients unable to exercise use echo or SPECT/PET with pharmacologic stress instead.
- CMR is only performed using pharmacologic stress.
- Patient characteristics should make a fully diagnostic coronary CTA scan highly probable (see section 6.2.5.1.2) consider result to be unclear in patients with severe diffuse or focal calcification.
- Proceed as in lower left coronary CTA box.
- Proceed as in stress testing for ischaemia box.

This slide corresponds to Figure 2 in the full text.

Management based on risk determination for prognosis in patients with chest pain and suspected SCAD



ICA = invasive coronary angiography; OMT = optimal medical therapy; PTP = pre-test probability; SCAD = stable coronary artery disease.

This slide corresponds to Figure 3 in the full text.



Definitions of risk for various test modalities^a

Exercise stress ECG ^b	High risk Intermediate risk Low risk	CV mortality >3%/year. CV mortality between 1 and 3%/year. CV mortality <1%/year.
Ischaemia imaging	High risk Intermediate risk Low risk	Area of ischaemia >10% (>10% for SPECT; limited quantitative data for CMR – probably $\geq 2/16$ segments with new perfusion defects or ≥ 3 dobutamine-induced dysfunctional segments; ≥ 3 segments of LV by stress echo). Area of ischaemia between 1 to 10% or any ischaemia less than high risk by CMR or stress echo. No ischaemia.
Coronary CTA ^c	High risk Intermediate risk Low risk	Significant lesions of high risk category (three-vessel disease with proximal stenoses, LM, and proximal anterior descending CAD). Significant lesion(s) in large and proximal coronary artery(ies) but not high risk category. Normal coronary artery or plaques only.

CAD = coronary artery disease; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; CV = cardiovascular; ECG = electrocardiogram; LM = left main; SPECT = single photon emission computed tomography.

- For detailed explanation on rationale for risk stratification scheme see web addenda.
- From nomogram (see web addenda, Figure W1) or <http://www.cardiology.org/tools/medcalc/duke/>
- Consider possible overestimation of presence of significant multivessel disease by coronary CTA in patients with high intermediate PTP ($\geq 50\%$) and/or severe diffuse or focal coronary calcifications and consider performing additional stress testing in patients without severe symptoms before ICA.

This slide corresponds to Table 17 in the full text.

Use of exercise or pharmacologic stress testing in combination with imaging

Recommendations	Class	Level
An imaging stress test is recommended as the initial test for diagnosing SCAD if the PTP is between 66–85% or if LVEF is <50% in patients without typical angina.	I	B
An imaging stress test is recommended in patients with resting ECG abnormalities which prevent accurate interpretation of ECG changes during stress.	I	B
Exercise stress testing is recommended rather than pharmacologic testing whenever possible.	I	C
An imaging stress test should be considered in symptomatic patients with prior revascularization (PCI or CABG).	IIa	B
An imaging stress test should be considered to assess the functional severity of intermediate lesions on coronary arteriography.	IIa	B

CABG = coronary artery bypass graft; ECG = electrocardiogram; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; PTP = pre-test probability; SCAD = stable coronary artery disease.
This slide corresponds to Table 15 in the full text.

Use of coronary CTA for the diagnosis of SCAD

Recommendations	Class	Level
Coronary CTA should be considered as an alternative to stress imaging techniques for ruling out SCAD in patients within the lower range of intermediate PTP for SCAD in whom good image quality can be expected.	IIa	C
Coronary CTA should be considered in patients within the lower range of intermediate PTP for SCAD after a non-conclusive exercise ECG or stress imaging test or who have contraindications to stress testing in order to avoid otherwise necessary invasive coronary angiography if fully diagnostic image quality of coronary CTA can be expected.	IIa	C
Coronary calcium detection by CT is not recommended to identify individuals with coronary artery stenosis.	III	C
Coronary CTA is not recommended in patients with prior coronary revascularization.	III	C
Coronary CTA is not recommended as a 'screening' test in asymptomatic individuals without clinical suspicion of coronary artery disease.	III	C

CT = computed tomography; CTA = computed tomography angiography; ECG = electrocardiogram; PTP = pre-test probability; SCAD = stable coronary artery disease.

This slide corresponds to Table 16 in the full text.

Risk stratification by resting echocardiography quantification of ventricular function in SCAD

Recommendation	Class	Level
Resting echocardiography is recommended to quantify LV function in all patients with suspected SCAD.	I	C

LV = left ventricular; SCAD = stable coronary artery disease.

This slide corresponds to Table 18 in the full text.

Risk stratification using ischaemia testing

Recommendations	Class	Level
Risk stratification is recommended based on clinical assessment and the result of the stress test initially employed for making a diagnosis of SCAD.	I	B
Stress imaging for risk stratification is recommended in patients with a non-conclusive exercise ECG ^a	I	B
Risk stratification using stress ECG (unless they cannot exercise or display ECG changes which make the ECG non-evaluable) or preferably stress imaging if local expertise and availability permit is recommended in patients with stable coronary disease after a significant change in symptom level.	I	B
Stress imaging is recommended for risk stratification in patients with known SCAD and a deterioration in symptoms if the site and extent of ischaemia would influence clinical decision making.	I	B
Pharmacological stress with echocardiography or SPECT should be considered in patients with LBBB.	IIa	B
Stress echocardiography or SPECT should be considered in patients with paced rhythm.	IIa	B

ECG = electrocardiogram; LBBB = left bundle branch block; SCAD = stable coronary artery disease; SPECT = single photon emission computed tomography.

^aStress imaging has usually been performed for establishing a diagnosis of SCAD in most of these patients. This slide corresponds to Table 19 in the full text.

Risk stratification by invasive or non-invasive coronary arteriography in patients with SCAD

Recommendations	Class	Level
ICA (with FFR when necessary) is recommended for risk stratification in patients with severe stable angina (CCS 3) or with a clinical profile suggesting a high event risk, particularly if the symptoms are inadequately responding to medical treatment.	I	C
ICA (with FFR when necessary) is recommended for patients with mild or no symptoms with medical treatment in whom non-invasive risk stratification indicates a high event risk and revascularization is considered for improvement of prognosis.	I	C
ICA (with FFR when necessary) should be considered for event risk stratification in patients with an inconclusive diagnosis on non-invasive testing, or conflicting results from different non-invasive modalities.	IIa	C
If coronary CTA is available for event risk stratification, possible overestimation of stenosis severity should be considered in segments with severe calcification, especially in patients at high intermediate PTP. Additional stress imaging may be necessary before referring a patient with few/no symptoms to ICA.	IIa	C

CCS = Canadian Cardiovascular Society; CTA = computed tomography angiography; FFR = fractional flow reserve; ICA = invasive coronary angiography; PTP = pre-test probability; SCAD = stable coronary artery disease. This slide corresponds to Table 20 in the full text.

Testing in asymptomatic patients at risk for SCAD

Recommendations	Class	Level
In asymptomatic adults with hypertension or diabetes a resting ECG should be considered for CV risk assessment.	IIa	C
In asymptomatic adults at intermediate risk (see SCORE for definition of intermediate risk - www.heartscore.org) measurement of carotid intima-media thickness with screening for atherosclerotic plaques by carotid ultrasound, measurement of ankle-brachial index or measurement of coronary calcium using CT should be considered for CV risk assessment.	IIa	B
In asymptomatic adults with diabetes, 40 years of age and older, measurement of coronary calcium using CT may be considered for CV risk assessment.	IIb	B
In asymptomatic adults without hypertension or diabetes a resting ECG may be considered.	IIb	C
In intermediate-risk asymptomatic adults (see SCORE for definition of intermediate risk - www.heartscore.org), (including sedentary adults considering starting a vigorous exercise programme), an exercise ECG may be considered for CV risk assessment particularly when attention is paid to non-ECG markers such as exercise capacity.	IIb	B
In asymptomatic adults with diabetes or asymptomatic adults with a strong family history of CAD or when previous risk assessment testing suggests high risk of CAD, such as a coronary artery calcium score of 400 or greater stress imaging tests (MPI, stress echocardiography, perfusion CMR) may be considered for advanced CV risk assessment.	IIb	C
In low- or intermediate-risk (based on SCORE) asymptomatic adults stress imaging tests are not indicated for further CV risk assessment.	III	C

CAD = coronary artery disease; CMR = cardiac magnetic resonance; CT = computed tomography; CV = cardiovascular; MPI = myocardial perfusion imaging; SCORE = systematic coronary risk evaluation.
This slide corresponds to Table 21 in the full text.

Reassessment in patients with SCAD

Recommendations	Class	Level
Follow-up visits are recommended every 4–6 months in the first year following institution of therapy for SCAD which may be extended to 1 year afterwards. Visits should be to the general practitioner who may refer to the cardiologist in case of uncertainty. These visits should include a careful history and biochemical testing as clinically appropriate.	I	C
An annual resting ECG is recommended and an additional ECG if a change in anginal status occurred or symptoms suggesting an arrhythmia appeared or medication has been changed which might alter electrical conduction.	I	C
An exercise ECG or stress imaging if appropriate is recommended in the presence of recurrent or new symptoms once instability has been ruled out.	I	C
Reassessment of the prognosis using stress testing may be considered in asymptomatic patients after the expiration of the period for which the previous test was felt to be valid (“warranty period”).	IIb	C
Repetition of an exercise ECG may only be considered after at least 2 years following the last test (unless there is a change in clinical presentation).	IIb	C

ECG = electrocardiogram; SCAD = stable coronary artery disease.

This slide corresponds to Table 22 in the full text.

Investigation in patients with suspected coronary microvascular disease

Recommendations	Class	Level
Exercise or dobutamine echocardiography should be considered in order to establish whether regional wall motion abnormalities occur in conjunction with angina and ST-changes.	IIa	C
Transthoracic Doppler echocardiography of the LAD with measurement of diastolic coronary blood flow following intravenous adenosine and at rest may be considered for non-invasive measurement of coronary flow reserve.	IIb	C
Intracoronary acetylcholine and adenosine with Doppler measurements may be considered during coronary arteriography, if the arteriogram is visually normal, to assess endothelium-dependent and non-endothelium-dependent coronary flow reserve, and detect microvascular/epicardial vasospasm.	IIb	C

FFR = fractional flow reserve; LAD = left anterior descending.

This slide corresponds to Table 23 in the full text.

Diagnostic tests in suspected vasospastic angina

Recommendations	Class	Level
An ECG is recommended during angina if possible.	I	C
Coronary arteriography is recommended in patients with characteristic episodic resting chest pain and ST-segment changes that resolve with nitrates and/or calcium antagonists to determine the extent of underlying coronary disease.	I	C
Ambulatory ST-segment monitoring should be considered to identify ST deviation in the absence of an increased heart rate.	IIa	C
Intracoronary provocative testing should be considered to identify coronary spasm in patients with normal findings or non-obstructive lesions on coronary arteriography and the clinical picture of coronary spasm to diagnose the site and mode of spasm.	IIa	C

ECG = electrocardiogram.

This slide corresponds to Table 24 in the full text.

Recommended diet intakes

- Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids.
- Trans unsaturated fatty acids <1% of total energy intake.
- <5 g of salt per day.
- 30-45 g of fibre per day, from wholegrain products, fruits and vegetables.
- 200 g of fruit per day (2–3 servings).
- 200 g of vegetables per day (2–3 servings).
- Fish at least twice a week, one being oily fish.
- Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/day of alcohol) for men and 1 glass per day (10 g/day of alcohol) for non-pregnant women.

This slide corresponds to Table 25 in the full text.

Blood pressure thresholds for definition of hypertension with different types of blood pressure measurement¹

	SBP (mmHg)	DPB (mmHg)
Office blood pressure	140	90
Home blood pressure	135	85
Ambulatory blood pressure		
24-hour	130	80
Daytime (or awake)	135	85
Nighttime (or asleep)	120	70

DPB = diastolic blood pressure; SBP = systolic blood pressure.

This slide corresponds to Table 26 in the full text.

¹Adapted from reference 275 in the Full Text (Mancia G , Fagard R et al, ESH-ESC Guidelines on Arterial Hypertension Eur Heart J:2013)

Major side-effects, contraindications, DDIs and precautions of anti-ischaemic drugs (1)

Drug class	Side-effects ^a	Contraindications	DDI	Precautions
Short-acting and long-acting nitrates	<ul style="list-style-type: none"> • Headache • Flushing • Hypotension • Syncope and postural hypotension • Reflex tachycardia • Methaemoglobinaemia 	<ul style="list-style-type: none"> • Hypertrophic obstructive cardiomyopathy 	<ul style="list-style-type: none"> • PDE5 inhibitors (sildenafil or similar agents) • α-adrenergic blockers • CCBs 	
β -blockers ^b	<ul style="list-style-type: none"> • Fatigue, depression • Bradycardia • Heart block • Bronchospasm • Peripheral vasoconstriction • Postural hypotension • Impotence • Hypoglycaemia/mask hypoglycaemia signs 	<ul style="list-style-type: none"> • Low heart rate or heart conduction disorder • Cardiogenic shock • Asthma • COPD caution; may use cardioselective β-blockers if fully treated by inhaled steroids and long-acting β-agonists • Severe peripheral vascular disease • Decompensated heart failure • Vasospastic angina 	<ul style="list-style-type: none"> • Heart-rate lowering CCB • Sinus-node or AV conduction depressors 	<ul style="list-style-type: none"> • Diabetics • COPD

AV = atrioventricular; CCBs = calcium channel blockers; COPD = chronic obstructive pulmonary disease; DDI = drug–drug interaction; PDE5 = phosphodiesterase type 5.

^aVery frequent or frequent; may vary according to specific drugs within the therapeutic class.

^bAtenolol, metoprolol CR, bisoprolol, carvedilol.

This slide corresponds to Table 27 in the full text.

Major side-effects, contraindications, DDIs and precautions of anti-ischaemic drugs (2)

Drug class	Side-effects ^a	Contraindications	DDI	Precautions
CCBs: heart-rate lowering	<ul style="list-style-type: none"> •Bradycardia •Heart conduction defect •Low ejection fraction •Constipation •Gingival hyperplasia 	<ul style="list-style-type: none"> • Low heart rate or heart rhythm disorder • Sick sinus syndrome • Congestive heart failure • Low blood pressure 	<ul style="list-style-type: none"> • Cardiodepressantn (β-blockers, flecainide) • CYP3A4 substrates 	
CCBs: Dihydro- pyridines	<ul style="list-style-type: none"> •Headache •Ankle swelling •Fatigue •Flushing •Reflex tachycardia 	<ul style="list-style-type: none"> • Cardiogenic shock • Severe aortic stenosis • Obstructive cardiomyopathy 	<ul style="list-style-type: none"> • CYP3A4 substrates 	
Ivabradine	<ul style="list-style-type: none"> • Visual disturbances • Headache, dizziness • Bradycardia • Atrial fibrillation • Heart block 	<ul style="list-style-type: none"> • Low heart rate or heart rhythm disorder • Allergy • Severe hepatic disease 	<ul style="list-style-type: none"> • QTc prolonging drugs • Macrolide antibiotics • Anti-HIV • Anti-fungal 	<ul style="list-style-type: none"> • Age >75 years • Severe renal failure

CCBs = calcium channel blockers; DDI = drug–drug interaction; HIV = human immunodeficiency virus.

^aVery frequent or frequent; may vary according to specific drugs within the therapeutic class.

This slide corresponds to Table 27 in the full text.

Major side-effects, contraindications, DDIs and precautions of anti-ischaemic drugs (3)

Drug class	Side-effects ^a	Contraindications	DDI	Precautions
Nicorandil	<ul style="list-style-type: none"> • Headache • Flushing • Dizziness, weakness • Nausea • Hypotension • Oral, anal, gastrointestinal ulceration 	<ul style="list-style-type: none"> • Cardiogenic shock • Heart failure • Low blood pressure 	<ul style="list-style-type: none"> • PDE5 inhibitors (sildenafil or similar agents) 	
Trimetazidine	<ul style="list-style-type: none"> • Gastric discomfort • Nausea • Headache • Movement disorders 	<ul style="list-style-type: none"> • Allergy • Parkinson's disease • Tremors and movement disorders • Severe renal impairment 	<ul style="list-style-type: none"> • None reported 	<ul style="list-style-type: none"> • Moderate renal impairment • Elderly
Ranolazine	<ul style="list-style-type: none"> • Dizziness • Constipation • Nausea • QT prolongation 	<ul style="list-style-type: none"> • Liver cirrhosis 	<ul style="list-style-type: none"> • CYP450 substrates (digoxin, simvastatin, cyclosporin) • QTc prolonging drugs 	
Allopurinol	<ul style="list-style-type: none"> • Rash • Gastric discomfort 	<ul style="list-style-type: none"> • Hypersensitivity 	<ul style="list-style-type: none"> • Mercaptopurine / azathioprine 	<ul style="list-style-type: none"> • Severe renal failure

CYP450 = cytochrome P450; DDI = drug–drug interaction; PDE5 = phosphodiesterase type 5.

^aVery frequent or frequent; may vary according to specific drugs within the therapeutic class.

This slide corresponds to Table 27 in the full text.

Definitions of risk for various test modalities^a

Exercise stress ECG ^b	High risk	CV mortality >3%/year.
	Intermediate risk	CV mortality between 1 and 3%/year.
	Low risk	CV mortality <1%/year.
Ischaemia imaging	High risk	Area of ischaemia >10% (>10% for SPECT; limited quantitative data for CMR – probably $\geq 2/16$ segments with new perfusion defects or ≥ 3 dobutamine-induced dysfunctional segments; ≥ 3 segments of LV by stress echo).
	Intermediate risk	Area of ischaemia between 1 to 10% or any ischemia less than high risk by CMR or stress echo.
	Low risk	No ischaemia.
Coronary CTA ^c	High risk	Significant lesions of high risk category (three-vessel disease with proximal stenoses, LM, and proximal anterior descending CAD).
	Intermediate risk	Significant lesion(s) in large and proximal coronary artery(ies) but not high risk category.
	Low risk	Normal coronary artery or plaques only.

CAD = coronary artery disease; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; CV = cardiovascular; ECG = electrocardiogram; ICA = invasive coronary angiography; LM = left main; PTP = pre-test probability; SPECT = single photon emission computed tomography.

^aFor detailed explanation on rationale for risk stratification scheme see web addenda.

^bFrom nomogram (see web addenda, Figure W1) or <http://www.cardiology.org/tools/medcalc/duke/>

^cSee Fig 2 in full text – consider possible overestimation of presence of significant multivessel disease by coronary CTA in patients with high intermediate PTP ($\geq 50\%$) and/or severe diffuse or focal coronary calcifications and consider performing additional stress testing in patients without severe symptoms before ICA.

This slide corresponds to Table 17 in the full text.

Pharmacological treatments in SCAD patients (1)

Indication	Class	Level
General considerations		
Optimal medical treatment indicates at least one drug for angina/ischemia relief plus drugs for event prevention.	I	C
It is recommended to educate patients about the disease, risk factors and treatment strategy.	I	C
It is indicated to review the patient's response soon after starting therapy.	I	C
Angina/ischaemia^a relief		
Short-acting nitrates are recommended.	I	B
First-line treatment is indicated with β -blockers and/or calcium channel blockers to control heart rate and symptoms.	I	A
For second-line treatment it is recommended to add long-acting nitrates or ivabradine or nicorandil or ranolazine, according to heart rate, blood pressure and tolerance.	IIa	B
For second-line treatment, trimetazidine may be considered.	IIb	B
According to comorbidities/tolerance it is indicated to use second-line therapies as first-line treatment in selected patients.	I	C

SCAD = stable coronary artery disease.

^aNo demonstration of benefit on prognosis

This slide corresponds to Table 28 in the full text.

Pharmacological treatments in SCAD patients (2)

Indication	Class	Level
Angina/ischaemia^a relief (cont'd)		
In asymptomatic patients with large areas of ischaemia (>10%) β -blockers should be considered.	IIa	C
In patients with vasospastic angina, calcium channel blockers and nitrates should be considered and beta-blockers avoided.	IIa	B
Event prevention		
Low-dose aspirin daily is recommended in all SCAD patients.	I	A
Clopidogrel is indicated as an alternative in case of aspirin intolerance.	I	B
Statins are recommended in all SCAD patients.	I	A
It is recommended to use ACE inhibitors (or ARBs) if presence of other conditions (e.g. heart failure, hypertension or diabetes).	I	A

ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker.

^aNo demonstration of benefit on prognosis

This slide corresponds to Table 28 in the full text.

Treatment in patients with microvascular angina

Recommendations	Class	Level
It is recommended that all patients receive secondary prevention medications including aspirin and statins.	I	B
β -blockers are recommended as a first-line treatment.	I	B
Calcium antagonists are recommended if β -blockers do not achieve sufficient symptomatic benefit or are not tolerated.	I	B
ACE inhibitors or nicorandil may be considered in patients with refractory symptoms.	IIb	B
Xanthine derivatives or non-pharmacological treatments such as neurostimulatory techniques may be considered in patients with symptoms refractory to the above listed drugs.	IIb	B

ACE = angiotensin converting enzyme.

This slide corresponds to Table 29 in the full text.

Stenting and peri-procedural antiplatelet strategies in SCAD patients

Recommendations	Class	Level
DES is recommended in SCAD patients undergoing stenting if there is no contraindication to prolonged DATP.	I	A
Aspirin is recommended for elective stenting.	I	B
Clopidogrel is recommended for elective stenting.	I	A
Prasugrel or ticagrelor should be considered in patients with stent thrombosis on clopidogrel without treatment interruption.	IIa	C
GP IIb/IIIa antagonists should be considered for bailout situation only.	IIa	C
Platelet function testing or genetic testing may be considered in specific or high risk situations (e.g. prior history of stent thrombosis; compliance issue; suspicion of resistance; high bleeding risk) if results may change the treatment strategy.	IIb	C
Prasugrel or ticagrelor may be considered in specific high risk situations of elective stenting (e.g. left main stenting; high risk of stent thrombosis; diabetes).	IIb	C
Pretreatment with clopidogrel (when coronary anatomy is not known) is not recommended.	III	A
Routine platelet function testing (clopidogrel and aspirin) to adjust antiplatelet therapy before or after elective stenting is not recommended.	III	A
Prasugrel or ticagrelor is not recommended in low risk elective stenting.	III	C

DATP = dual antiplatelet therapy; GP = glycoprotein; SCAD = stable coronary artery disease. This slide corresponds to Table 30 in the full text.

Use of fractional flow reserve, intravascular ultrasound, & optical coherence tomography in SCAD

Recommendations	Class	Level
FFR is recommended to identify hemodynamically relevant coronary lesion(s) when evidence of ischaemia is not available.	I	A
Revascularization of stenoses with FFR <0.80 is recommended in patients with angina symptoms or a positive stress test.	I	B
IVUS or OCT may be considered to characterize lesions.	IIb	B
IVUS or OCT may be considered to improve stent deployment.	IIb	B
Revascularization of an angiographically intermediate stenosis without related ischaemia or without FFR <0.80 is not recommended.	III	B

FFR = fractional flow reserve; IVUS = intravascular ultrasound; OCT = optical coherence tomography; SCAD = stable coronary artery disease.

This slide corresponds to Table 31 in the full text.

Revascularization of SCAD patients on OMT

(Adapted from the ESC/EACTS 2010 Guidelines)

Indication ^a	To improve prognosis		To improve symptoms persistent on OMT	
	Class	Level	Class	Level
A Heart Team approach to revascularization is recommended in patients with unprotected left main, 2–3 vessel disease, diabetes or comorbidities.	I	C	I	C
Left main >50% diameter stenosis. ^b	I	A	I	A
Any proximal LAD >50% diameter stenosis. ^b	I	A	I	A
2–3 vessel disease with impaired LV function/CHF.	I	B	IIa	B
Single remaining vessel (>50% diameter stenosis ^b).	I	C	I	A
Proven large area of ischaemia (>10% LV ^c)	I	B	I	B
Any significant stenosis with limiting symptoms or symptoms non responsive/intolerant to OMT.	NA	NA	I	A
Dyspnoea/cardiac heart failure with >10% ischaemia/viability supplied by stenosis >50%.	IIb	B	IIa	B
No limiting symptoms with OMT in vessel other than left main or proximal LAD or single remaining vessel or vessel subtending area of ischaemia <10% of myocardium or with FFR ≥0.80.	III	A	III	C

CHF = congestive heart failure; FFR = fractional flow reserve; LAD = left anterior descending; LV = left ventricular; OMT = optimal medical therapy; SCAD = stable coronary artery disease. ^aIn asymptomatic patients, the decision will be guided by the extent of ischaemia on stress testing. ^bWith documented ischaemia or FFR <0.80 for angiographic diameter stenoses 50–90%. ^cAs assessed by non-invasive test (SPECT, MRI, stress echocardiography).

This slide corresponds to Table 32 in the full text.

Characteristics of the seven more recent randomized trials

	TIME	MASS II	SWISSI II	COURAGE	BARI-2D	JSAP	FAME-2
Recruitment (years)	1996-2000	1995-2000	1991-97	1999-2004	2001-2005	2002-2004	2010-2012
Study size (n)	301	611	201	2287	2368	384	888
Mean age (years)	80	60	55	61	62	64	64
Angina CCS	II-IV	II-III	0	0-III	0-II	0-II	I-IV
Stress ischaemia (% of patients)	69	NA	100	NA	NA	NA	100
Prior MI (% of patients)	47	44	100	39	38	15	37
Mean LVEF (%)	52	67	57	62	NA	65	16% with EF <0.50
Angiographic selection	No	Yes	Yes	Yes	Yes	Yes	Yes
Mandatory documented ischaemia	No	No	Yes	No	No	No	Yes
Revascularization	PCI or CABG	PCI or CABG	PCI	PCI	PCI or CABG	PCI	PCI
PEP	Angina	Death/MI/ refractory angina	Death/MI/ revasc	Death/MI	Death	Death/ACS	Death/MI/ Urgent revasc
Revascularization better on PEP	Yes	No at 1 year Yes at 5 years (CABG)	Yes	No	No	Yes	Yes

ACS = acute coronary syndrome; CABG = coronary artery bypass graft; CCS = Canadian Cardiovascular Society; EF = ejection fraction; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; PEP = primary endpoint; revasc = revascularization. This slide corresponds to Table 33 in the full text.



Follow-up of revascularized SCAD patients (1)

Recommendations	Class	Level
General measures		
It is recommended that all revascularized patients receive a secondary prevention and be scheduled for follow-up visit.	I	A
It is recommended to instruct patients before discharge about return to work and reuptake of full activities. Patients have to be advised to seek immediate medical contact if symptoms (re-)occur.	I	C
Antiplatelet therapy		
SAPT, usually aspirin, is recommended indefinitely.	I	A
DAPT is indicated after BMS for at least 1 month.	I	A
DAPT is indicated for 6 to 12 months after 2nd generation DES.	I	B
DAPT may be used for more than 1 year in patients at high ischaemic risk (e.g. stent thrombosis, recurrent ACS on DAPT, post MI/diffuse CAD) and low bleeding risk.	IIb	B
DAPT for 1 to 3 months may be used after DES implantation in patients at high bleeding risk or with undeferrable surgery or concomitant anticoagulant treatment.	IIb	C

ACS = acute coronary syndrome; BMS = bare-metal stent; CAD = coronary artery disease; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; MI = myocardial infarction; SAPT = single antiplatelet therapy.

This slide corresponds to Table 34 in the full text.

Follow-up of revascularized SCAD patients (2)

Recommendations	Class	Level
Imaging management		
In symptomatic patients, stress imaging (stress echocardiography, MRI or MPS) is indicated rather than stress ECG.	I	C
In patients with low risk ischaemic findings (<5% of the myocardium) at stress imaging, optimal medical therapy is recommended.	I	C
In patients with high risk ischaemic findings (>10% of myocardium) at stress imaging, coronary angiography is recommended.	I	C
Late (6 months) stress imaging test after revascularization may be considered to detect patients with restenosis after stenting or graft occlusion irrespective of symptoms.	IIb	C
After high risk PCIs (e.g. LM disease) late (3–12 months) control angiography may be considered, irrespective of symptoms. ^a	IIb	C
Systematic control angiography, early or late after PCI, is not recommended.	III	C

ECG = electrocardiogram; LM = left main; MPS = myocardial perfusion scintigraphy; MRI = magnetic resonance imaging; PCI = percutaneous coronary intervention.

^aSpecific patient subsets indicated for early stress testing:

- patients with safety critical professions (e.g. pilots, drivers, divers) and competitive athletes.
- patients who would like to engage in activities for, which high oxygen consumption is required.

This slide corresponds to Table 34 in the full text

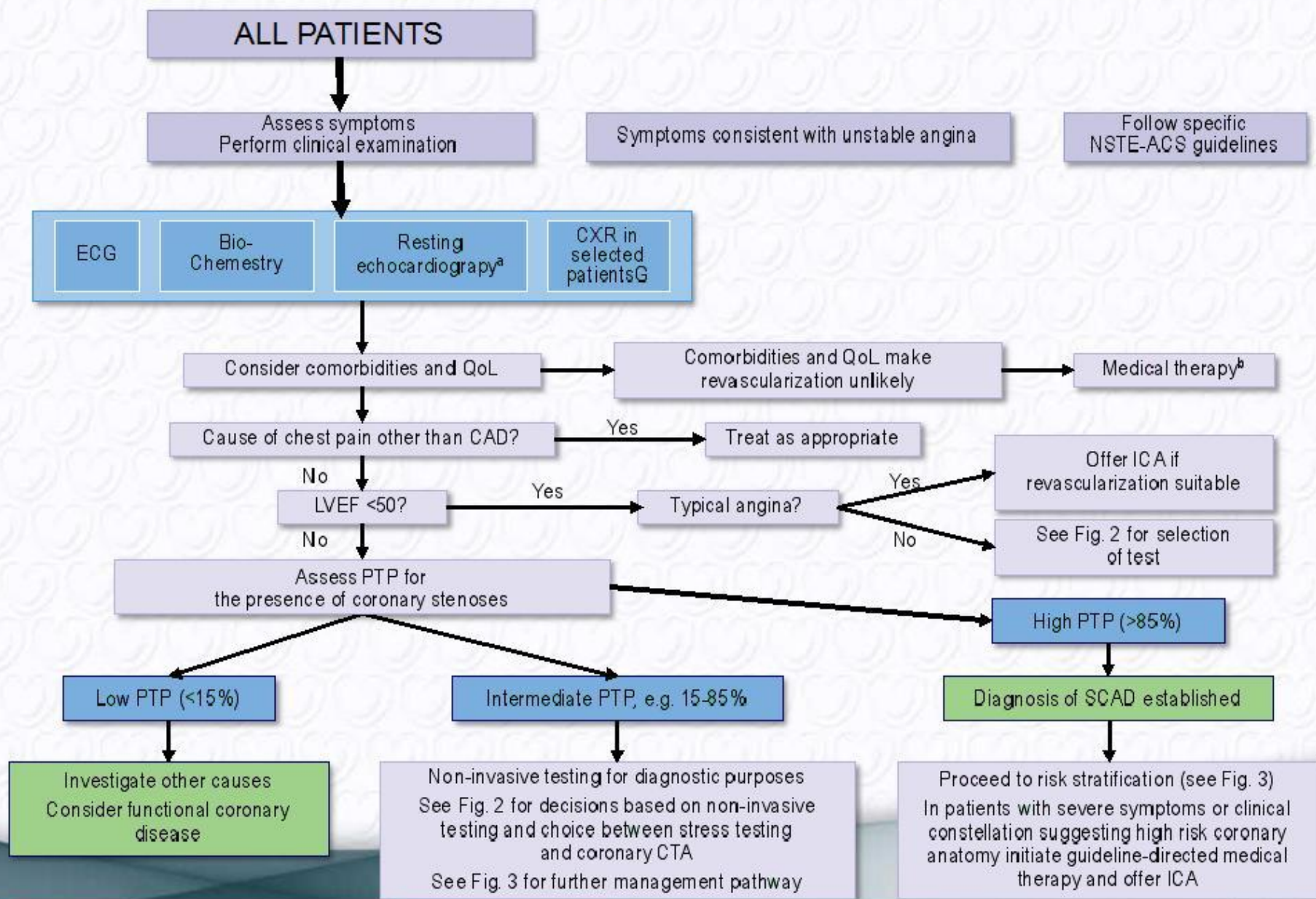
Treatment options in refractory angina

Recommendations	Class	Level
EECP should be considered for symptom relief in patients with invalidating angina refractory to optimal medical and revascularization strategies.	IIa	B
TENS may be considered to ameliorate symptoms of invalidating angina refractory to optimal medical and revascularization strategies.	IIb	C
SCS may be considered to ameliorate symptoms and quality of life in patients with invalidating angina refractory to optimal medical and revascularization strategies.	IIb	B
TMR is not indicated in patients with invalidating angina refractory to optimal medical and revascularization strategies.	III	A

EECP = enhanced external counterpulsation; TENS = transcutaneous electrical nerve stimulation;
TMR = transmyocardial revascularization; SC = spinal cord stimulation.

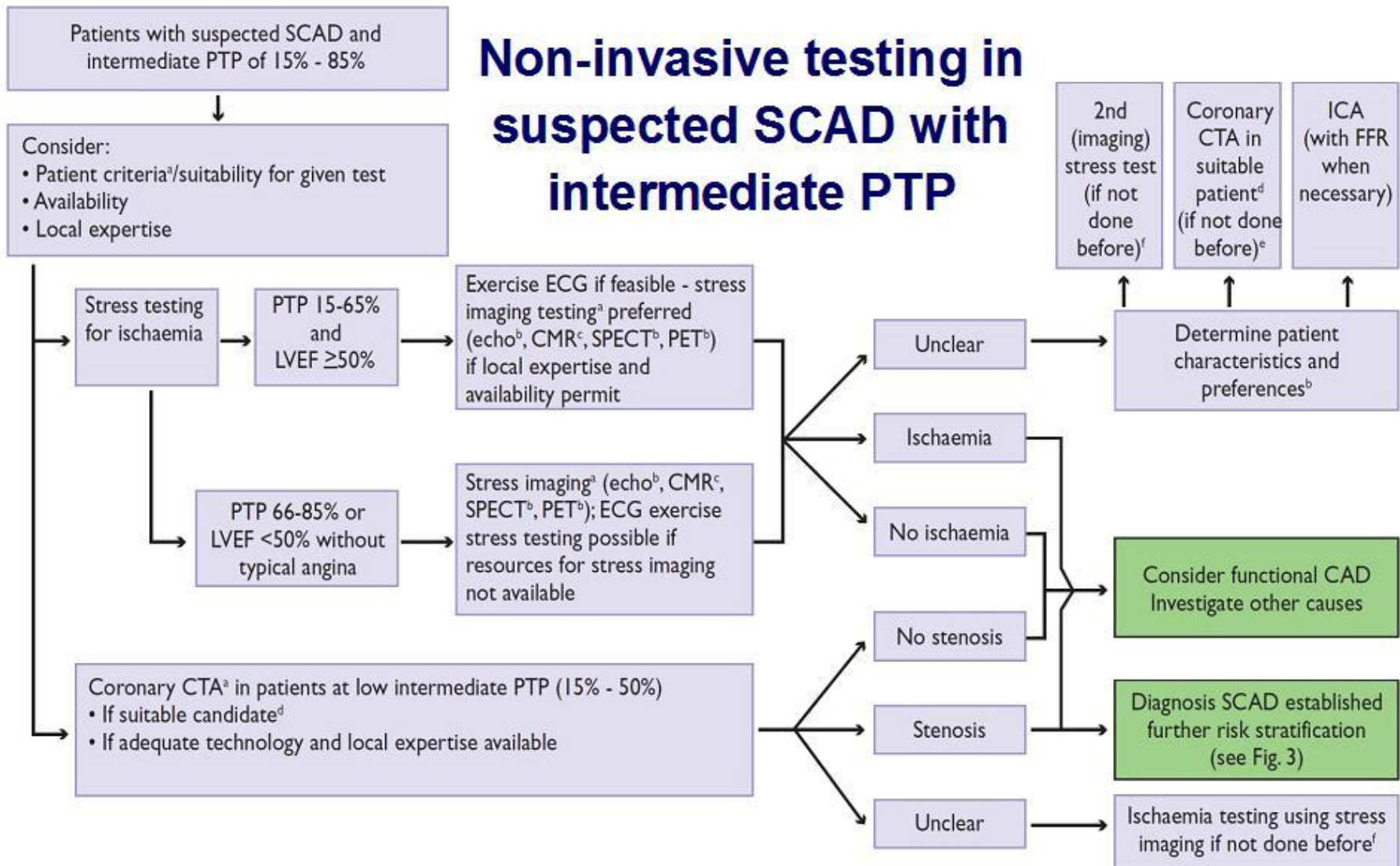
This slide corresponds to Table 35 in the full text.

Figure 1. Initial diagnostic management of patients with suspected SCAD



CTA = computed tomography angiography; CXR = chest X-ray; ICA = invasive coronary angiography; NSTE-ACS, non-ST-elevation acute coronary syndrome; PTP = pre-test probability; QoL = quality of life. ^aMay be omitted in very young and healthy patients with a high suspicion of an extra-cardiac cause of chest pain and in multimorbid patients in whom the echo result has no consequence for further patient management. ^bIf diagnosis of SCAD is doubtful, establishing a diagnosis using pharmacological stress imaging prior to treatment may be reasonable.

Non-invasive testing in suspected SCAD with intermediate PTP

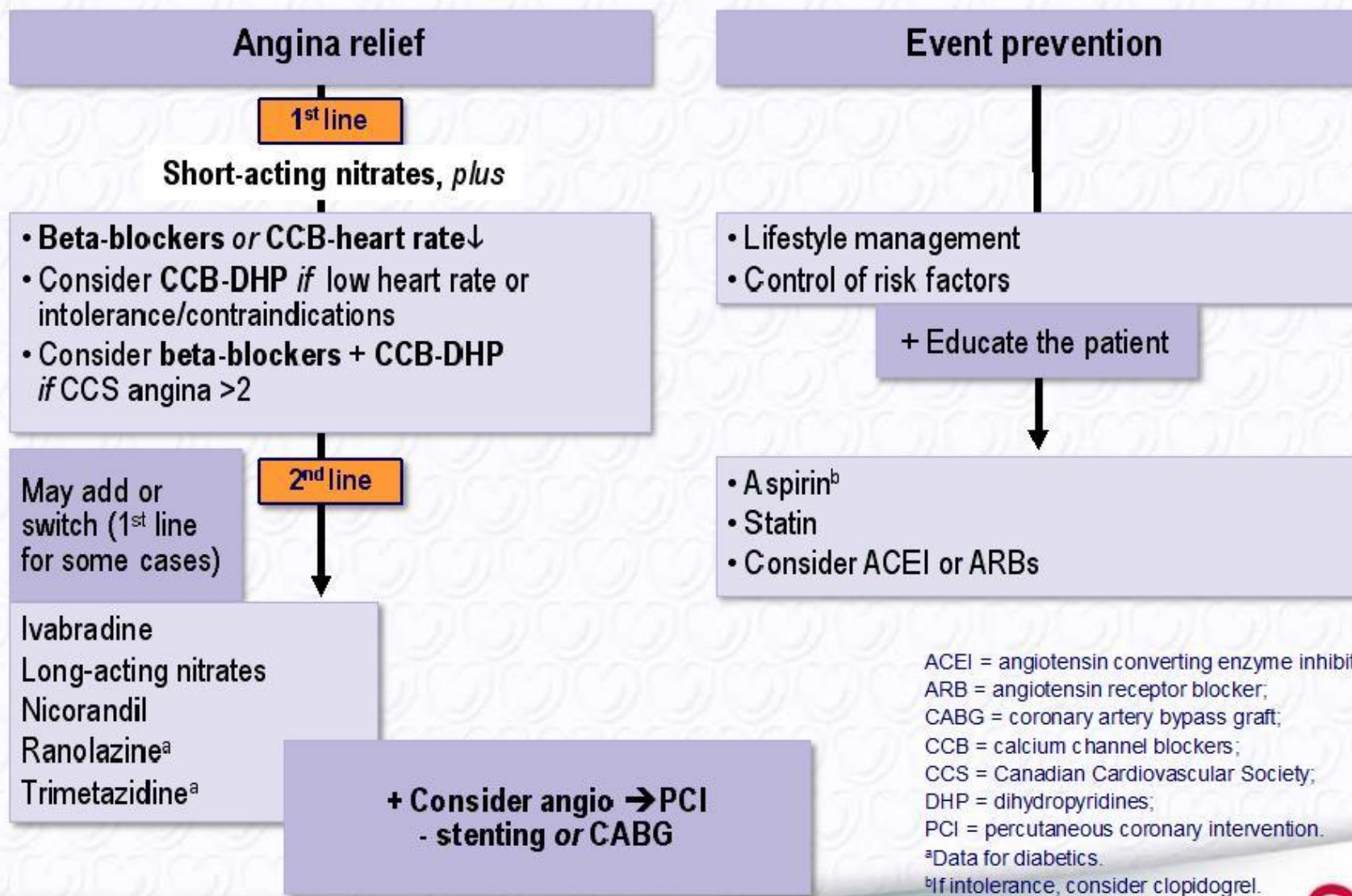


CAD = coronary artery disease; CTA = computed tomography angiography; CXR = chest X-ray; ECG = electrocardiogram; ICA = invasive coronary angiography; LVEF = left ventricular ejection fraction; PTP = pre-test probability; SCAD = stable coronary artery disease.

- Consider age of patient versus radiation exposure.
- In patients unable to exercise use echo or SPECT/PET with pharmacologic stress instead.
- CMR is only performed using pharmacologic stress.
- Patient characteristics should make a fully diagnostic coronary CTA scan highly probable (see section 6.2.5.1.2) consider result to be unclear in patients with severe diffuse or focal calcification.
- Proceed as in lower left coronary CTA box.
- Proceed as in stress testing for ischaemia box.

This slide corresponds to Figure 2 in the full text.

Medical management of patients with SCAD



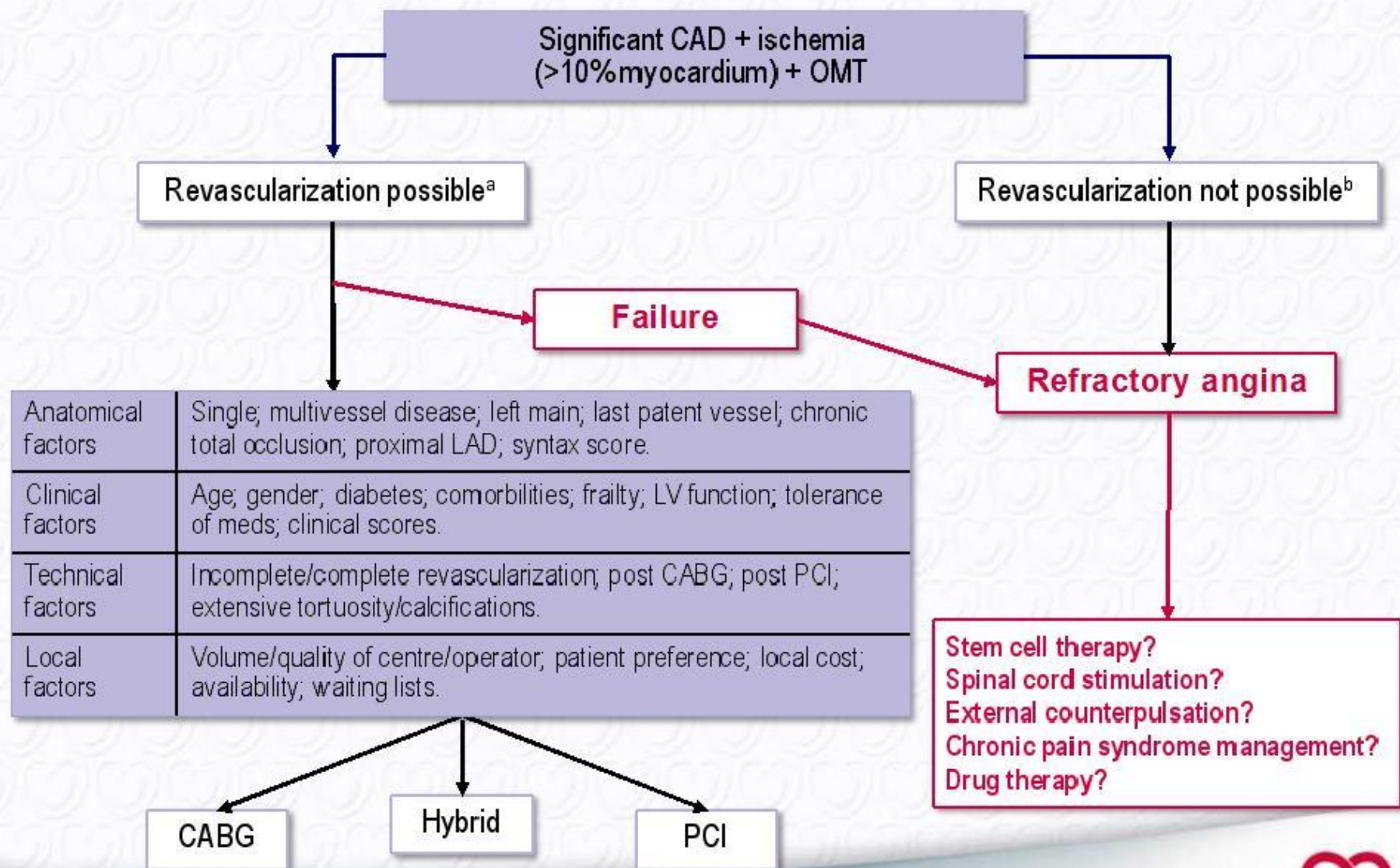
ACEI = angiotensin converting enzyme inhibitors;
ARB = angiotensin receptor blocker;
CABG = coronary artery bypass graft;
CCB = calcium channel blockers;
CCS = Canadian Cardiovascular Society;
DHP = dihydropyridines;
PCI = percutaneous coronary intervention.

^aData for diabetics.

^bIf intolerance, consider clopidogrel.

This slide corresponds to Figure 4 in the full text.

Global strategy of intervention in SCAD patients with demonstrated ischaemia

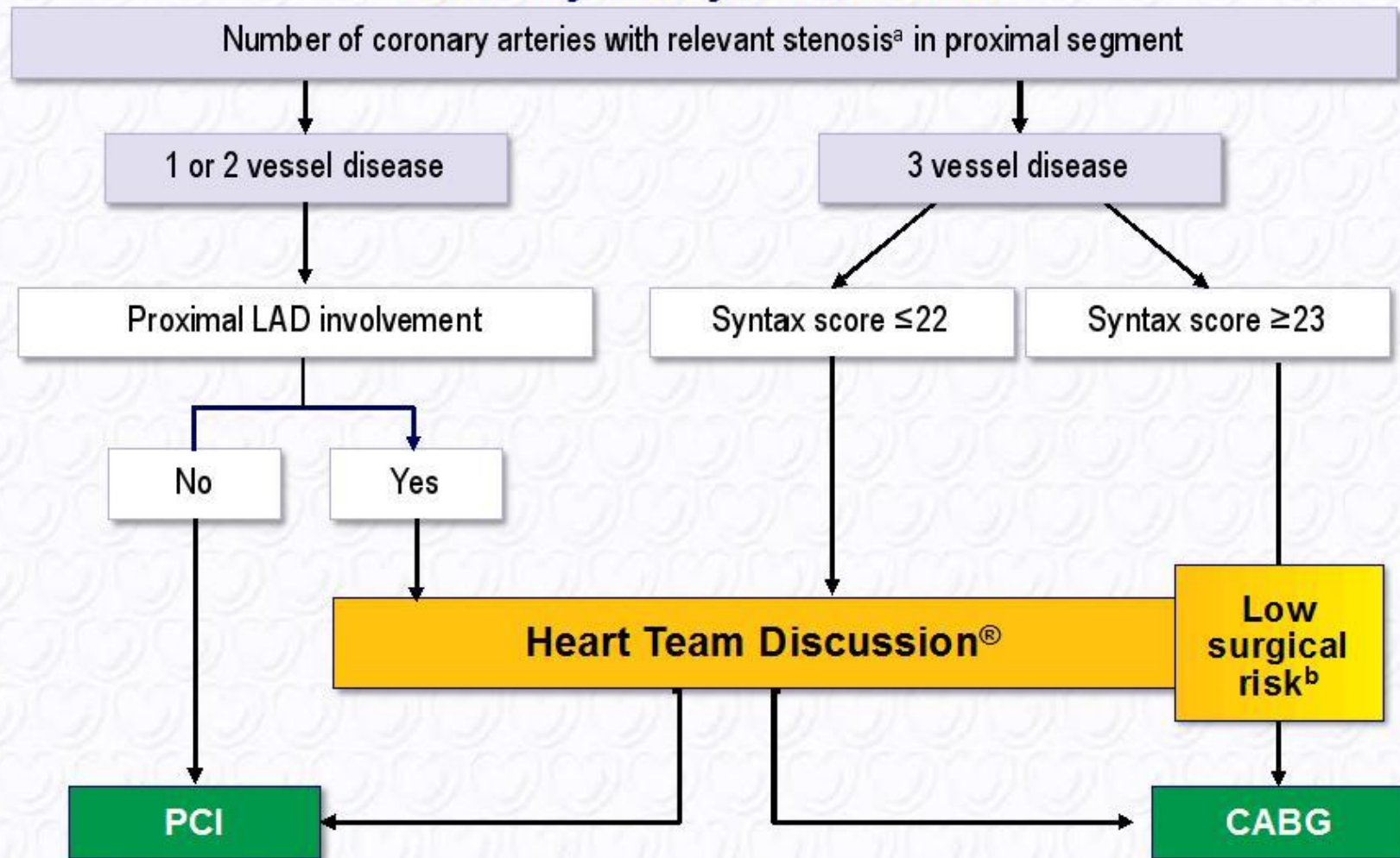


CABG = coronary artery bypass graft; CAD= coronary artery disease; LAD = left anterior descending; LV = left ventricular; OMT = optimal medical treatment, PCI = percutaneous coronary intervention. ^aIndication of revascularization for prognosis or symptoms (see Table 32). ^bNot suitable for revascularization due to anatomy or clinical conditions.

This slide corresponds to Figure 5 in the full text.

Eur Heart J 2013;34:2949–3003. doi:10.1093/eurheartj/eh296

PCI or CABG surgery in SCAD without left main coronary artery involvement

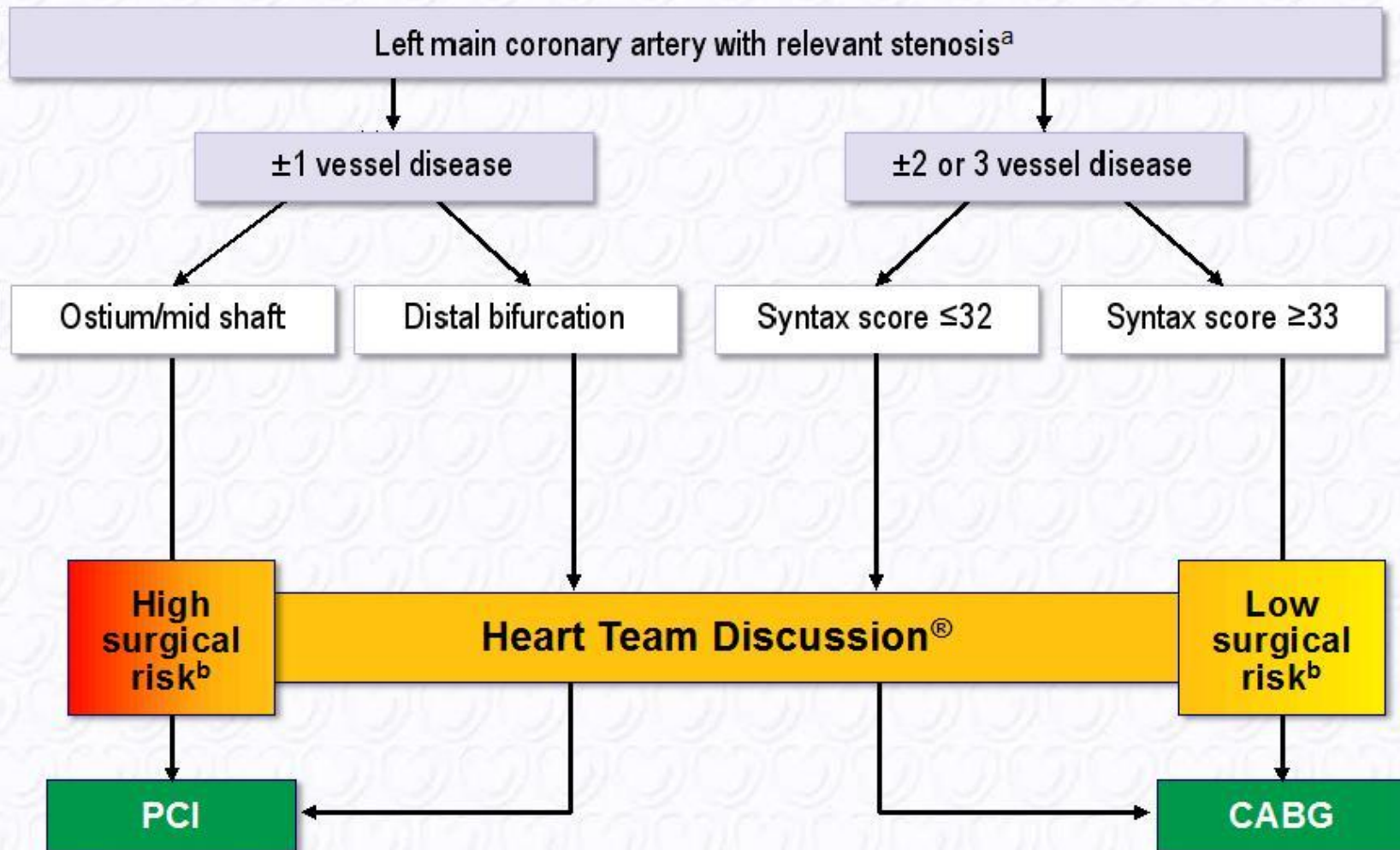


CABG = coronary artery bypass graft; LAD = left anterior descending; PCI = percutaneous coronary intervention.

^a >50% stenosis and proof of ischaemia, >90% stenosis in two angiographic views, or FFR < 0.80. ^b CABG is the preferred option in most patients unless patients comorbidities or specificities deserve discussion by the Heart Team. According to local practice (time constraints, workload) direct transfer to CABG may be allowed in these low risk patients, when formal discussion in a multidisciplinary team is not required (adapted from ESC/EACTS Guidelines on Myocardial Revascularization 2010).

This slide corresponds to Figure 6 in the full text.

PCI or CABG surgery in SCAD with left main coronary artery involvement



CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.

^a>50% stenosis and proof of ischaemia, >70% stenosis in two angiographic views, or fractional flow reserve < 0.80.

^bPreferred option in general. According to local practice (time constraints, workload) direct decision may be taken without formal multidisciplinary discussion, but preferably with locally agreed protocols (adapted from ESC/EACTS Guidelines on Myocardial Revascularization 2010).

This slide corresponds to Figure 7 in the full text.

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2013 ESC Guidelines on Management of Stable Coronary Artery Disease*

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* Adapted from the ESC Guidelines on the management of stable coronary artery disease (Eur Heart J 2013 - doi: 10.1093/eurheartj/ehz296).

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