

A collection of overlapping squares in various shades of light blue and white, some with solid fills and some as outlines, arranged in a scattered pattern in the top left corner of the slide.

Dr Rohit Khurana

Senior Consultant General and Interventional Cardiologist

A cluster of overlapping, light blue-outlined squares and rectangles of various sizes and orientations, scattered in the upper left quadrant of the slide.

Optimizing Treatment for patients with Coronary Artery Disease and Diabetes

Definition

Stable coronary artery disease

- Generally characterized by episodes of reversible myocardial demand/supply mismatch, related to ischaemia or hypoxia – causes transient chest discomfort (angina)
- Usually inducible by exercise, emotion or other stress and reproducible—but, which may also be occurring spontaneously.
- SCAD also includes the stabilized, often asymptomatic, phases that follow an acute coronary syndrome.

Montalescot G, et al. Guidelines on the management of stable coronary artery disease. Eur Heart J. 2013;34(38):2949-3003.

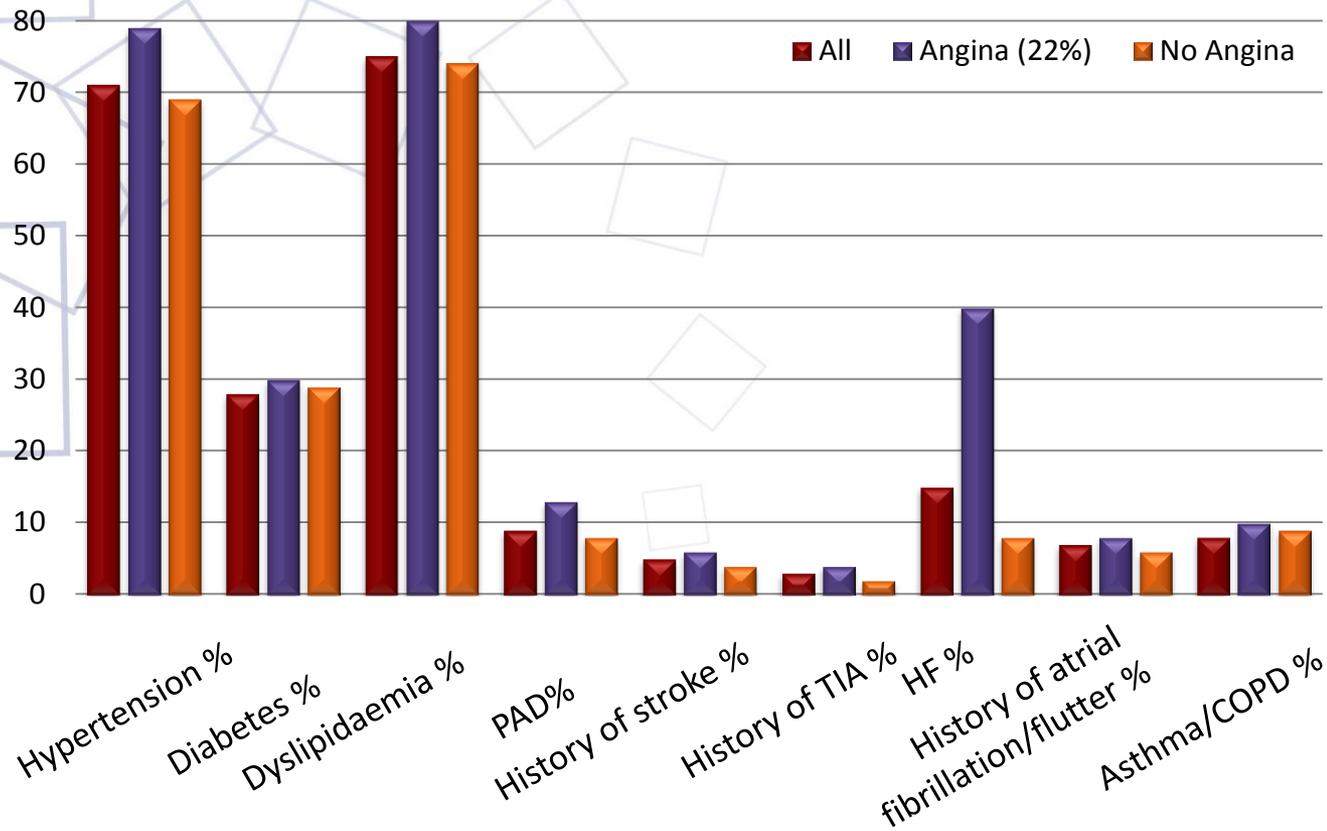
Classification of Chest Pain

- **Typical angina (definite)**
 - ❑ **Substernal chest discomfort: characteristic quality, duration**
 - ❑ **Provoked by stress;**
 - ❑ **relieved by rest or nitroglycerin**

- **Atypical angina (probable)**
 - ❑ **Meets 2 of the above characteristics**

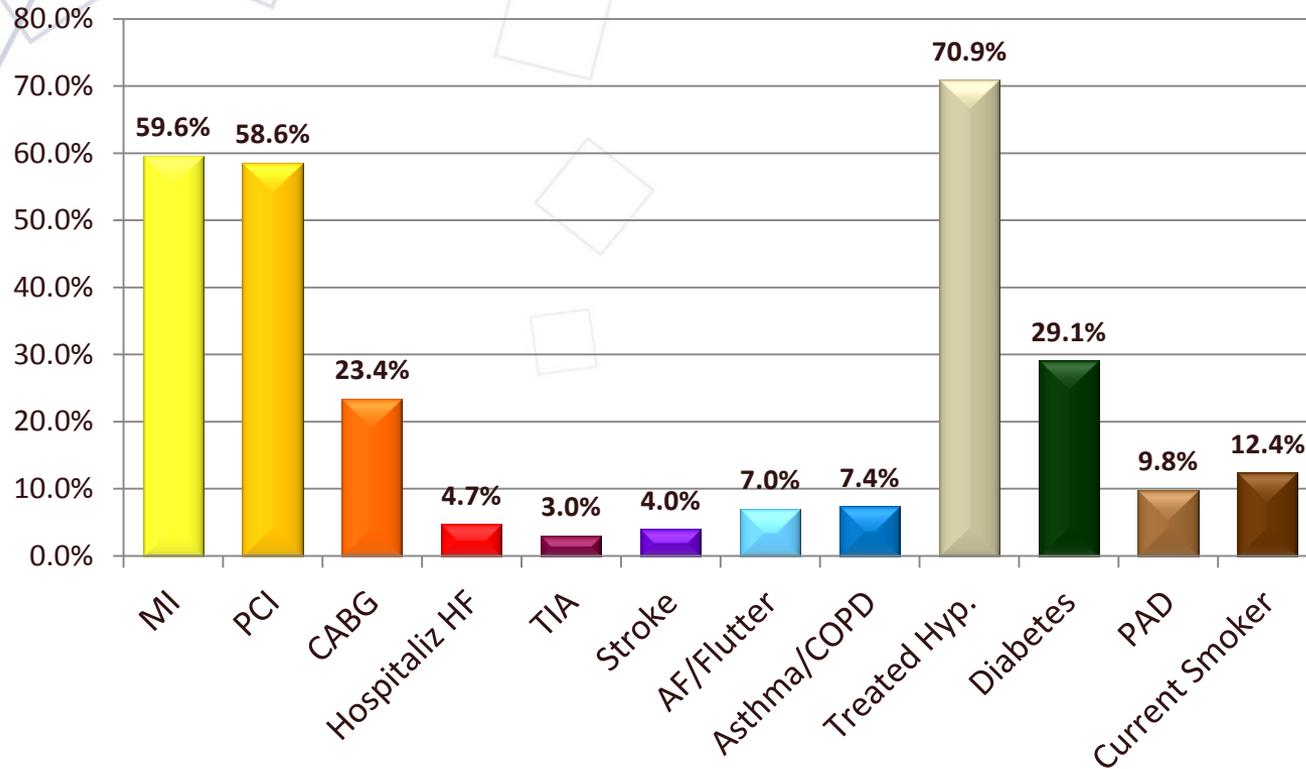
- **Non-cardiac chest pain**
 - ❑ **Meets ≤ 1 of typical angina characteristics**

Prevalence of co-morbidities in patients with SCAD



CLARIFY is an international, prospective, observational, longitudinal cohort study in stable CAD outpatients (more than 33,000 from 45 countries). Patients were enrolled between 2009 and 2010, with a 5-year follow-up.

Medical History and lifestyle in patients with CAD. Data from CLARIFY registry



Data extrapolated from: Ferrari et al. *Int J Cardiol* 2013;167:2938-2943

Investigation of Patients referred for Chest Pain

- **Electrocardiogram**
 - ❑ **All patients: resting ECG**
- **Chest X-ray**
 - ❑ **If no obvious noncardiac cause of angina**
- **Echocardiography (rest) – for most patients**
 - ❑ **To document LV systolic function and exclude cardiac valvular lesions**
 - ❑ **If ECG findings show a pathologic Q-wave**

How should information from the physical exam be used to evaluate people with SIHD?

- May reveal related conditions (HF, valvular heart disease)
- **Signs suggesting CAD (only present during chest pain)**
 - ❑ **S3 or S4 gallop, mitral regurgitant murmur, bibasilar rales, paradoxically split S2, or chest wall heave**
- **Signs of CHD**
 - ❑ **Jugular venous pulsation, S3 gallop, mitral regurgitation murmur, displaced apical impulse, pulmonary crackles, diminished breath sounds, dullness to percussion, abdomino-jugular reflux, hepatomegaly, lower extremity edema**
- **Signs of noncoronary atherosclerotic vascular disease**
 - ❑ **Carotid bruit, diminished / absent pedal pulses, abdominal aneurysms**
- **Xanthelasma and xanthomas: hyperlipidemias**

Which diagnostic tests should follow preliminary Investigations?

- Standard exercise ECG
- If exercise ECG can't be interpreted / performed:
BBB, Repolarization abnormalities

Consider

Exercise Stress ECHO

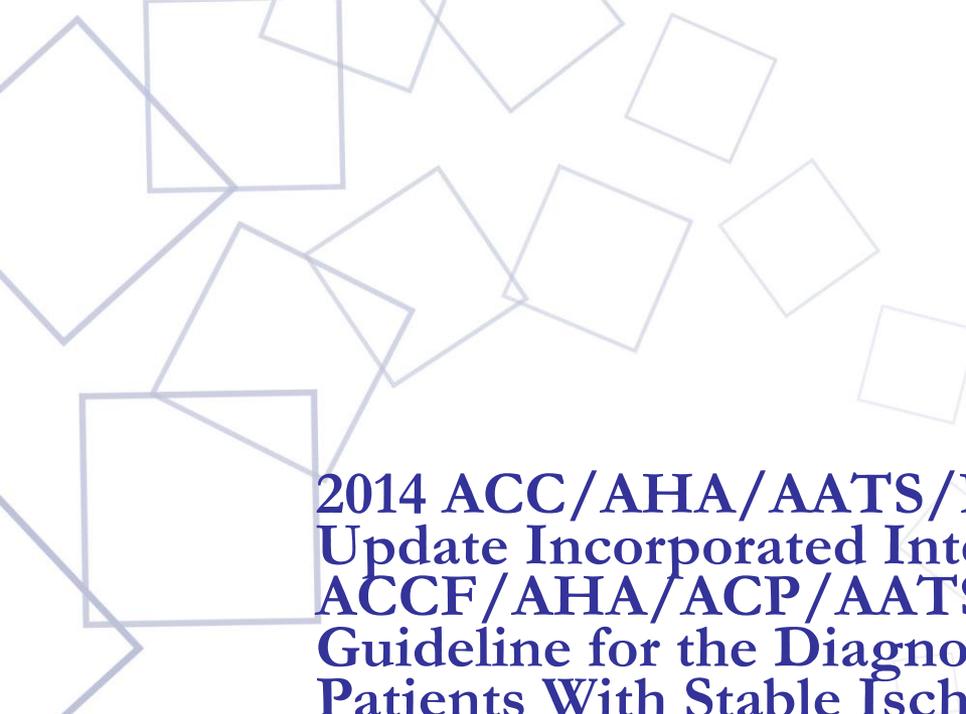
Pharmacologic (Dobutamine) Stress ECHO

Important to estimate the probability of disease separately from the mortality risk?

- If <5% probability of CAD: look for **other causes of pain**
 - ❑ Predictors of CAD
 - Patient age, sex, and type of angina
 - Smoking history, hyperlipidemia, diabetes
- Nonischemic CV: aortic dissection, pericarditis
- Pulmonary: embolus, pneumothorax, pneumonia, pleuritis

In the majority of cases, it is possible to make a confident diagnosis on the basis of the **history alone**, although **physical examination and objective tests** are often necessary to **confirm the diagnosis** exclude alternative diagnoses, and **assess the severity** of underlying disease.

- Pancreatitis
- Chest wall: costochondrosis, fibrositis, rib fracture, sternoclavicular arthritis, herpes zoster (before the rash)
- Psychiatric: anxiety/ affective/ somatoform/ thought disorders



**2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused
Update Incorporated Into the 2012
ACCF/AHA/ACP/AATS/PCNA/SCAI/STS
Guideline for the Diagnosis and Management of
Patients With Stable Ischemic Heart Disease**

© American College of Cardiology Foundation and American Heart Association, Inc.

When is Cardiac CT Indicated?



CCTA is reasonable for patients with an intermediate pretest probability of IHD who a) have **continued symptoms with prior normal test findings**, or b) have **inconclusive results from prior exercise or pharmacological stress testing**, or c) are unable to undergo stress with nuclear MPI or echocardiography.



For patients with a low to intermediate pretest probability of obstructive IHD, CAC score may be considered.

➤ Coronary artery calcium scoring:

- ↓ Score identifies people w/o CAD
- ↑ Score is less reliable in ruling in CAD

When is Coronary Angiography Indicated?



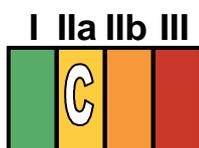
Patients with SIHD who have **survived sudden and MI, cardiac death or potentially life-threatening ventricular arrhythmia** should undergo coronary angiography to assess cardiac risk.



Patients with SIHD who **develop symptoms and signs of heart failure** should be evaluated to determine whether coronary angiography should be performed for risk assessment.



Patients with presumed SIHD who have **unacceptable ischemic symptoms despite Medical therapy** and who are amenable to, and candidates for, **coronary** revascularization.



To define the extent and severity of CAD in patients with suspected SIHD whose clinical characteristics and results of noninvasive testing (*exclusive of stress testing*) **indicate a high likelihood of severe IHD** and who are amenable to, and candidates for, coronary revascularization.

CAD Prognostic Index

Extent of CAD	Prognostic Weight (0–100)	5-Year Survival Rate (%)*
1-vessel disease, 75%	23	93
1-vessel disease, 50% to 74%	23	93
1-vessel disease, $\geq 95\%$	32	91
2-vessel disease	37	88
2-vessel disease, both $\geq 95\%$	42	86
1-vessel disease, $\geq 95\%$ proximal LAD artery	48	83
2-vessel disease, $\geq 95\%$ LAD artery	48	83
2-vessel disease, $\geq 95\%$ proximal LAD artery	56	79
3-vessel disease	56	79
3-vessel disease, $\geq 95\%$ in ≥ 1 vessel	63	73
3-vessel disease, 75% proximal LAD artery	67	67
3-vessel disease, $\geq 95\%$ proximal LAD artery	74	59

*Assuming medical treatment only.

What are the Goals of treatment?

- Minimize likelihood of death & maximize health and function
 - Reduce premature CV death
 - Prevent complications that impair functional well-being
- **Strategies for achieving treatment goals**
 - Patient education**
 - Lifestyle modification**
 - Medical therapy**
 - Revascularization (coronary artery bypass grafting or PCI)**
 - Use guideline-directed medical therapy — whether or not revascularization occurs**

Which Patients deserve immediate revascularization?

- To improve survival if mortality risk is high
 - Left main or complex CAD
 - >50% stenosis in left main coronary artery
 - >70% in 3 major coronary arteries
 - >70% in proximal left anterior descending artery + 1 other major coronary artery
 - Survivors of sudden cardiac death (presumed ischemia-mediated ventricular tachycardia from >70% stenosis in major coronary artery)
- **To relieve symptoms if they persist despite therapy**
 - ❑ **For stenosis likely to affect survival: same recommendations**
 - ❑ **Other patients with >70% stenosis in ≥ 1 coronary arteries**

Special Considerations for: Women, Older Adults, Diabetics and CKD

▶ **Women**

- More atypical chest pain + angina-equivalent symptoms
- Tend to be treated less aggressively (bc different presentation and testing compared to men?)

▶ **Older adults**

- ❑ Diagnosis and stress testing harder due to physiologic changes of aging, coexisting conditions
- ❑ Receive less evidence-based care (bc pharmacotherapy more difficult? bc of increased CABG morbidity, mortality?)

▶ **Diabetes mellitus**

- ❑ Greater risk of SIHD + magnified effects of other risk factors

▶ **Chronic kidney disease**

- ❑ Greater risk of SIHD + poor outcomes after AMI interventions

Case Vignette

56 y/o Singaporean Chinese lady – referred for upper back pain

Worse with exertion

Sometimes worse after meals

Radiates to the front of chest

Informed by orthopedic surgeon to have scoliosis

Continuing for ~ 2 yrs; “not helped by physiotherapy”

Pains now almost daily

Cardiovascular examination unremarkable

Risk factors

Chronic dyslipidemia – resistant for many years to commencing statins

Medications: Lipitor 20mg on

QRISK 2: 4.2% 10 yr risk

Cardiac Investigations

ECHOcardiogram: Normal LV function, morphologically normal valves & function

Treadmill Test

Case Vignette

THE HARLEY STREET HEART & CANCER CENTRE EXERCISE STRESS TEST REPORT

Patient ID: S1424091H
 Height: [REDACTED]
 Study Date: 26.07.2016
 Test Type: --
 Protocol: BRUCE

DOB: 05.04.1960
 Age: 56yrs
 Gender: Female
 Race:
 Referring Physician: --
 Attending Physician: DR REGIN.
 Technician: IAN CORPUZ

Medications:
 --

Reason for Exercise Test:
 --

Exercise Test Summary

Phase Name	Stage Name	Time in Stage	Speed (km/h)	Grade (%)	HR (bpm)	BP (mmHg)	Comment
PRETEST	SUPINE	07:36	1.60	0.00	96	136/72	
EXERCISE	STAGE 1	03:00	2.70	10.00	150		
	STAGE 2	00:07	4.00	12.00	150		
RECOVERY		01:00	0.00	0.00	126	171/97	
		04:21	0.00	0.00	88	133/77	

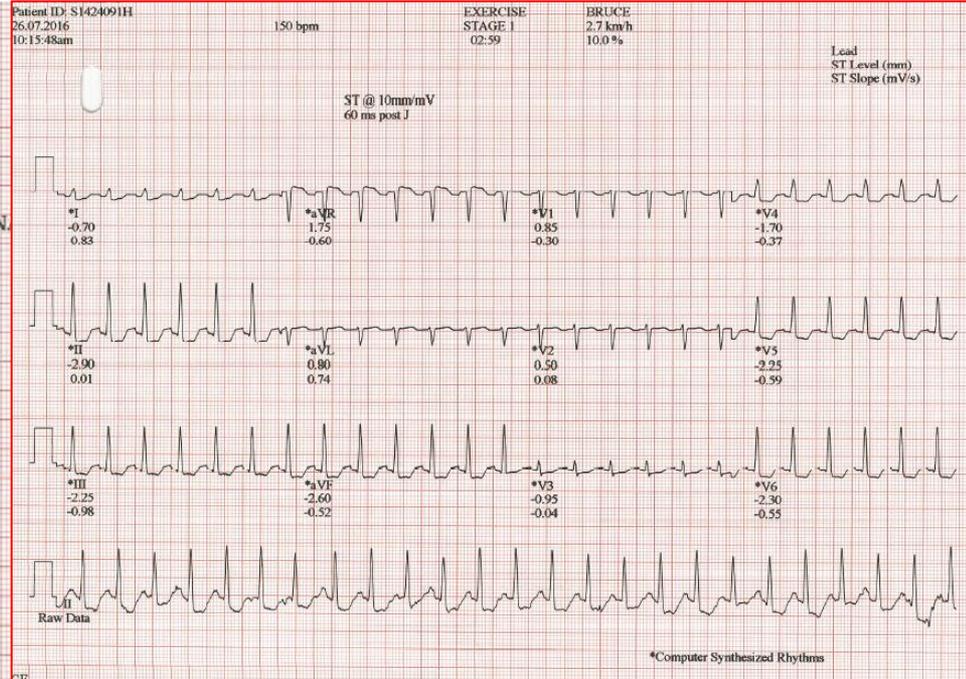
The patient exercised according to the BRUCE for 3:07 min:s, achieving a work level of Max. METS: 4.80. The resting heart rate of 82 bpm rose to a maximal heart rate of 151 bpm. This value represents 92 % of the maximal, age-predicted heart rate. The resting blood pressure of 136/72 mmHg, rose to a maximum blood pressure of 179/87 mmHg. The exercise test was stopped due to back pain.

Interpretation

Summary: Functional Capacity: Limited exercise capacity.
 Symptoms/Chest Pain: No Chest Pain with exercise, Back pain during exercise.
 ST Changes: 1-2 mm inferolateral ST depression at low workload.

Conclusions

POSITIVE treadmill test.



Case Vignette

56 y/o Singaporean Chinese lady – referred for upper back pain

Risk factors

Chronic dyslipidemia – resistant for many years to commencing statins

Pre-treatment Fasting lipid profile

Total chol 304

HDL chol 54

LDL chol 232

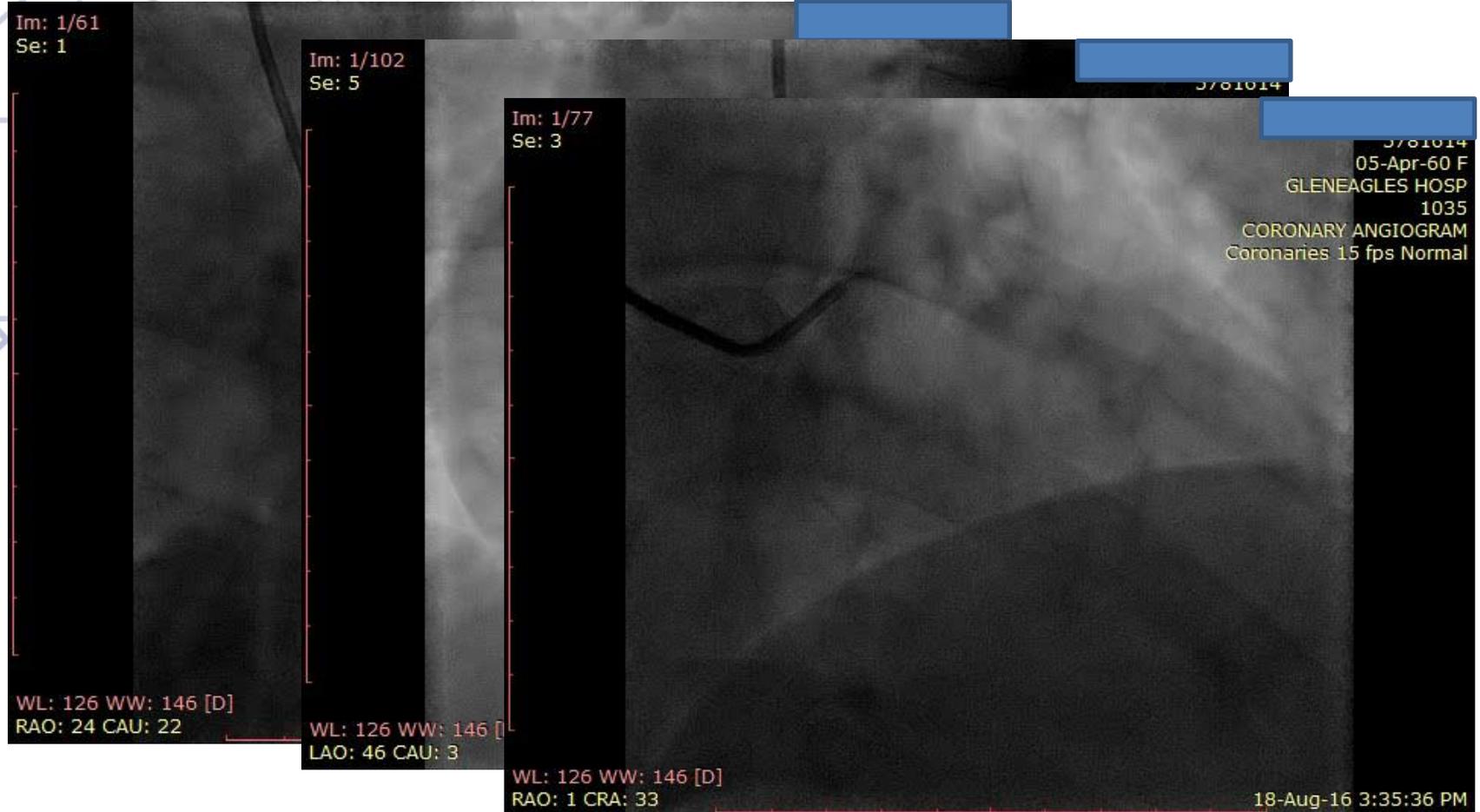
TG 89

Medications: Lipitor 20mg on

High Pre-test likelihood of CAD

Advised to proceed with angiography

Coronary Angiogram



Case Vignette

56 y/o Singaporean Chinese lady – referred for upper back pain

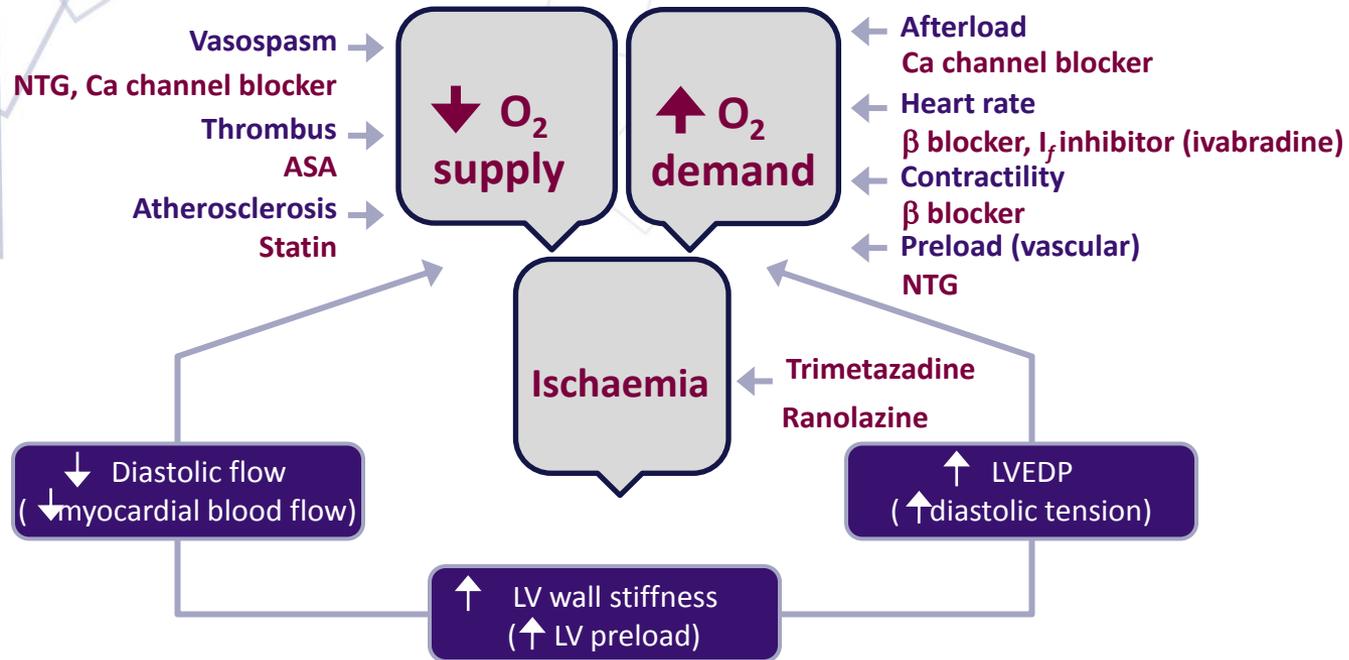
Medications: Lipitor 20mg on

Aspirin 75mg od, Plavix 75mg od, Pariet 20mg od

Bisoprolol 2.5mg od, Vasteral MR 35 mg bd

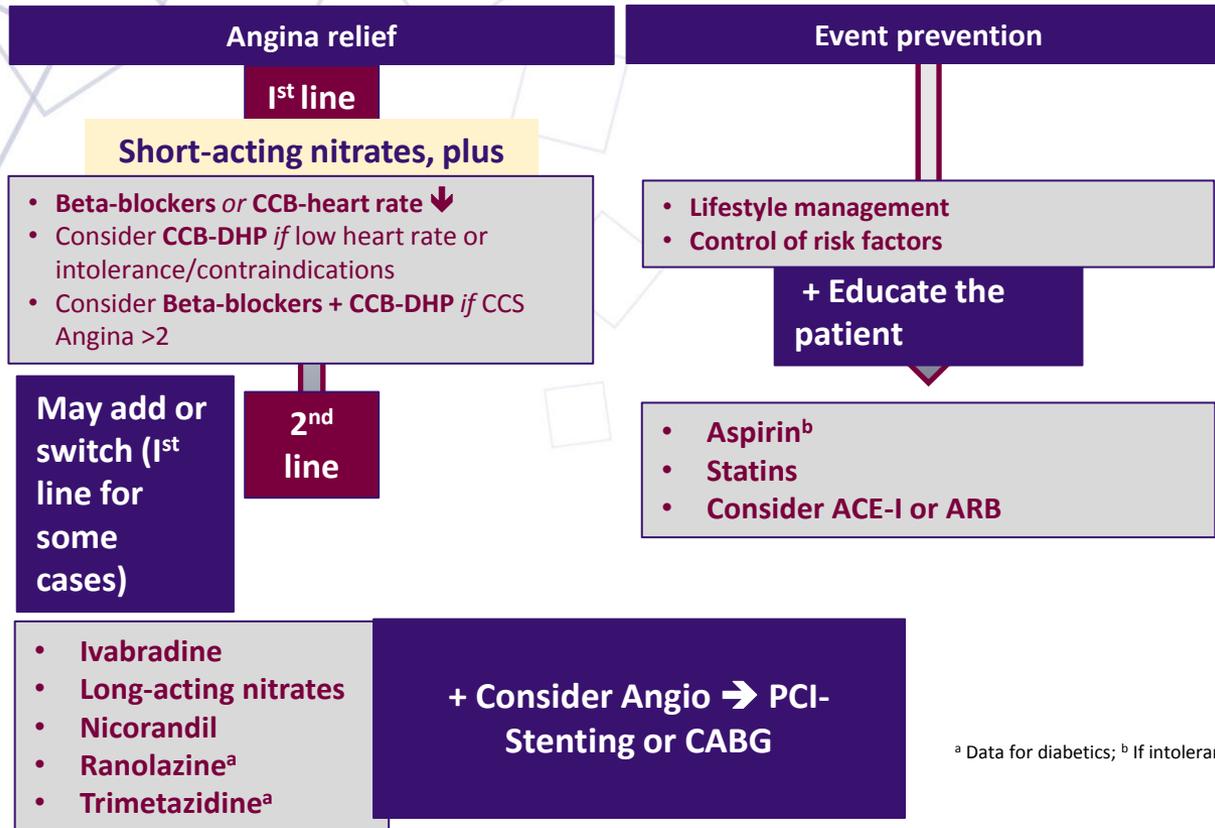
For revascularization → to alleviate angina, improve prognosis

Principles of Medical Therapy



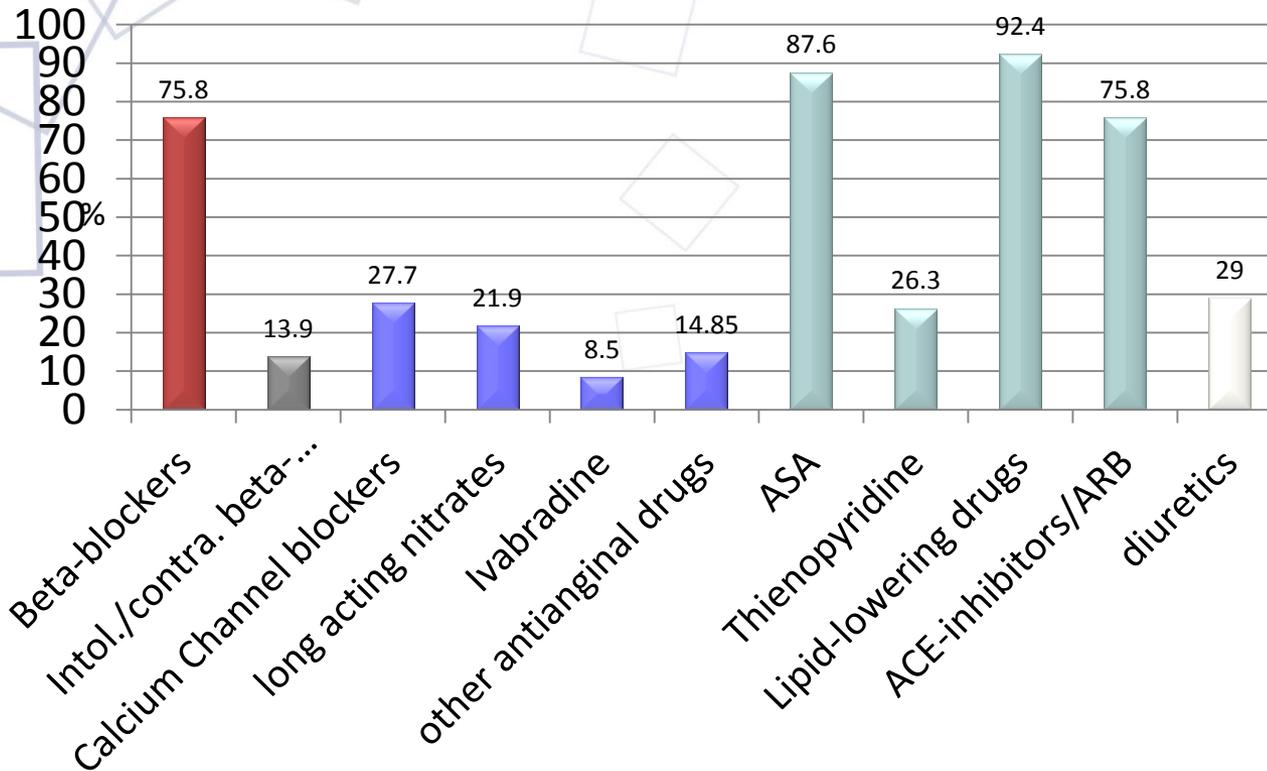
Adapted from Morrow DA, Boden WE. Chapter 57: Stable Ischemic Heart Disease. In: Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 9th ed. (2012). Saunders; pp 1210-1269. Michel T, Hoffman BB. Chapter 27: Treatment of myocardial Ischemia & Hypertension. In: Brunton LL, et al. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 12th ed. (2011). McGraw-Hill. Stone PH, et al. *Cardiol Clin* 2008;26:603-614.

ESC 2013 algorithm for the medical management of stable CAD



^a Data for diabetics; ^b If intolerance, consider clopidogrel.

CLARIFY registry : Treatment Strategies



Data extrapolated from Pozzoli et al. *G Ital Cardiol* 2014;15(4):226-232

ESC Guidelines

New ESC Guidelines published on stable coronary artery disease

The Guidelines give imaging a greater role in CAD diagnosis and introduce controlling heart rate as the new treatment goal for medical therapy



Gilles Montalescot



Udo Sechtem

“Controlling heart rate is the new treatment goal for medical therapy in the 2013 Guidelines.

First line treatment should be with β -blockers or calcium channel blockers, both of which are readily available.

Second line treatment includes long-acting nitrates and new drugs on the market such as ivabradine or ranolazine.”

ESC Guidelines

Recommended Management of Stable Angina: Where is the Evidence?

ESC Guidelines: β -blockers

Extrapolated from the post-MI trials that beta-blockers *may be cardioprotective* also in patients with SCAD

However : **Not been proven in a placebo-controlled trial.**

The beta-blockers trials post-MI were performed before the implementation of other secondary preventive therapy, such as treatment with statins and ACE-I's, *which leaves some uncertainty* regarding their efficacy on top of a modern treatment strategy.

ESC Guidelines: Calcium Channel Blockers

Heart rate lowering CCBs *may improve* the prognosis of post-MI patients
... prognostic documentation in stable CHD *has not been available*
for dihydropyridine CCBs until recently

European Heart Journal (2013) 34, 2927–2930

ESC Guidelines: β -blockers vs CCB

Concluded *that there is no evidence* to discriminate between BB and CCB for the initial treatment of people with stable angina.

Randomized trials of BBs and CCBs in people with stable angina have mainly studied older drugs. The trials *selectively* recruited patients who were suitable for treatment with either a BB or CCB.

Limitations of Current Evidence

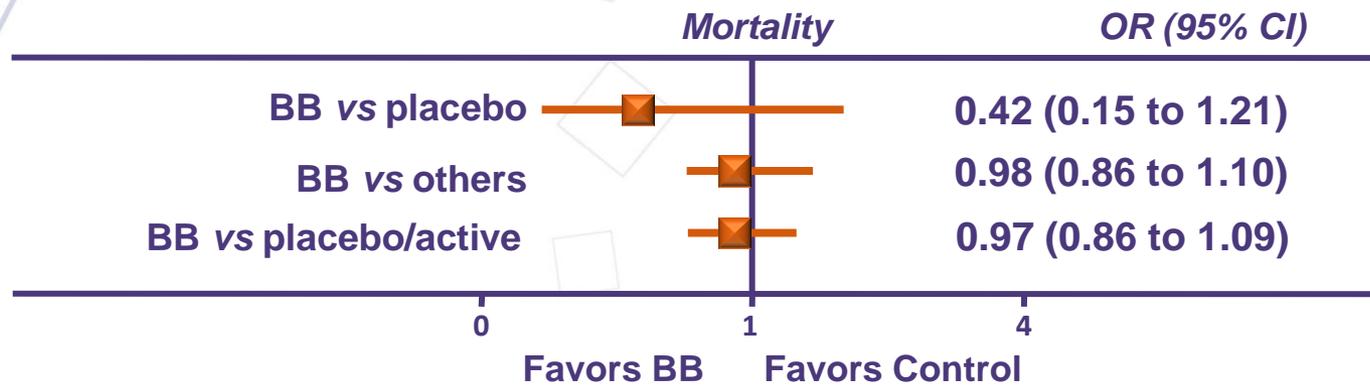
Information about long term effects of BBs and CCBs *is very limited*

Most trials were not designed to study the effects of treatment on mortality or other major CV outcomes, are limited by small study size, and only report short to medium term follow-up.

National Clinical Guidelines Centre; 2011. Stable angina: FULL guideline (July 2011)

The impact of beta-blockers on mortality in stable angina: a meta-analysis

89 randomized trials with 21,674 patients with stable angina



Beta-blockers did not have statistically significant impact on mortality versus placebo or versus other active comparators.

OR, odds ratio; CI, confidence interval

Published literature was searched from 1966 to 2009 in online databases, including MEDLINE, EMBASE and CINAHL. 29 trials of beta-blockers (n=2,315 patients) versus placebo and 60 trials of beta-blockers (n=19,343) versus other antianginals were identified that met the criteria. Cardiovascular mortality was selected as the primary outcome measure.

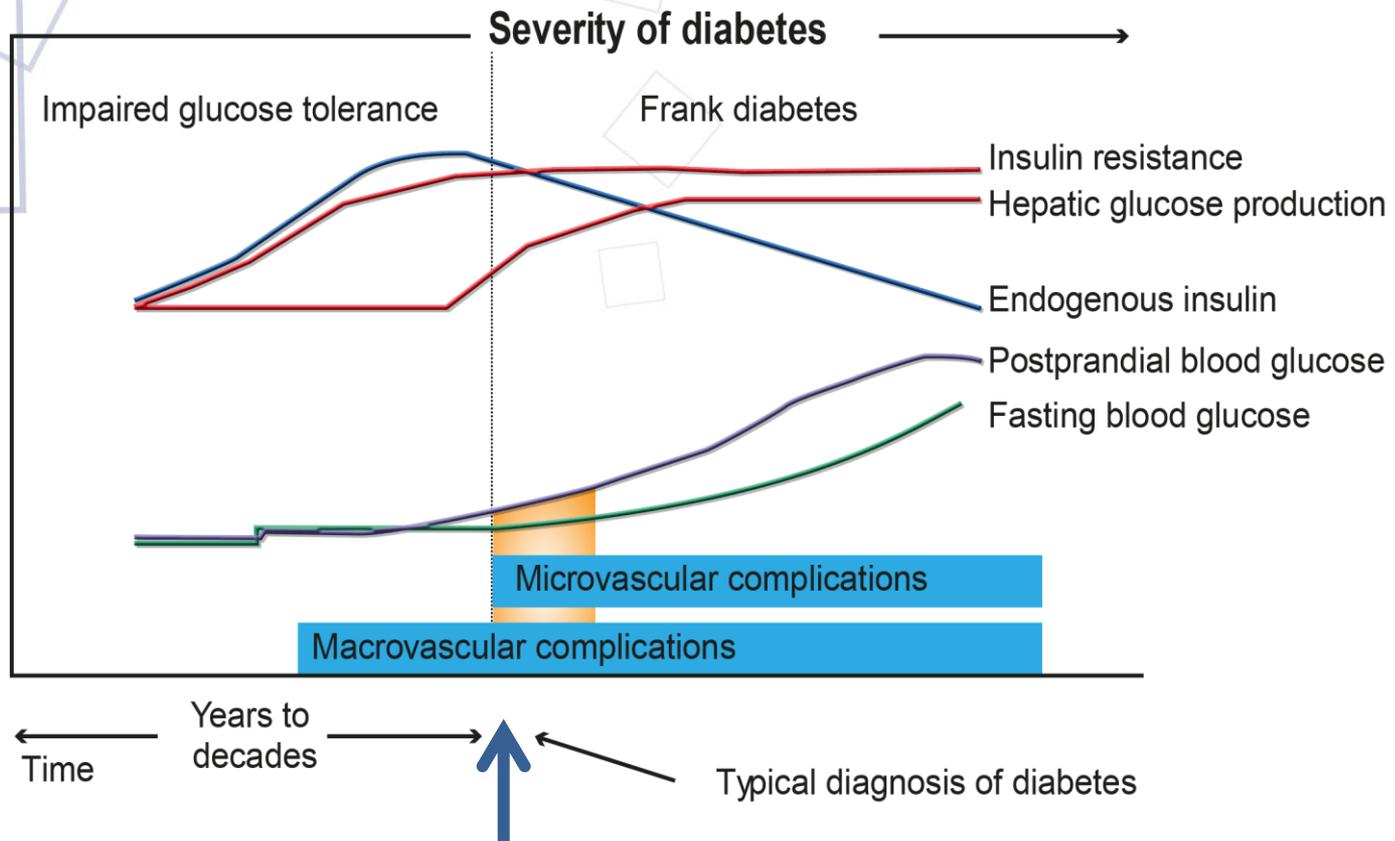
SCAD and DIABETES : Epidemiology

- Over 60% of patients with T2D develop CVD (2)
- Mortality due to CVD is increased 3x in diabetic men and 2-5x in diabetic women, compared with age and sex-matched non-diabetic persons.(1)
- CVD risk assessment should be given a higher priority in T2 diabetes patients

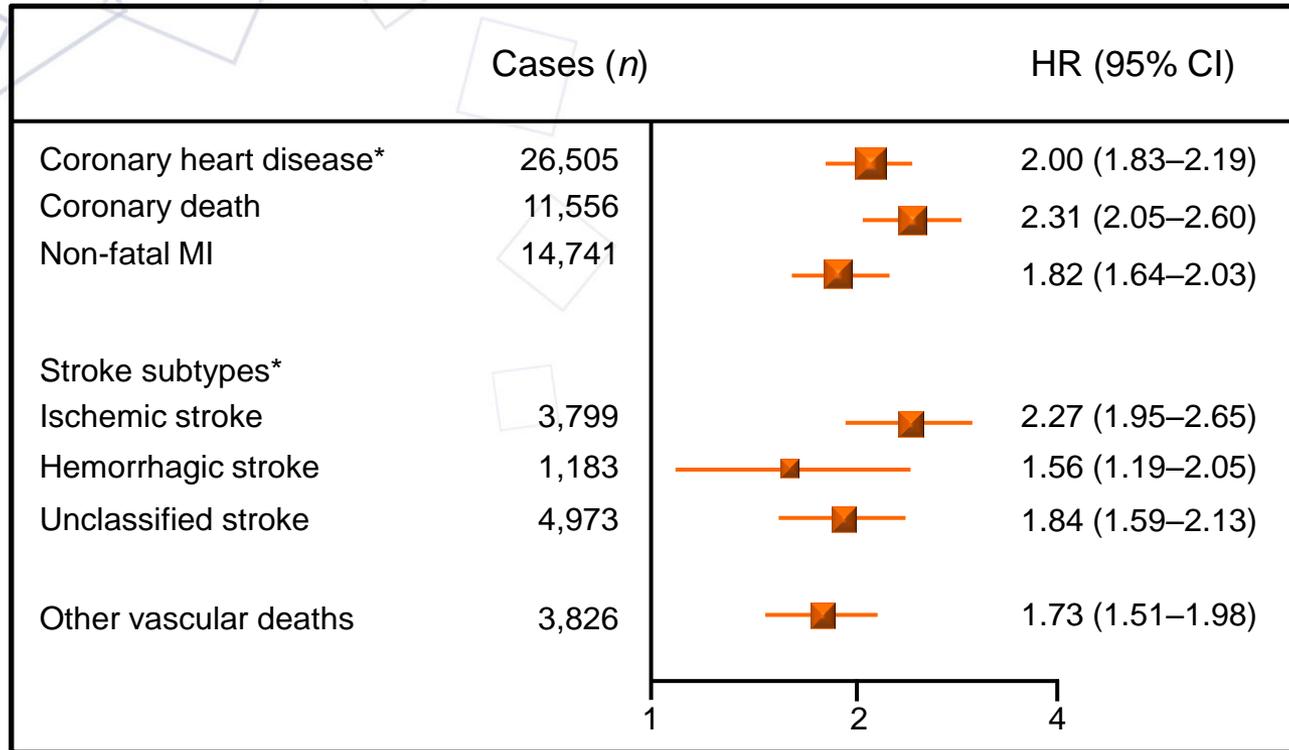
1. *Eur Heart J.* 2013;34(38):2949-3003

2. *Eur Heart J* 2013; 34, 3035–3087

Glycaemic continuum and cardiovascular disease



Vascular outcomes are worse in people with diabetes *versus* those without



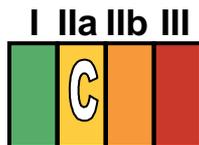
Meta-analysis of 102 prospective studies

*Includes both fatal and non-fatal events

Diabetes Management in SCAD patients



For selected individual patients, such as those with a short duration of diabetes mellitus and a long life expectancy, **a goal HbA1c of 7% or less is reasonable.**



A goal HbA1c **between 7% and 9% is reasonable for certain patients** according to age, history of hypoglycemia, presence of microvascular or macrovascular complications, or presence of coexisting medical conditions.



Initiation of pharmacotherapy interventions to achieve target HbA1c might be reasonable.



Therapy with rosiglitazone **should not be initiated** in patients with SIHD.

Harm

Changes in ESC guidelines and new indication in Canada

- 2016 European Society of Cardiology Guidelines for the diagnosis and treatment of acute and chronic heart failure

Recommendations to prevent or delay the development of overt heart failure or prevent death before the onset of symptoms

Recommendations	Class ^a	Level ^b	Ref ^c
Treatment of hypertension is recommended to prevent or delay the onset of HF and prolong life.	I	A	126, 129, 150, 151
Treatment with statins is recommended in patients with or at high-risk of CAD whether or not they have LV systolic dysfunction, in order to prevent or delay the onset of HF and prolong life.	I	A	137–140, 152
Counselling and treatment for smoking cessation and alcohol intake reduction is recommended for people who smoke or who consume excess alcohol in order to prevent or delay the onset of HF.	I	C	131–134
Treating other risk factors of HF (e.g. obesity, dysglycaemia) should be considered in order to prevent or delay the onset of HF.	IIa	C	130, 141, 153–155
Empagliflozin should be considered in patients with type 2 diabetes in order to prevent or delay the onset of HF and prolong life.	IIa	B	130
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life.	I	A	5, 144, 145
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction without a history of myocardial infarction, in order to prevent or delay the onset of HF.	I	B	5

- Canada approves new indication “to reduce the incidence of cardiovascular (CV) death in patients with type 2 diabetes and established CV disease who have inadequate glycemic control”. (source: http://www.boehringer-ingenheim.ca/en/news/press_releases/2016/11Aug20161111.html)

Key Guideline Messages (1)

- A standard exercise test is the first choice to diagnose IHD for patients with an interpretable ECG and able to exercise

Those who have an *uninterpretable* ECG and can exercise, should undergo exercise stress test with nuclear MPI or echocardiography, particularly if likelihood of IHD is >10%. If unable to exercise, MPI or echocardiography with pharmacologic stress is recommended.

Threshold for ischaemia and therefore prognosis also determined from stress testing

Key Guideline Messages (2)

- Patients should generally receive a “package” of optimized medical management that include lifestyle interventions and medications shown to improve outcomes which includes (as appropriate):
 - Diet, weight loss and regular physical activity;
 - If a smoker, smoking cessation;
 - Aspirin 75-162mg daily;
 - A statin medication in moderate dosage;
 - If hypertensive, antihypertensive medication to achieve a BP <140/90
 - If diabetic, appropriate glycemic control.

Key Guideline Messages (3)

- First line medical therapies:
Beta blockers, calcium-channel blocker or long-acting nitrate
- Coronary arteriography should be considered for patients whose clinical characteristics and results of noninvasive testing indicate a high likelihood of severe IHD and when the benefits are deemed to exceed risk
- Prior to revascularization to improve symptoms, coronary anatomy should be correlated with functional studies to ensure lesions responsible for symptoms are targeted
- Patients should be carefully followed to monitor progression of disease, complications and adherence

THE HARLEY STREET HEART & CANCER CENTRE



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