



The Role of Non-Invasive Multimodality Imaging in Chronic Coronary Syndrome: Anatomical and Functional Pathways

6th Myanmar Cardiac Society Conference.
23rd -24th November 2024

Dr K.H. Lam
MRCP. FNHAM. FASPIC. FAsCC. FESC. FACC
Assunta Hospital. Malaysia

Disclosure Information



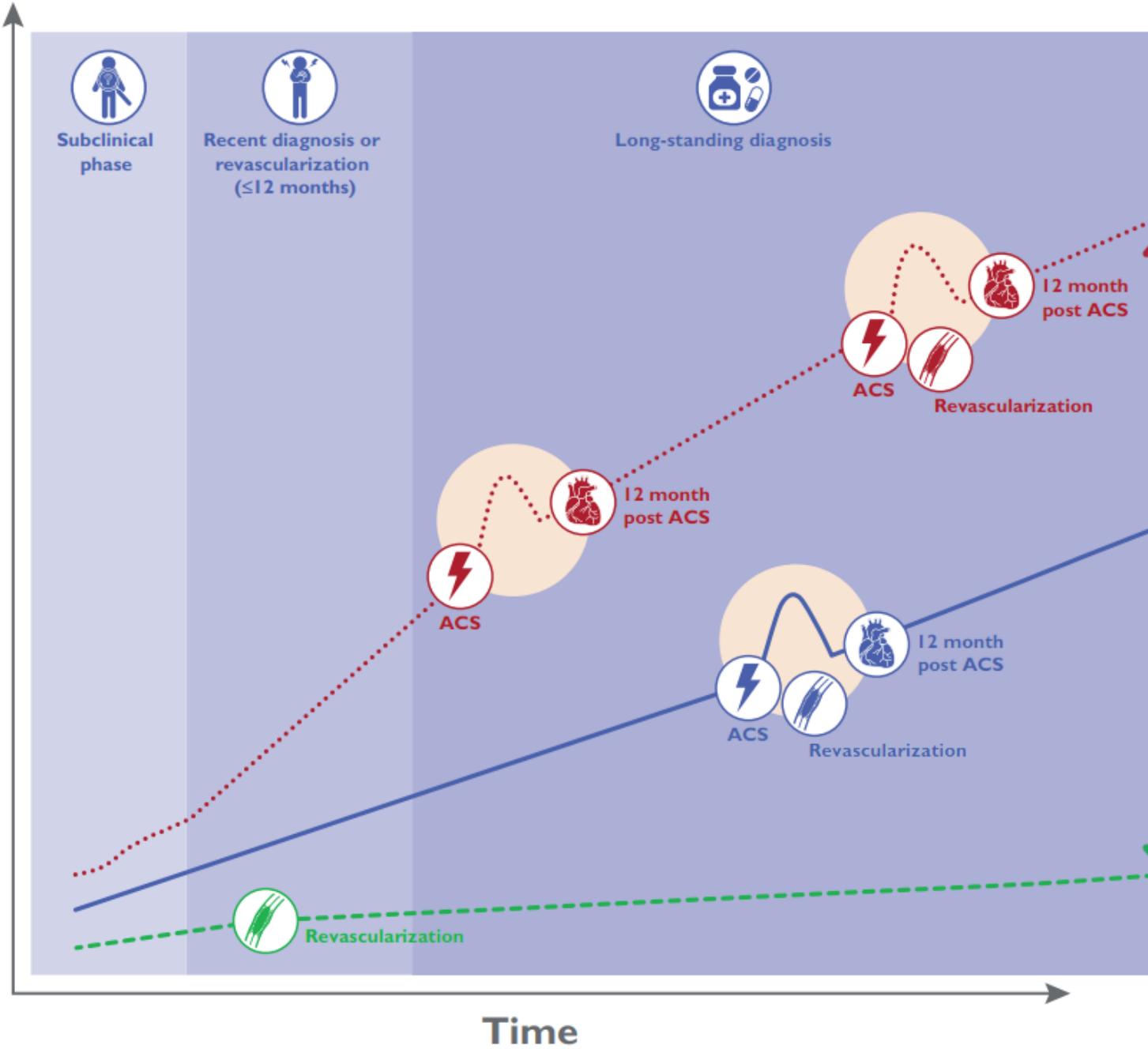
I have no actual or potential conflict of interest in relation to this presentation.

Speaker's Bureau: MSD, Novartis, Servier, Pfizer, Astra Zeneca , Bayer and Boehringer Ingelheim.

What is Coronary artery disease

- * Coronary artery disease is a pathological process characterized by atherosclerotic plaque accumulation in the epicardial arteries, whether obstructive or non-obstructive.
- * This process can be modified by lifestyle adjustments, pharmacological therapies, and invasive interventions designed to achieve disease stabilization or regression.
- * The disease can have long, stable periods but can also become unstable at any time, typically due to an acute atherothrombotic event caused by plaque rupture or erosion.
- * However, the disease is chronic, most often progressive, and hence serious, even in clinically apparently silent periods.
- * The dynamic nature of the CAD process results in various clinical presentations which can be categorized as either acute coronary syndromes (ACS) or chronic coronary syndromes (CCS)

Cardiac risk (death, MI)



Higher risk with insufficiently controlled risk factors, suboptimal lifestyle modifications and/or medical therapy, large area at risk of myocardial ischaemia

Lower risk with optimally controlled risk factors, lifestyle changes, adequate therapy for secondary prevention (e.g. aspirin, statins, ACE inhibitors) and appropriate revascularization

Time

The Role of Non-Invasive
Multimodality Imaging in Chronic
Coronary Syndrome: Anatomical
and Functional Pathways

Functional and Anatomy Assessment.....What does it means

- * Functional assessment measures an individual's level of function and ability to perform specific tasks on a safe and dependable basis over a defined period.
- * Anatomy assessment measures the structure of an individual lesion without any level of functional understanding or specific safety task over a period of time.

Principletreat a coronary stenosis on the basis of whether it is hemodynamically significant rather than the degree of luminal stenosis

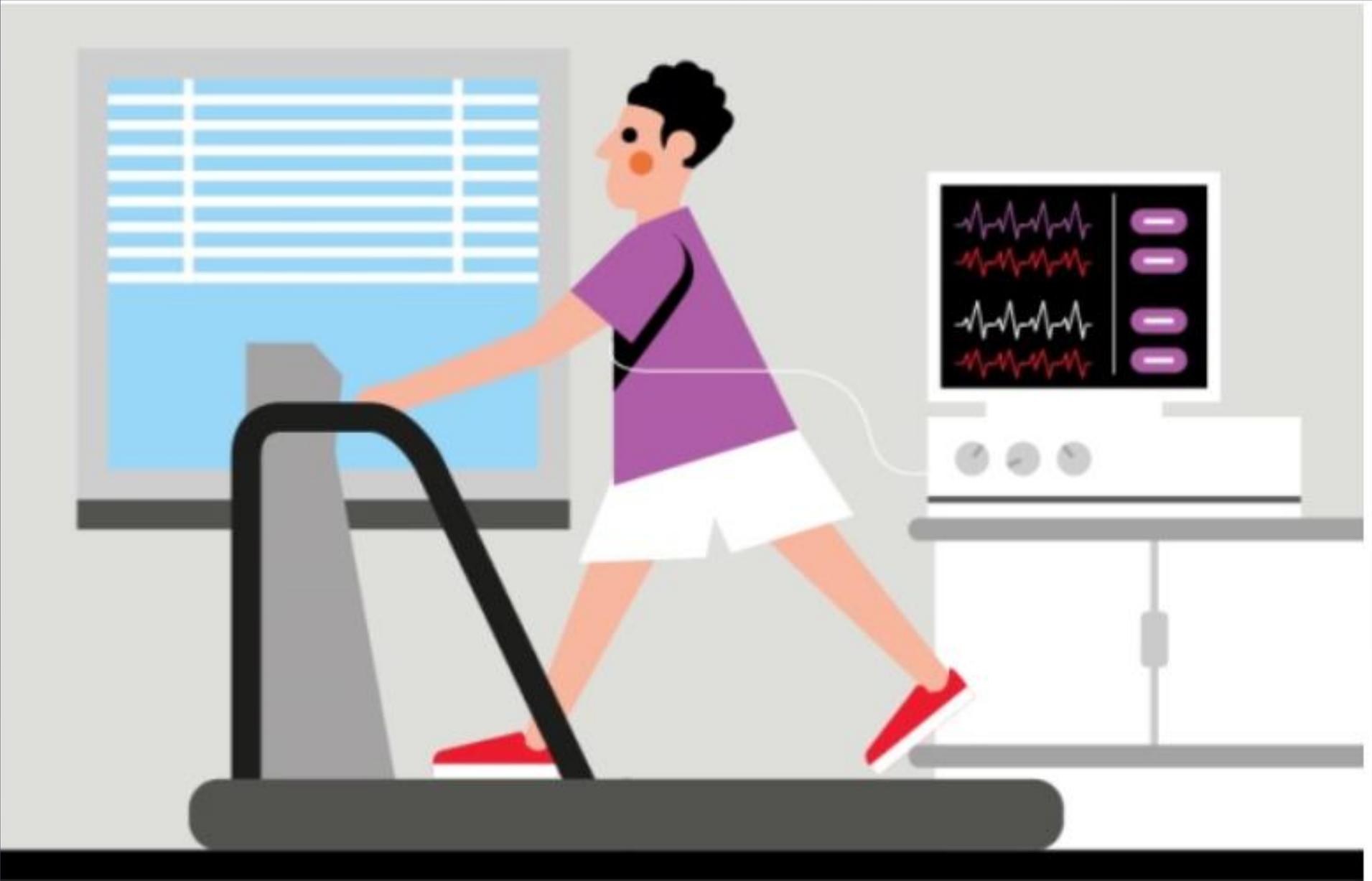
Non-invasive testing of CAD

- * The primary purpose of non-invasive diagnostic testing of patients suspected to have CAD is to *rule out the presence of significant underlying CAD and/or myocardial ischemia* and thus avoid unnecessary testing for those who gain no benefit from invasive catheterization.
- * The non-invasive testing seeks to provide *risk-stratification* to determine the need of medical therapy as well as determine conditions, when revascularization results in fewer future events, specifically in left main and three vessel disease.
- * Hence, an ideal first-line non-invasive diagnostic strategy is desired to have *high diagnostic accuracy* to identify significant CAD. In addition a testing strategy should be proven to fit the standard *cost effectiveness* criteria.
- * However, unless specific recommendations are available, test selection ultimately depends on availability, local expertise, cost, radiation considerations and patient characteristics leading to a degree of geographic variability.

Which Modality to choose?

- * It is essential to understand the limitations and strengths of each imaging method and, specifically, when to choose a functional approach focused on the ischemia versus a coronary anatomy-based one.
- * Ultimately the goal of using non-invasive testing is to guide further non-invasive medical or invasive therapy.
- * Overview of non-invasive imaging modalities for the comprehensive management of CCS patients

Stress Testing



Exercise Stress Testing

- ✓ Stress testing is generally safe. There is a small risk of acute myocardial infarction (~1:5000 tests) and death (~1:10 000 tests)
- ✓ The is sensitivity 68% and the specificity is 70-77%
- ✓ Advantage : Assessment of exercise capacity, Cost effective, First line test in absence of contraindications.
- ✓ Disadvantage : Lowest sensitivity of all stress tests: risk of false negative test and Lower diagnostic accuracy in women.

Stress ECG is functional tests and it cannot state a percentage of coronary stenosis (as commonly reported in CT coronary angiography). Stress ECG does not specify which coronary artery is the culprit vessel.

When should cardiac stress testing be ordered?

- * Risk stratification of known or possible CAD. The annual risk of cardiovascular mortality can be quantified from stress test results by measures such as the Duke treadmill score (low risk equating to <1% per year cardiovascular mortality, high risk >5% per year cardiovascular mortality).
- * Work-up for potential cardiac causes of dyspnoea (noting dyspnoea can be a cardiac equivalent symptom of CAD)
- * Evaluation of the effects of exercise on valvular dysfunction, pulmonary pressures or arrhythmia (eg. chronotropic incompetence),
- * Risk assessment in the postinfarct, preoperative or high risk patient populations.

Who should not have an Exercise Stress testing

- * Stress ECG should not be ordered when the baseline ECG shows a complete LBBB.
- * Paced ventricular rhythm.
- * Pre-excitation syndrome (Wolf-Parkinson-White syndrome) or AF
- * More than 1 mm ST segment depression (eg. associated with left ventricular hypertrophy or digitalis effect).

In these cases, ischaemic ECG changes cannot be identified and an imaging stress test should be considered.

Acute myocardial infarction , high risk unstable angina, symptomatic severe aortic stenosis, uncontrolled arrhythmia causing symptoms or haemodynamic instability, unstable heart failure, acute pulmonary embolus and acute aortic dissection.... Big NO NO ...!

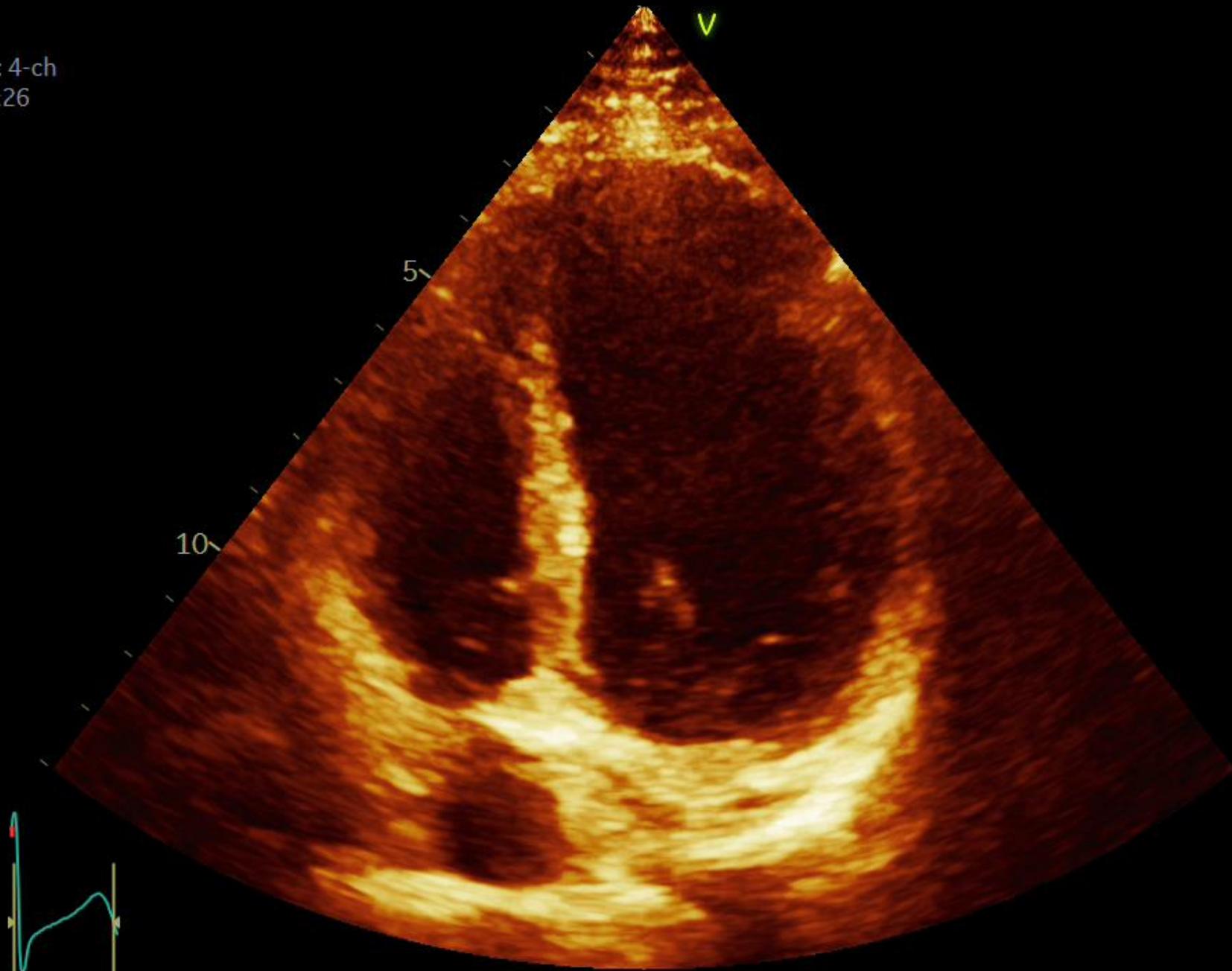
Stress test results... What does it means

Test result	What it could mean	What could still happen	What is the next step?
Normal	You do not have significant coronary artery disease (70% or greater artery blockage).	You could still have a heart attack if a smaller blockage (less than 70%) ruptures and forms a clot.	Your doctor may want to do further testing if you have other risk factors for heart disease that raise concern.
Abnormal	You may have significant coronary artery disease (70% or greater blockage).	The abnormal result may be a false alarm, and could require further testing to confirm.	The doctor may order additional tests to confirm that you have coronary artery disease.

Where do Exercise stress testing Stand now

2019	Class^a
Exercise ECG is recommended for the assessment of exercise tolerance, symptoms, arrhythmias, BP response, and event risk in selected patients.	I
Exercise ECG may be considered as an alternative test to rule-in or rule-out CAD when other non-invasive or invasive imaging methods are not available.	IIb
Exercise ECG may be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIb

ACE
Rest : 4-ch
T1: 1:26



50
2:59HR

Stress Echocardiography Imaging

- * Stress echocardiography is the combination of 2D echo cardiography with a physical, pharmacological, or electrical stress . The diagnostic endpoint for the detection of myocardial ischaemia is the induction of a transient change in regional function during stress.
- * Stress Echocardiography is the first-line method for ischemia detection because of its low cost, availability, and non radiation exposure.
- * Physicians have become more familiar with this method and echocardiography technology has been improved, expanding the indications of SE.
- * This method can be used in CAD diagnosis and prognosis, especially after acute coronary syndrome or in myocardial viability assessment.
- * They are expanded to a broad spectrum of Non ischaemic cardiac diseases by using different stressors and protocols.

Indications to stress echocardiography

- * Diagnosis of CAD in patients in whom exercise ECG is contraindicated, not feasible, uninterpretable, non-diagnostic or gives ambiguous results.
- * Risk stratification in patients with established diagnosis.
- * Pre-operative risk assessment (high-risk non emergent).
- * Evaluation after revascularization (not in the early post-procedure period, with change in symptoms).
- * Search for viability in patients with ischemic cardiomyopathy eligible for revascularization.
- * Coronary artery disease of unclear significance at angiography or computed tomography.

Types of Stress echocardiography

- * There are two main techniques for the evaluation of myocardial ischemia: PSE (frequently using dobutamine) or ESE with either semi supine bicycle or treadmill.
- * ESE is the preferable technique in patients who exercise as it follows the natural stress response. ESE provides functional prognostic information, hemodynamic assessment, and presents a better and more predictable safety profile than PSE.
- * Moreover, treadmill exercise induces a greater magnitude of ischemia than dobutamine-atropine infusion owing to the higher rate-product achieved by exercise.



Vasodilator stress Imaging

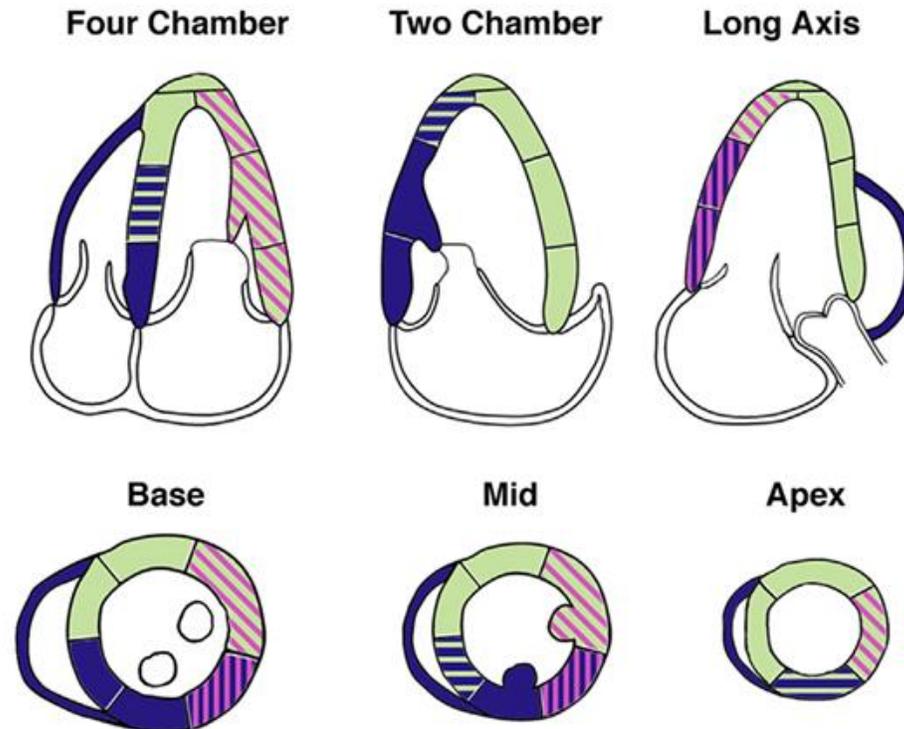
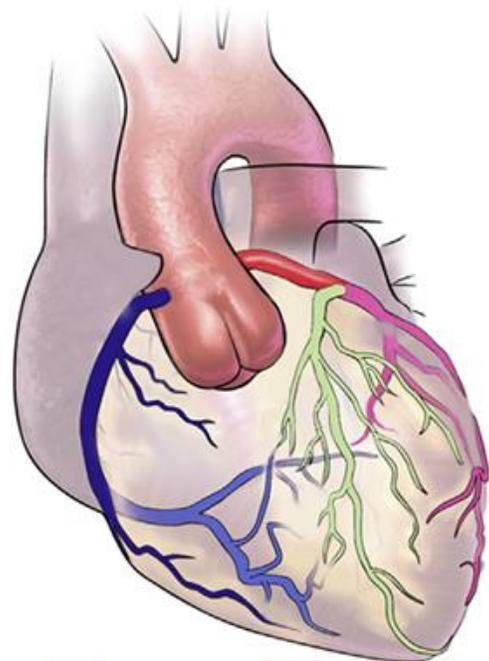
- ❖ Stress testing with vasodilators (dipyridamole or adenosine) may be performed for assessment of ischemia, myocardial perfusion, and myocardial viability. These agents are contraindicated in patients with reactive airway obstruction or severe hypotension.
- ❖ Dipyridamole is safely given up to 0.84 mg/kg over 6 to 10 minutes. Atropine administration or handgrip exercise at peak infusion increases test sensitivity.
- ❖ Adenosine, in concert with contrast echocardiography, can also be used to assess myocardial perfusion. The adenosine infusion rate is 140 mg/kg/min over 4 to 6 minutes to a maximum of 60 mg. Adenosine has a shorter half-life and thus, shorter action time than dipyridamole.
- ❖ DSE rather than vasodilator stress echocardiography is preferred by most because of higher sensitivity for detection of CAD unless perfusion can also be assessed.

	Exercise	Inotropes and/or Chronotropes
	Bicycle/Treadmill	Dobutamine (synthetic catecholamine)
Physiology	- Preserves integrity of the electro-mechanical response	- Stimulates beta-1 adrenoceptors with the effect of increased heart rate and/or contractility
Test selection	- Preferred stress for patients who can attain an adequate level of exercise for known or suspected CAD - Bicycle stress is preferred for assessment of diastolic function	- Performed when a patient is unable to exercise and for known or suspected CAD - Preferred choice for assessment of myocardial viability
Characteristics	- Increases myocardial oxygen demand	-Increases myocardial oxygen demand
Hemodynamic response		
Heart rate	↑↑	↑↑
Stroke volume	↑↑ through Frank-Starling mechanism	↓ or no change
Systolic blood pressure	↑↑ by 50%	↑
Contractility	↑	↑ 4 to 5-fold
Myocardial blood flow	↑	↑
Contraindications	- Unstable or complicated acute coronary syndrome - Serious cardiac arrhythmias (VT, complete A-V block). - Moderate to severe systemic hypertension (resting systolic blood pressure >180 mmHg)	- Hemodynamically significant LV outflow tract obstruction - Unstable or complicated acute coronary syndrome - Serious cardiac arrhythmias (VT, complete A-V block) - Severe systemic hypertension (resting systolic blood pressure >180 mmHg)

Exercise and pharmacologic testing modalities, including physiologic effect, test selection, hemodynamic response, and contraindications

Pellikka et al. Guidelines for Performance, Interpretation, and Application of Stress Echocardiography in Ischemic Heart Disease: Journal of the American Society of Echocardiography . Volume 33 Number 1. January 2020

Typical distributions of the right coronary artery, the LAD, and the circumflex coronary artery



- | | |
|---|--|
|  RCA |  RCA or CX |
|  LAD |  LAD or CX |
|  CX |  RCA or LAD |

Wall Motion Scoring

- 1 = normal or hyperkinesis (systolic increase in thickening >50%)
- 2 = hypokinesis
- 3 = akinesis, or severe hypokinesis (<10% systolic thickening)
- 4 = dyskinesis (paradoxical systolic motion)
- 5 = aneurysmal (diastolic deformation)

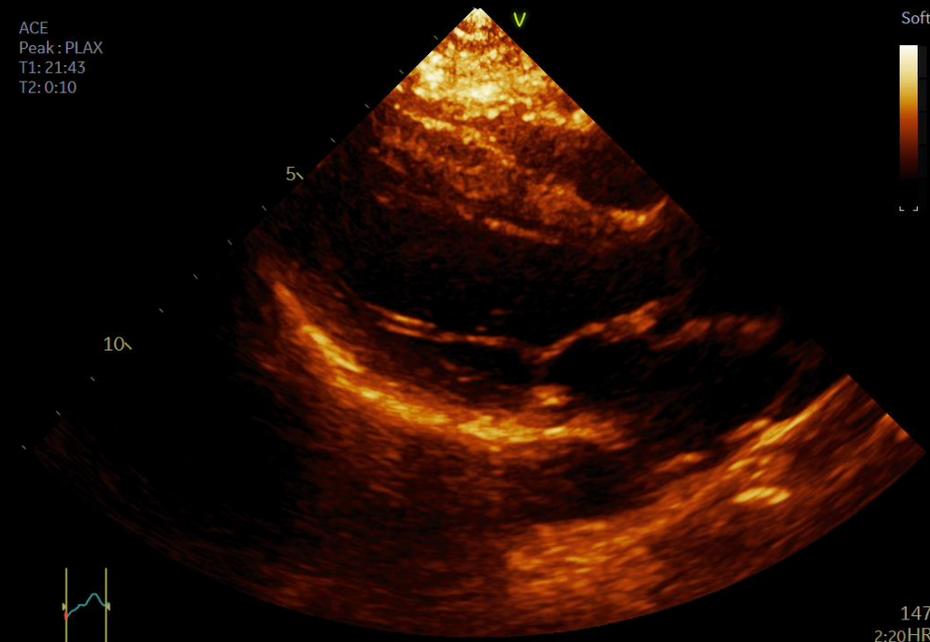
Endpoints of stress echocardiogram

1. Achievement of target HR (85% of maximal, age-predicted HR)
2. Completion of protocol (maximal drug dose) or limiting symptoms (chest pain, fatigue)
3. Obvious echocardiographic findings of extensive myocardial ischemia
4. Marked ischemic ECG changes: symptomatic ST elevation > 1 mm (other than aVR or V1) in 12-lead ECG recording
5. Symptomatic drop in SBP > 10 mmHg from baseline (only in ESE)
6. Sustained ventricular tachycardia
7. Central nervous system symptoms (ataxia, pre-syncope)

ACE
Rest : PLAX
T1: 0:07



ACE
Peak : PLAX
T1: 21:43
T2: 0:10

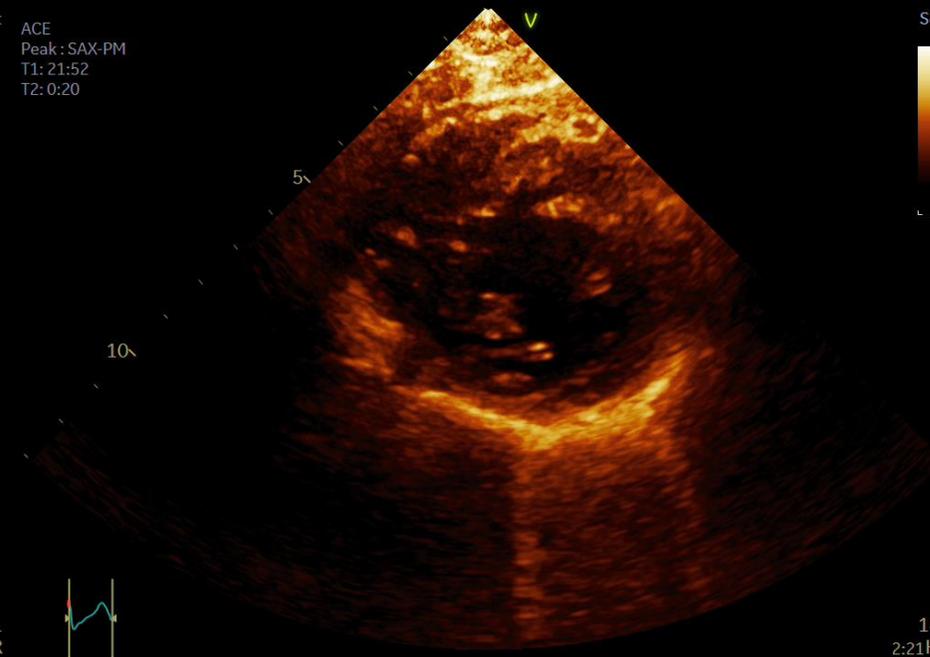


63
2:44HR

ACE
Rest : SAX-PM
T1: 0:17



ACE
Peak : SAX-PM
T1: 21:52
T2: 0:20

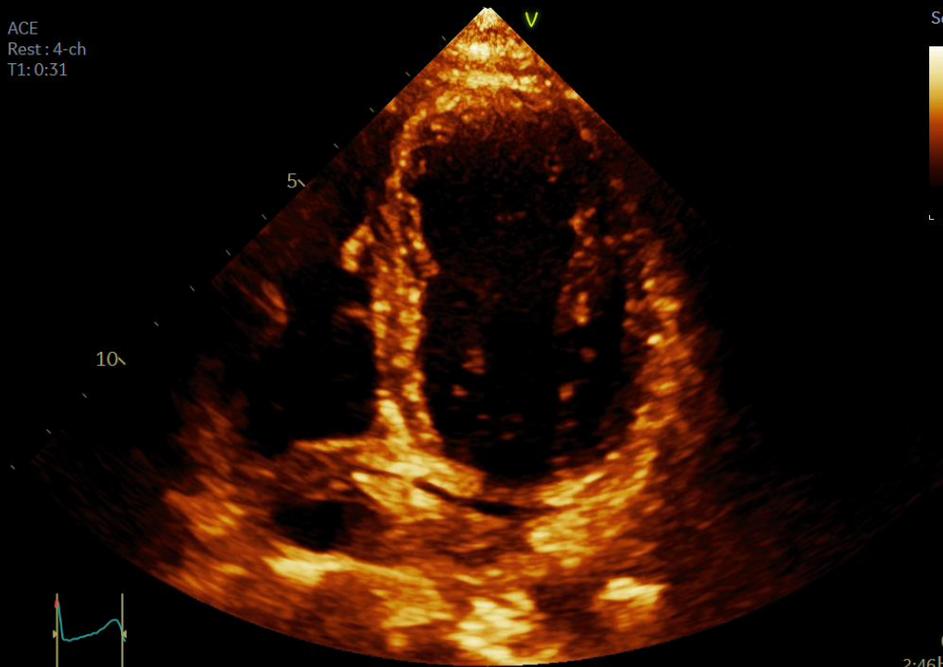


61
2:46HR

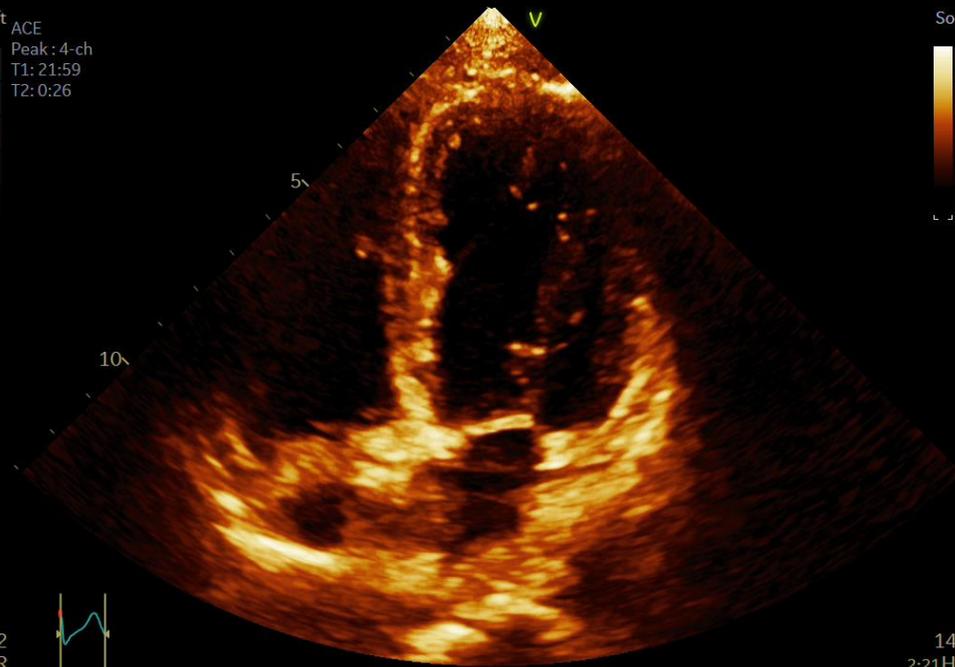
147
2:20HR

146
2:21HR

ACE
Rest : 4-ch
T1: 0:31



Soft ACE
Peak : 4-ch
T1: 21:59
T2: 0:26



Soft

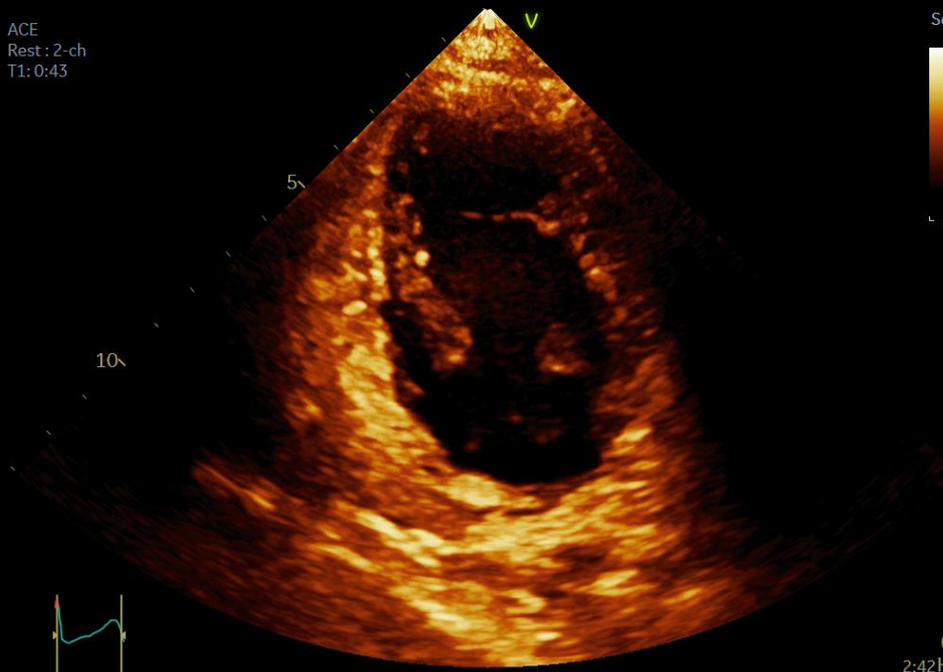


62
2:46HR

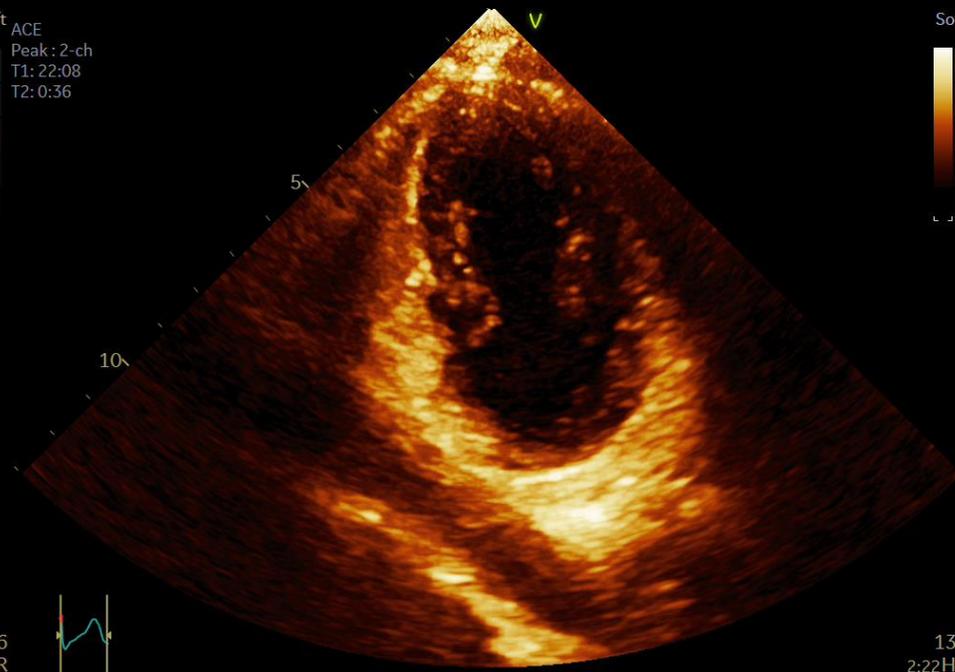


144
2:21HR

ACE
Rest : 2-ch
T1: 0:43



Soft ACE
Peak : 2-ch
T1: 22:08
T2: 0:36



Soft



66
2:42HR

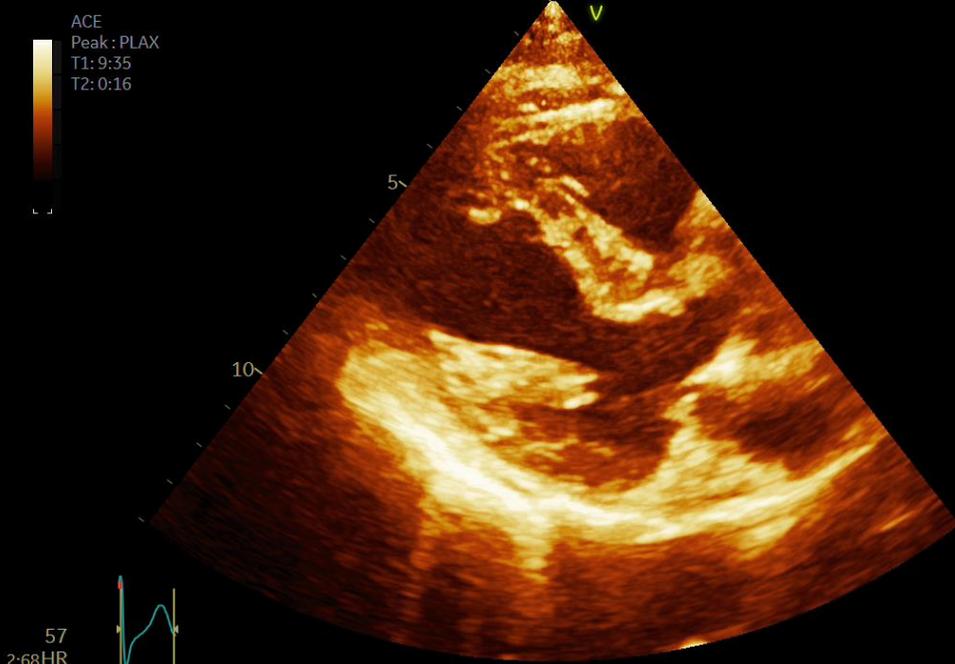


139
2:22HR

ACE
Rest : PLAX
T1: 0:35



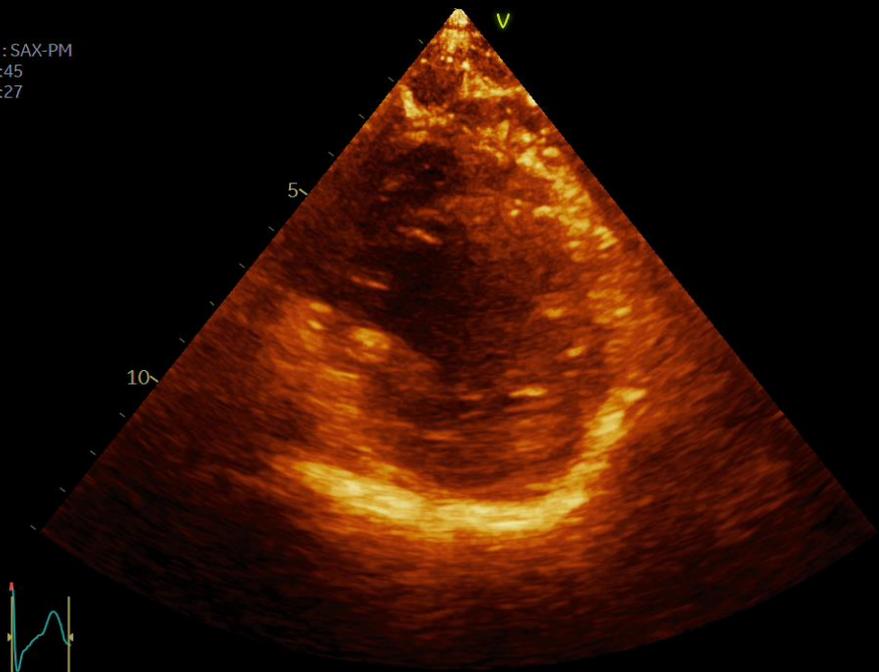
ACE
Peak : PLAX
T1: 9:35
T2: 0:16



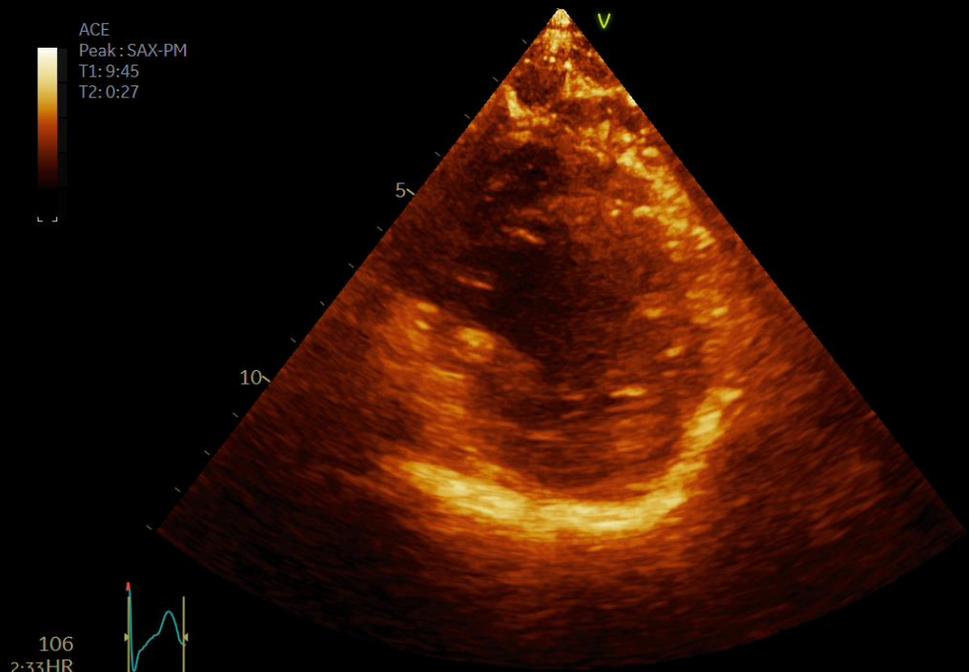
57
2:68HR

112
2:32HR

ACE
Peak : SAX-PM
T1: 9:45
T2: 0:27



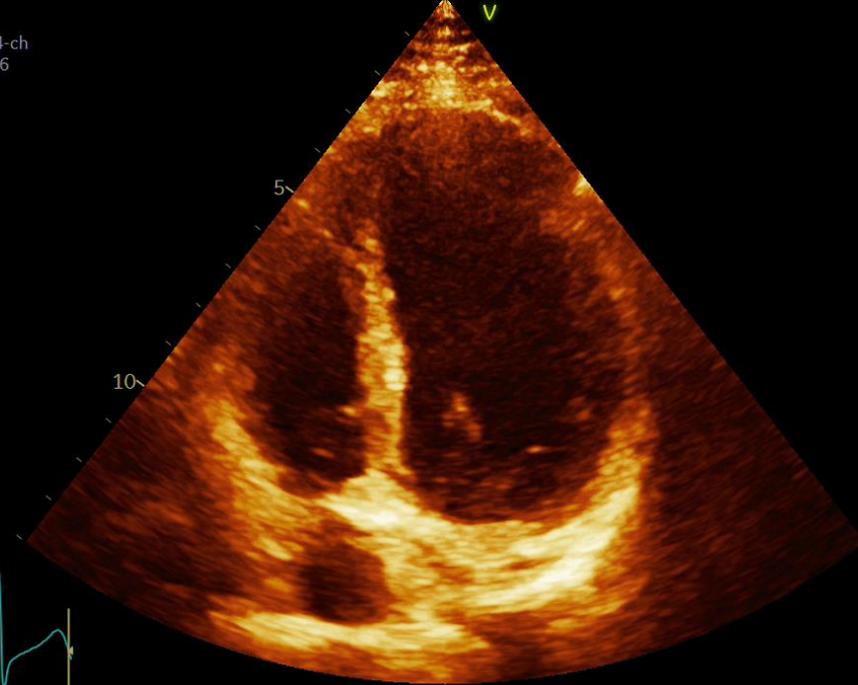
ACE
Peak : SAX-PM
T1: 9:45
T2: 0:27



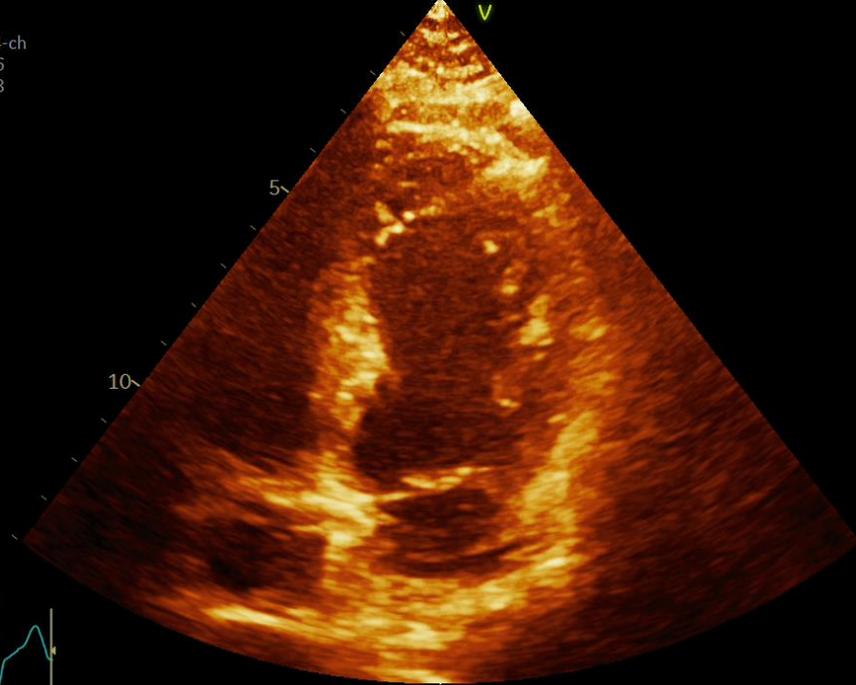
106
2:33HR

106
2:33HR

ACE
Rest : 4-ch
T1: 1:26



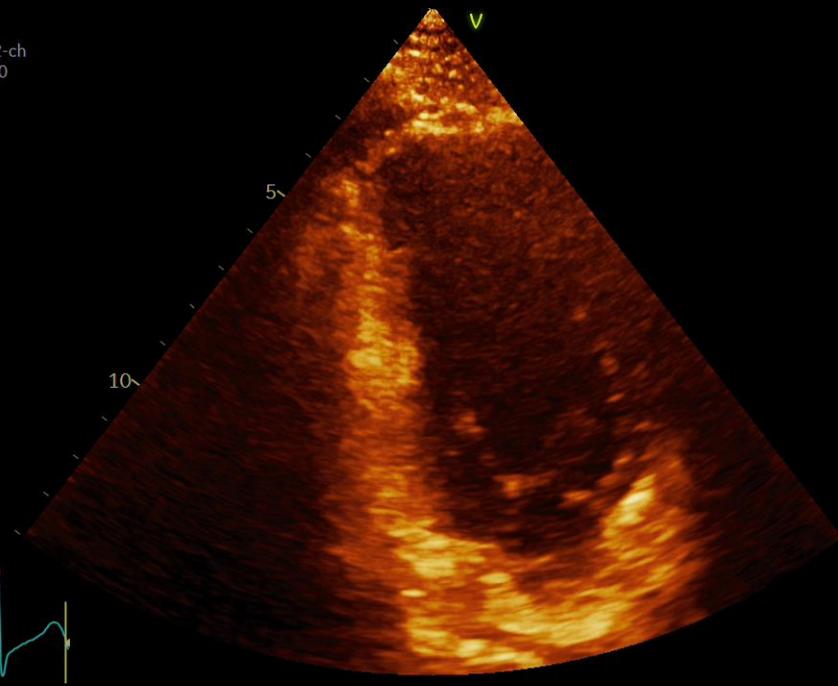
ACE
Peak : 4-ch
T1: 9:56
T2: 0:38



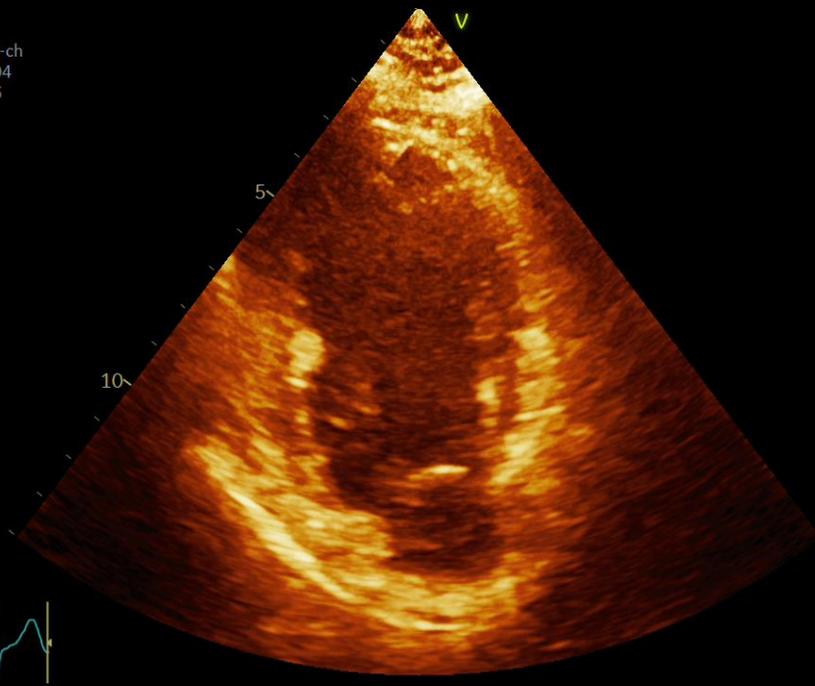
50
2:59HR

101
2:34HR

ACE
Rest : 2-ch
T1: 1:40



ACE
Peak : 2-ch
T1: 10:04
T2: 0:46



51
2:64HR

99
2:35HR

Caveat of Stress Echocardiography Interpretation

A negative SE for ischemia does not entirely rule out the presence of angiographically obstructive CAD. There are several common technical reasons which lower the sensitivity of the method ("false negative"):

- 1) low-quality views of the lateral and inferolateral walls when the culprit lesion is located at the territory of LCX artery,
- 2) patients with suboptimal imaging owing to body habitus,
- 3) submaximal level of stress,
- 4) antianginal treatment.

Finally, the diagnosis of a single-vessel disease may become challenging in less severe (50-70%) stenosis, where ischemia may not be detected depending on the anatomy of the rest of the vessels supplying the same myocardial wall

Accuracy of stress Echo cardiography

- * ESE sensitivity is between 80% and 85%
- * DSE sensitivity is between 79% and 83%
- * ESE specificity is between 80% and 88%
- * DSE specificity is between 82% and 85%

Pellikka PA, Arruda-Olson A, Chaudhry FA, Chen MH, Marshall JE, Porter TR, et al. Guidelines for performance, interpretation, and application of stress echocardiography in ischemic heart disease: from the American society of echocardiography. *J Am Soc Echocardiogr.* (2020) 33(1):1–41

Lee C, Columbo JA, Stone DH, Creager MA, Henkin S. Preoperative evaluation and perioperative management of patients undergoing major vascular surgery. *Vasc Med.* (2022) 27(5):496–512.

Comparison of imaging modalities for CAD diagnosis regarding their sensitivity and specificity

Diagnosis of coronary artery disease

	Sensitivity (%)	Specificity (%)
Exercise ECG	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	79-88	81-91
Vasodilator stress Echocardiography	72-79	92-95
Vasodilator stress SPECT	90-91	75-84
Vasodilator stress MRI	67-94	61-85
Coronary CTA	95-99	64-83
Vasodilator stress PET	81-97	74-91

Complications	ESE (%)	DSE (%)
Acute myocardial infarction	0.01	0.02
Sustained Ventricular Tachycardia (sVT)	0.05	0.15
Ventricular Fibrillation (VF)	<0.01	0.04
Cardiac rupture	-	0.01
Stroke	0.01	0.01
Syncope	0.01	-
Complete atrio-ventricular block	0.02	-
Death (VF and cardiac rupture)	0.01	0.01
Conduction abnormalities other than complete A-V block	0.04	0.23
Non-sustained ventricular tachycardia	0.25	1-3
Atrial fibrillation/flutter	0.05	0.9
Paroxysmal supraventricular tachycardia (SVT)	0.14	1.3

Complications of Exercise Echocardiography. Analysis of a Cohort of 19,239 patients J Peteiro, A Bouzas-Mosquera - International Cardiovascular Forum Journal, 2017

Varga A, Garcia MA, Picano E. International Stress Echo Complication Registry. Safety of stress echocardiography (from the International Stress Echo. Complication Registry). Am J Cardiol. 2006;98:541e543.



Exercise stress echocardiography: Where are we now?

Carlos Alberto Cotrim, Hugo Café, Isabel João, Nuno Cotrim, Jorge Guardado, Pedro Cordeiro, Hortense Cotrim, Luis Baquero

Specialty type: Cardiac and cardiovascular systems

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

Carlos Alberto Cotrim, Luis Baquero, Heart Center, Hospital da Cruz Vermelha Portuguesa, Lisboa 1549-008, Portugal

Hugo Café, Hortense Cotrim, Faculdade de Medicina, Algarve University, Faro 8005-139, Portugal

Isabel João, Department of Cardiology, Garcia de Orta Hospital, Almada 2805-267, Portugal

Nuno Cotrim, Department of Medicine, Garcia de Orta Hospital, Almada 2805-267, Portugal

Jorge Guardado, Cardiovascular Unit, UCARDIO, Centro Clinico, Riachos 2350-325, Portugal

Pedro Cordeiro, Department of Cardiology, Hospital Particular do Algarve, Faro 8005-226, Portugal

Corresponding author: Carlos Alberto Cotrim, MD, PhD, Professor, Heart Center, Hospital da Cruz Vermelha Portuguesa, Rua Duarte Galvão, 54, Lisboa 1549-008, Portugal.

carlosadcotrim@gmail.com

Exercise stress echocardiography: Where are we now?

- * Exercise is the most physiologic stressor of all and should thus be preferable in patients who are able to exercise. In coronary artery disease diagnosis, exercise echocardiography is the appropriate first-line test for patients who are asymptomatic or with chest pain or dyspnea as the chief complaint.
- * A major advantage of exercise echocardiography over the other forms of stress is that it may offer helpful and versatile evaluation of valve function and pulmonary hemodynamics and of special subsets of patients, such as patients with heart failure, pulmonary hypertension, valve disease, congenital heart disease, or athletes with symptoms of unknown etiology in search of intraventricular gradients.
- * More importantly, the option of ESE is advantageous over techniques with higher cost and radiation burden for effective primary prevention of cancer, which should begin in the cardiac imaging laboratory.

Dobutamine stress echocardiography: a review and update

This article was published in the following Dove Press journal:

Research Reports in Clinical Cardiology

5 April 2014

[Number of times this article has been viewed](#)

Lauren Gray Gilstrap¹

R Sacha Bhatia²

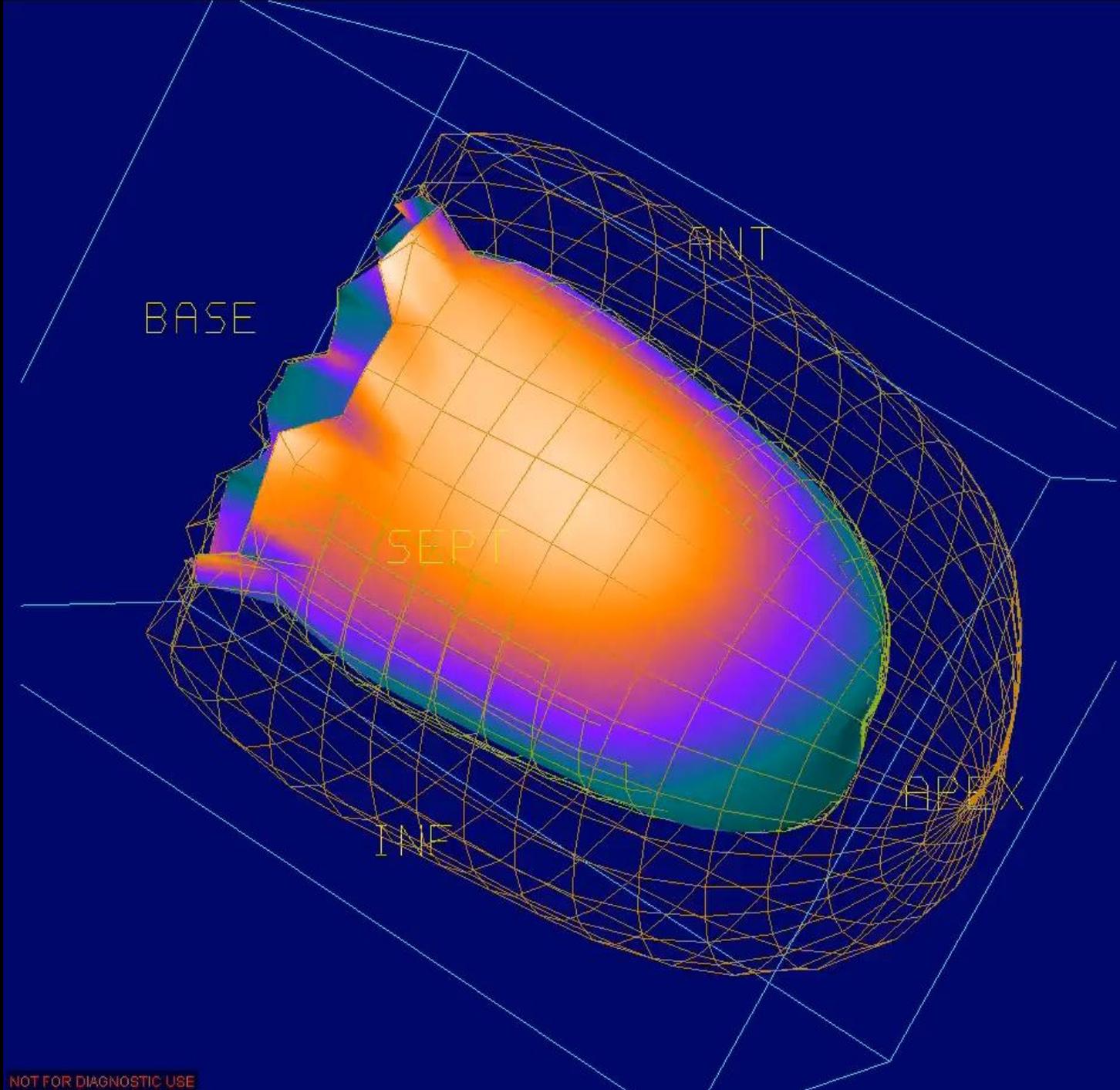
Rory B Weiner³

David M Dudzinski³

¹Division of Cardiology, Brigham and Women's Hospital, Boston, MA, USA; ²Institute for Health Systems Solutions, Women's College Hospital, Toronto, ON, Canada; ³Cardiology Division, Massachusetts General Hospital, Boston, MA, USA

Abstract: Stress echocardiography is a noninvasive cardiovascular diagnostic test that provides functional and hemodynamic information in the assessment of a number of cardiac diseases. Performing stress echocardiography with a pharmacologic agent such as dobutamine allows for simulation of increased heart rate and increased myocardial physiologic demands in patients who may be unable to exercise due to musculoskeletal or pulmonary comorbidities. Dobutamine stress echocardiography (DSE), like exercise echocardiography, has found its primary application in ischemic heart disease, with roles in identification of obstructive epicardial coronary artery disease, detection of viable myocardium, and assessment of the efficacy of anti-ischemic medical therapy in patients with known coronary artery disease. DSE features prominently in the evaluation and management of valvular heart disease by helping to assess the effects of mitral and aortic stenoses, as well as a specific use in differentiating true severe valvular aortic stenosis from pseudostenosis that may occur in the setting of left ventricular systolic dysfunction. DSE is generally well tolerated, and its side effects and contraindications generally relate to consequences of excess inotropic and/or chronotropic stimulation of the heart. The aim of this paper is to review the indications, contraindications, advantages, disadvantages, and risks of DSE.

Keywords: stress echocardiography, dobutamine, coronary artery disease, myocardial ischemia



BASE

ANIT

SEPT

INF

RIGHT

Nuclear perfusion study

- * Sensitivity is about 85-90% and the specificity is 70-75%
- * Advantage : Exercise capacity can be assessed and High sensitivity.
- * Disadvantage : Radiation (9-10 mSv) and False positives due to higher sensitivity/ diaphragmatic attenuation as in SPECT scan BUT have improved with PET scan.

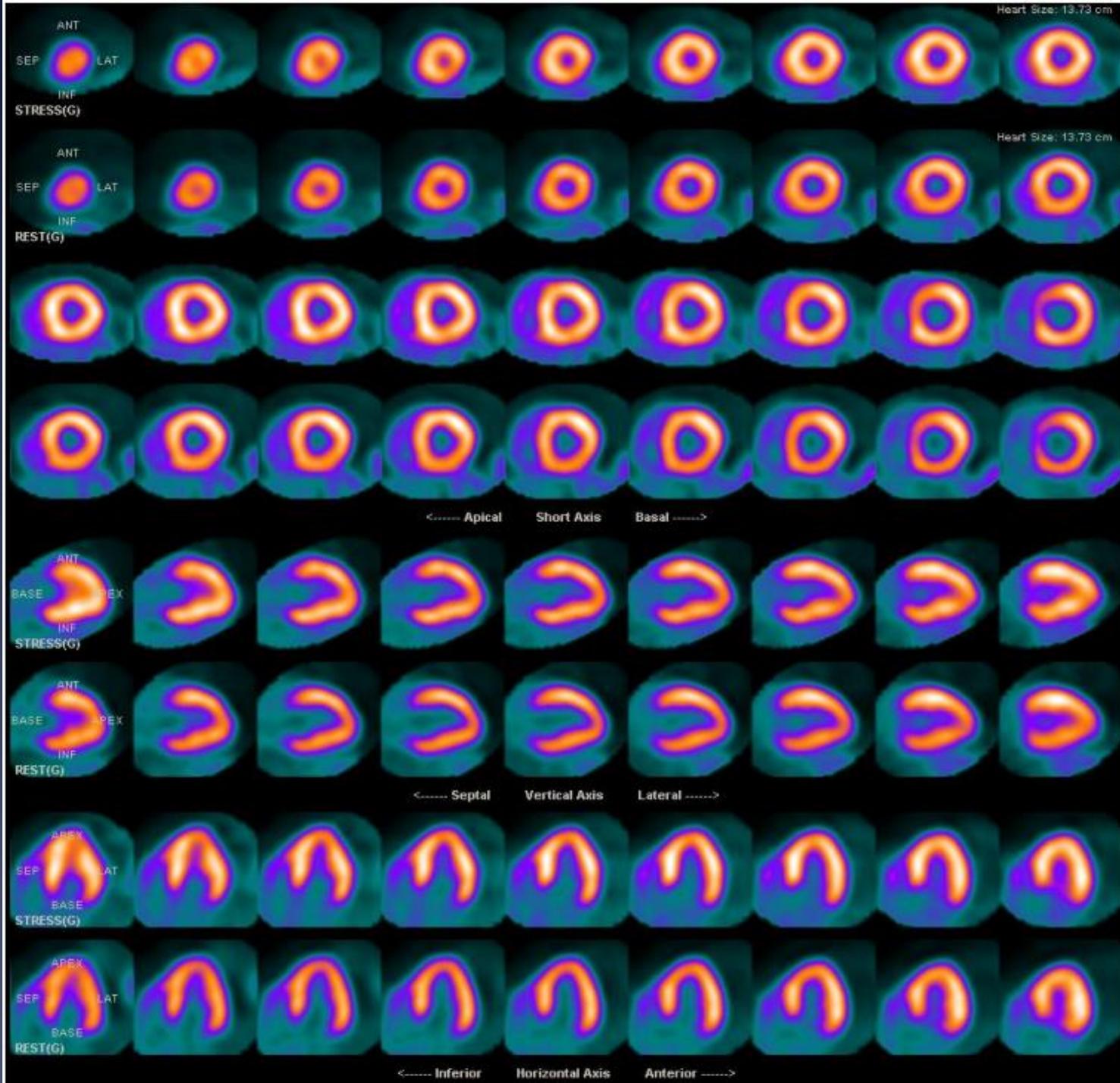
BASE

ANT

SEMI

PEX

TH



Cardiac Single photon emission computed tomography (SPECT)

- ✓ is lower cost
- ✓ uses gamma emitting radioisotope (tracer):
 - technetium-99m
 - iodine-123
 - iodine-131
- ✓ gives poorer contrast and spatial resolution (cf. PET)
- ✓ usually one large crystal based detector

Cardiac Positron emission tomography

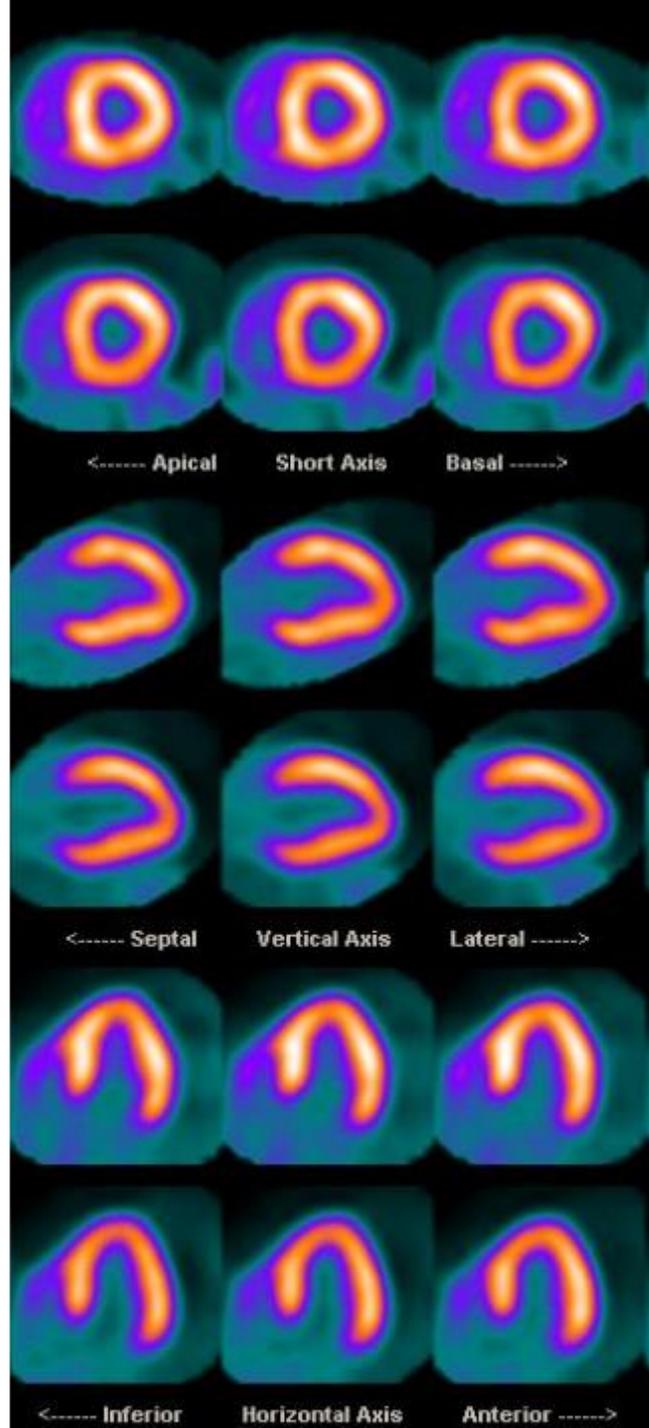
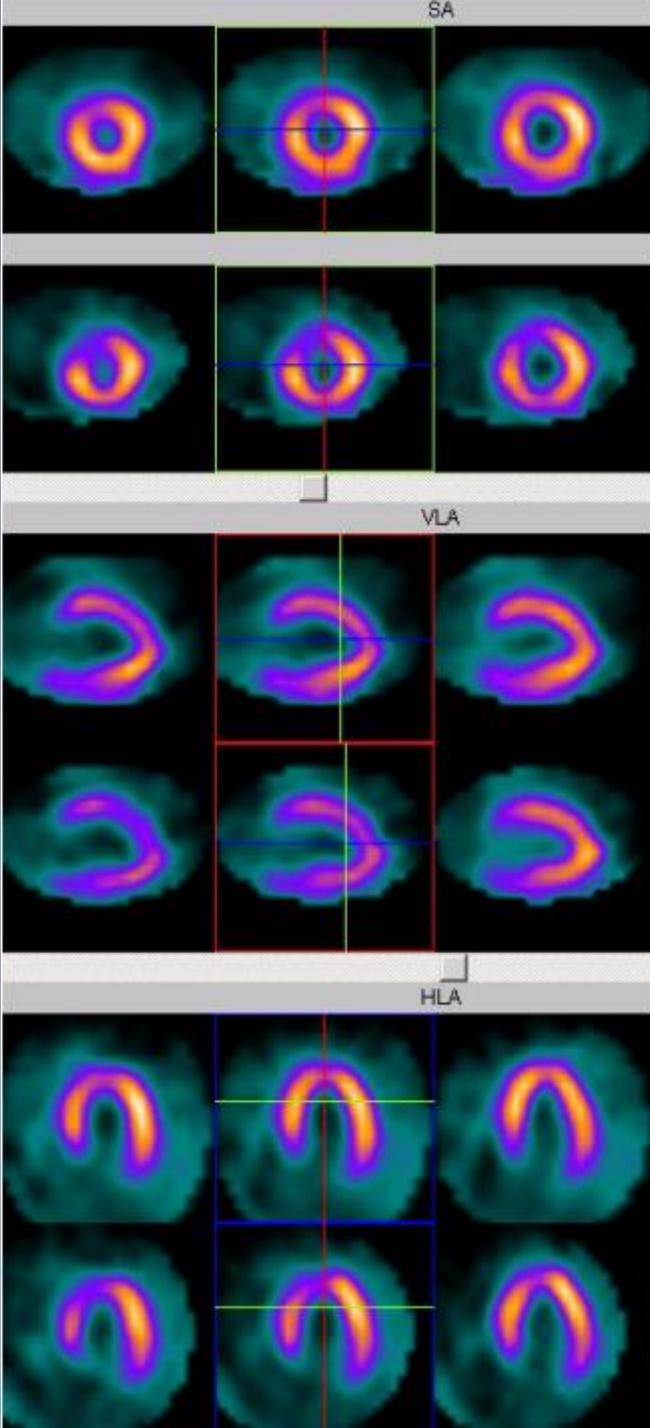
- ✓ is very expensive
- ✓ uses positron emitting radioisotope (tracer)
rubidium-82 as the radiotracer
- ✓ gives better contrast and spatial resolution (cf. SPECT)
- ✓ has a ring of multiple detectors

Clinical PET Myocardial Perfusion Imaging and Flow Quantification



Daniel Juneau, MD, FRCPC^{a,1}, Fernanda Erthal, MD^{a,1},
Hiroshi Ohira, MD, PhD^{a,b}, Brian Mc Ardle, MD^a,
Renée Hessian, MD, FRCPC^a,
Robert A. deKemp, PhD, PEng, PPhys^a,
Rob S.B. Beanlands, MD, FRCPC^{a,*}

- * Cardiac PET has inherent advantages over single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI), including better imaging characteristics and the ability to quantify blood flow routinely.
- * PET MPI has better sensitivity, specificity and accuracy than SPECT MPI in the detection of obstructive coronary artery disease.
- * Myocardial flow reserve assessment can overcome the pitfall of balanced ischemia otherwise observed using conventional MPI in some patients with multivessel disease.
- * PET MPI and flow quantification provide independent and incremental prognostic information for risk stratification



SPECT MPI Report

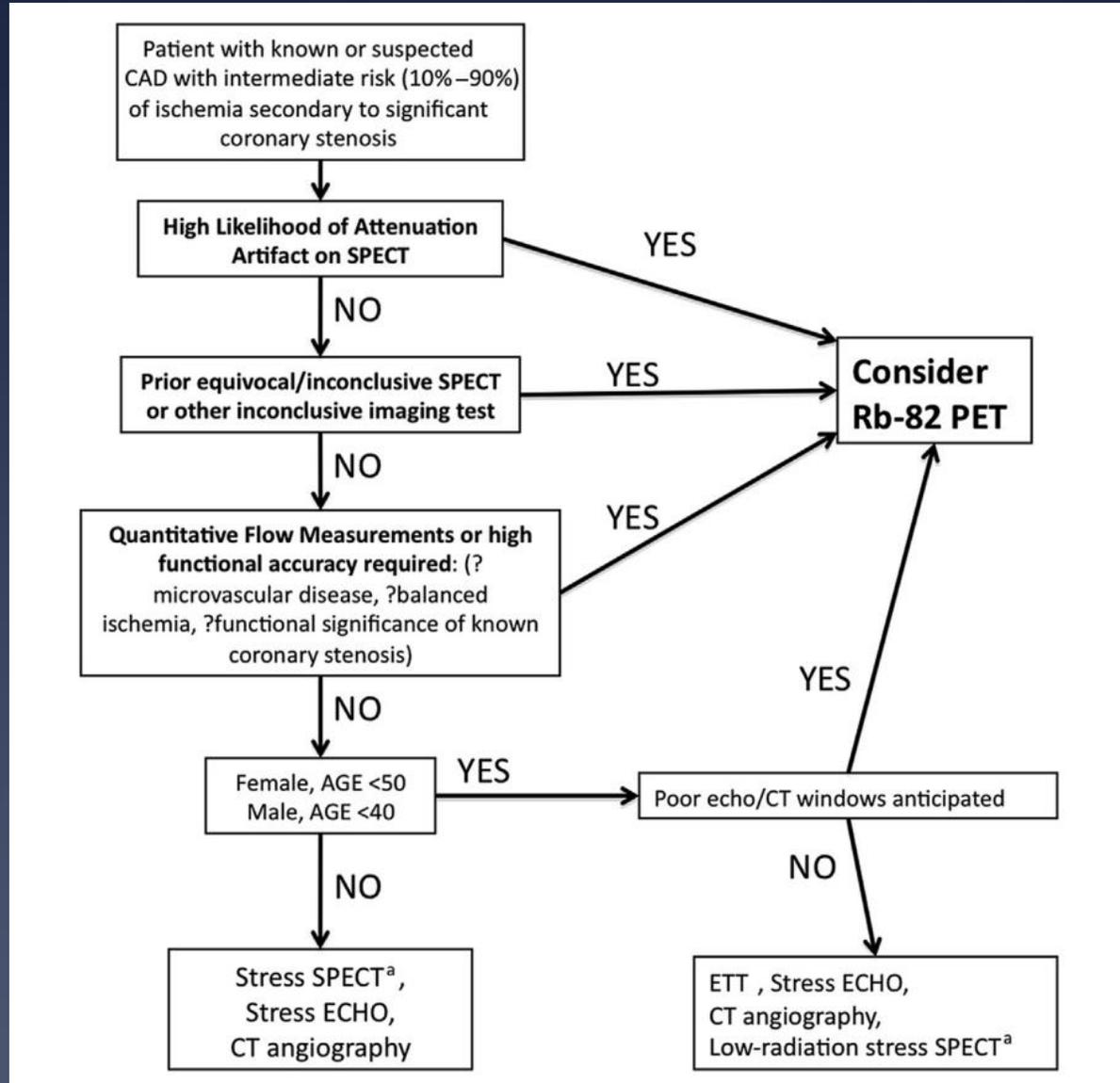
There was a small defect of moderate intensity in the mid to apical anterior wall that remained fixed on the rest images and most likely is due to breast attenuation artifact; however a non-transmural myocardial scar cannot be excluded.

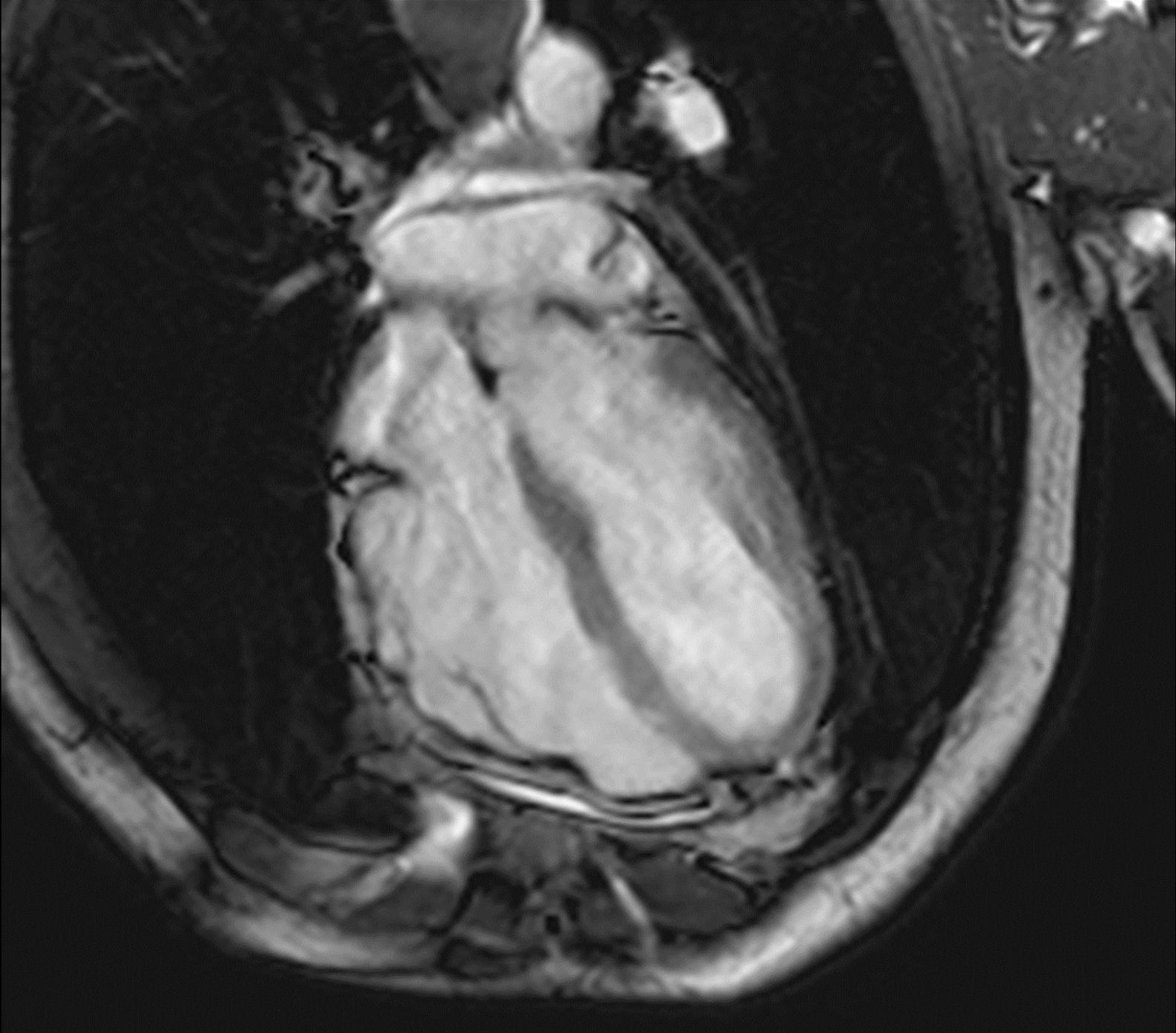
PET MPI Report

There were no regional perfusion defects seen on the stress or rest images. The patient's PET/CT test results are normal and suggest no evidence of flow-limiting CAD. The results suggest that the previously described fixed anterior wall defect (her prior SPECT study) is likely to represent an attenuation artifact.

Cardiac catheterization was not performed because the PET MPI study was normal.

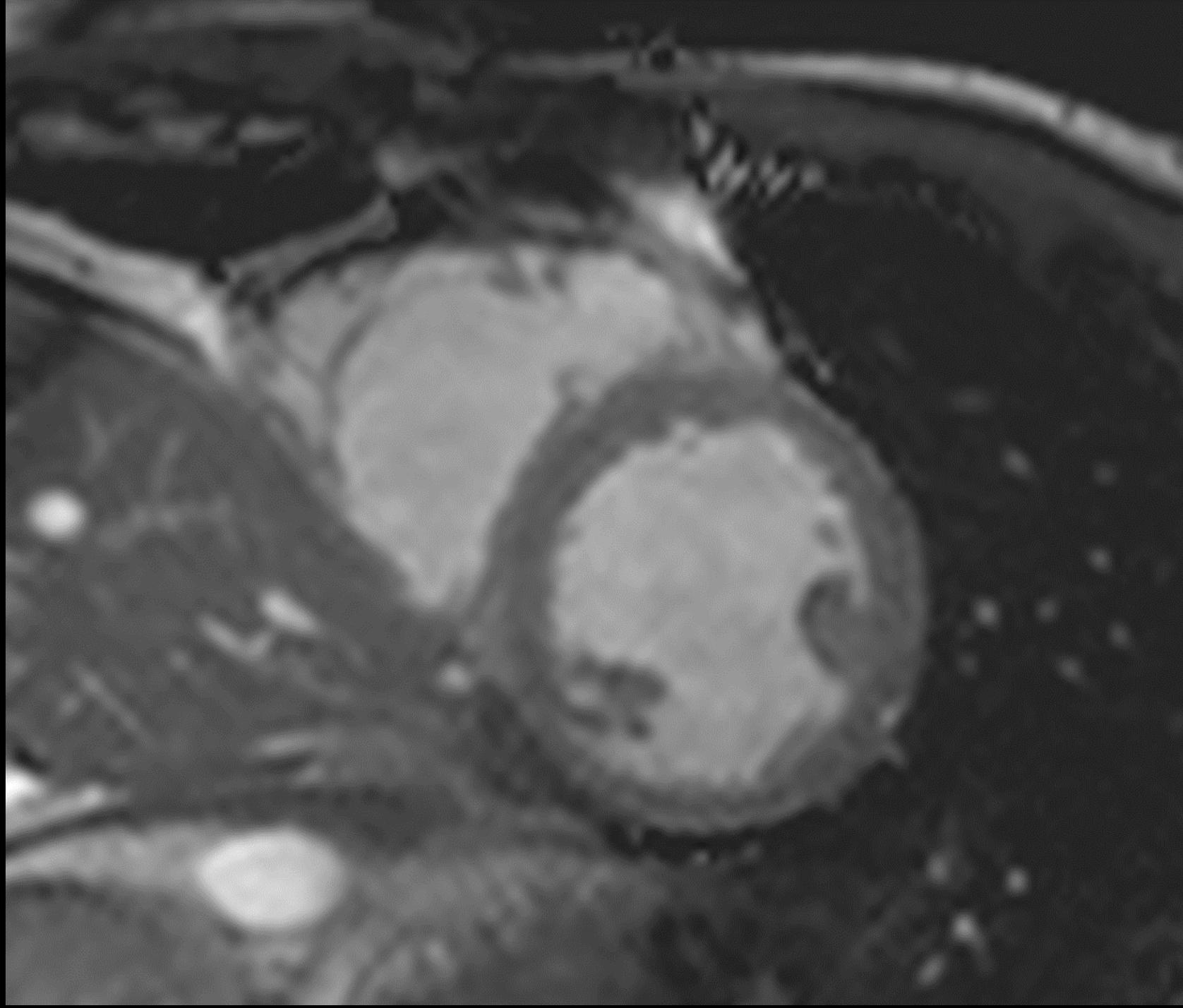
Proposed clinical algorithm for use of rubidium-82-chloride (Rb-82) PET myocardial perfusion imaging

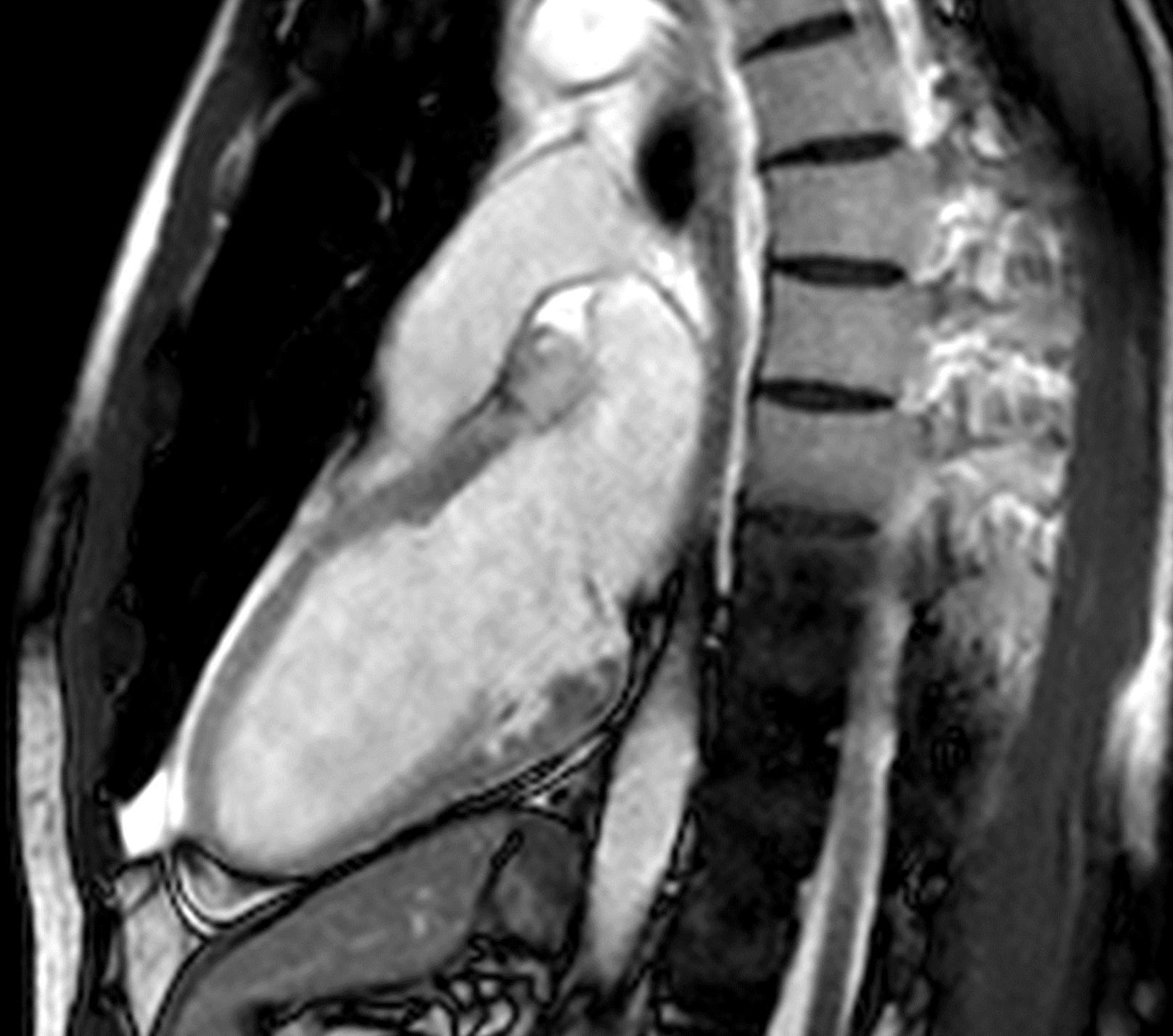




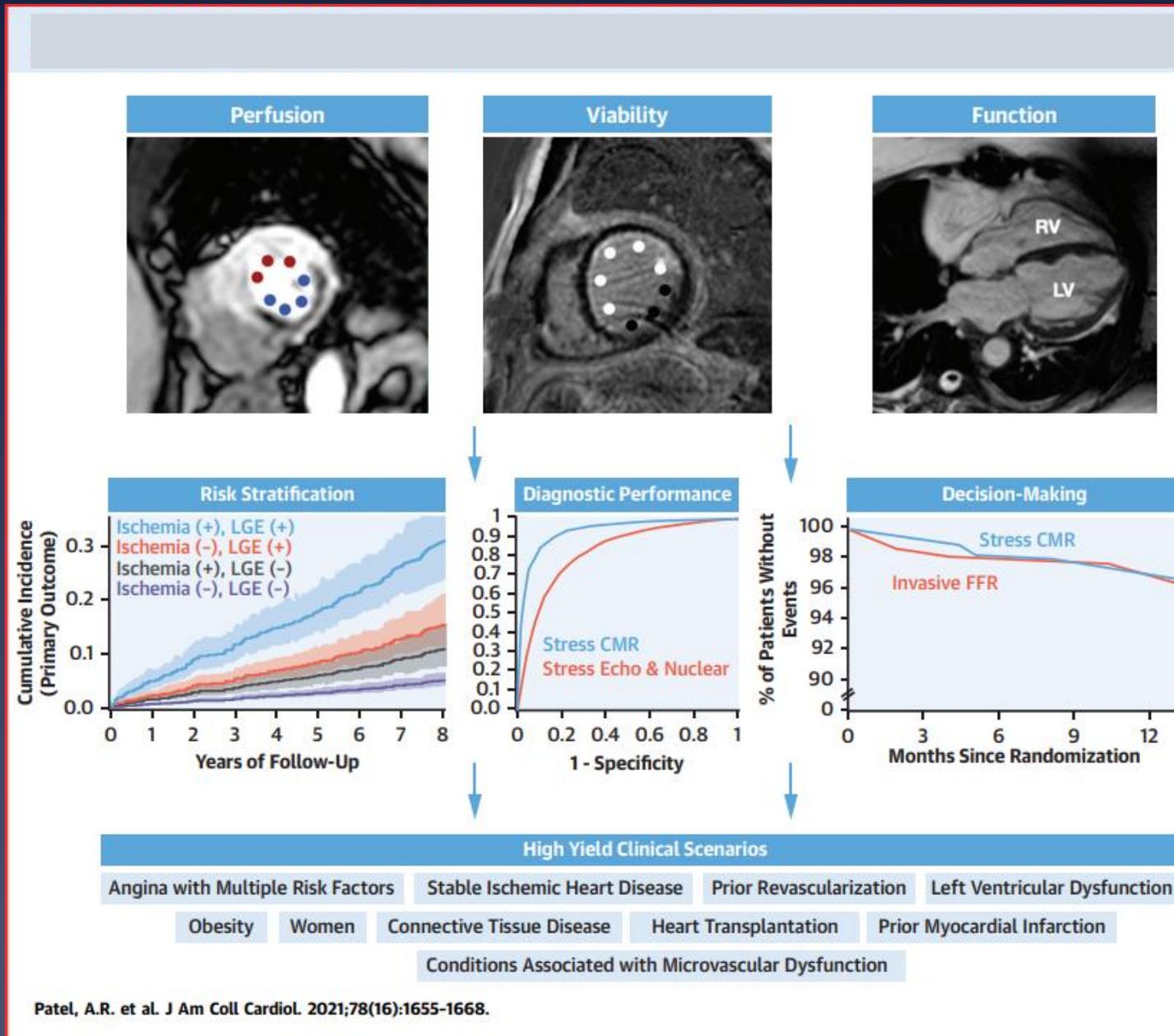
Cardiac MRI Imaging

- * CMR reported high sensitivity 89% and specificity of 87%.
- * CMR also has a g high spatial and temporal resolution in detecting subendocardial ischemia or infarction, freedom from soft tissue attenuation or the requirement of an acoustic window, sensitive tissue characterization for silent myocardial infarction and myocardial viability.
- * Excellent safety profile, and lack of ionizing radiation or iodinated contrast exposure.





The Key Elements of A Stress Cardiac Magnetic Resonance Imaging Examination Include Assessment of Ischemia, Viability, and Function



Cardiac MRI Imaging limitations

- * Stress CMR cannot readily be combined with exercise at present.
- * Claustrophobic and obese patients may not be able to tolerate the study.
- * Patients with implantable devices including ferromagnetic materials may not be ideal candidates for stress CMR due to device-related imaging artifacts that limit interpretability of the images.
- * The utilization of stress CMR is also hampered by cost and expertise.

Stress Cardiac Magnetic Resonance Myocardial Perfusion Imaging

JACC Review Topic of the Week



Amit R. Patel, MD,^{a,b} Michael Salerno, MD, PhD, MS,^{c,d,e} Raymond Y. Kwong, MD, MPH,^f Amita Singh, MD,^a Bobak Heydari, MD,^g Christopher M. Kramer, MD^{c,d}

ABSTRACT

Stress cardiovascular magnetic resonance imaging (CMR) is a cost-effective, noninvasive test that accurately assesses myocardial ischemia, myocardial viability, and cardiac function without the need for ionizing radiation. There is a large body of literature, including randomized controlled trials, validating its diagnostic performance, risk stratification capabilities, and ability to guide appropriate use of coronary intervention. Specifically, stress CMR has shown higher diagnostic sensitivity than single-photon emission computed tomography imaging in detecting angiographically significant coronary artery disease. Stress CMR is particularly valuable for the evaluation of patients with moderate to high pretest probability of having stable ischemic heart disease and for patients known to have challenging imaging characteristics, including women, individuals with prior revascularization, and those with left ventricular dysfunction. This paper reviews the basic principles of stress CMR, the data supporting its clinical use, the added-value of myocardial blood flow quantification, and the assessment of myocardial function and viability routinely obtained during a stress CMR study.

(J Am Coll Cardiol 2021;78:1655-1668) © 2021 by the American College of Cardiology Foundation.

Review

Qualitative and Quantitative Stress Perfusion Cardiac Magnetic Resonance in Clinical Practice: A Comprehensive Review

Wenli Zhou ¹, Jason Sin ², Andrew T. Yan ³, Haonan Wang ⁴, Jing Lu ¹, Yuehua Li ¹ , Paul Kim ⁵ , Amit R. Patel ⁶ and Ming-Yen Ng ^{7,8,*} 

¹ Department of Radiology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, No. 600, Yishan Road, Shanghai 200233, China

² Department of Diagnostic Radiology, The University of Hong Kong, Hong Kong SAR, China

³ St. Michael's Hospital, University of Toronto, Toronto, ON M5B 1W8, Canada

⁴ General Electric, Boston, MA 02210, USA

⁵ Department of Medicine, University of California San Diego, San Diego, CA 92093, USA

⁶ Department of Cardiovascular Medicine, University of Virginia, Charlottesville, VA 22903, USA

⁷ Department of Medical Imaging, HKU-Shenzhen Hospital, Shenzhen 518009, China

⁸ Department of Diagnostic Radiology, School of Clinical Medicine, The University of Hong Kong, Hong Kong SAR, China

* Correspondence: myng2@hku.hk

Abstract: Stress cardiovascular magnetic resonance (CMR) imaging is a well-validated non-invasive stress test to diagnose significant coronary artery disease (CAD), with higher diagnostic accuracy than other common functional imaging modalities. One-stop assessment of myocardial ischemia, cardiac function, and myocardial viability qualitatively and quantitatively has been proven to be a cost-effective method in clinical practice for CAD evaluation. Beyond diagnosis, stress CMR also provides prognostic information and guides coronary revascularisation. In addition to CAD, there is a large body of literature demonstrating CMR's diagnostic performance and prognostic value in other common cardiovascular diseases (CVDs), especially coronary microvascular dysfunction (CMD). This review focuses on the clinical applications of stress CMR, including stress CMR scanning methods, practical interpretation of stress CMR images, and clinical utility of stress CMR in a setting of CVDs with possible myocardial ischemia.

Keywords: stress imaging; cardiac magnetic resonance imaging; myocardial ischemia; coronary artery disease; coronary microvascular dysfunction



Citation: Zhou, W.; Sin, J.; Yan, A.T.; Wang, H.; Lu, J.; Li, Y.; Kim, P.; Patel, A.R.; Ng, M.-Y. Qualitative and Quantitative Stress Perfusion Cardiac Magnetic Resonance in Clinical Practice: A Comprehensive Review. *Diagnostics* **2023**, *13*, 524. <https://>

This Issue

Views **4,591** | Citations **0** | Altmetric **50**

Original Investigation

June 7, 2023

Diagnostic and Prognostic Value of Stress Cardiovascular Magnetic Resonance Imaging in Patients With Known or Suspected Coronary Artery Disease

A Systematic Review and Meta-analysis

Fabrizio Ricci, MD, PhD, MSc^{1,2,3}; Mohammed Y. Khanji, MBBCh, PhD^{3,4,5}; Giandomenico Bisaccia, MD¹; [et al](#)

» [Author Affiliations](#)

JAMA Cardiol. 2023;8(7):662-673. doi:10.1001/jamacardio.2023.1290

This systematic review and meta-analysis pooling 74,470 patients with stable chest pain over 381,357 person-years of follow-up, stress CMR yielded high diagnostic accuracy and accurate risk stratification in patients with known or suspected coronary artery disease, particularly when 3-T imaging was used.

The presence of stress-inducible ischemia and late gadolinium enhancement was associated with higher mortality and likelihood of cardiovascular events, while normal stress CMR results were associated with a lower likelihood of cardiovascular events for at least 3.5 years.

3D phase 75%

PS

....

Volume Rendering No cut

DFOV 13.2cm
STND Ph:75% (No Fil.)

R
S
A

L
I
P

No VOI

W = 4095 L = 2048

AI

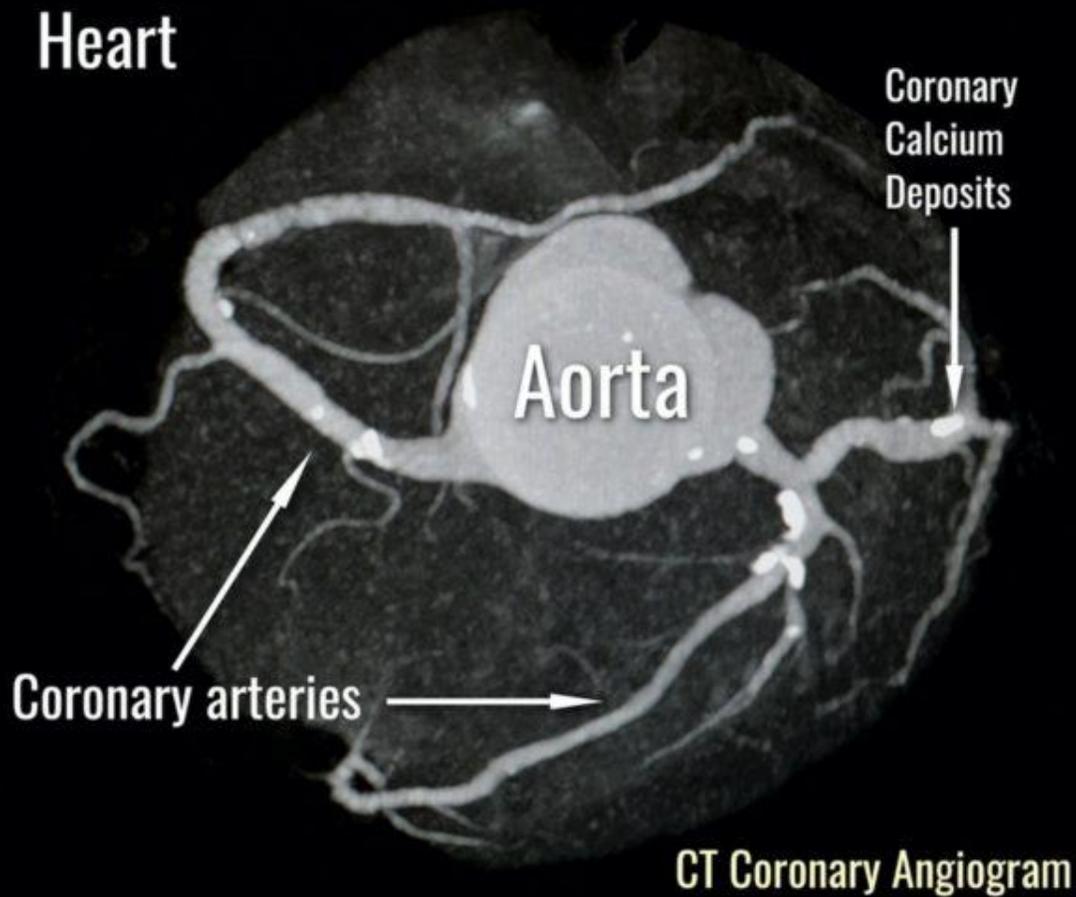


CT coronary angiogram study

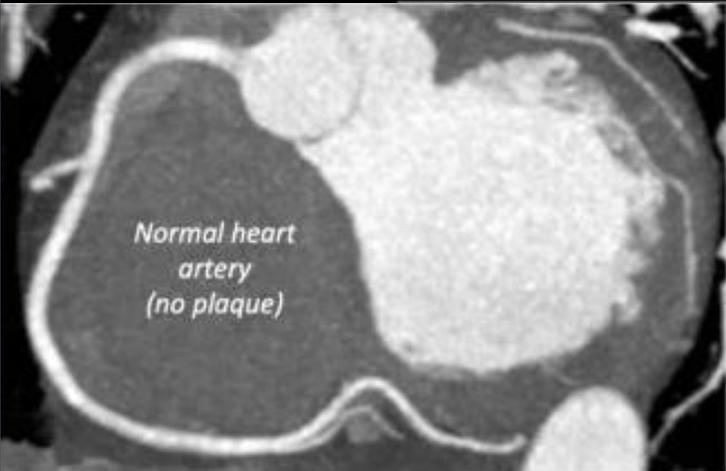
- * Sensitivity is about 85-90% and the specificity is 64-90%
- * Advantage : High negative predictive value (especially in low to intermediate risk subjects)
- * Disadvantage : Radiation (12-20 mSv) and Functional effect of stenosis not usually assessed, nor exercise capacity

Coronary artery calcium score CT radiation is about 1–3 mSv

Heart



CT Coronary Angiogram



Update for the Performance of CT Coronary Angiography

Evidence-Based Application and Technical Guidance According to Current Consensus Guidelines and Practical Advice from the Clinical Routine

Update zur Durchführung der CT-Koronarangiografie

Evidenzbasierter Einsatz und technische Anleitung entsprechend den aktuellen Empfehlungen sowie praktische Tipps aus der Routine am eigenen Standort

Authors

Martin Soschynski¹, Muhammad Taha Hagar¹, Jana Taron^{1,2}, Tobias Krauss¹, Philipp Ruile³, Manuel Hein³, Thomas Nührenberg³, Maximilian Frederik Russe¹, Fabian Bamberg¹, Christopher L Schlett¹

- * cCTA is recommended in the current guidelines of the ESC primarily in the case of low and intermediate clinical probability of coronary artery disease.
- * This study and the consensus recommendations of the Society of Cardiovascular Computed Tomography (SCCT) can be used as an orientation guide for the practical workflow for cCTA preparation and acquisition.
- * Image quality and radiation dose still depend on the examination preparation and the selection of the scan protocol.

CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial



The SCOT-HEART investigators*

Summary

Background The benefit of CT coronary angiography (CTCA) in patients presenting with stable chest pain has not been systematically studied. We aimed to assess the effect of CTCA on the diagnosis, management, and outcome of patients referred to the cardiology clinic with suspected angina due to coronary heart disease.

Methods In this prospective open-label, parallel-group, multicentre trial, we recruited patients aged 18–75 years referred for the assessment of suspected angina due to coronary heart disease from 12 cardiology chest pain clinics across Scotland. We randomly assigned (1:1) participants to standard care plus CTCA or standard care alone. Randomisation



Lancet 2015; 385: 2383–91

Published Online
March 15, 2015
[http://dx.doi.org/10.1016/S0140-6736\(15\)60291-4](http://dx.doi.org/10.1016/S0140-6736(15)60291-4)

This online publication has been corrected. The corrected version first appeared at

.....the PROMISE and SCOT-HEART trials — that compared CT with functional testing in patients with stable symptomsThe investigators found that CT was as good as functional testing as a preliminary evaluation before possible ICA.

Findings Between Nov 18, 2010, and Sept 24, 2014, we randomly assigned 4146 (42%) of 9849 patients who had been referred for assessment of suspected angina due to coronary heart disease. 47% of participants had a baseline clinic diagnosis of coronary heart disease and 36% had angina due to coronary heart disease. At 6 weeks, CTCA reclassified the diagnosis of coronary heart disease in 558 (27%) patients and the diagnosis of angina due to coronary heart disease in 481 (23%) patients (standard care 22 [1%] and 23 [1%]; $p < 0.0001$). Although both the certainty (relative risk [RR] 2.56, 95% CI 2.33–2.79; $p < 0.0001$) and frequency of coronary heart disease increased (1.09, 1.02–1.17; $p = 0.0172$), the certainty increased (1.79, 1.62–1.96; $p < 0.0001$) and frequency seemed to decrease (0.93, 0.85–1.02; $p = 0.1289$) for the diagnosis of angina due to coronary heart disease. This changed planned investigations (15% vs 1%; $p < 0.0001$) and treatments (23% vs 5%; $p < 0.0001$) but did not affect 6-week symptom severity or subsequent admittances to hospital for chest pain. After 1.7 years, CTCA was associated with a 38% reduction in fatal and non-fatal myocardial infarction (26 vs 42, HR 0.62, 95% CI 0.38–1.01; $p = 0.0527$), but this was not significant.

Interpretation In patients with suspected angina due to coronary heart disease, CTCA clarifies the diagnosis, enables targeting of interventions, and might reduce the future risk of myocardial infarction.

Edinburgh, Centre for Cardiovascular Science, Chancellor's Building, Edinburgh EH16 4SA, Scotland
d.e.newby@ed.ac.uk

ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The use of CTA in addition to standard care in patients with stable chest pain resulted in a significantly lower rate of death from coronary heart disease or nonfatal myocardial infarction at 5 years than standard care alone, without resulting in a significantly higher rate of coronary angiography or coronary revascularization.

The 5-year rate of the primary end point was lower in the CTA group than in the standard-care group (2.3% [48 patients] vs. 3.9% [81 patients]; hazard ratio, 0.59; 95% confidence interval [CI], 0.41 to 0.84; $P=0.004$).

METHODS

In an open-label, multicenter, parallel-group trial, we randomly assigned 4146 patients with stable chest pain who had been referred to a cardiology clinic for evaluation to standard care plus CTA (2073 patients) or to standard care alone (2073 patients). Investigations, treatments, and clinical outcomes were assessed over 3 to 7 years of follow-up. The primary end point was death from coronary heart disease or nonfatal myocardial infarction at 5 years.

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

APRIL 28, 2022

VOL. 386 NO. 17

CT or Invasive Coronary Angiography in Stable Chest Pain

The DISCHARGE Trial Group

ABSTRACT

- * Pragmatic, randomized trial comparing CT with ICA as initial diagnostic imaging strategies for guiding the treatment of patients with stable chest pain.
- * 3561 patients followed up for 3.5 years. The primary outcome was major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke)

Among patients referred for ICA because of stable chest pain and intermediate pretest probability of CAD, the risk of major adverse cardiovascular events was similar in the CT group and the ICA group.

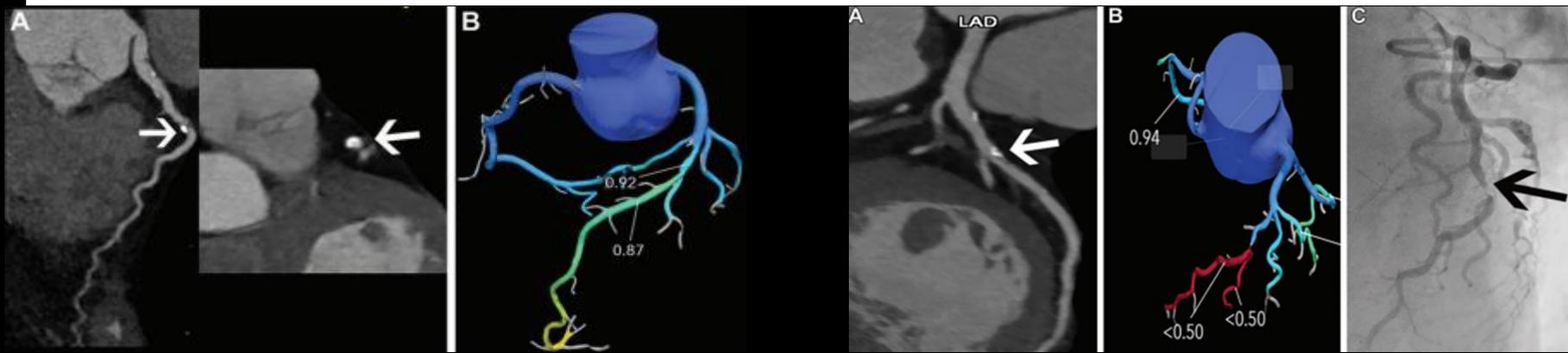
ORIGINAL RESEARCH

Anatomical and Functional Computed Tomography for Diagnosing Hemodynamically Significant Coronary Artery Disease

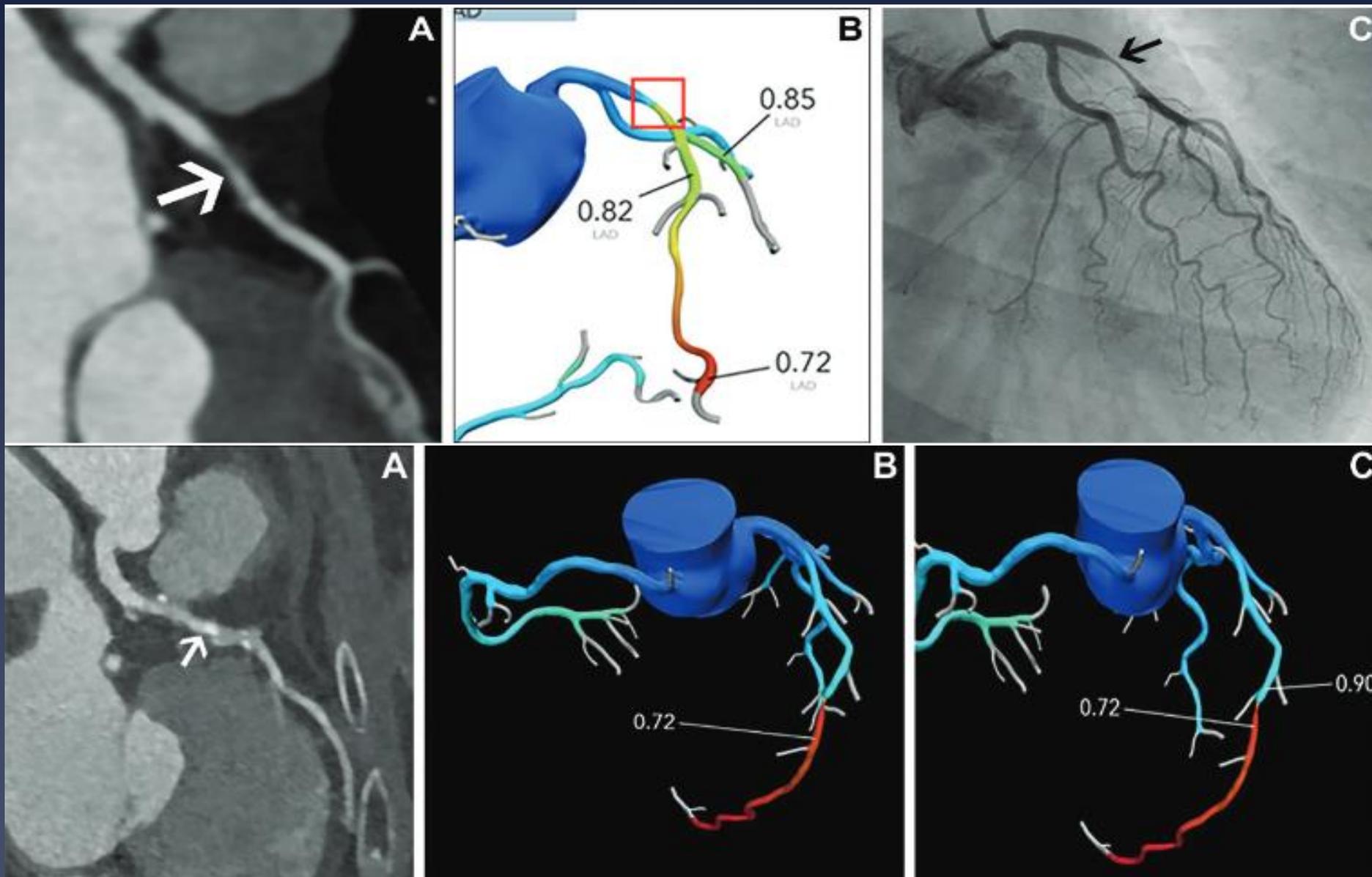


A Meta-Analysis

Csilla Celeng, MD, PhD,^a Tim Leiner, MD, PhD,^a Pál Maurovich-Horvat, MD, PhD, MPH,^b Béla Merkely, MD, PhD,^b
Pim de Jong, MD, PhD,^a Jan W. Dankbaar, MD, PhD,^a Hendrik W. van Es, MD, PhD,^c Brian B. Ghoshhajra, MD, MBA,^d
Udo Hoffmann, MD, MPH,^d Richard A.P. Takx, MD, PhD, MSc^{a,c,d}



CT FFR (FFR_{CT})



CT Fractional Flow Reserve: A Practical Guide to Application, Interpretation, and Problem Solving

Prabhakar Rajiah, MBBS, MD, FRCR
Kristopher W. Cummings, MD
Eric Williamson, MD
Phillip M. Young, MD

Abbreviations: ACS = acute coronary syndrome, CAD = coronary artery disease, CTA = CT angiography, FFR_{CT} = fractional flow reserve CT, ICA = invasive coronary angiography, LAD = left anterior descending artery, LCx = left circumflex artery, MACE = major adverse cardiovascular events, MPR = multiplanar reconstruction, OMT = optimal medical therapy, PCI = percutaneous coronary intervention, TAVR = transcatheter aortic valve replacement, 3D = three dimensional

RadioGraphics 2022; 42:340–358

<https://doi.org/10.1148/rg.210097>

Content Codes: **CA** **CT**

From the Department of Radiology, Mayo Clinic, 200 1st St SW, Rochester, MN 55905 (P.R., E.W., P.M.Y.); and Department of Radiology, Mayo Clinic, Phoenix, Ariz (K.W.C.). Recipient of a Cum Laude award for an education exhibit at the 2020 RSNA Annual Meeting. Received March 29, 2021; revision requested April 30 and received June 22; accepted July 2. For this journal-based SA-CME activity, the author P.R. has provided disclosures (see end of article); all other authors, the editor, and the reviewers have disclosed no relevant relationships. **Address correspondence to** P.R. (e-mail: radpr73@gmail.com).

©RSNA, 2022

CT fractional flow reserve (FFR_{CT}) is a physiologic simulation technique that models coronary flow from routine coronary CT angiography (CTA). To evaluate lesion-specific ischemia, FFR_{CT} is measured 2 cm distal to a stenotic lesion. FFR_{CT} greater than 0.8 is normal, 0.76–0.8 is borderline, and 0.75 or less is abnormal. FFR_{CT} should always be interpreted in correlation with clinical and anatomic coronary CTA findings. FFR_{CT} increases the specificity of coronary CTA in the evaluation of coronary artery disease, decreases the prevalence of nonobstructive disease in invasive coronary angiography (ICA), and helps with revascularization decisions and planning. Patients with intermediate-risk coronary anatomy at CTA and abnormal FFR_{CT} can undergo ICA and revascularization, whereas those with normal FFR_{CT} can be safely deferred from ICA. In borderline FFR_{CT} values, management is decided in the context of the clinical scenario, but many cases could be safely managed with medical treatment. There are some limitations and pitfalls of FFR_{CT} . Abnormal FFR_{CT} values can be seen in mild stenosis, and normal FFR_{CT} values can be seen in severe stenosis. Gradually decreasing or abnormal low FFR_{CT} values at the distal vessel without a proximal focal lesion could be due to diffuse atherosclerosis. Coronary stents, bypass grafts, coronary anomalies, coronary dissection, transcatheter aortic valve replacement, unstable angina, and acute or recent myocardial infarction are situations in which FFR_{CT} has not been validated and should not be used at this time. The authors provide a practical guide to the applications and interpretation of FFR_{CT} , focusing on common pitfalls and challenges.

Online supplemental material is available for this article.

Coronary angiogram study



- * Sensitivity is about 100% and the specificity is 100%
- * Advantage : Gold standard.
- * Disadvantage : Invasive, Radiation (8 to 10 mSv) and Functional effect of stenosis not routinely.



Coronary angiography	5.6 mSv
PTCA	6.9 mSv
Coronary angiography with PTCA	9.3 mSv
Coronary Angiography + PTCA + Stent	13 mSv

100 mSv	Above about 100 mSv, the probability of cancer (rather than the severity of illness) increases with dose. The estimated risk of fatal cancer is 5 of every 100 persons exposed to a dose of 1000 mSv (ie. if the normal incidence of fatal cancer were 25%, this dose would increase it to 30%).
50 mSv	Is, conservatively, the lowest dose at which there is any evidence of cancer being caused in adults. It is also the highest dose which is allowed by regulation in any one year of occupational exposure. Dose rates greater than 50 mSv/yr arise from natural background levels in several parts of the world but do not cause any discernible harm to local populations.
20 mSv/yr	Averaged over 5 years is the limit for radiological personnel such as employees in the nuclear industry, uranium or mineral sands miners and hospital workers (who are all closely monitored).
10 mSv/yr	Is the maximum actual dose rate received by any Australian uranium miner.
3-5 mSv/yr	Is the typical dose rate (above background) received by uranium miners in Australia and Canada.
3 mSv/yr	(approx) is the typical background radiation from natural sources in North America, including an average of almost 2 mSv/yr from radon in air.
2 mSv/yr	(approx) is the typical background radiation from natural sources, including an average of 0.7 mSv/yr from radon in air. This is close to the minimum dose received by all humans anywhere on Earth.
0.3-0.6 mSv/yr	Is a typical range of dose rates from artificial sources of radiation, mostly medical.
0.05 mSv/yr	A very small fraction of natural background radiation, is the design target for maximum radiation at the perimeter fence of a nuclear electricity generating station. In practice the actual dose is less.

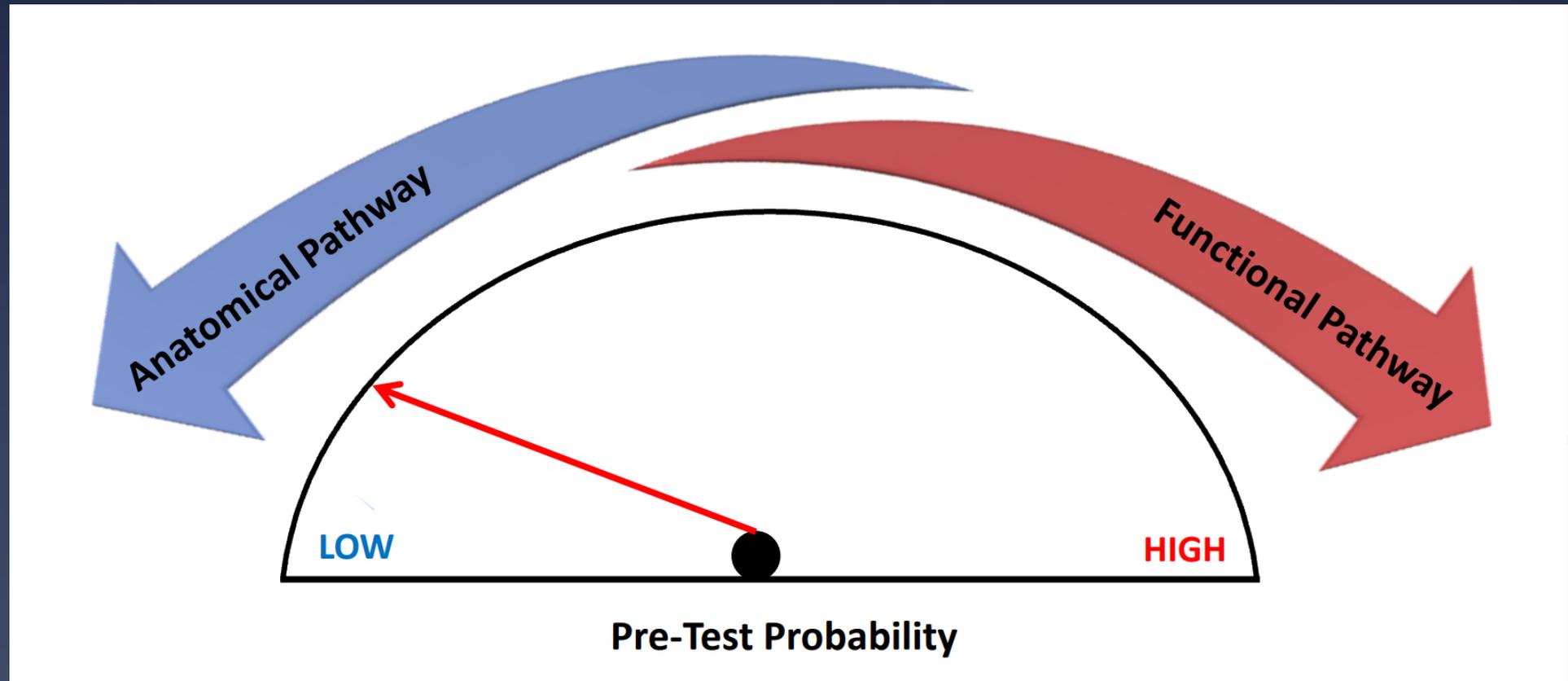
How much ionising radiation is dangerous?...
 Maybe
 Cardiologist is not telling me the truth !!!



Conclusion

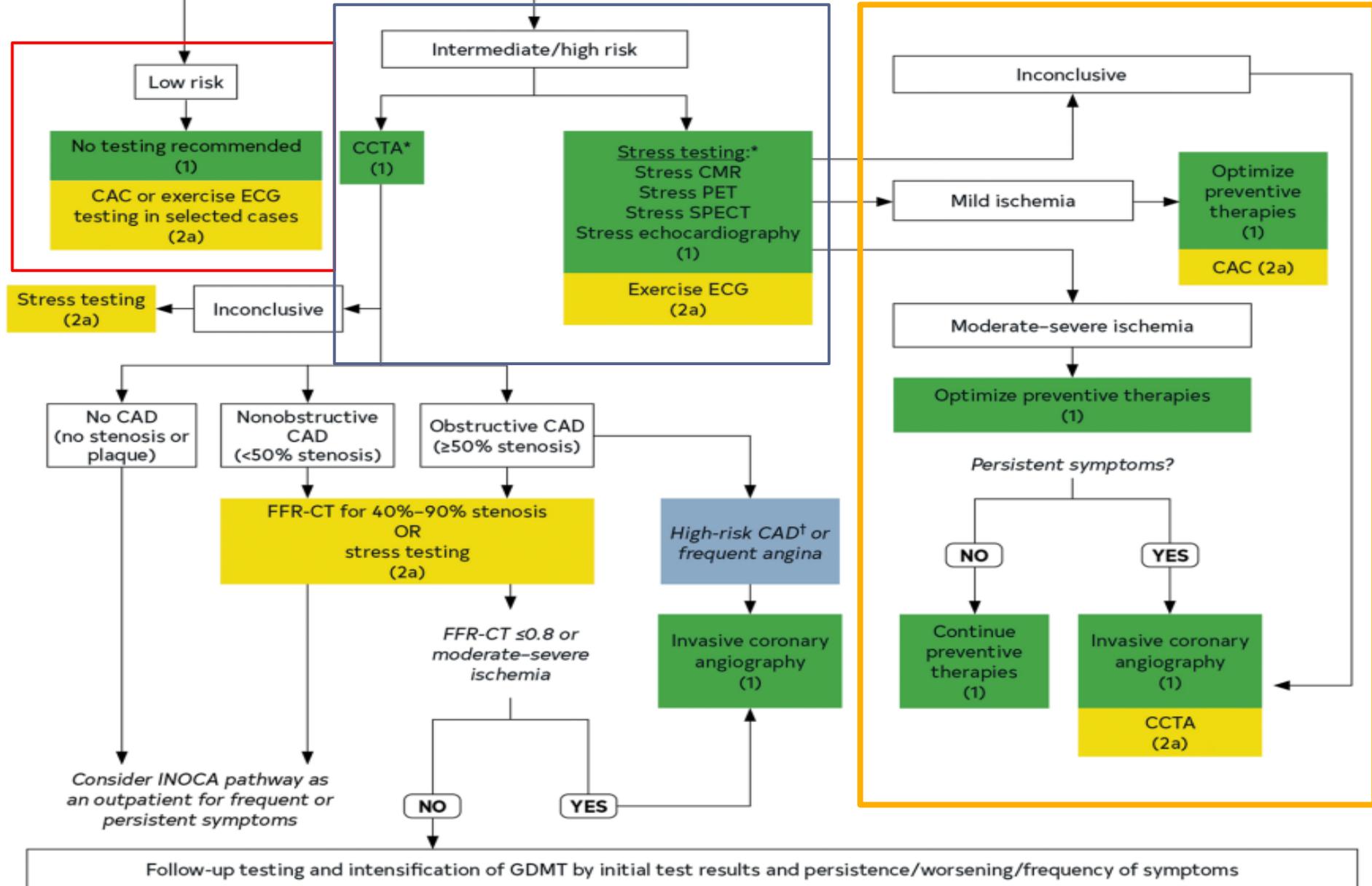
- * Which test to prescribe can be sometimes difficult to decide. Both anatomic and functional imaging techniques have strengths and limitations.
- * CCTA is the preferred test in patients with a lower range of clinical likelihood of CAD..... Hence rule-out power.
- * Non-invasive functional tests for ischemia have a better rule-in power and should be therefore preferred in those with higher clinical risk of coronary atherosclerosis.

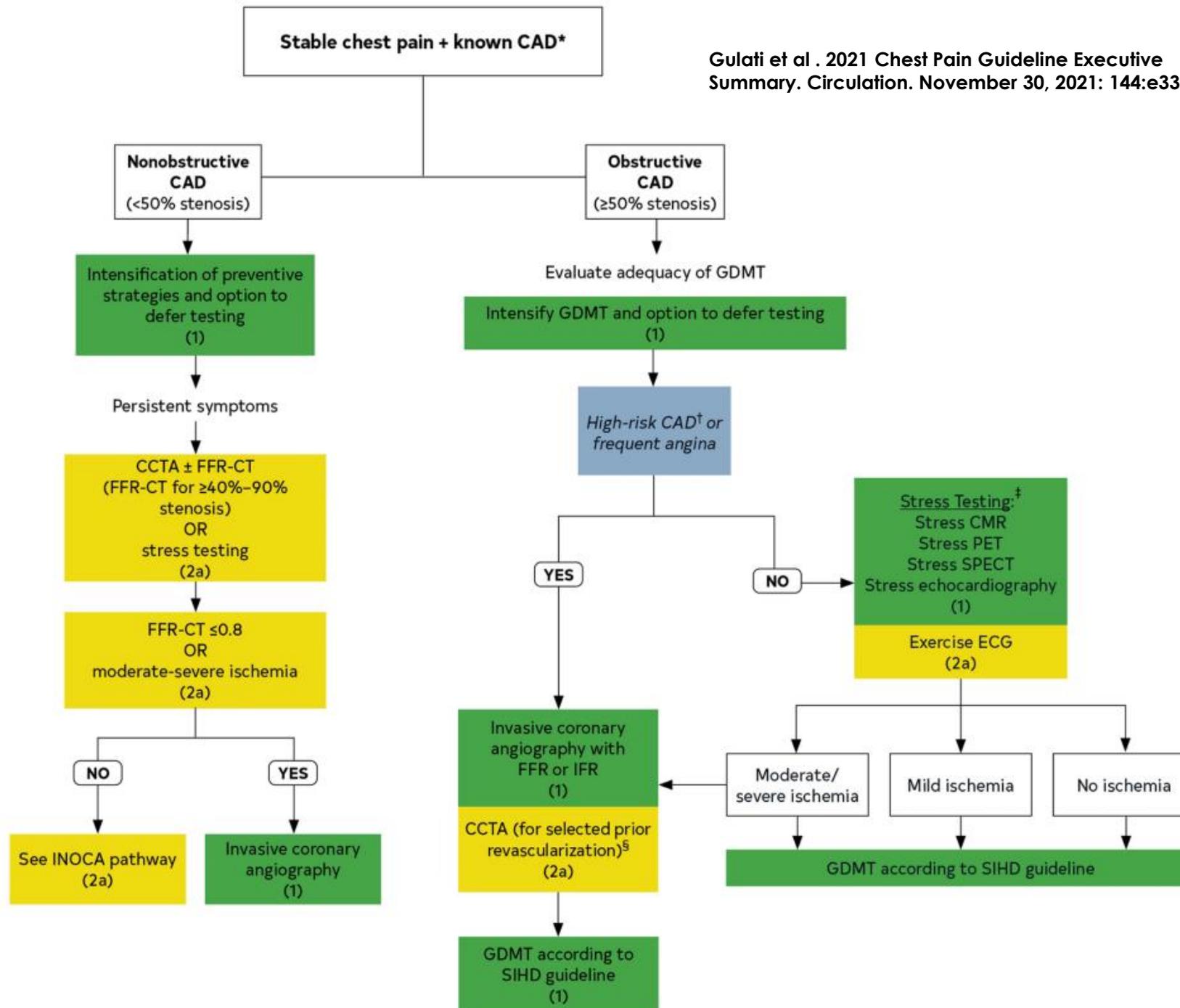
Non-invasive imaging in Chronic Coronary Syndrome



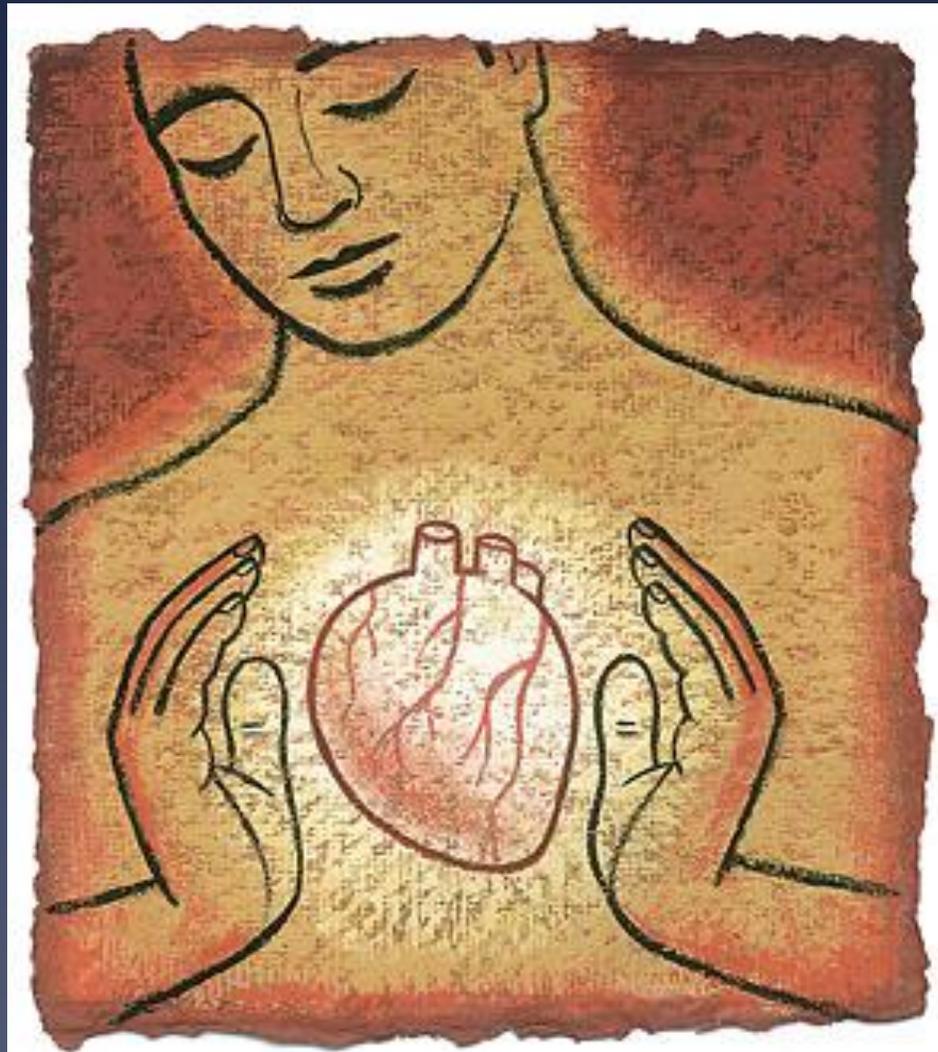
Stable Chest Pain + No Known CAD

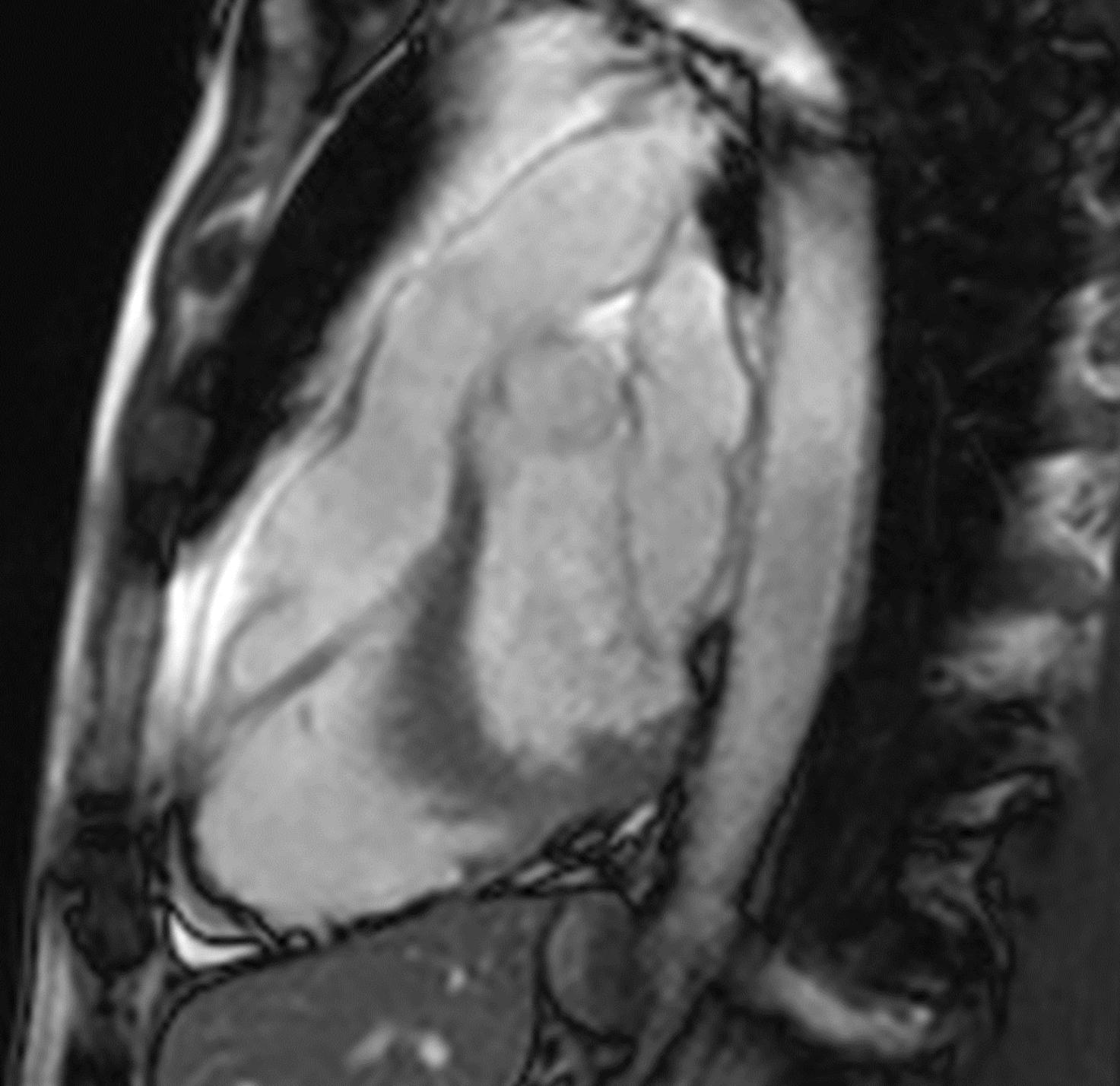
Gulati et al . 2021 Chest Pain Guideline Executive Summary. Circulation. November 30, 2021: 144:e336–e367

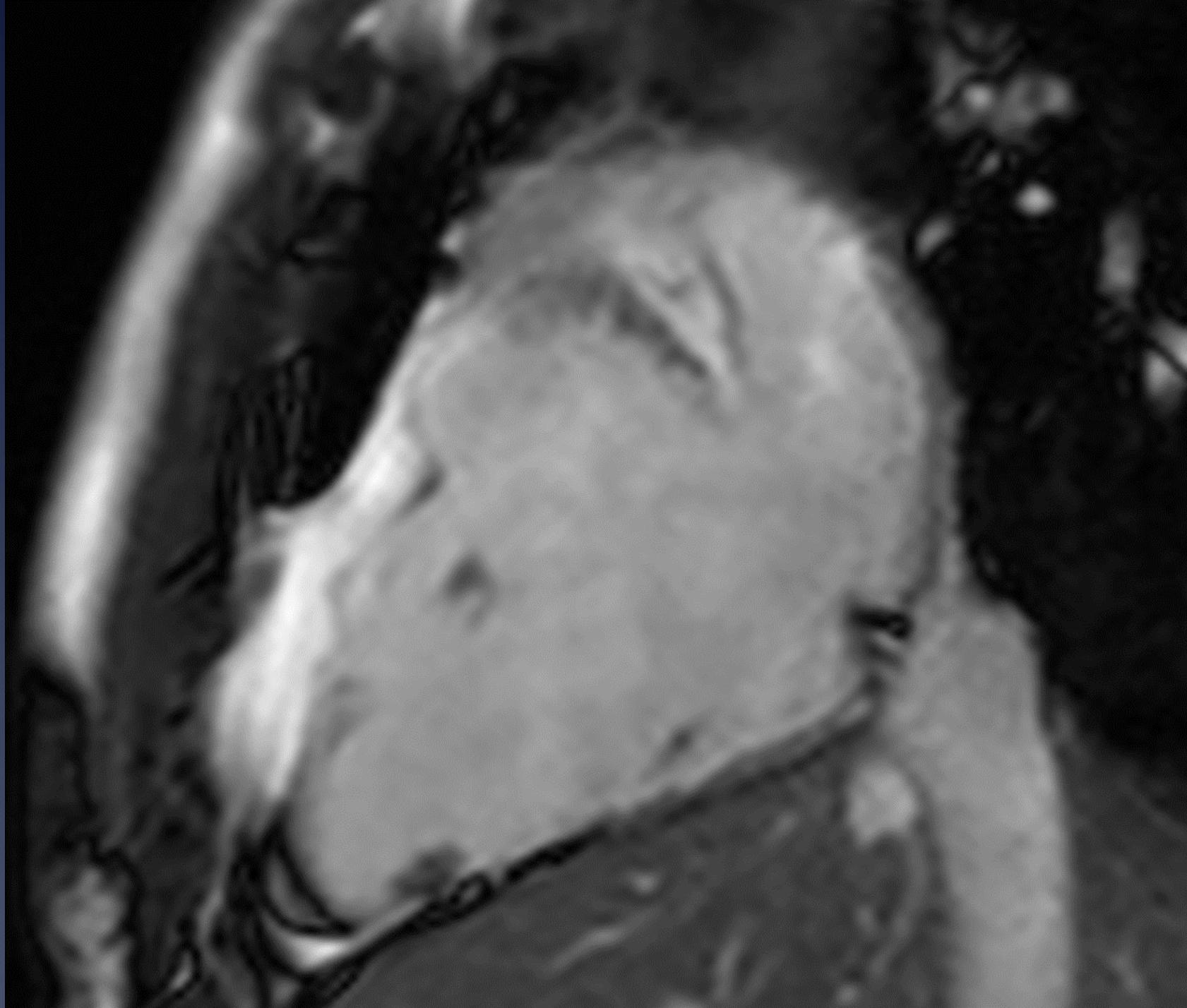




Thank You







Case study

- * 68 yr old Malay lady. Active lady
- * Known hypertension and hyperlipidemia 10 year.
- * Current medications:

Cardiprin	100 mg daily
Felodipine	5 mg daily
Simvastatin	20 mg on

Case study

- * Angina on exertion 1 month. On and off. Height 155 cm, Weight 69 kg (BMI 28.7).
- * The BP is 140/80 mmHg and the is pulse 84 bpm. Clinical examination normal
- * Blood: Total cholesterol 4.7 mmol/L , LDL 2.6 mmol/L , HDL 1.0 mmol/L, TG 2.0 mmol/L FBS 8.0 mmol/L, HbA1c 8.0%. Renal profile and urine normal.
- * ECG normal. Echocardiography was done and it showed a normal cardiac anatomy with no regional LV wall abnormalities seen at rest.
- * Positive stress Echo for ischeamia at High work load mainly at the inferior and posterior territory.

What is Optimal Medical treatment

- * The combination of intensive, evidence-based pharmacologic intervention with life-saving interventions comprises optimal medical therapy (OMT).
- * OMT is recommended by guidelines for all stable IHD patients, regardless of whether revascularization is performed.
- * Optimal medical therapy consisted of antiplatelet therapy, anti-ischemic therapy, and aggressive lipid and blood pressure control.
- * Based on the strength of the evidence, recommending more-aggressive medical therapy for patients with moderate-to-severe angina, and PCI or CABG for many patients in whom symptoms persist

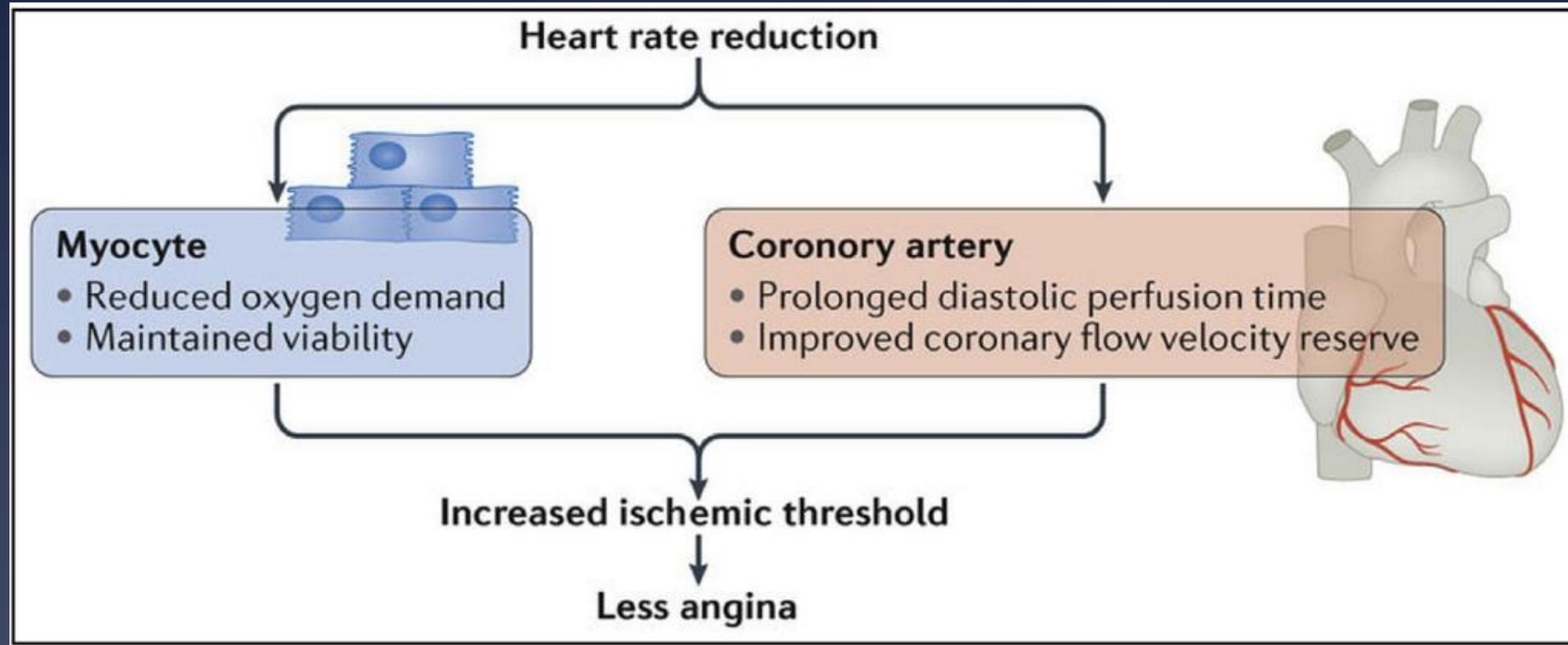
Case study : How would You managed her

- * Risk factor modification and go on medical treatment.
- * Do other test like MSCT angiogram.
- * Counselling patient for Invasive coronary angiogram.

That the Diabetic need to be address with Metformin in combination with SGLT2 inhibitor and the Felodipine was replace with ACEI and for the angina I started with Bisoprolol and Trimetazidine

- * Ultimately the goal of using non-invasive testing is to guide further non-invasive medical or invasive therapy.
- * Anatomical testing is recommended for patients with low to intermediate risk for future events, while stress testing is preferred in higher risk patients due to its greater rule in power

Beneficial effects of heart rate reduction in angina

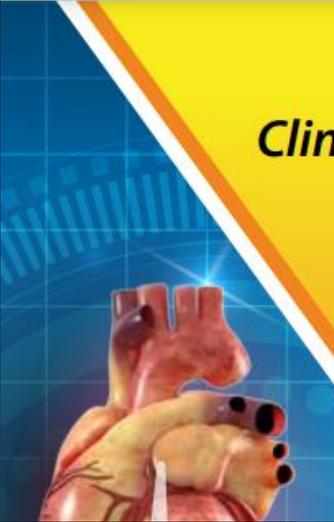


Problems with Guidelines

- * All guidelines take into consideration evidence provided by published trial data and meta-analysis of the different studies.
- * However, in absence of these data which unfortunately is not uncommon, the recommendations are made according to previously reported guidelines, tradition-driven beliefs, and opinion of the experts on the guideline committees.
- * Some guideline suggestions are inevitably, therefore, not evidence-based. The lack of reliable, objective data is indicated by providing a lower class to the recommendation.

Angina Guidelines

- * The absence of objective data is particularly relevant to the guidelines for antianginal drug therapy. The AHA/ACC , ESC , and NICE recommendations suggest a first-choice therapy with sublingual or short-acting nitroglycerin, β -blockers, and calcium-channel blockers.
- * *Ivabradine, nicorandil, ranolazine, and trimetazidine are reserved for patients who have contraindications to the first-choice agents, do not tolerate them, or remain symptomatic, even though more evidence-based clinical data that are more contemporary are available for them than for the first-choice drugs.*
- * No head-to-head comparisons between first-choice and second-choice treatments are available that demonstrate superiority of one over any other in terms of antianginal effects.
- * Sometimes double and sometimes triple therapy with different classes of antianginal drugs is often needed, and the guidelines do not provide an indication of the optimal combination.



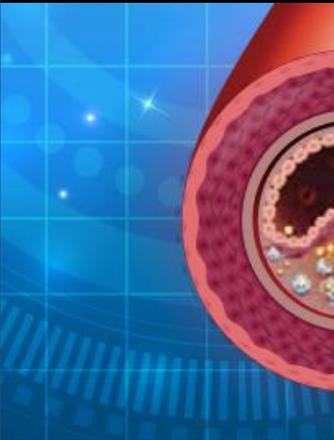
8.2.2. Management of symptoms - Anti-ischemic therapy (Fig 2, pg 25)

Anti-ischemic therapy is used to treat the symptoms of angina. While these medications have been shown to reduce symptoms, none have been shown to prevent MI or death in patients with stable CAD.

These medications prevent attacks of angina by:

- decreasing myocardial oxygen consumption (lowering heart rate, blood pressure, myocardial loading, or myocardial contractility) and/or
- increasing myocardial oxygen supply (increasing coronary blood flow)

.....That the Diabetic need to be address with Metformin in combination with SGLT2 inhibitor and the Felodipine was replace with ACEI and for the angina I started with Bisoprolol and Trimetazidine.....



- Ivabradine
- Ranolazine
- Nicorandil

The choice of anti-ischemic therapy should be individualised depending upon:

- presence of co-morbidities (such as asthma) and/or
- physiological parameters such as resting heart rate, blood pressure, LV function and/or
- Cost and availability

Combination of anti-ischemic therapy may be necessary to control symptoms.

OPEN

EXPERT CONSENSUS DOCUMENT

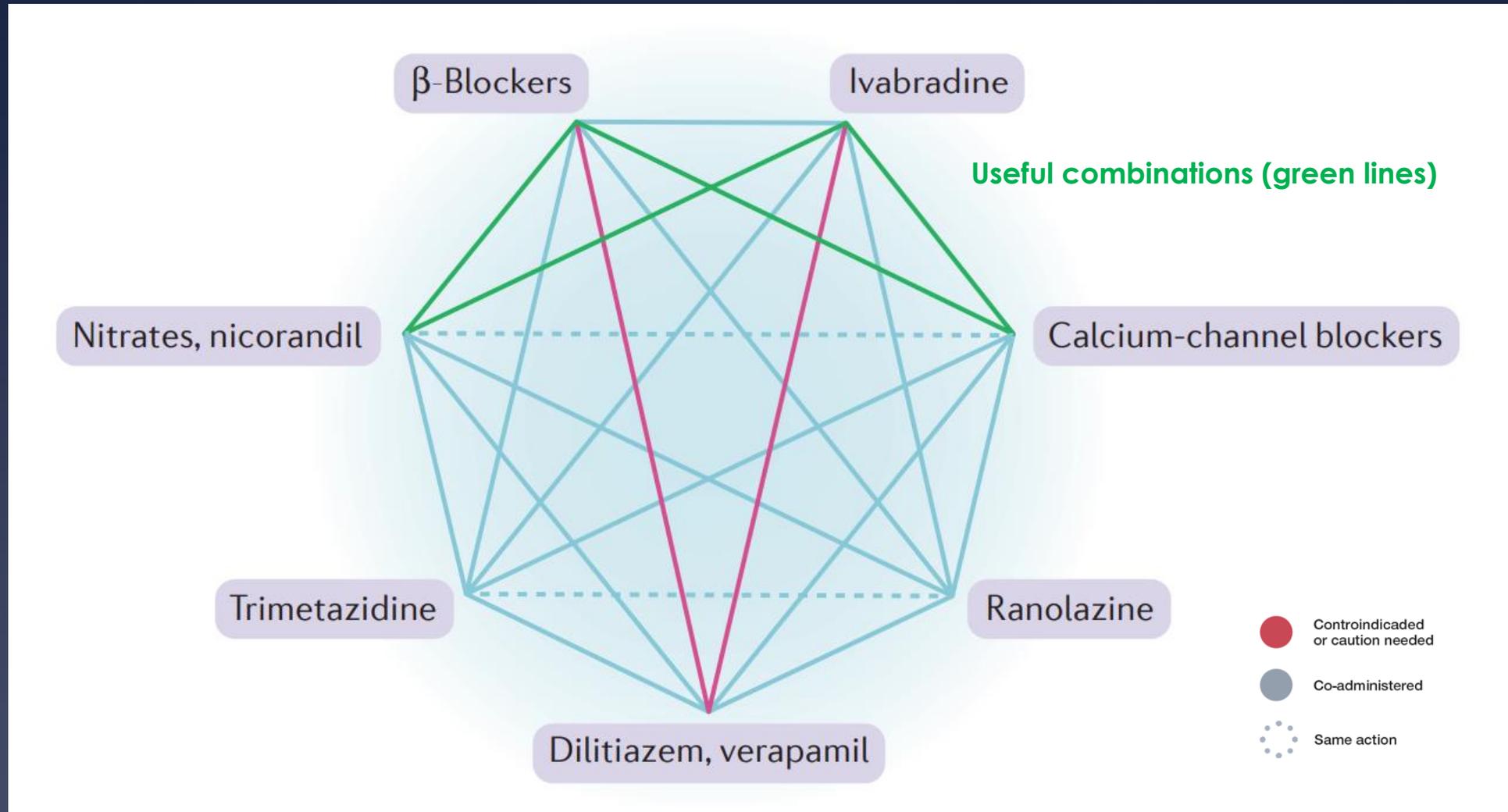
A 'diamond' approach to personalized treatment of angina

Roberto Ferrari^{1,2}, Paolo G. Camici³, Filippo Crea⁴, Nicolas Danchin⁵, Kim Fox⁶, Aldo P. Maggioni⁷, Athanasios J. Manolis⁸, Mario Marzilli^{9,10}, Giuseppe M. C. Rosano^{11,12} and José L. Lopez-Sendon¹³

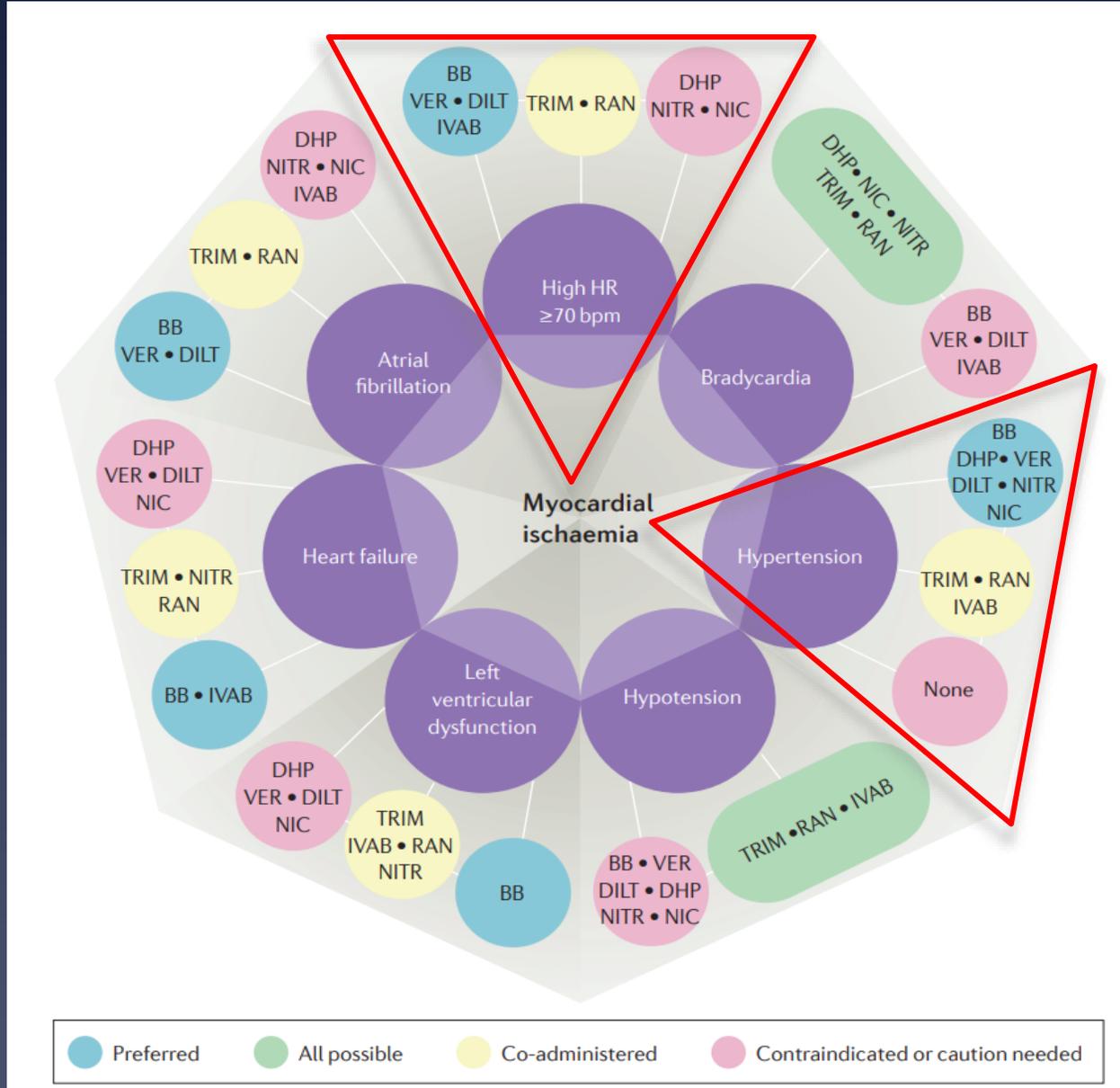
Abstract | In clinical guidelines, drugs for symptomatic angina are classified as being first choice (β -blockers, calcium-channel blockers, short-acting nitrates) or second choice (ivabradine, nicorandil, ranolazine, trimetazidine), with the recommendation to reserve second-choice medications for patients who have contraindications to first-choice agents, do not tolerate them, or remain symptomatic. No direct comparisons between first-choice and second-choice treatments have demonstrated the superiority of one group of drugs over the other.

Meta-analyses show that all antianginal drugs have similar efficacy in reducing symptoms, but provide no evidence for improvement in survival. The newer, second-choice drugs have more evidence-based clinical data that are more contemporary than is available for traditional first-choice drugs. Considering some drugs, but not others, to be first choice is, therefore, difficult. Moreover, double or triple therapy is often needed to control angina. Patients with angina can have several comorbidities, and symptoms can result from various underlying pathophysiologies. Some agents, in addition to having antianginal effects, have properties that could be useful depending on the comorbidities present and the mechanisms of angina, but the guidelines do not provide recommendations on the optimal combinations of drugs. In this Consensus Statement, we propose an individualized approach to angina treatment, which takes into consideration the patient, their comorbidities, and the underlying mechanism of disease.

Possible combinations of different classes of antianginal drugs

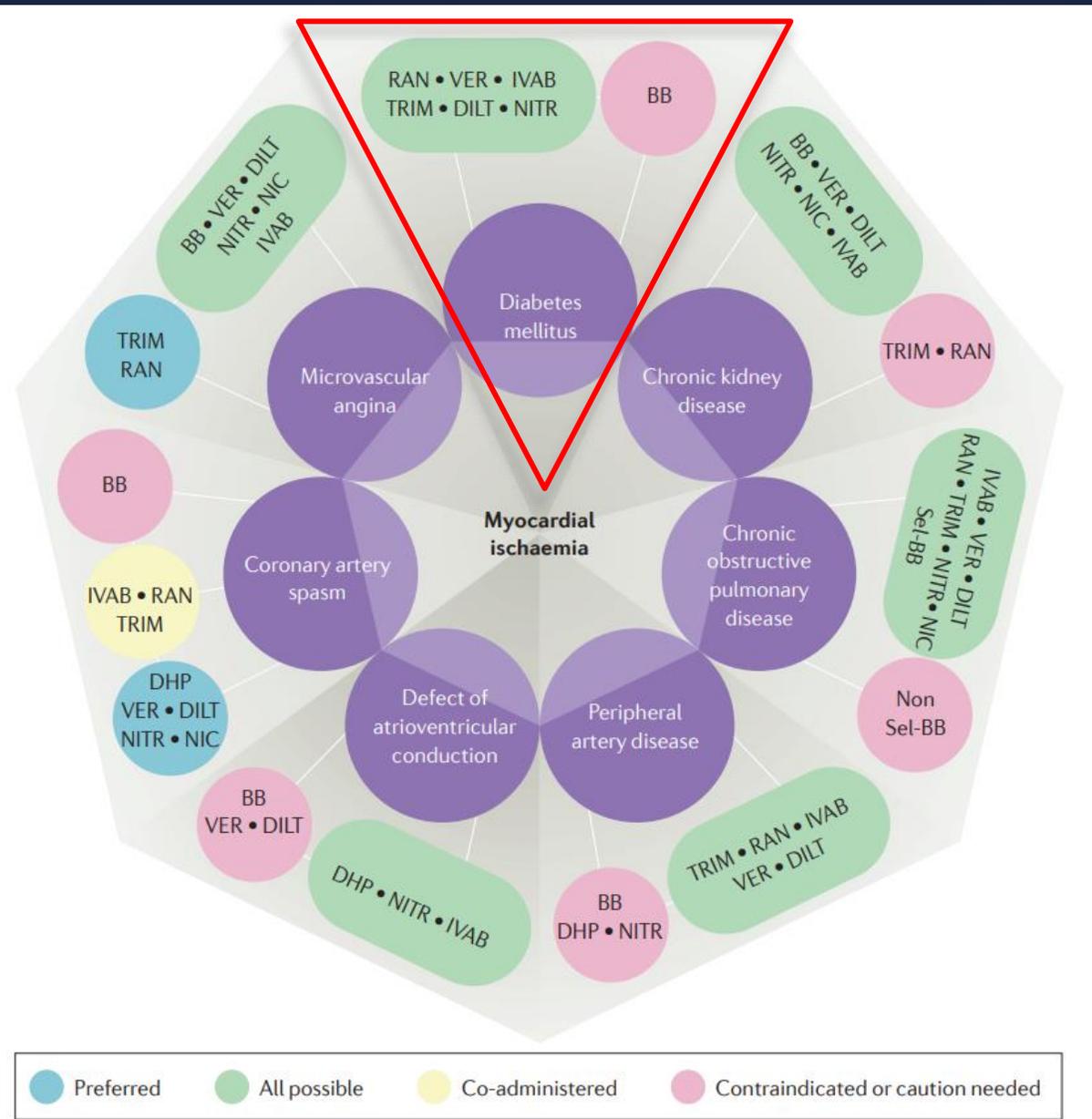


Possible combinations of classes of antianginal drugs according to different comorbidities



Expert Consensus Document. A 'diamond' approach to personalized treatment of angina. Roberto Ferrari et al. Nature Reviews | Cardiology. 15 | February 2018

Possible combinations of classes of antianginal drugs according to different comorbidities



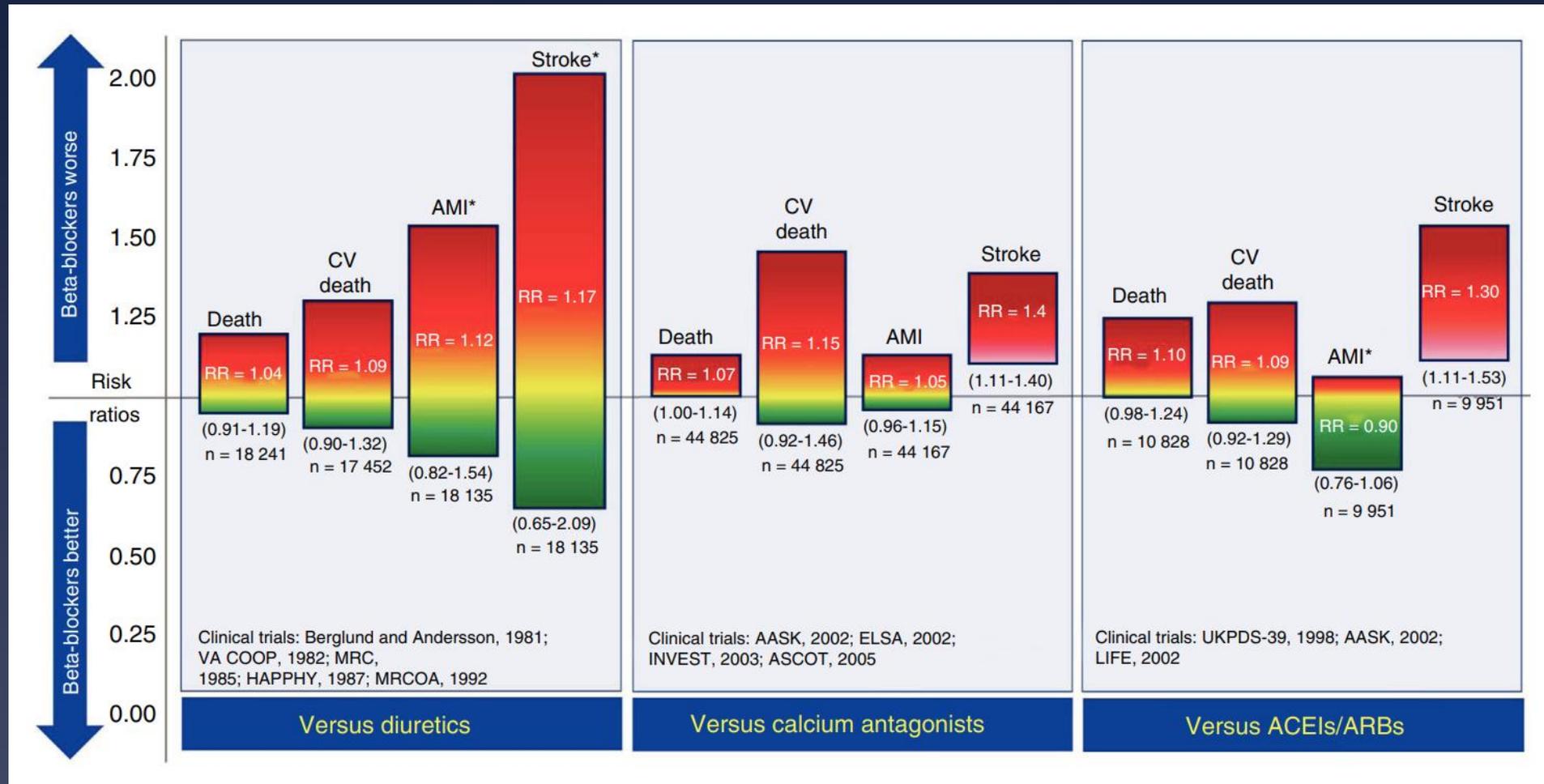
Expert Consensus Document. A 'diamond' approach to personalized treatment of angina. Roberto Ferrari et al. Nature Reviews | Cardiology. 15 | February 2018

Case Study

- * Came back earlier to see me because she felt fatigue and “Mengah” .
- * The BP is 130/80 mmHg and the is pulse 74 bpm. Clinical examination normal.
- * Stopped Bisoprolol and started Ivabradine at 5 mg Bid

Have been with me for the last 5 years with no cardiac events with fairly good control of the Risk factors and a pulse rate between 60-70 bpm with Ivabradine 7.5 mg bd

Beta Blockers in Hypertension



Compared with placebo, BBs have not been shown to reduce all-cause or cardiovascular mortality in patients with uncomplicated essential hypertension but there was reduction of stroke. Compared with diuretics, CCB and ACEi/ARB, BBs do not reduce cardiovascular events and may even be associated with a higher incidence of stroke.

The new European guidelines on hypertension rule out BBs as first-line drug therapy for uncomplicated hypertension.

Main clinical studies analyzing beta-blockers in the treatment of essential hypertension

Study	Population	Beta-blocker	Comparison	Result
Berglund and Andersson ³⁰	47-54 y	Propranolol	Thiazide	No difference in mortality
VA COOP ³¹	21-65 y	Propranolol	Thiazide	No difference in mortality, AMI, or stroke
MRC ³²	35-64 y	Propranolol	Thiazide Placebo	Lower risk of stroke vs placebo; no difference in AMI or mortality Higher risk of stroke vs thiazide
Coope and Warrender ³³	60-79 y	Atenolol ± thiazide	Placebo	Lower risk of stroke vs placebo; no difference in AMI or mortality
HAPPHY ³⁴	40-65 y (only men)	Metoprolol Atenolol	Thiazide	Tendency for less stroke vs diuretics No difference in mortality or AMI
MAPHY ³⁵	40-64 y (only white men)	Metoprolol	Thiazide	Reduction in total mortality, AMI, and stroke
STOP-Hypertension ³⁶	70-84 y	Pindolol Metoprolol Atenolol	Placebo	Reduction in cardiovascular mortality, AMI, and stroke
MRCOA ³⁷	65-74 y	Atenolol Diuretics	Placebo	No difference in cardiovascular death, stroke, or AMI vs placebo (diuretic vs placebo did reduce such events)
UKPDS ³⁸	Diabetic patients	Atenolol	Captopril	No difference in total mortality, AMI, or stroke
STOP-2 ³⁹	70-84 y	Pindolol Metoprolol Atenolol	Enalapril Lisinopril Felodipine Isradipine	No difference in mortality, AMI, or stroke
CAPP ⁴⁰	20-66 y	Metoprolol Atenolol	Captopril	Tendency for higher cardiovascular mortality No difference in AMI Lower risk of stroke
ELSA ⁴¹	Carotid atherosclerosis	Atenolol	Lacidipine	Increased atherosclerotic plaque progression
LIFE ⁴²	55-80 y	Atenolol	Losartan	Same cardiovascular mortality Same risk of AMI More stroke More DM
INVEST ⁴³	≥50 y Ischemic heart disease	Atenolol ± thiazide	Verapamil ± trandolapril	No difference in mortality, AMI, or stroke
CONVINCE ⁴⁴	≥ 55 years with 1 CVRF	Atenolol	Verapamil	No difference in mortality, AMI, or stroke
ASCOT-BPLA ⁴⁵	40-79 y High cardiovascular risk	Atenolol ± thiazide	Amlodipine ± perindopril	Tendency for higher risk of AMI Higher risk of stroke Higher cardiovascular mortality Higher risk of DM

Beta Blockers in Heart failure

Design and results of the main clinical trials of beta-blockers in heart failure

Study (y, patients)	Drug, mean (mg/d)	NYHA	LVEF	Ischemic	Mean follow-up, mo	NYHA class III/IV	NNT 1 life 1 y	Reduction in risk of death			Reduction in risk of hospitalization		
								Total	CV	Sudden	Due to HF	Total	Due to HF
CIBIS-II ⁶ (1999, n=2647)	Bisoprolol 7.5 mg/d	III-IV	≤35%	50%	15	100%	23	34%	29%	44%	26%	20%	36%
MERIT-HF ⁷ (1999, n=3991)	Metoprolol 159 mg/d	II-IV	≤40%	65%	12	59%	27	34%	38%	41%	49%	18%	35%

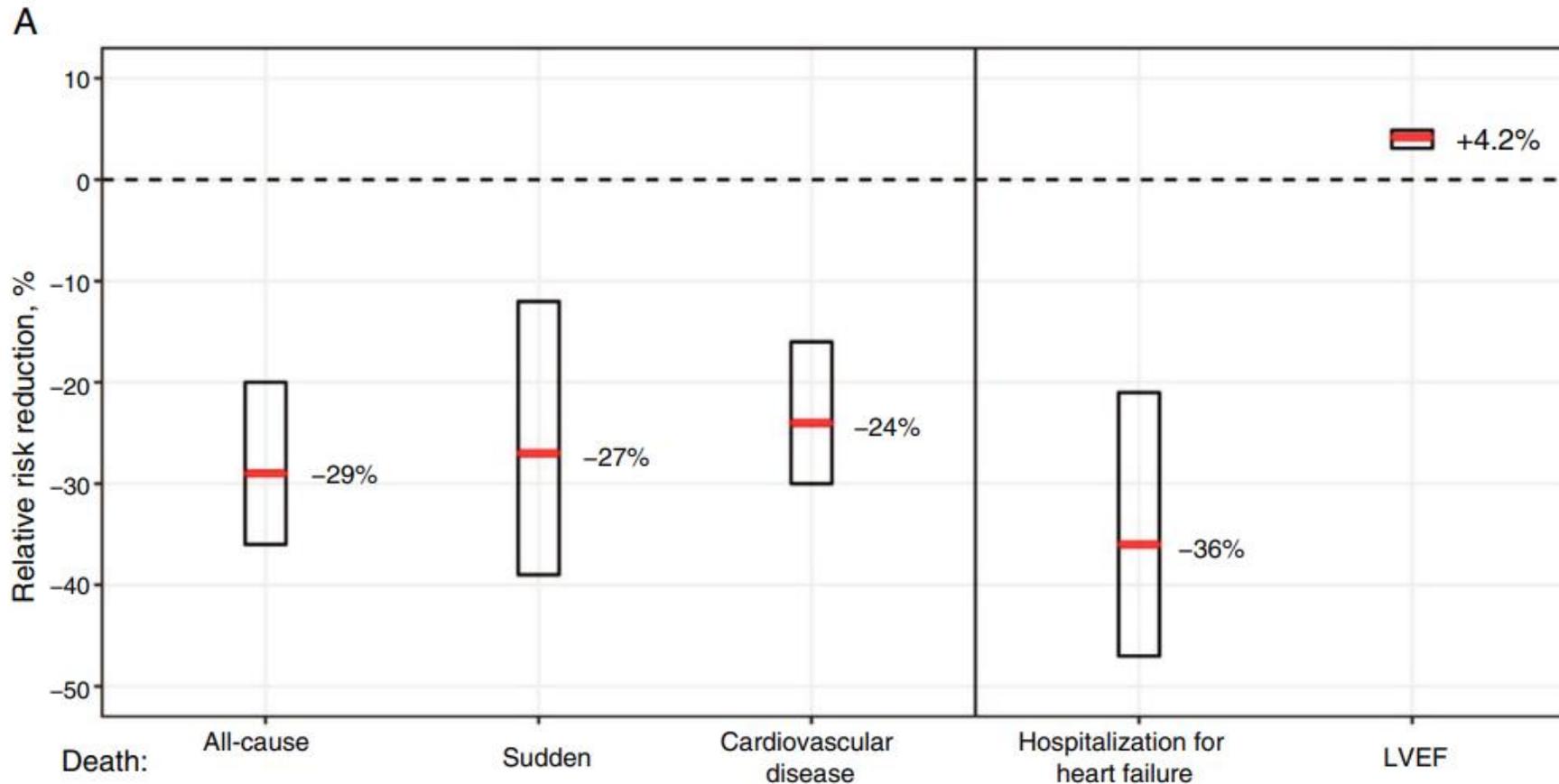
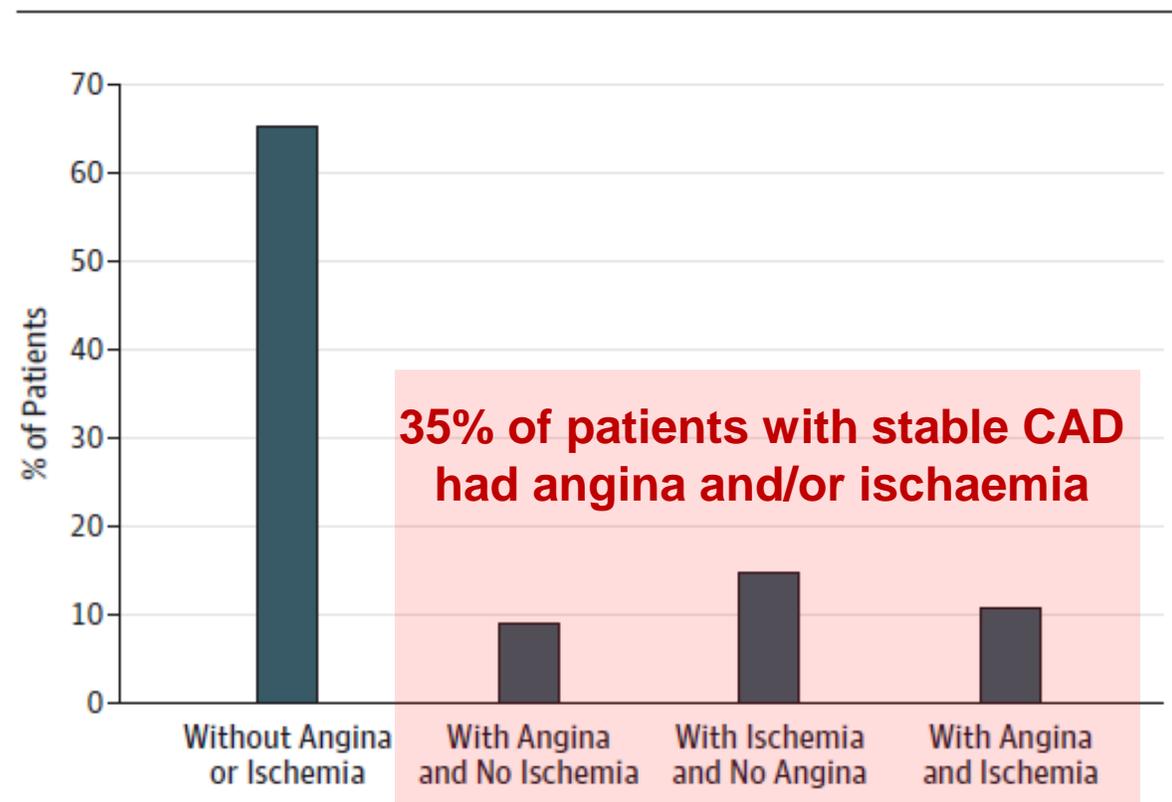
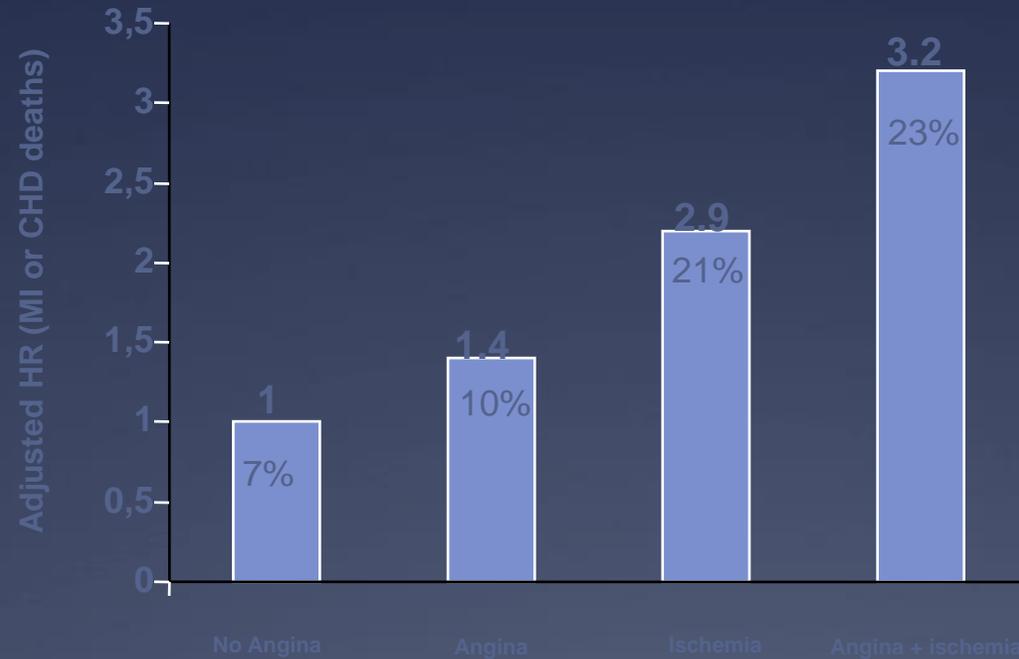


Figure 2. Clinical Patterns of Stable Coronary Artery Disease



myocardial ischaemia increases the risk of coronary events

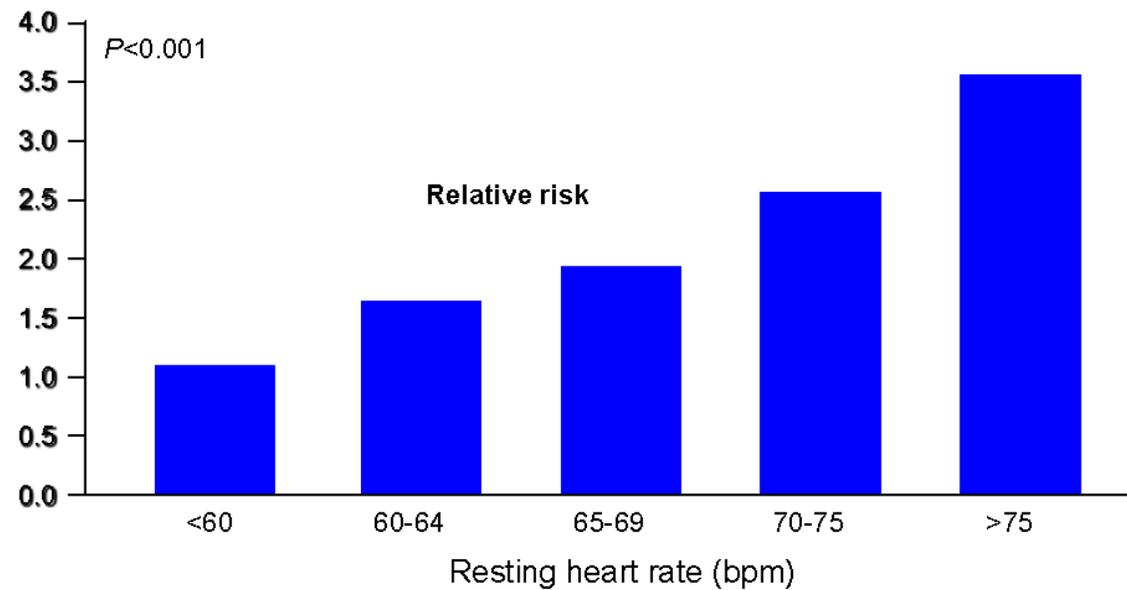
The Heart and Soul Study; 937 outpatients with stable CHD, 3.9 years of follow-up



Gehi AK et al. Arch Intern Med. 2008;168(13):1423-1428

Sudden death risk increases progressively with resting heart rate in the general population

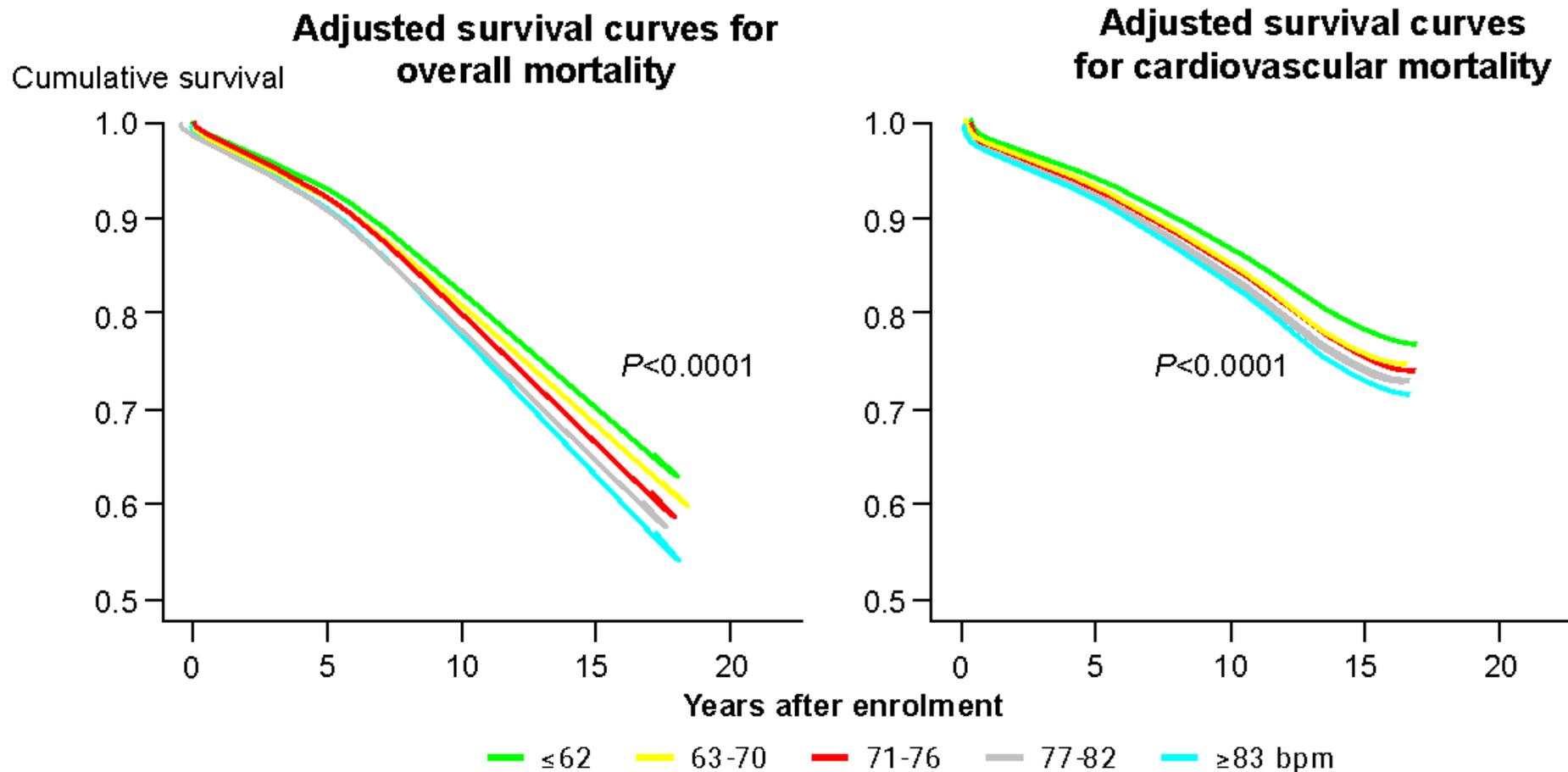
The Paris Prospective Study I, general population, 5713 men; 23-year follow-up



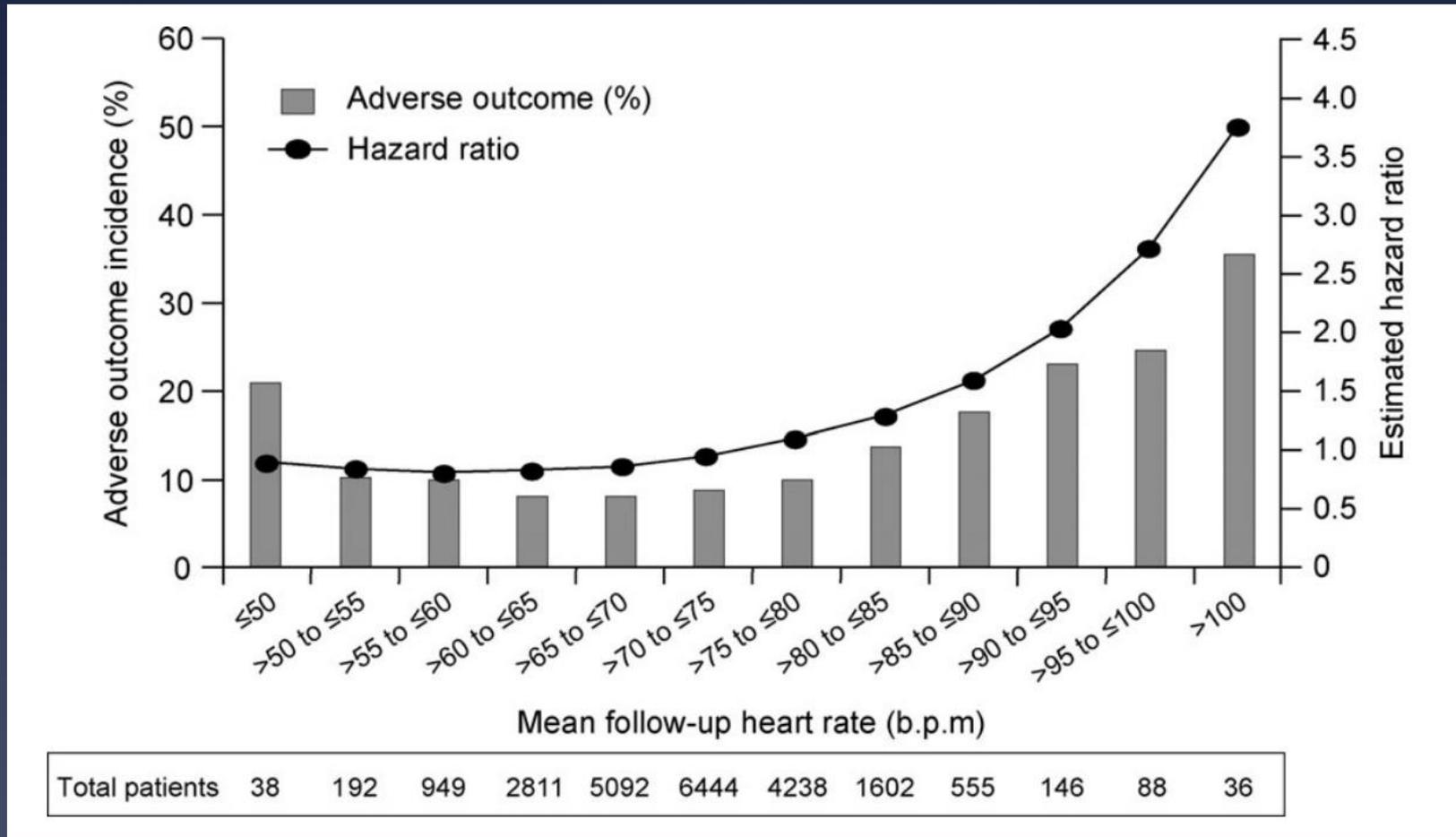
Jouven X, et al., *N Engl J Med.* 2005;352:1951-1958.

Resting heart rate is an independent predictor of mortality in patients with CAD

The Coronary Artery Surgery Study (CASS) registry; 24 913 CAD patients;
14.1-year follow-up



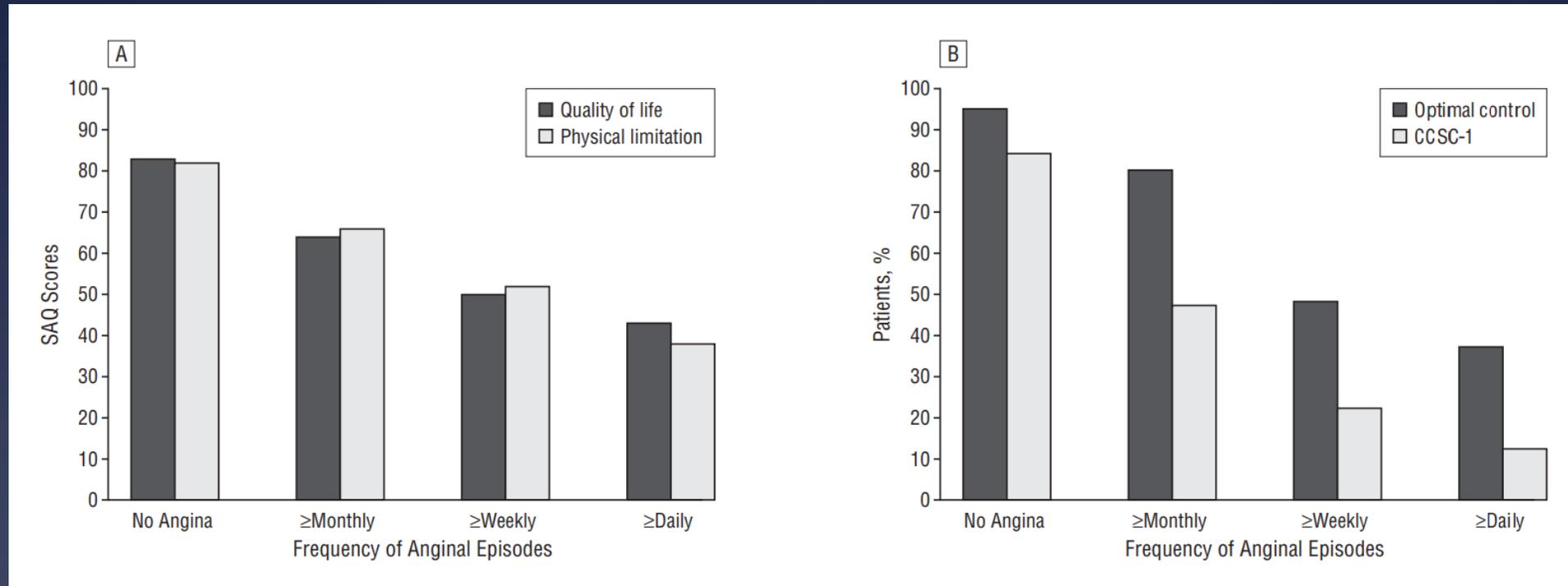
Impact of resting heart rate on outcomes in hypertensive patients with CAD



Relationship between follow-up resting heart rate for all patients and incidence of adverse outcomes (left axis, bars) and risk (right axis –†–, hazard ratio) derived from a stepwise Cox proportional hazards model. Among all patients, the nadir for follow-up resting heart rate was 59 b.p.m

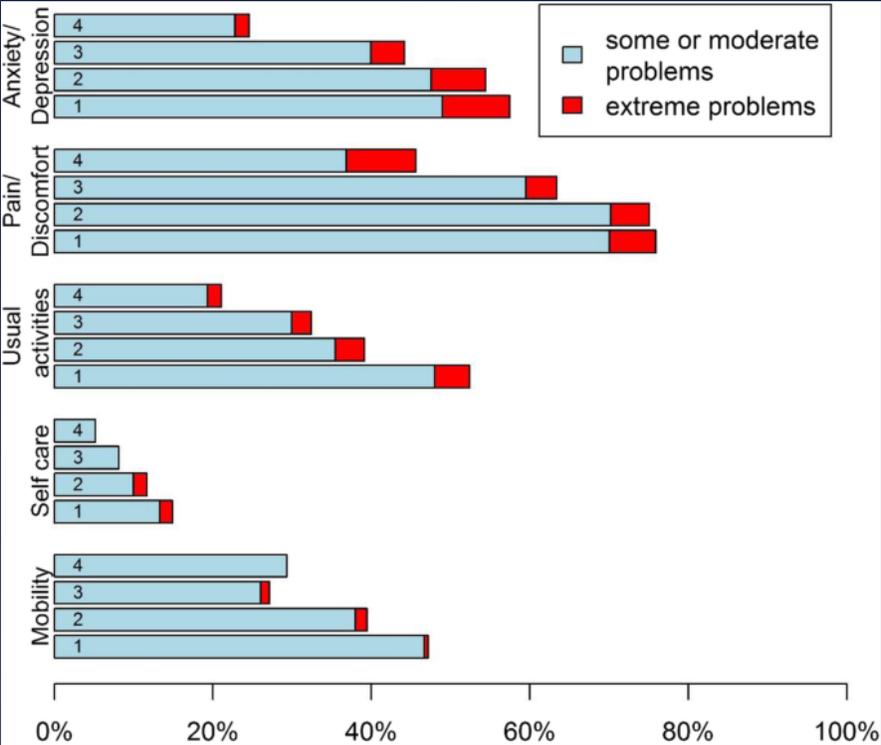
Prevalence of angina increases with age in
both sexes

Angina associated with greater physical limitation and poorer quality of life



Relationship between angina frequency and patient-assessed quality-of-life indices and general practitioner (GP) perception. Relationship between the frequency of anginal episodes (over the preceding 4 weeks) and (A) patient-assessed Seattle Angina Questionnaire (SAQ) quality-of-life indices or (B) GP-perceived physical limitation by angina (Canadian Cardiovascular Society Classification 1 [CCSC-1]) and optimal therapeutic control.

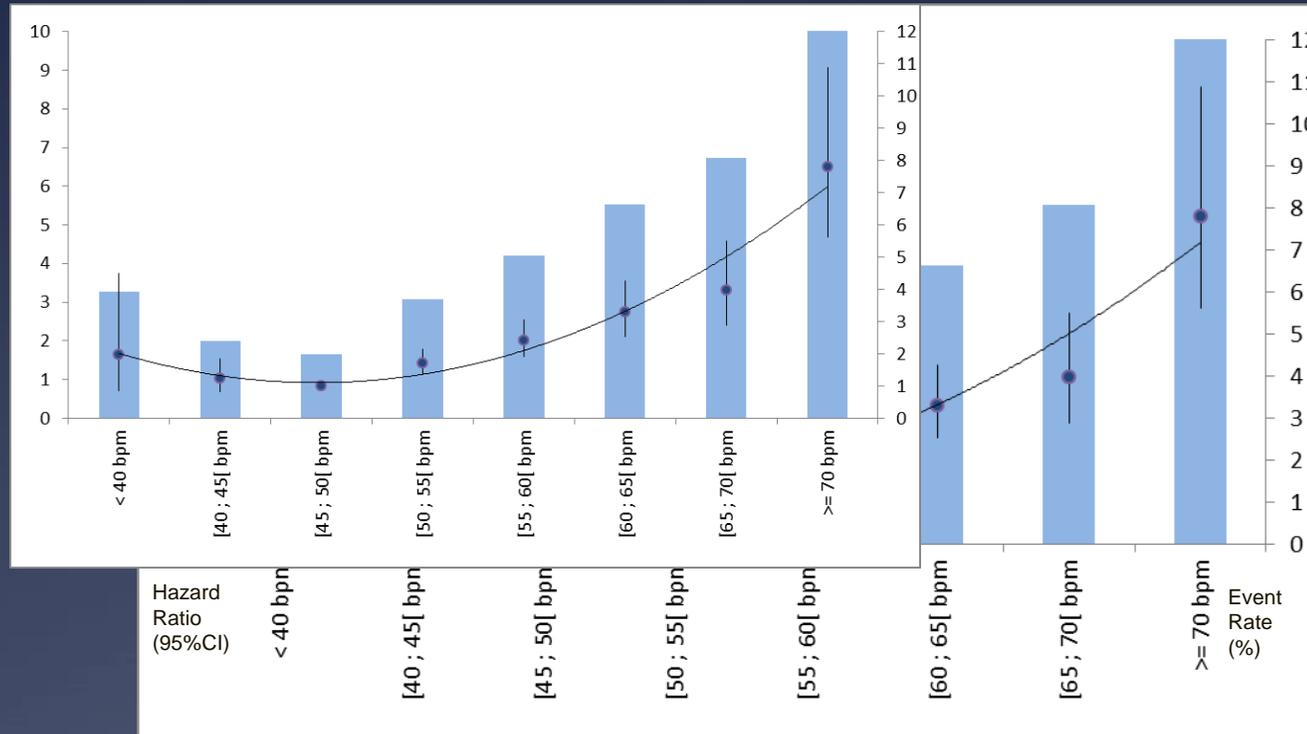
Angina impacts patient mobility, self-care, usual activities, pain/discomfort, and anxiety/depression



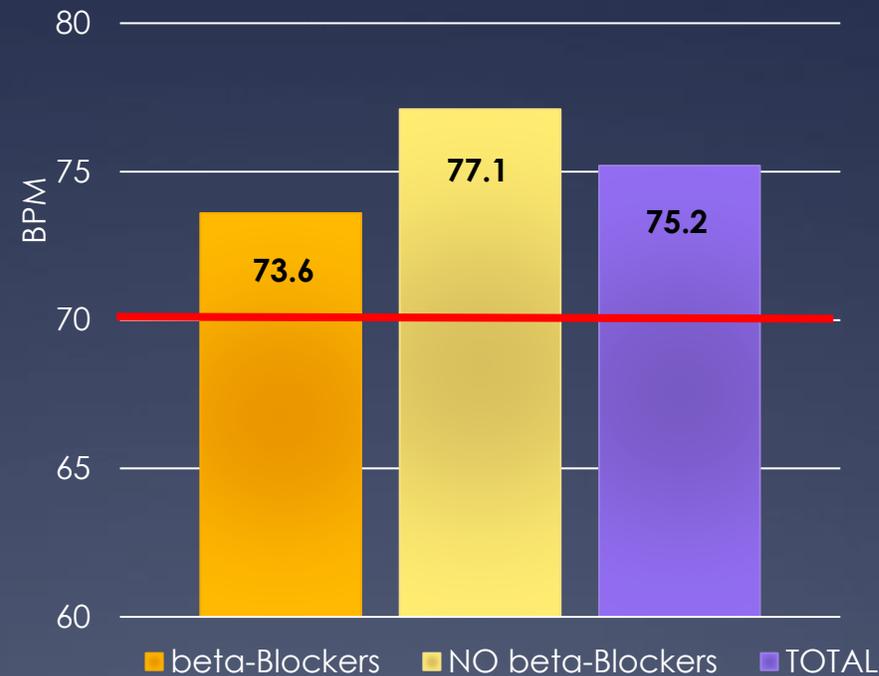
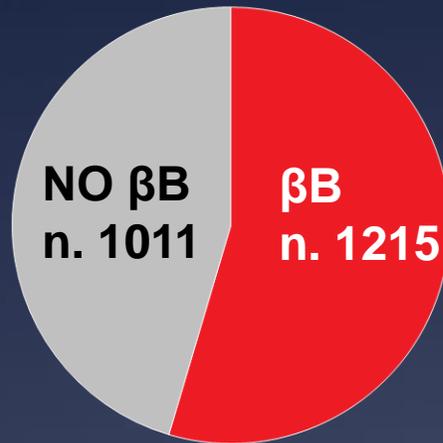
- 1. Typical angina
- 2. Atypical angina
- 3. Non-anginal chest discomfort
- 4. Other chest discomfort

Rieckmann N et al. Health Qual Life Outcomes. 2020;18(140):e2112800.

Shifting the paradigm from threshold to target HR in patients receiving HR lowering drugs



Heart rate control and β -Blocker use in patients with CAD

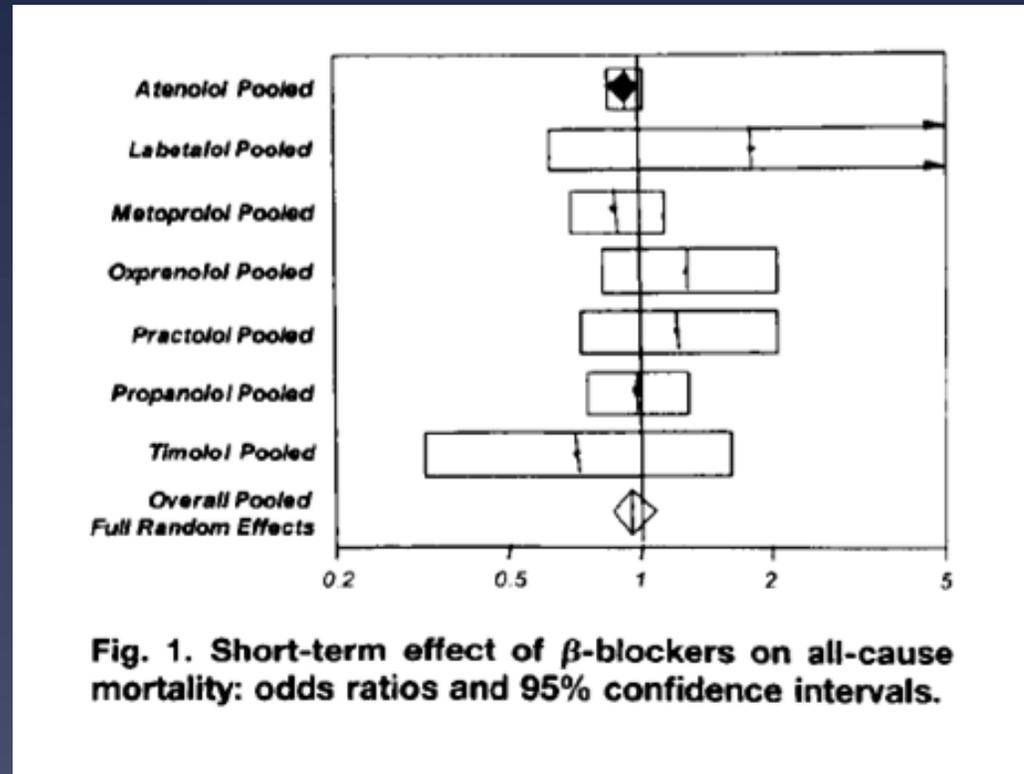


This observational, cross-sectional, multicenter survey patients with chronic CAD attending outpatient clinics. N = 2226 . F/U 6 months

Beta-blockers in CAD without LVD

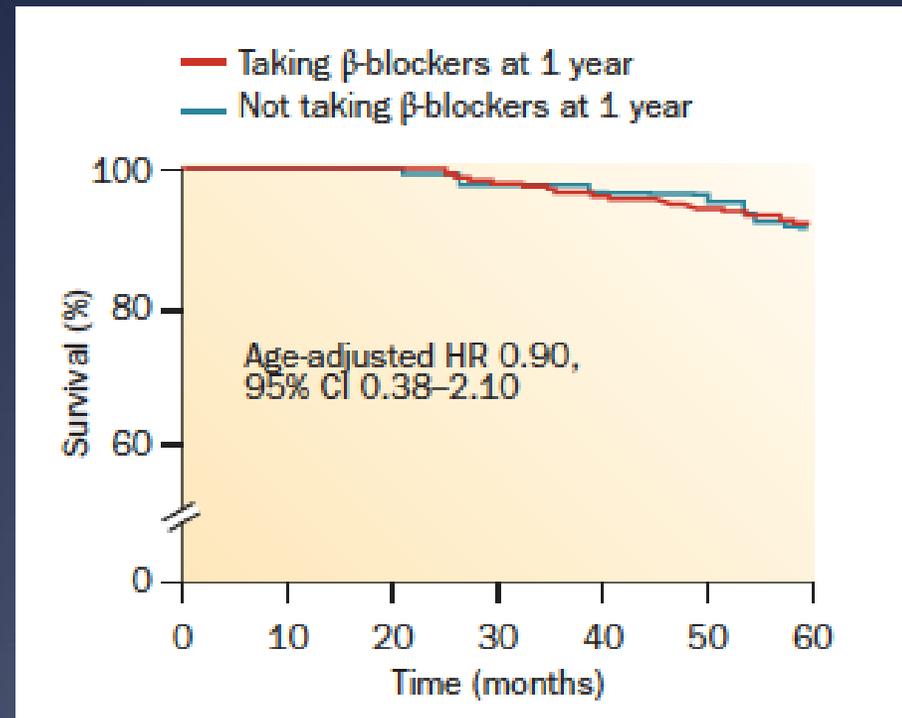
- * Beta-blockers have been approved on the basis of small studies that are not adequate according to current standards
- * No real evidence exists from the small and relatively old (1979–2003) randomized trials in patients with chronic angina that β -blockers reduce mortality

Beta-blockade in post-MI patients with preserved LV function



Beta Blockers at 1 year after MI

The FAST-MI 2005 registry



Lack of Effect of Oral Beta-Blocker Therapy at Discharge on Long-Term Clinical Outcomes of ST-Segment Elevation Acute Myocardial Infarction After Primary Percutaneous Coronary Intervention

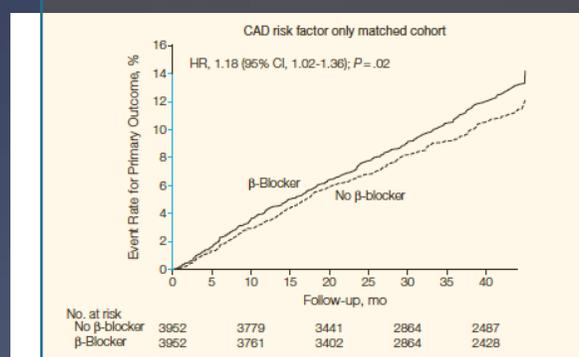
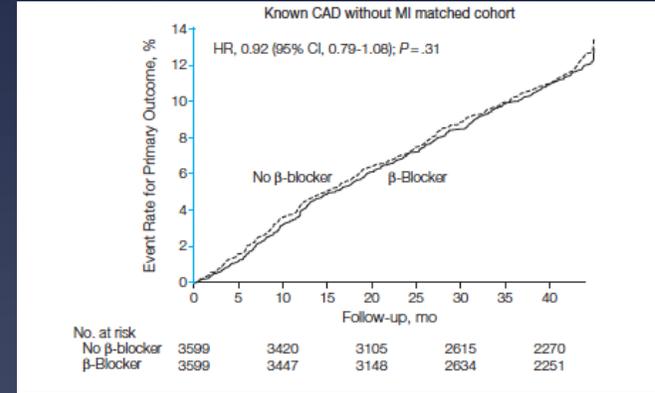
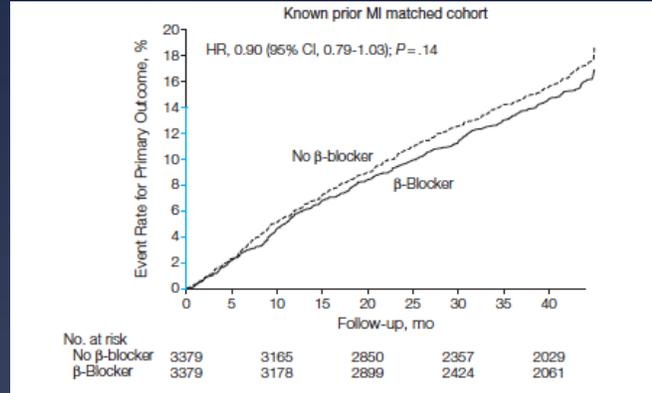
Neiko Ozasa, MD^a, Takeshi Kimura, MD^{a,*}, Takeshi Morimoto, MD, MPH^b, Heigen Hou, MD^a, Toshihiro Tamura, MD^a, Satoshi Shizuta, MD^a, Yoshihisa Nakagawa, MD^c, Yutaka Furukawa, MD^d, Yasuhiko Hayashi, MD^e, Koichi Nakao, MD^f, Masunori Matsuzaki, MD^g, Masakiyo Nobuyoshi, MD^h, and Kazuaki Mitsudo, MDⁱ, on behalf of the j-Cypher Registry Investigators

Am J Cardiol 2010;106:1225–1233

- 12,824 consecutive patients
- 910 patients who underwent PCI within 24 hours from onset of STEMI

β -blocker use and clinical outcomes

The REACH registry - CV death, MI, Stroke

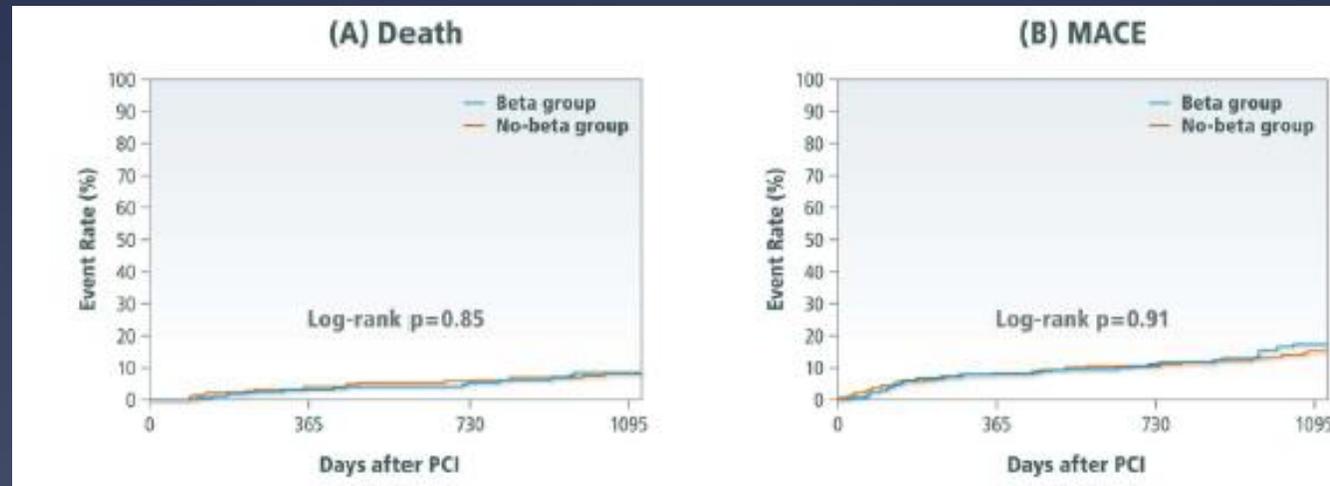


Am J Cardiol 2010;106:1225-1233

Long term effect of BB administered at discharge after primary-PCI

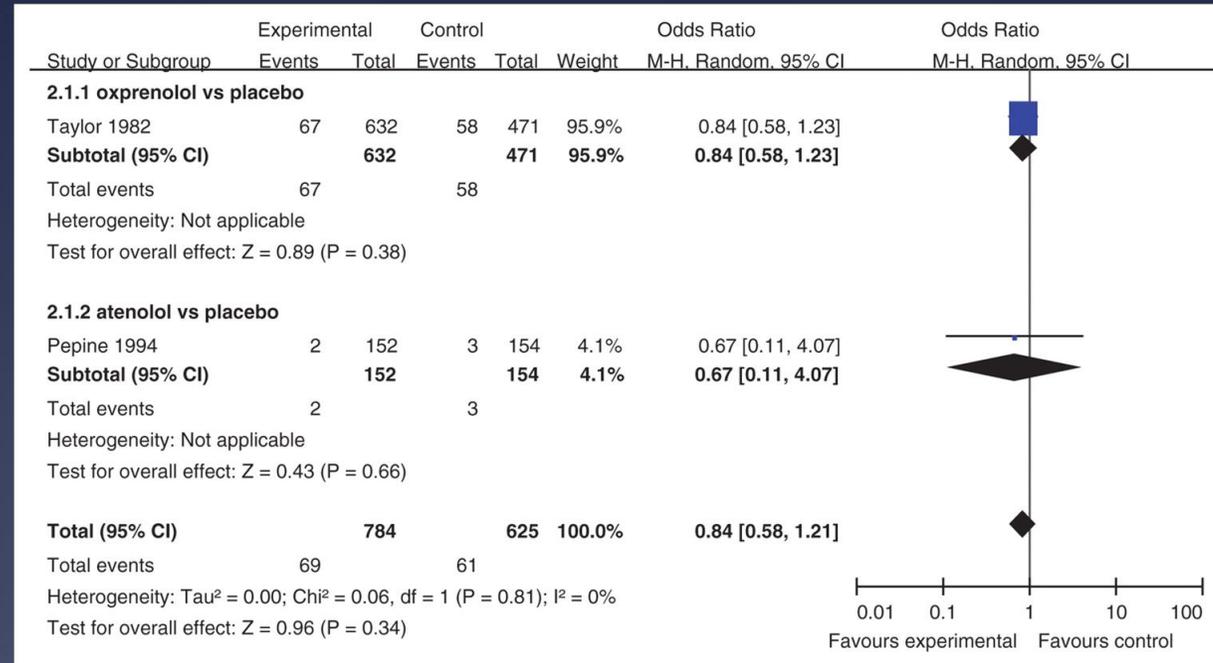
The j-cypher Registry

- 12,824 consecutive patients
- 910 patients who underwent PCI within 24 hours from onset of STEMI



Ozasa N et al. *Am J Cardiol.* 2010;106:1225-33

Long-term beta blockers for stable angina: systematic review and meta-analysis



therapy trials: Chronic angina/stable CAD (1992-2014)

Trial	Mortality	Prevent MI	Short-Term Anginal Relief	Short-Term QoL ↑	Long-Term QoL ↑
RITA-2	No diff	No diff	PCI	PCI	No diff
ACME	No diff	No diff	PCI	PCI	N/A
ACME-2	No diff	No diff	PCI	No diff	N/A
MASS	No diff	No diff	PCI	N/A	N/A
MASS-II	No diff	No diff	PCI	PCI	N/A
AVERT	No diff	No diff	PCI	No diff	No diff
TIME	No diff	No diff	PCI	PCI	No diff
COURAGE	No diff	No diff	PCI*	PCI	No diff
BARI-2D	No diff	No diff	PCI	PCI	No diff
FAME 2	No diff	No diff	PCI	N/A	N/A

*No difference at 5 years

Approach to the treatment of CAD/Angina

- In patients with angina OMT is able to control symptoms in most patients, improves QoL, at a very low cost compared with PCI
- Evidence shows that OMT is equal to PCI in controlling symptoms and it is superior in reducing events
- PCI is not one off but often leads to repetitive procedures with increasing costs (in EU the mean cost of PCI is between 3K and 8K/procedure. This cost is increased by the need of double anti-platelet therapy)

Treatment approach of Angina in 2021

- Best initial management strategy for patients with Angina?

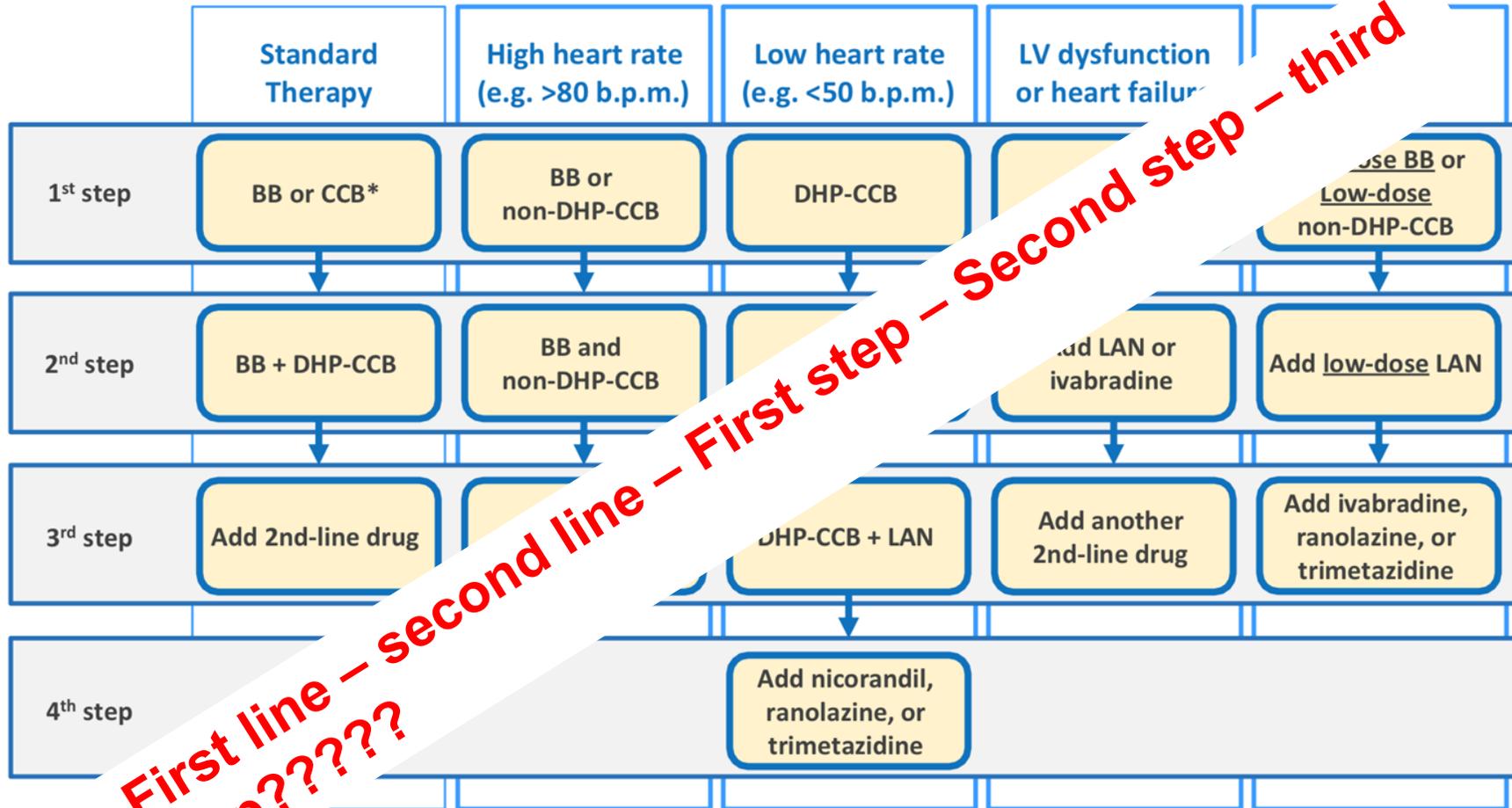
ESC and ACC/AHA Guidelines Recommend an “OMT First” Treatment Approach

- Does early revascularization improve prognosis compared to OMT in CCS?

In the past 25 years not one single trial has demonstrated any additional benefit of PCI

- Is PCI superior to OMT for durable angina relief?

Results of early studies, the ORBITA and ISCHEMIA Trials demonstrate that most patients remain symptomatic after PCI

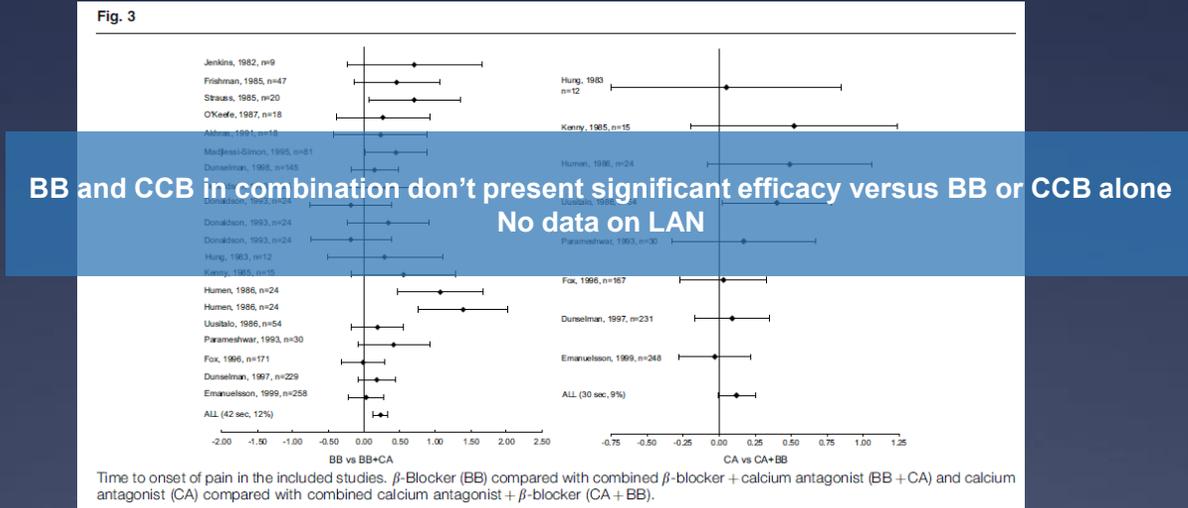


First line – second line – First step – Second step – third step?????

* Combination of a BB with a DHP-CCB should be considered as first step;
 Combination of a BB or a CCB with a second-line drug may be considered as a first step.

CCS 2019 Guidelines acknowledge the unconvincing data of combining first-line anti-anginal therapy - BB and CCB

22 studies



Meta-analysis in angina pectoris Klein et al. Coronary Artery Disease 2002, Vol 13 No 8

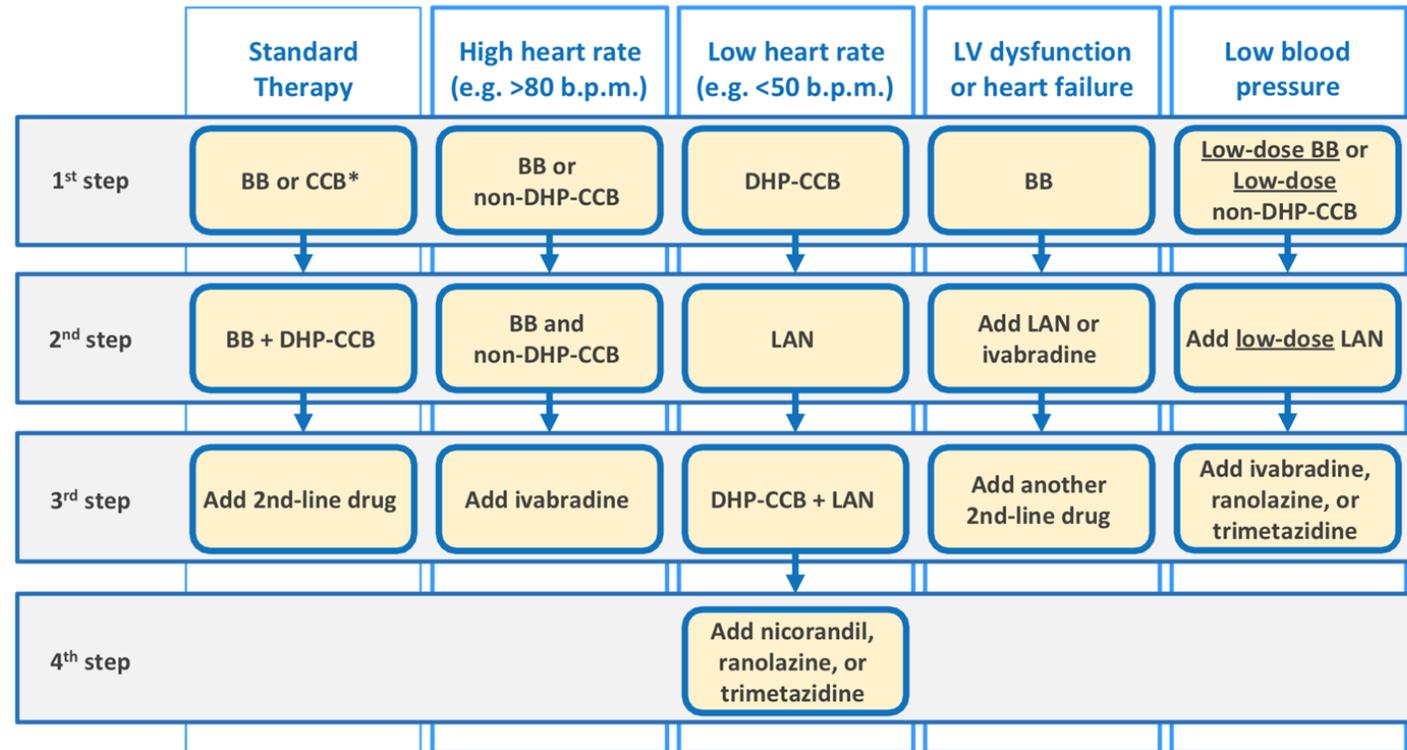


Figure 8 Suggest stepwise strategy for long term anti-*ischaemic* drug therapy in patients with chronic coronary syndromes and specific baseline characteristics. The proposed stepwise approach must be adapted to each patient's characteristics and preferences. Given the limited evidence on various combinations of drugs in different clinical conditions, the proposed options are only indicative of potential combinations and do not represent formal recommendations. BB = beta-blocker; bpm = beats per minute; CCB = [any class of] calcium channel blocker; DHP-CCB = dihydropyridine calcium channel blocker; HF = heart failure; LAN = long-acting nitrate; LV = left ventricular; non-DHP-CCB = non-dihydropyridine calcium channel blocker.

Limitations of conventional anti-anginal drugs

Contraindications/ Side effects	Nitrates	β -Blockers	Ca Antagonists
Decompensated HF	Yes	No	No
Asthma	No	Yes	No
Closed angle glaucoma	Yes	No	No
AV block 3rd degree	No	Yes	Yes
Hypotension	Yes	Yes	Yes
Fatigue	No	Yes	Yes
Bradycardia	No	Yes	Yes
Reflex tachycardia	Yes	No	Yes
Erectile dysfunction	No	Yes	Yes
Peripheral edema	No	No	Yes
Bronchospasm	No	Yes	No
Mood disorders, nightmares	No	Yes	No
Flushing	Yes	No	Yes
Headaches	Yes	No	Yes
Dyslipidemia	No	Yes	No
Worsening of glucose intolerance	No	Yes	Yes
Tolerance	Yes	No	No
Phosphodiesterase inhibitors	Yes	No	No

The average dosage of β -blockers in CLARIFY is at 50 % of the recommended range

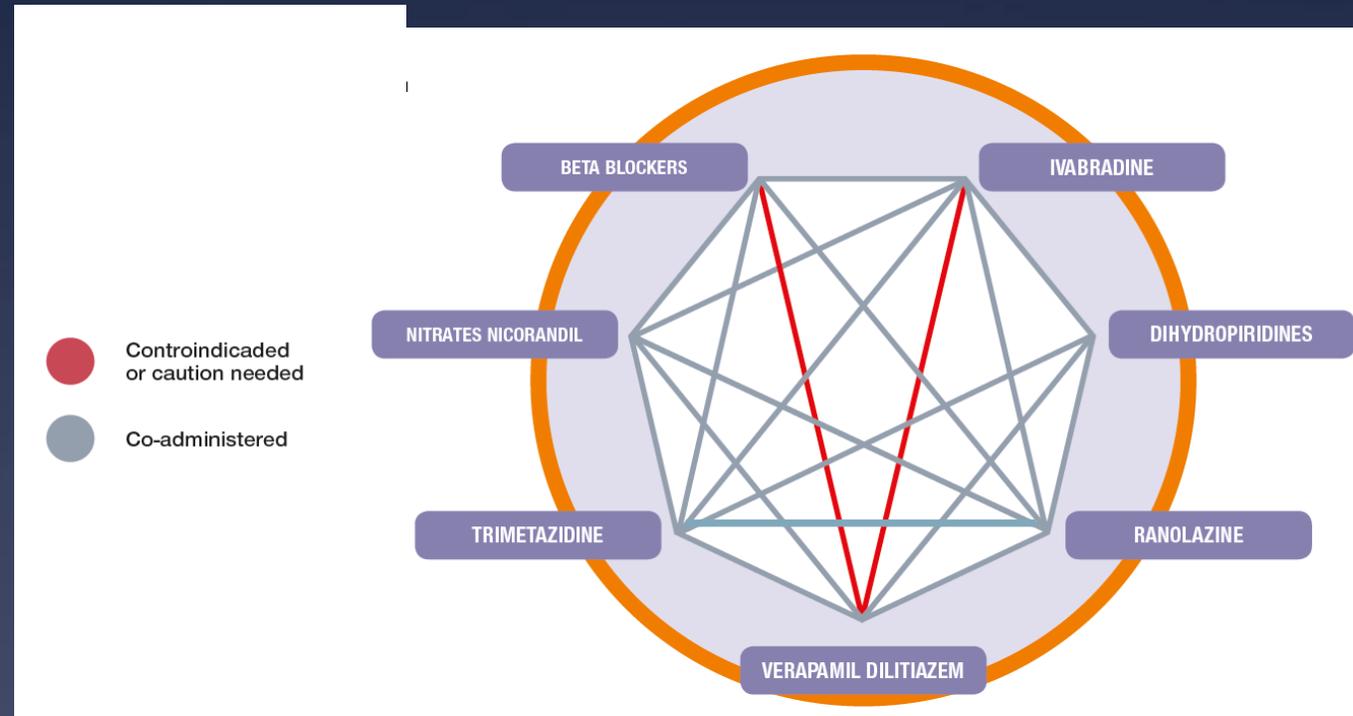


Table 1

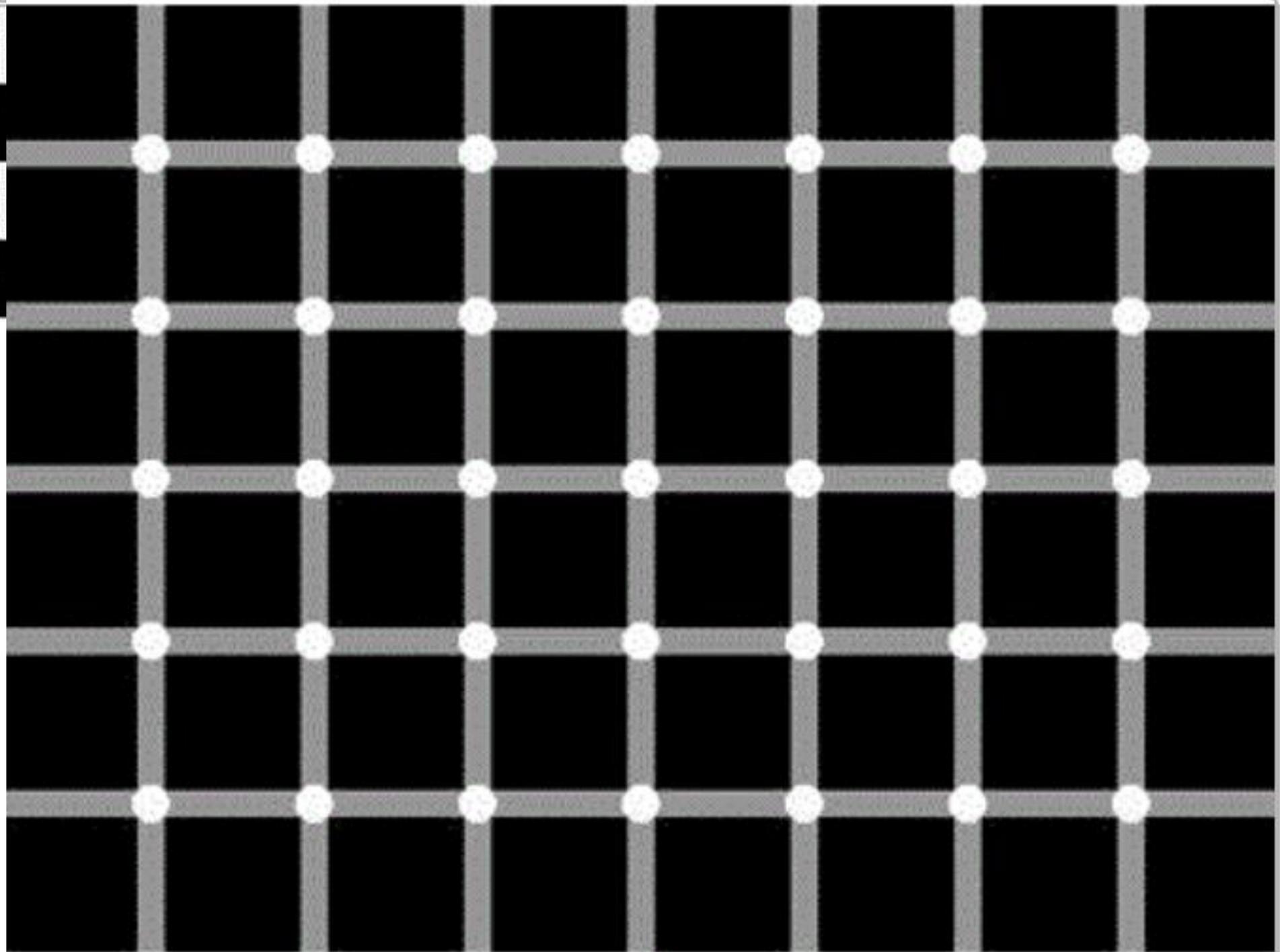
The use of beta-blockers in the CLARIFY population (32,914 patients). ^aPercentages of patients receiving any beta-blocker (patients could be taking more than one beta-blocker at the baseline visit). According to recommendations in stable angina^b [21,22] and/or chronic heart failure^c [23]. ^d75% of the total CLARIFY population.

	Patients, n (%) ^a	Dosage (mg/day), mean \pm SD	Recommended range ^b (mg/day)
Any beta-blocker	24,754 ^d		
Atenolol	3685 (15%)	52.88 \pm 27.11	25–100 ^b
Bisoprolol	8446 (34%)	4.92 \pm 2.96	2.5–10 ^b /10 ^c
Carvedilol	2872 (12%)	22.71 \pm 15.92	50 ^c
Metoprolol tartrate	3838 (16%)	75.67 \pm 51.94	50–100 ^b
Metoprolol succinate	3125 (13%)	70.85 \pm 44.56	200 ^c
Nebivolol	1404 (6%)	4.68 \pm 1.83	2.5–5 ^b /10 ^c
At least one other beta-blocker	1373 (5%)		

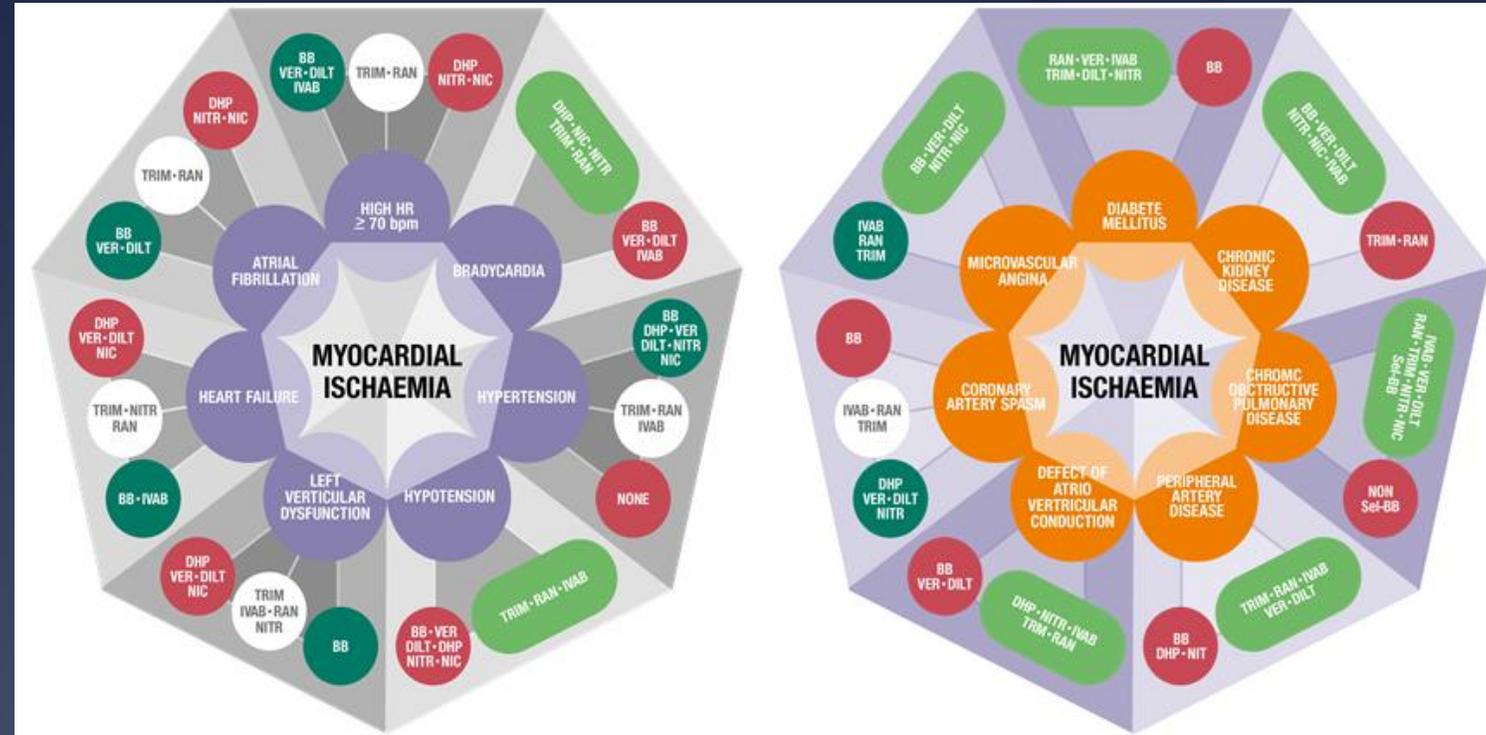
Pharmacological management of angina



Ferrari R, et al. *Nature Reviews Cardiology* volume 15, pages 120–132 (2018)

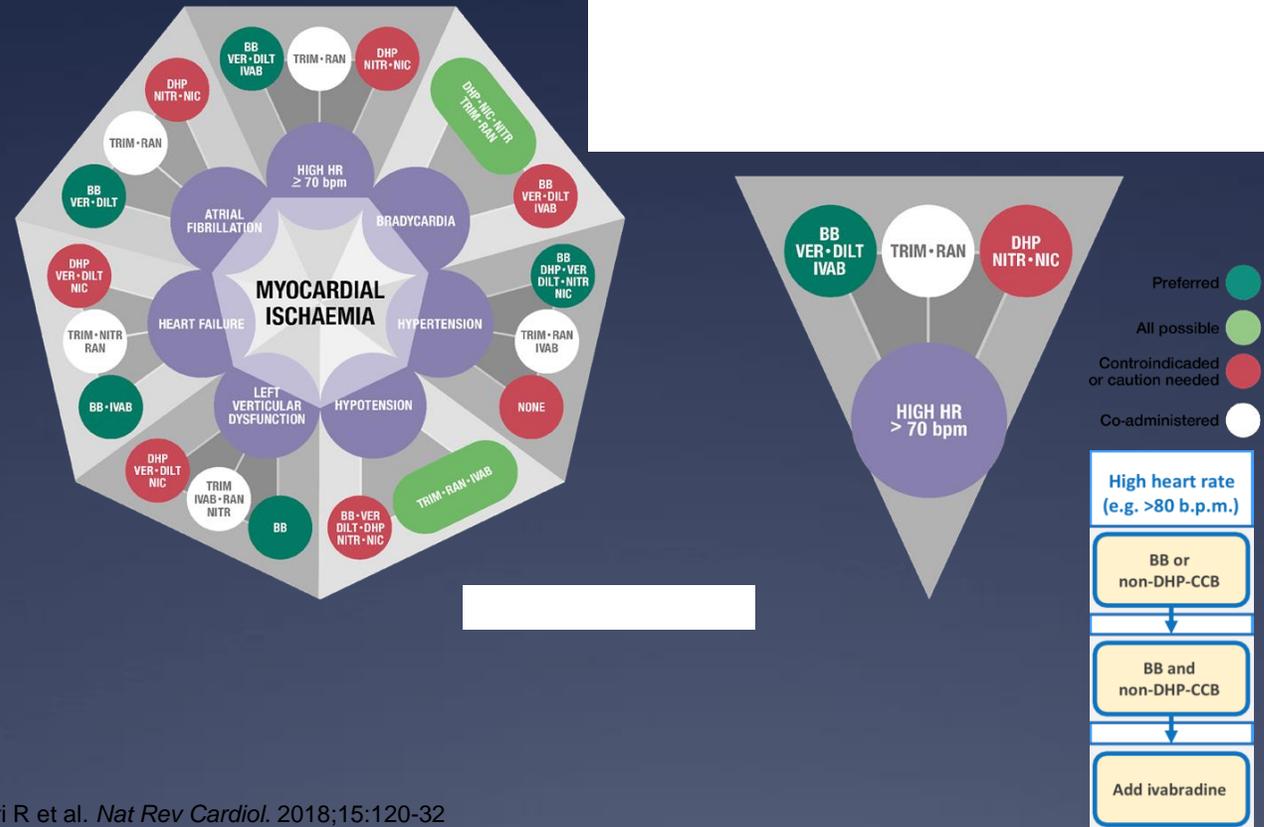


Therapeutic approach according to clinical features and comorbidities



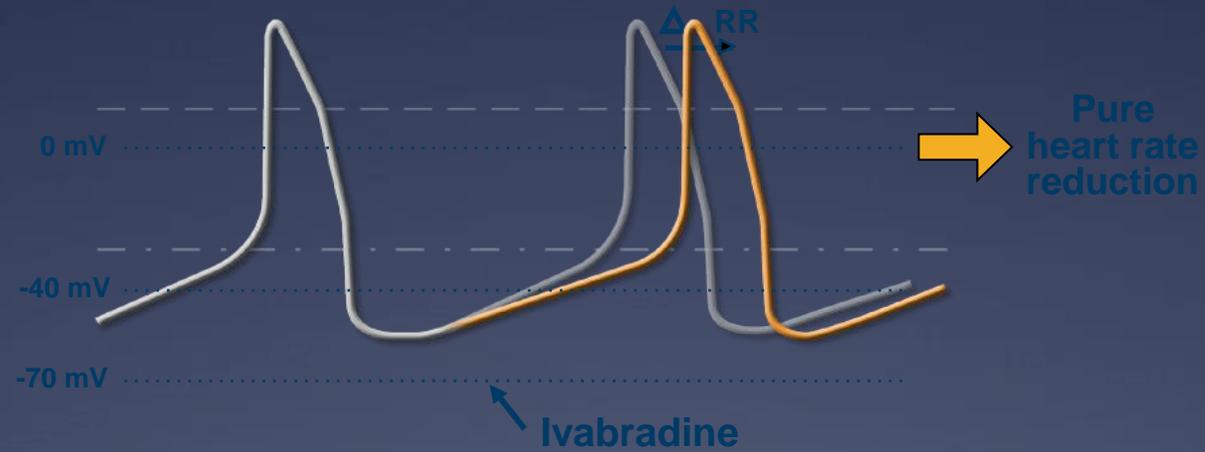
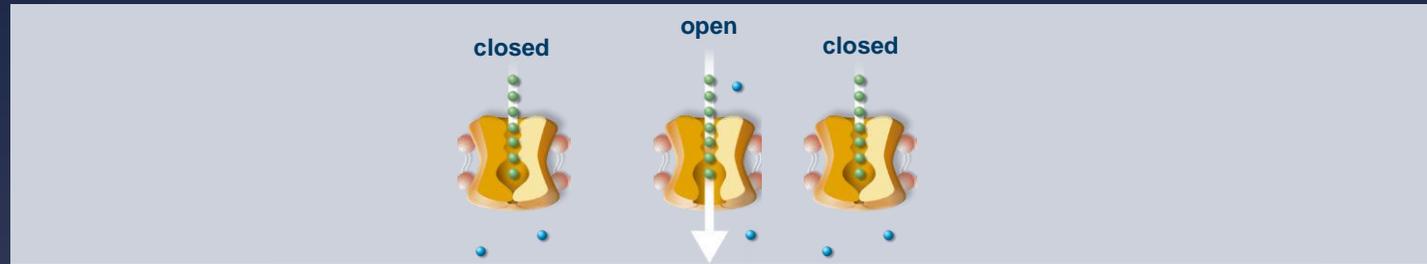
Ferrari R et al. *Nat Rev Cardiol.* 2018;15:120-32

Flexibility of the DIAMOND approach according to patient features and comorbidities



Ferrari R et al. *Nat Rev Cardiol.* 2018;15:120-32

Ivabradine: pure heart rate reduction



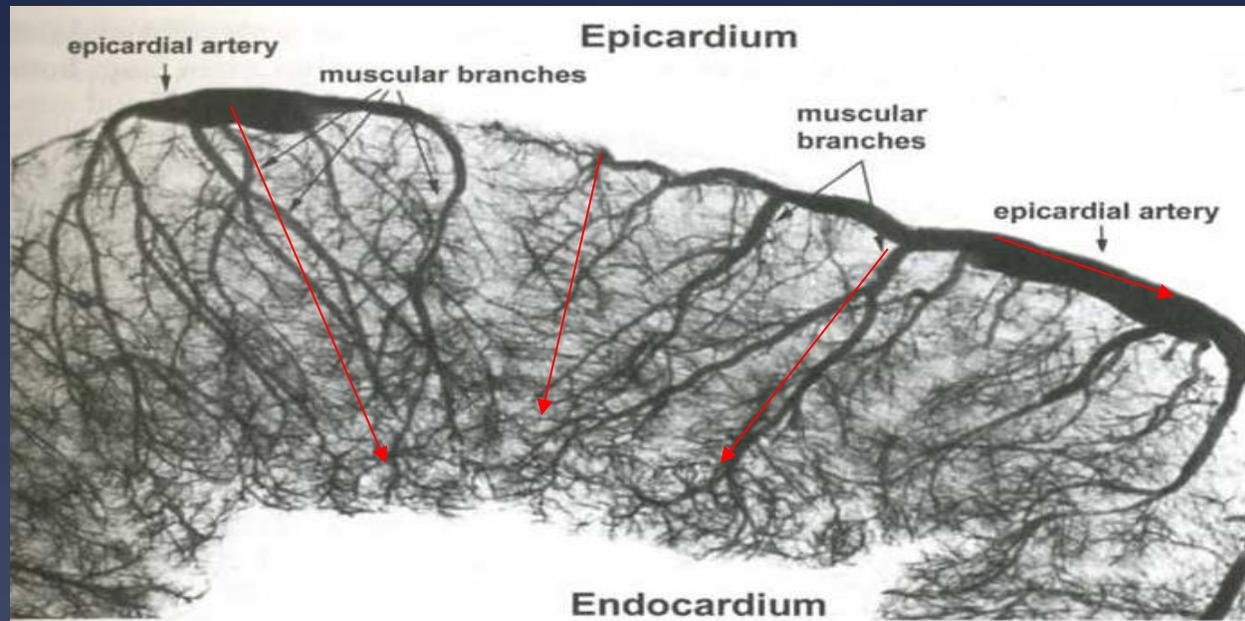
I_f inhibition reduces the diastolic depolarization slope, and thereby lowers heart rate

differently:
dependent on the initial level of
HR thus avoiding bradycardia,



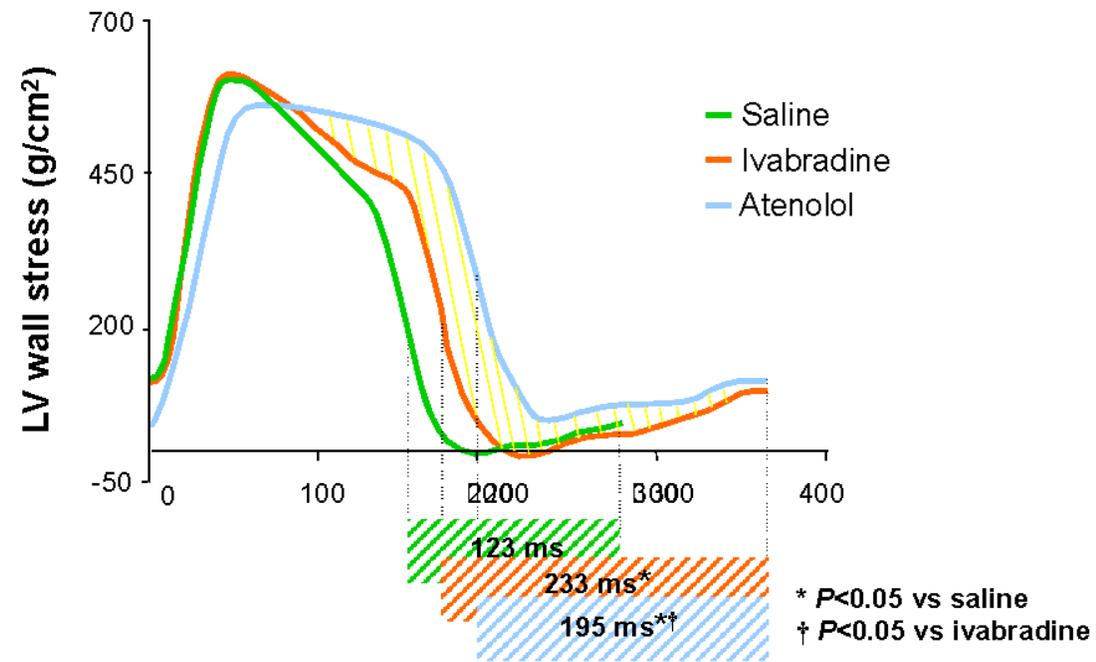
Borer JS, Heuzey JY. Characterization of the heart rate-lowering action of Corlentor. *Am J Ther.* 2008;15:461-473.

Circulation of blood in coronary arteries

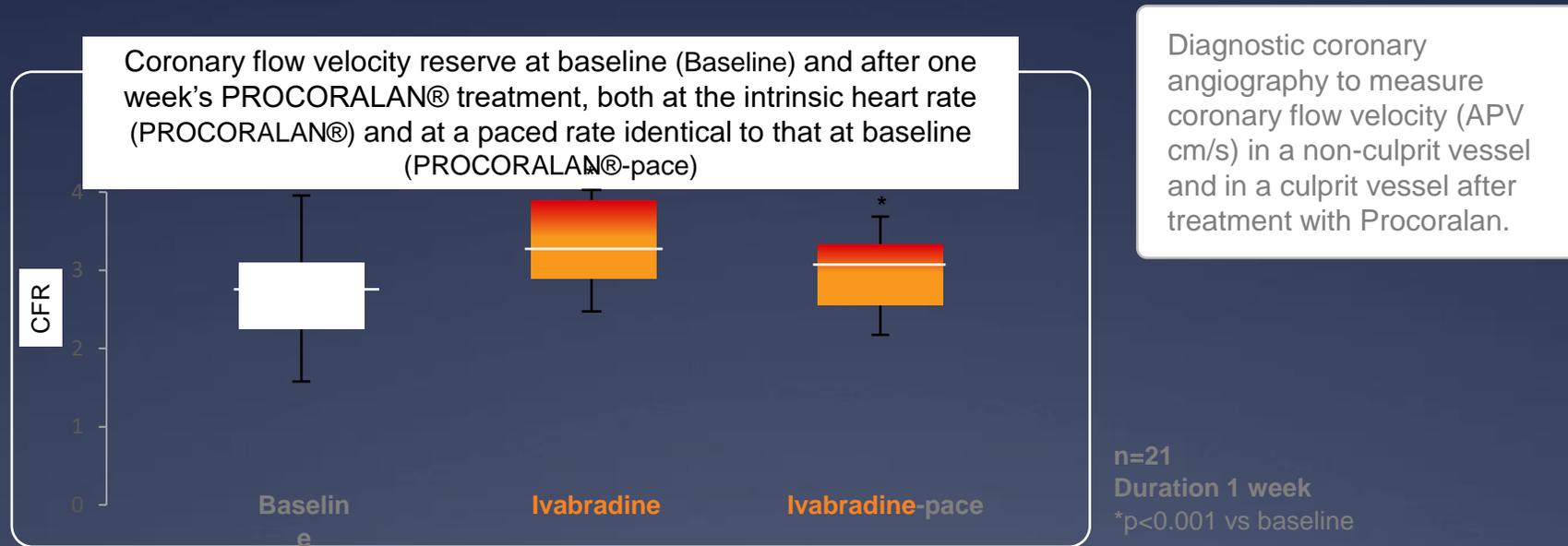


Coronary flow occurs only in diastole « An increase of 1% of diastolic time, increases blood flow by 2,6 to 6% in the subendocardium » - **The difference between coronary artery pressure and LVEDP drives subendocardial perfusion**

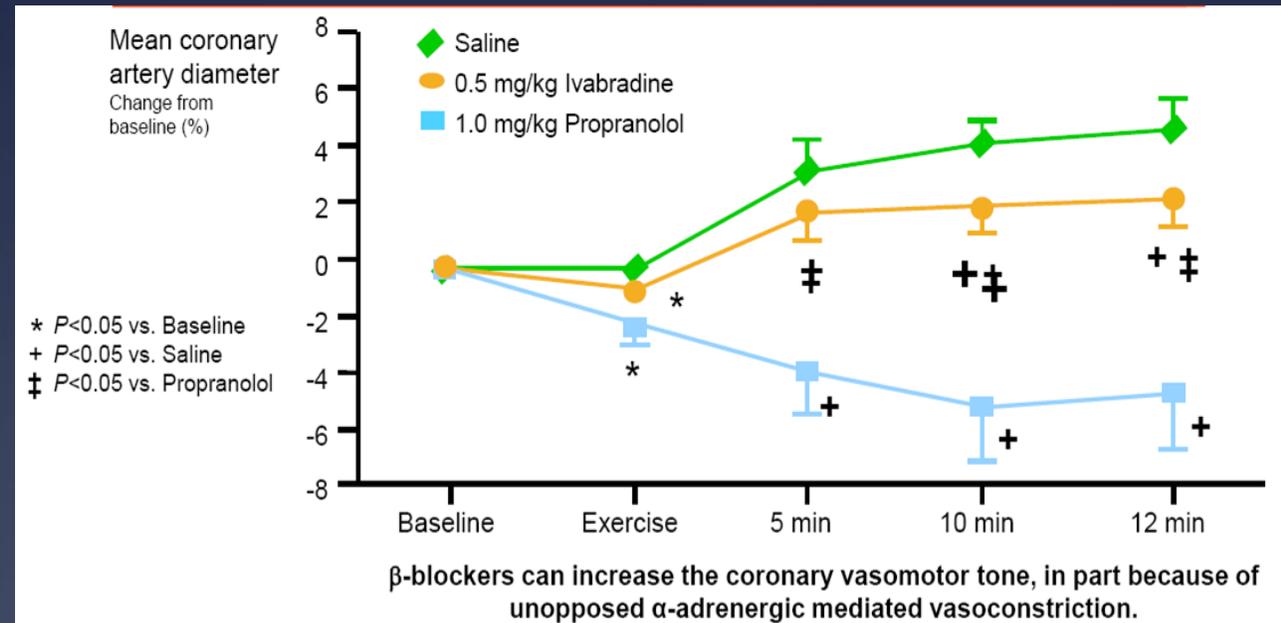
Ivabradine increases diastolic time by 6min/hour



Ivabradine increases coronary flow reserve 1 week after treatment initiation

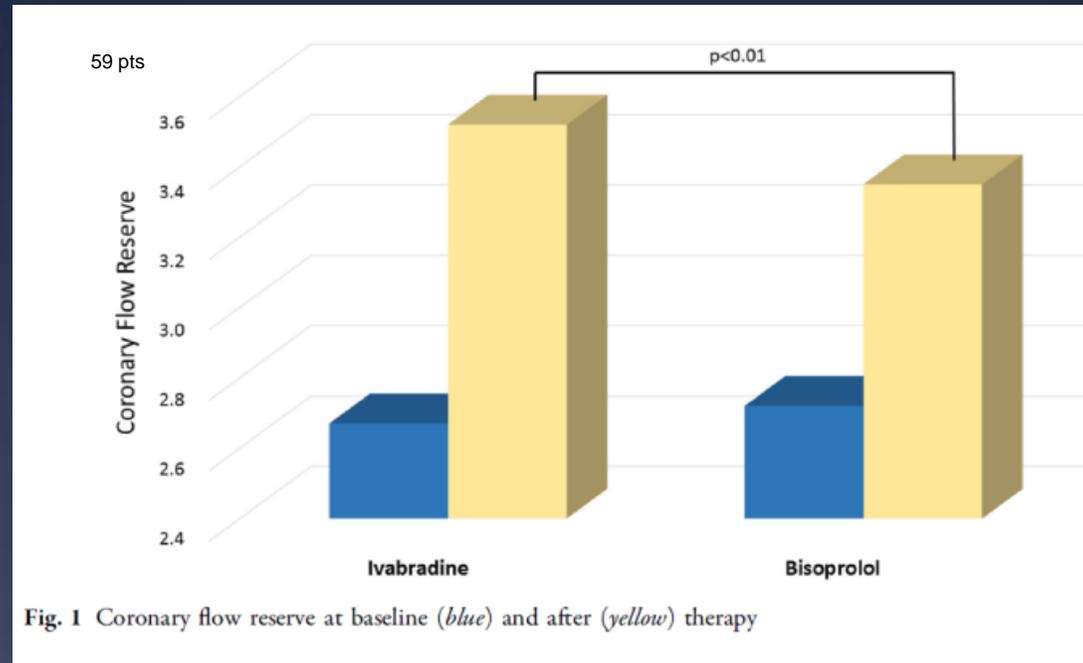


Ivabradine preserves coronary vasodilation during effort

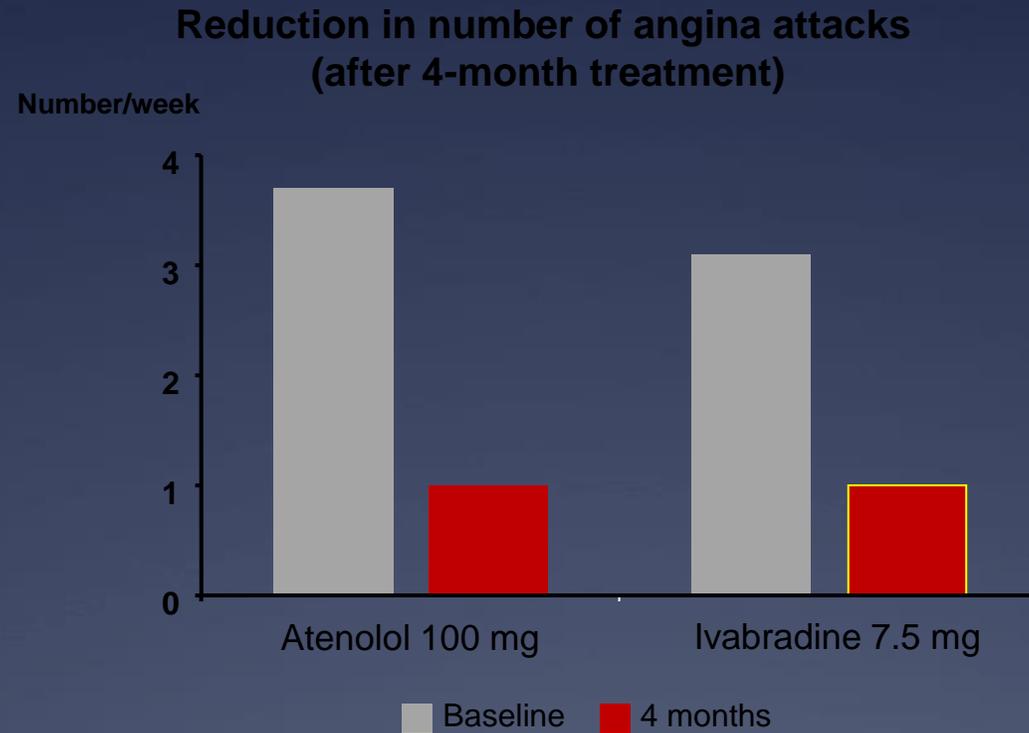


Simon L, et al. *J Pharmacol Exp Ther.* 1995;275:659-666.

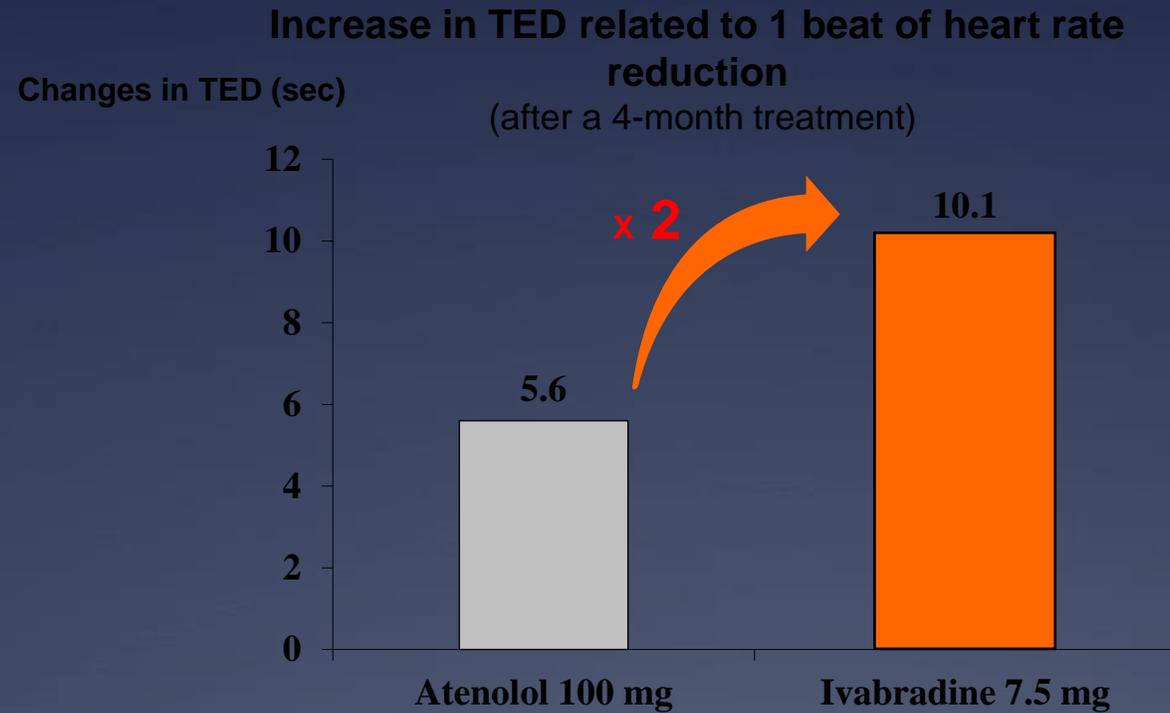
Ivabradine provides better coronary flow reserve than Bisoprolol for the same HR reduction



Antianginal effect of ivabradine

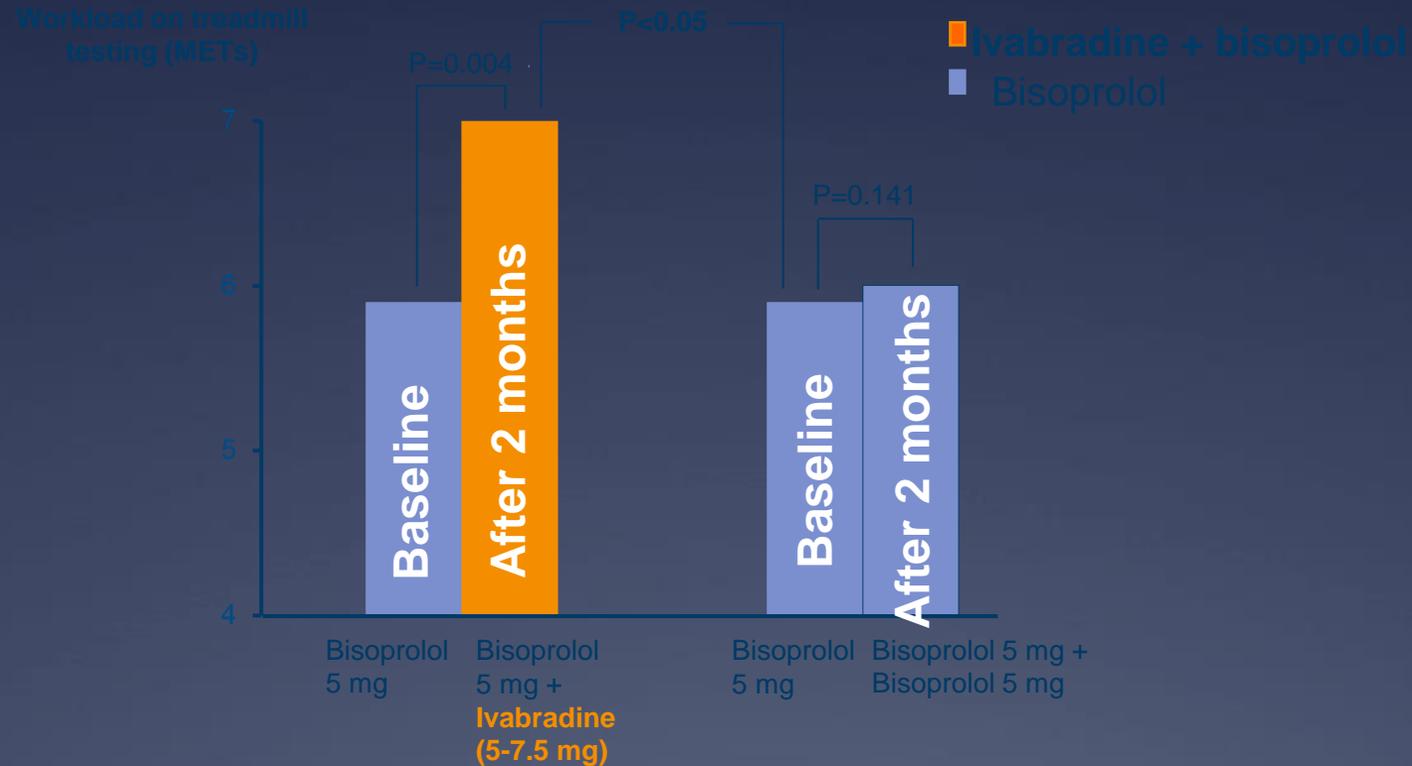


Comparative anti-ischaemic effect of ivabradine and beta-blocker



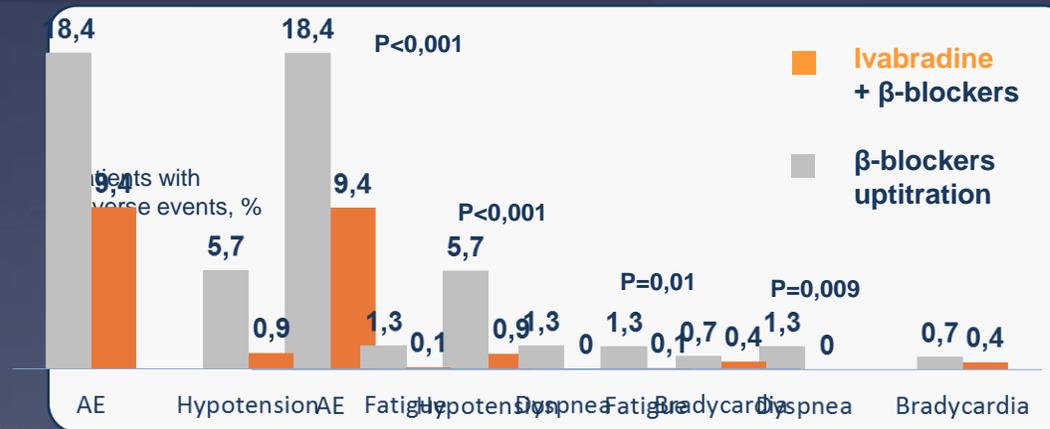
Tardif JC. *Drugs of Today*. 2008;44:171-181.

Combining ivabradine with beta-blocker provides additional anti-ischemic efficacy



Amosova E. et al. *Cardiovasc Drugs Ther.* 2011.

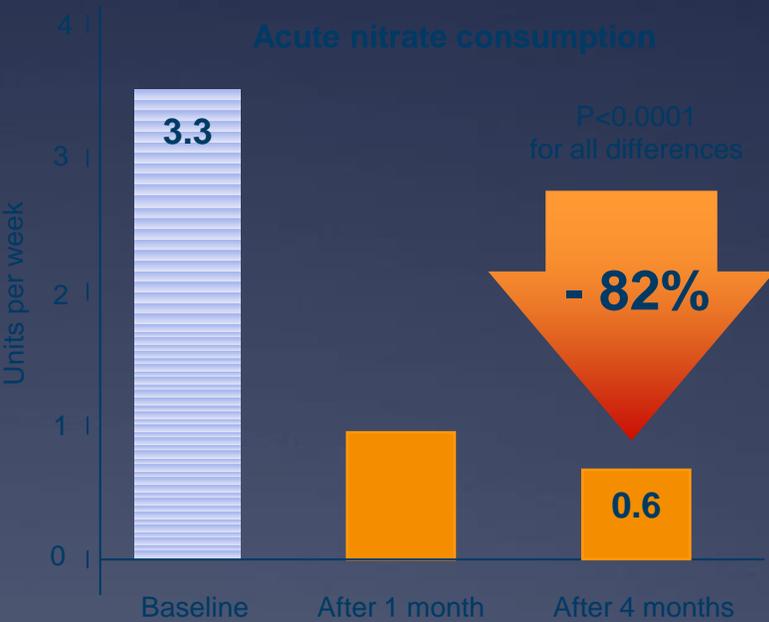
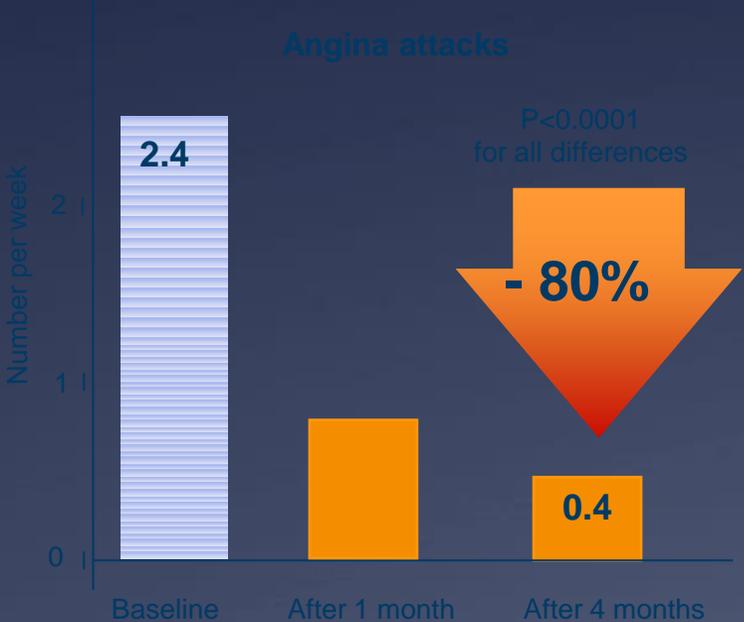
Efficacy of ivabradine/BBs compared to uptitration of BBs in patients with stable angina (CONTROL-2 study)



REDUCTION: antianginal efficacy of ivabradine in clinical practice

Multicenter, prospective, open label study (Germany):

4 954 angina patients, 4 months follow-up



Efficacy graded by physicians as being "excellent/very good" in 97% of the patients

Köster R, Kaehler J, Meinertz T, for the REDUCTION Study Group. *Am Heart J.* 2009;158:e51-e57.

Effect of Ivabradine in 14,256 patients with coronary artery disease

	Baseline	Follow up
Heart Rate	83	69
Angina/week	3.3	0.67
GTN Use	1.7	0.3
Cardiac deaths		8
Discontinuation		136
Severe adverse reactions		9
Confirmed SARs		0

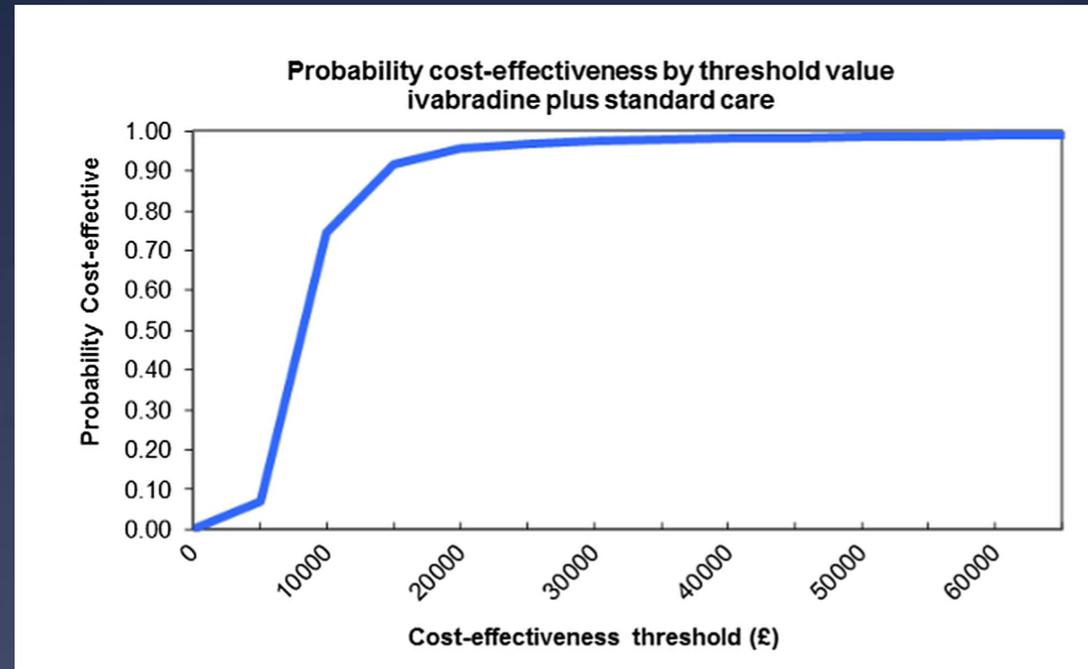
Consistent antianginal efficacy of ivabradine across all subpopulations of angina patients

Data pooled from 5 randomized trials in patients with stable angina pectoris receiving ivabradine for 3 or 4 months (n=2425)



*CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; PTCA: percutaneous transluminal coronary angioplasty; PVD: peripheral vascular disease

Cost-effectiveness of ivabradine



Ivabradine is expected to have a 95% chance of being cost-effective in the EU licensed population using the current National Institute of Health and Care Excellence (NICE)

Griffiths A, et al. Heart 2014;100:1031–1036. doi:10.1136/heartjnl-2013-304598

COST-EFFECTIVENESS ANALYSIS OF IVABRADINE IN CHRONIC STABLE ANGINA PATIENTS IN A FINNISH SETTING

Félix J¹, Almeida J¹, Joutseno J², Alegre P³

¹Exigo Consultores, Alhos Vedros, Lisbon, Portugal, ²Servier Finland OY, Vantaa, Finland,

RESULTS: For each 100 patients using ivabradine in comparison with amlodipine we estimate a 36 LYs (95%CI: [18;57]) or 30 QALYs (95%CI: [17;47]) gain.

Incremental cost-effectiveness ratios for ivabradine utilization were a12,886/LY and a 15,060/QALY.

CONCLUSIONS: Ivabradine is a cost- effective alternative for the treatment of SA when compared to generic amlodipine in a Finnish setting of patients with contraindication or intolerance to beta-blockers and resting HR 70 bpm.

Insights for clinical practice

- Angina with or without ischemia carries an adverse prognosis
- Medical therapy for the treatment of angina should be implemented using the Diamond approach that goes beyond the indications of the guidelines and should be implemented in daily practice
- Ivabradine is effective in reducing angina and ischaemia in patients with CCS and, in association with BB, confers greater anti-ischemic effect than BB alone, increases tolerability, exercise capacity and QOL in patients with angina
- Ivabradine is cost-effective and should be implemented in the majority patients with IHD and co-morbidities

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 18, 2014

VOL. 371 NO. 12

Ivabradine in Stable Coronary Artery Disease without Clinical Heart Failure

Kim Fox, M.D., Ian Ford, Ph.D., Philippe Gabriel Steg, M.D., Jean-Claude Tardif, M.D., Michal Tendera, M.D.

Concluding that..... Among patients who had stable coronary artery disease without clinical heart failure, the addition of ivabradine to standard background therapy to reduce the heart rate did not improve outcomes

- * A randomized, double-blind, placebo-controlled trial of ivabradine, added to standard background therapy, in 19,102 patients who had both stable CAD without clinical heart failure and a heart rate of 70 beats per minute or more.
- * After a median follow-up of 27.8 months, there was no significant difference between the ivabradine group and the placebo group in the incidence of the primary end point (6.8% and 6.4%, respectively; hazard ratio, 1.08; 95% confidence interval, 0.96 to 1.20; P=0.20), nor were there significant differences in the incidences of death from cardiovascular causes and nonfatal myocardial infarction.

Signify Study

- * randomized, double-blind, placebo-controlled trial of ivabradine, added to standard background therapy, in 19,102 patients who had both stable coronary artery disease without clinical heart failure and a heart rate of 70 beats per minute or more
- * No significant differences in the incidences of death from cardiovascular causes and nonfatal myocardial infarction.
- * Ivabradine was associated with an increase in the incidence of the primary end point among patients with activity-limiting angina but not among those without activity-limiting angina ($P=0.02$ for interaction). The incidence of bradycardia was higher with ivabradine than with placebo (18.0% vs. 2.3%, $P<0.001$).

Why Signify study fails

- * SIGNIFY had a high prevalence of risk factors owing to the inclusion criteria, the annual incidence of the primary end point was relatively low (approximately 2.8%), probably owing to the background therapy the patients were receiving, which was administered according to current guidelines
- * It is possible that ivabradine decreased the heart rate too much or that there may be a J-shaped.
- * It is also possible that heart-rate-reducing antianginal agents have no effect on outcomes in patients with stable coronary artery disease. Although there is historical evidence of a benefit of beta-blockers after myocardial infarction, there is little current evidence of their benefit with respect to hard clinical outcomes in patients who have stable coronary artery disease without left ventricular dysfunction.
- * The benefit observed with lowering the heart rate in patients with heart failure but not in those with stable coronary artery disease may reflect the fact that an elevated heart rate is due to different pathophysiological mechanisms in these two conditions. In patients with heart failure, there is neurohormonal activation, which in itself leads to ventricular remodeling, further left ventricular dysfunction, and a vicious cycle of decline. In contrast, there is no neurohormonal activation in stable coronary artery disease without left ventricular dysfunction.

Beautiful Study

- * Enrolled 10 917 eligible patients who had coronary artery disease and a left-ventricular ejection fraction of less than 40% in a randomised, double-blind, placebo-controlled, parallel-group trial.
- * 5479 patients received 5 mg ivabradine, with the intention of increasing to the target dose of 7.5 mg twice a day, and 5438 received matched placebo in addition to appropriate cardiovascular medication.
- * no affect the primary composite outcome (hazard ratio 0.91, 95% CI 0.81–1.04, $p=0.17$), cardiovascular death, or admission to hospital for new-onset or worsening heart failure.
- * There was a reduce secondary endpoints: admission to hospital for fatal and non-fatal myocardial infarction (0.64, 95% CI 0.49–0.84, $p=0.001$) and coronary revascularisation (0.70, 95% CI 0.52–0.93, $p=0.016$).

Subanalysis of Beautiful study

- * Of the BEAUTIFUL population, 13.8% had limiting angina at baseline (734 ivabradine, 773 placebo); of these, 712 patients had heart rate \geq 70 b.p.m. *Median duration of follow-up was 18 months. Ivabradine was associated with a 24% reduction in the primary endpoint (cardiovascular mortality or hospitalization for fatal and non-fatal myocardial infarction [MI] or heart failure) (HR, 0.76; 95% CI, 0.58-1.00) and a 42% reduction in hospitalization for MI (HR, 0.58, 95% CI, 0.37-0.92).*
- * *In patients with heart rate \geq 70 b.p.m., there was a 73% reduction in hospitalization for MI (HR, 0.27, 95% CI, 0.11-0.66) and a 59% reduction in coronary revascularization (HR, 0.41, 95% CI, 0.17-0.99). Ivabradine was safe and well tolerated.*

SHIFT study

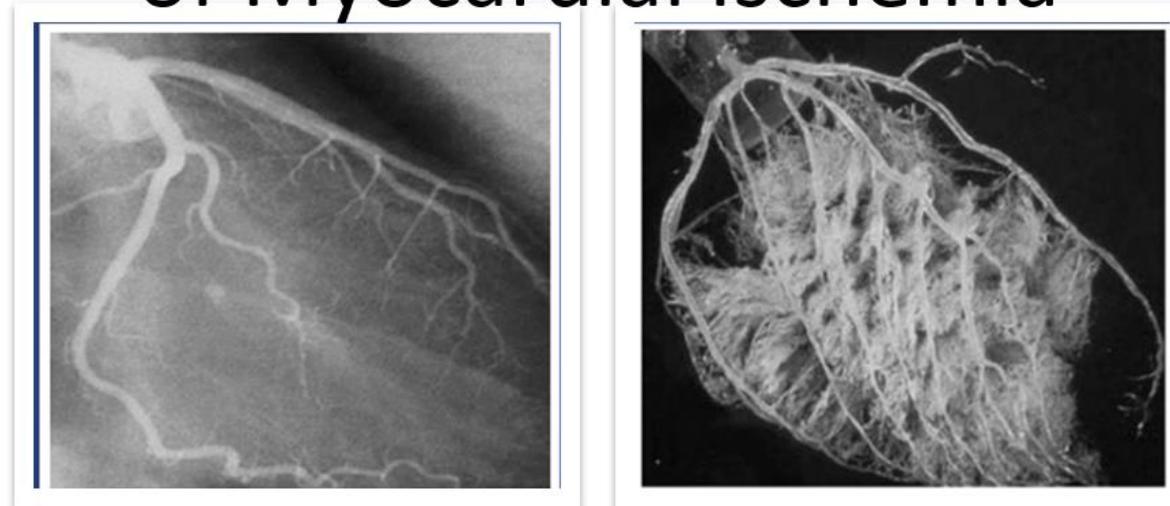
- * 6558 patients with stable symptomatic chronic HF of New York Heart Association (NYHA) class II–IV, with severe left ventricular systolic dysfunction ($EF \leq 35\%$) of both ischaemic and nonischaemic aetiology. Follow up 23 month.
- * ivabradine use was associated with a reduction in the primary endpoint of the composite of cardiovascular death or hospitalization for worsening HF symptoms (HR 0.82, 95% CI 0.75–0.90, $p < 0.0001$). These findings were principally driven by hospital admissions for worsening HF (21% in the placebo group versus 16% in the ivabradine group; HR 0.74, 95% CI 0.66–0.83, $p < 0.0001$).
- * For the secondary end points, there was no difference in the all-cause or CV mortality (HR 0.90, $p = 0.092$ and HR 0.91, $p = 0.128$ respectively). Ivabradine was associated with a reduction in all-cause hospitalization (HR 0.89, $p = 0.003$).

Incidence of angina in different populations

Table 8. Age-standardized incidence rate of stable angina pectoris per 1,000 persons, age ≥30 years, 2010

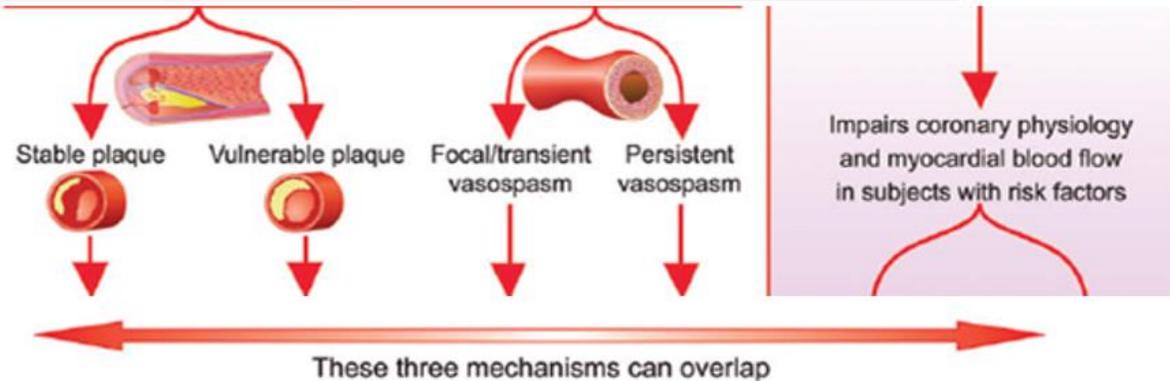
Region	Women	Men	Total
Asia Pacific, High Income	2.26	2.87	2.56
Asia, Central	4.56	6.39	5.37
Asia, East	2.53	3.15	2.84
Asia, South	2.74	3.57	3.16
Asia, Southeast	2.26	2.85	2.54
Australasia	2.42	3.11	2.76
Caribbean	2.50	3.14	2.80
Europe, Central	2.99	4.01	3.46
Europe, Eastern	3.84	5.54	4.54
Europe, Western	2.28	3.06	2.65
Latin America, Andean	2.22	2.58	2.39
Latin America, Central	2.41	2.96	2.67
Latin America, Southern	2.11	3.02	2.53
Latin America, Tropical	3.12	4.08	3.57
North Africa/Middle East	3.40	4.27	3.83
North America, High Income	2.45	3.35	2.88
Oceania	2.48	3.88	3.15
Sub-Saharan Africa, Central	2.22	3.10	2.63
Sub-Saharan Africa, East	2.66	3.21	2.92
Sub-Saharan Africa, Southern	2.33	2.95	2.61
Sub-Saharan Africa, West	2.80	3.18	2.98

Macrovascular and Microvascular Causes of Myocardial Ischemia



Epicardial coronary arteries

Coronary microcirculation



These **functional** and **structural** phenomena can act **simultaneously** in the same patient

Case study

- * 68 yr old Malay lady. Active lady
- * Known hypertension and hyperlipidemia 10 year.
- * Current medications:

Cardiprin	100 mg daily
Felodipine	5 mg daily
Simvastatin	20 mg on

Case study

- * Angina on exertion 1 month. On and off. Height 155 cm, Weight 69 kg (BMI 28.7).
- * The BP is 140/80 mmHg and the is pulse 84 bpm. Clinical examination normal
- * Blood: Total cholesterol 4.7 mmol/L , LDL 2.6 mmol/L , HDL 1.0 mmol/L, TG 2.0 mmol/L FBS 8.0 mmol/L, HbA1c 8.0%. Renal profile and urine normal.
- * ECG normal. Echocardiography was done and it showed a normal cardiac anatomy with no regional LV wall abnormalities seen at rest.
- * Positive stress Echo for ischeamia at High work load mainly at the inferior and posterior territory.

Case study : How would You managed her

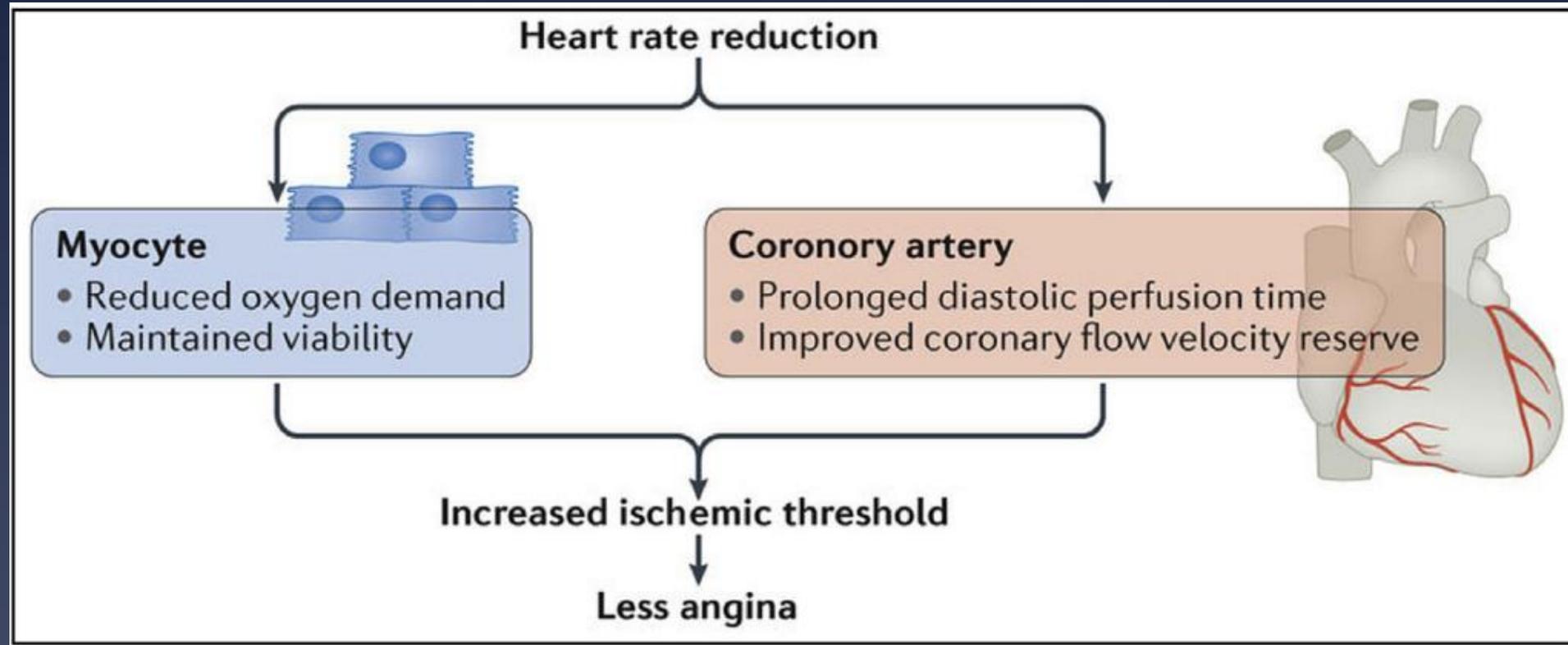
- * Risk factor modification and go on medical treatment.
- * Do other test like MSCT angiogram.
- * Counselling patient for Invasive coronary angiogram.

That the Diabetic need to be address with Metformin in combination with SGLT2 inhibitor and the Felodipine was replace with ACEI and for the angina I started with Bisoprolol and Trimetazidine

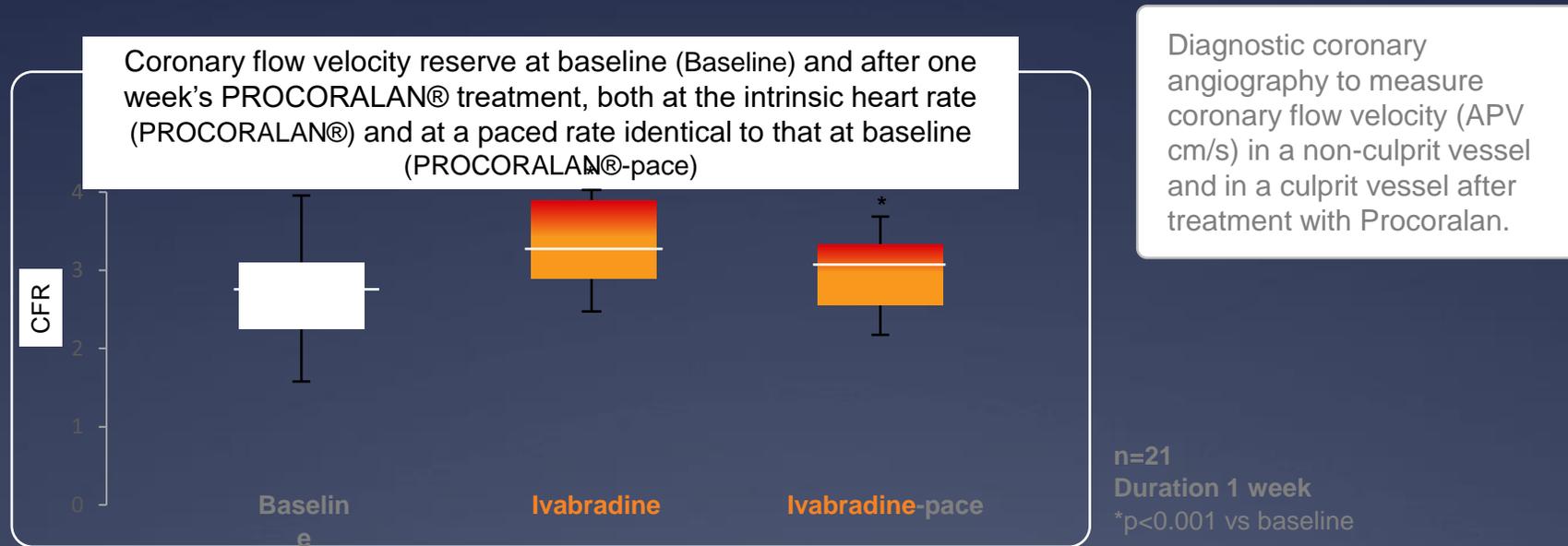
What is Optimal Medical treatment

- * The combination of intensive, evidence-based pharmacologic intervention with life-saving interventions comprises optimal medical therapy (OMT).
- * OMT is recommended by guidelines for all stable IHD patients, regardless of whether revascularization is performed.
- * Optimal medical therapy consisted of antiplatelet therapy, anti-ischemic therapy, and aggressive lipid and blood pressure control.
- * Based on the strength of the evidence, recommending more-aggressive medical therapy for patients with moderate-to-severe angina, and PCI or CABG for many patients in whom symptoms persist

Beneficial effects of heart rate reduction in angina



Ivabradine increases coronary flow reserve 1 week after treatment initiation



Strengths and weaknesses of stress echocardiography: key points

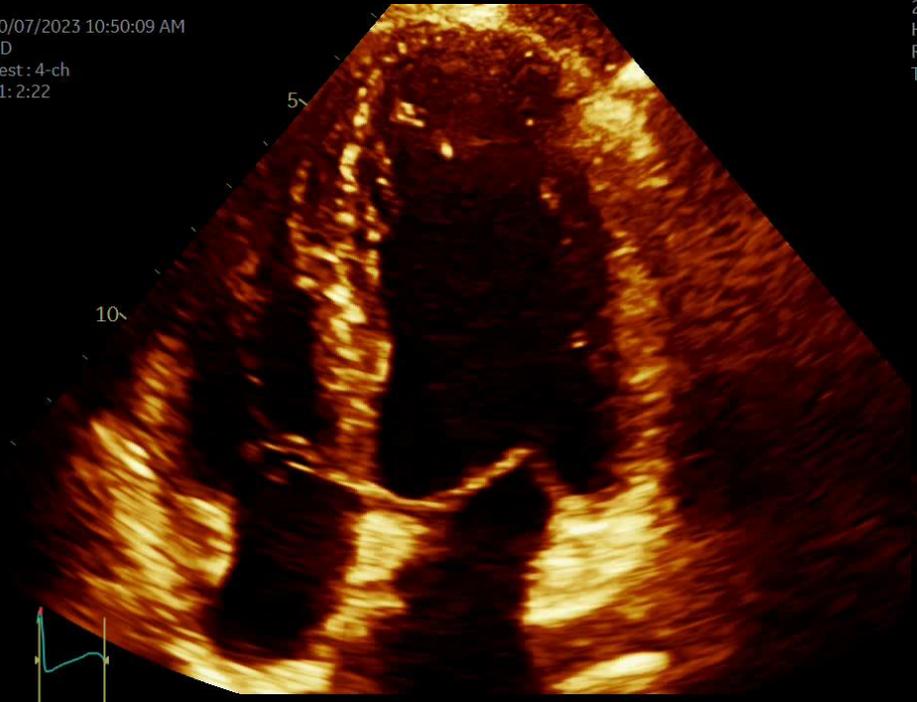
Strengths

- “patient friendly”, versatility
- accuracy
- prognostic value
- detection of viable myocardium after infarction
- assessment of left ventricular reserve (for example, valvar heart disease)

Weaknesses

- dependence on image quality
- subjectivity, need for an expert reader
- dependence on ischaemia (hence problems with mild disease, submaximal stress, and testing on treatment)
- recognition of ischaemia with resting wall motion abnormalities
- recognition of multivessel disease

20/07/2023 10:50:09 AM
HD
Rest : 4-ch
T1: 2:22



20/07/2023 10:50:41 AM
HD
Rest : 2-ch
T1: 2:53

