Non-invasive Ischemic Evaluation

Bryan C. Lee, MD
Assistant Professor
Division of Cardiovascular Medicine
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

The Ohio State University
Wexner Medical Center

Objectives

- Clinical Evaluation/Pre-test Probability
- Stress Modalities
  - Exercise
  - Pharmacologic
- Traditional Imaging modalities
  - Nuclear Perfusion
  - Echocardiography

Clinical Evaluation

History

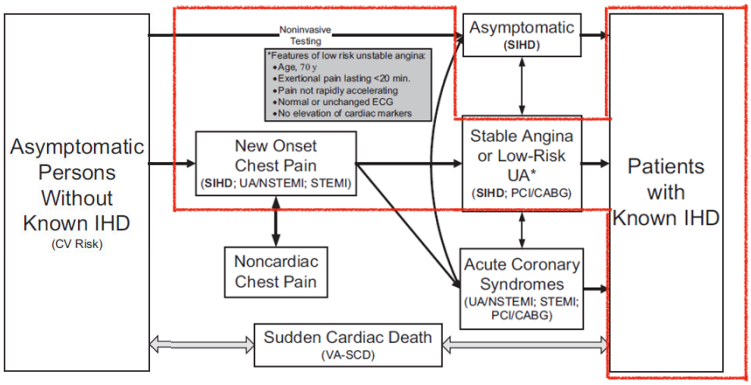


Figure 1. Spectrum of IHD

Guidelines relevant to the spectrum of IHD are in parentheses. CABG indicates coronary artery bypass graft; CV, cardiovascular; ECG, electrocardiogram; IHD, ischemic heart disease; PCI, percutaneous coronary intervention; SCD, sudden cardiac death; SIHD, stable ischemic heart disease; STEMI, ST-elevation myocardial infarction; UA, unstable angina; UA/NSTEMI, unstable angina/non–ST-elevation myocardial infarction; and VA, ventricular arrhythmia.

Source: https://www.ahajournals.org/doi/pdf/10.1161/cir.0b013e318277d6a0 http://dx.doi.org/10.1016/j.jacc.2012.07.013

Clinical Evaluation

Goal

Effectively **diagnose** and **risk stratify** coronary artery disease.

Table 13. CAD Prognostic Index

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

*Assuming medical treatment only. CAD indicates coronary artery disease; LAD, left anterior descending.
Reproduced from Califf et al. (55).

Source: https://www.ahajournals.org/doi/pdf/10.1161/cir.0b013e318277d6a0

Clinical Evaluation

History

Table 5. Clinical Classification of Chest Pain

Typical angina (definite)	1) Substernal chest discomfort with a characteristic quality and duration that is 2) provoked by exertion or emotional stress and 3) relieved by rest or nitroglycerin
Atypical angina (probable)	Meets 2 of the above characteristics
Noncardiac chest pain	Meets 1 or none of the typical anginal characteristics

Adapted from Braunwald et al. (6).

Table 10. Comparing Pretest Likelihood of CAD in Low-Risk Symptomatic Patients With High-Risk Symptomatic Patients (Duke Database)

	Nonanginal Chest Pain		Atypical Angina		Typical Angina	
Age, y	Men	Women	Men	Women	Men	Women
35	3–35	1–19	8–59	2–39	30–88	10–78
45	9–47	2–22	21–70	5–43	51–92	20–79
55	23–59	4–21	45–79	10–47	80–95	38–82
65	49–69	9–29	71–86	20–51	93–97	56–84

Each value represents the percentage with significant CAD. The first is the percentage for a low-risk, mid-decade patient without diabetes mellitus, smoking, or hyperlipidemia. The second is that of a patient of the same age with diabetes mellitus, smoking, and hyperlipidemia. Both high- and low-risk patients have normal resting ECGs. If ST-T-wave changes or Q waves had been present, the likelihood of CAD would be higher in each entry of the table.
CAD indicates coronary artery disease; and ECG, electrocardiogram.
Reprinted from Pryor et al. (71).

Table 7. Alternative Diagnoses to Angina for Patients With Chest Pain

Nonischemic Cardiovascular	Pulmonary	Gastrointestinal	Chest Wall	Psychiatric
Aortic dissection	Pulmonary embolism	Esophageal	Costochondritis	Anxiety disorders
		Esophagitis	Fibrositis	Hyperventilation
		Spasm	Rib fracture	Panic disorder
		Reflux	Sternoclavicular arthritis	Primary anxiety
			Herpes zoster (before the rash)	
Pericarditis	Pneumothorax	Biliary		Affective disorders (i.e., depression)
	Pneumonia	Colic		Somatiform disorders
	Pleuritis	Cholecystitis Choledocholithiasis		Thought disorders (i.e., fixed delusions)
		Cholangitis		
		Peptic ulcer		
		Pancreatitis		

Source: https://www.ahajournals.org/doi/pdf/10.1161/cir.0b013e318277d6a0

Clinical Evaluation

History

- Tests performance relies on prevalence (pre-test probability) of obstructive CAD in the population
  - If a test is 70% sensitive and 90% specific
    - Pretest Probability = 50%; PPV = 88%
    - Pretest Probably = 5%; PPV 27%

Clinical Evaluation

Key Points

- Noninvasive diagnostic testing is most useful when the pretest probability of ischemic heart disease is **intermediate**
  - **(10-90%; annual rate hard CV events 1-3%)**

- For many patients, determination of low, intermediate or high probability may be done quickly and reliably in clinic based on **age, sex, presence of risk factors, and description of pain (± resting EKG)**

Ischemic Cascade

- Graded ischemia of increasing severity and duration produces sequential changes
- Depends on the severity of stress imposed (i.e., submaximal exercise can fail to produce ischemia) and the severity of the flow disturbance
- Perfusion: more sensitive
- Wall motion: more specific

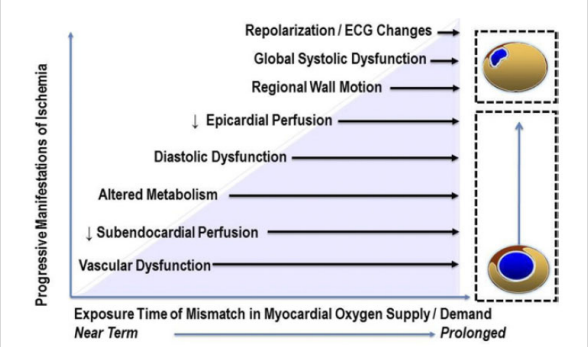


Figure 7. The Ischemic Cascade

Reproduced with permission from Shaw et al. (75).

Source: https://www.ahajournals.org/doi/pdf/10.1161/cir.0b013e318277d6a0

Exercise

Modality of Choice

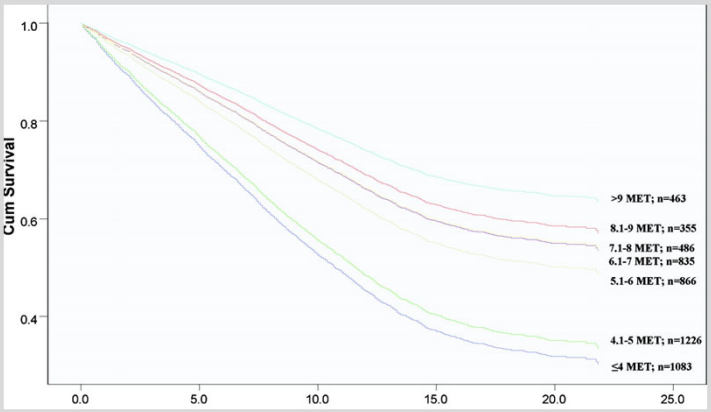
- Superior ability to detect ischemia
- Correlation to symptom burden and physical work capacity
- Exercise capacity itself is a strong prognostic indicator

Circulation
Volume 122, Issue 8, 24 August 2010, Pages 790-797
https://doi.org/10.1161/CIRCULATIONAHA.110.938852

EXERCISE PHYSIOLOGY

Exercise Capacity and Mortality in Older Men

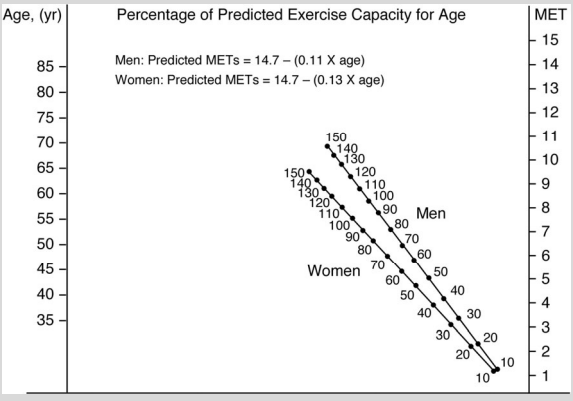
A 20-Year Follow-Up Study



MET

Metabolic Equivalent of Task

- A metabolic equivalent (MET) is the ratio of oxygen uptake by the body at a given activity level to resting oxygen uptake by the body
  - 3.5 ml/min/kg O_2



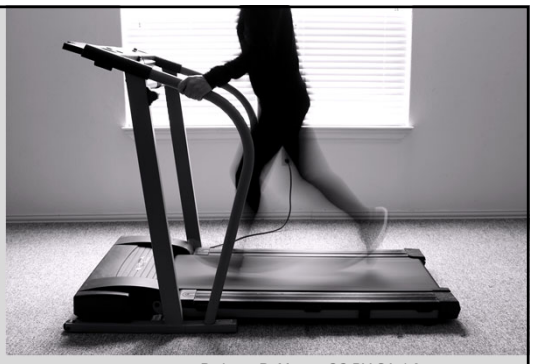
https://doi.org/10.1161/CIRCULATIONAHA.105.561944Circulation. 2006;114:2070–2082

Physical activity	MET
Light intensity activities	**< 3**
writing, desk work, using computer	1.5[10]
walking slowly	2.0[10]
Moderate intensity activities	**3 to 6**
walking, 3.0 mph (4.8 km/h)	3.0[10]
sweeping or mopping floors, vacuuming carpets	3 to 3.5[10]
yoga session with asanas and pranayama	3.3[11]
Tennis doubles	5.0[10]
sexual activity, aged 22	5.8[12]
Vigorous intensity activities	**≥6**
aerobic dancing, medium effort	6.0[13]
bicycling, on flat, 10–12 mph (16–19 km/h), light effort	6.0[10]
jumping jacks	>6.0[14]
sun salutation (Surya Namaskar, vigorous with transition jumps)	7.4[11]
basketball game	8.0[10]
swimming moderately to hard	8 to 11[10]
jogging, 5.6 mph (9.0 km/h)	8.8[13]
rope jumping (66/min)	9.8[13]
rope jumping (84/min)	10.5[13]
rope jumping (100/min)	11.0[13]
jogging, 6.8 mph (10.9 km/h)	11.2[13]

Exercise Testing

Goals

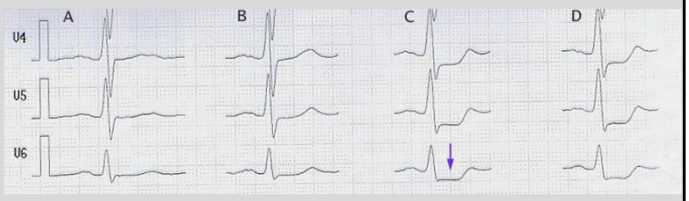
- Achieve high levels of exercise (i.e., maximal exertion), which in the setting of a negative ECG generally and reliably excludes obstructive CAD.
- Document the extent and severity of ECG changes and angina at a given workload to predict the likelihood of underlying significant or severe CAD.
- Failure to reach peak heart rate or to achieve adequate levels of exercise results in an indeterminate estimation of CAD.



Exercise ECG

Modality of Choice

- Diagnostic endpoint
  - **≥ 1 mm horizontal/downsloping ST depression**
  - ST elevation
- Performance
  - **Sensitivity: 68%**
  - **Specificity: 77% (slightly lower in women)**
  - Test performance is improved when non-EKG factors are considered
    - Exercise duration, heart rate recovery
    - Angina
    - Ventricular arrhythmias, hemodynamic response to exercise (eg BP drop)



Exercise ECG

Modality of Choice

- **Patients must be able to exercise and have an interpretable resting EKG**
- Resting EKG abnormalities which reduce test accuracy
  - LVH
  - LBBB
  - Ventricular pacing
  - Resting ST-depression ≥ 0.5 mm
  - Digitalis effect

Table 1. Contraindications to Exercise Testing (Table view)

Absolute
Acute myocardial infarction (within 2 d)
Unstable angina not previously stabilized by medical therapy[1]
Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise
Symptomatic severe aortic stenosis
Uncontrolled symptomatic heart failure
Acute pulmonary embolus or pulmonary infarction
Acute myocarditis or pericarditis
Acute aortic dissection
Relative[2]
Left main coronary stenosis
Moderate stenotic valvular heart disease
Electrolyte abnormalities
Severe arterial hypertension[3]
Tachyarrhythmias or bradyarrhythmias
Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
Mental or physical impairment leading to inability to exercise adequately
High-degree atrioventricular block

[1] Appropriate timing of testing depends on level of risk of unstable angina, as defined by the Agency for Health Care Policy and Research Unstable Angina Guidelines.
[2] Relative contraindications can be superseded if the benefits of exercise outweigh the risks.
[3] In the absence of definitive evidence, the committee suggests a systolic blood pressure >200 mm Hg and/or diastolic blood pressure >110 mm Hg.
Modified from Fletcher GF, Balady G, Froelicher VF, Hartley LH, Haskell WL, Pollock ML. Exercise standards: a statement for healthcare professionals from the American Heart Association. Special report. *Circulation.* 1995;91:580-615.

https://www.ahajournals.org/doi/epub/10.1161/01.CIR.96.1.345.

Exercise ECG

Modality of Choice

- Exercise is almost always the stressor of choice in capable individuals who require noninvasive testing
- Exercise capacity itself offers strong prognostic information following stress testing by its association with mortality

CLASS I

1. Standard exercise ECG testing is recommended for patients with an intermediate pretest probability of IHD who have an interpretable ECG and at least moderate physical functioning or no disabling comorbidity (114,145–147). *(Level of Evidence: A)*

CLASS IIa

1. For patients with a low pretest probability of obstructive IHD who do require testing, standard exercise ECG testing can be useful, provided the patient has an interpretable ECG and at least moderate physical functioning or no disabling comorbidity. *(Level of Evidence: C)*

https://www.sciencedirect.com/science/article/pii/S0735109712027015?via%3Dihub –

Pharmacologic Stress

Agents

Beta-agonists

- Mechanism: increased heart rate and inotropy
- Agent: dobutamine (Dobutrex®)
- Adverse effects: ventricular arrhythmias, palpitations, chest pain, hypotension (10%)

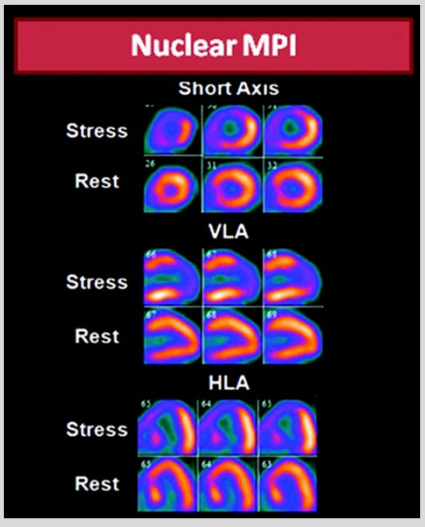
Vasodilators

- Mechanism: increase flow to normal arteries, decrease perfusion to stenotic vessels
- Agents
  - Dipyridamole (Persantine®)
  - Adenosine (Adenoscan®)
  - Regadenoson (Lexiscan®)
    - May be given as a bolus (no infusion)
    - Lower likelihood of bronchospasm
- Cause bronchospasm in COPD/asthma, reversed by aminophylline

Nuclear Myocardial Perfusion

Pros & Cons

- Advantages
  - Compared to EKG, more sensitive in detection of single vessel disease
  - May use with abnormal baseline EKG
  - May use to assess myocardial viability
- Disadvantages
  - Attenuation artifacts
    - Men: inferior wall (diaphragmatic motion)
    - Women: anterior wall (breast tissue overlay)
  - Perfusion is relative: study may appear normal in triple vessel disease

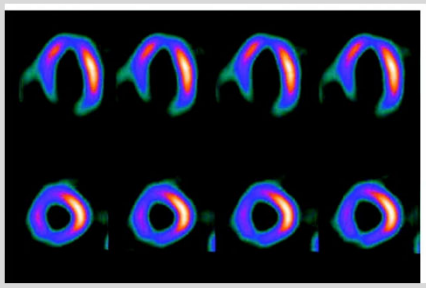


12 Oct 2010https://doi.org/10.1161/CIRCULATIONAHA.109.903351Circulation. 2010;122:1514–1518

Nuclear Myocardial Perfusion

Pros & Cons

- Performance
  - Sensitivity: 85%
  - Specificity: 85%
  - Caution not for LBBB or V pacing
    - False positive reversible perfusion defects of the septum (abnormal septal motion, reduced diastolic filling)

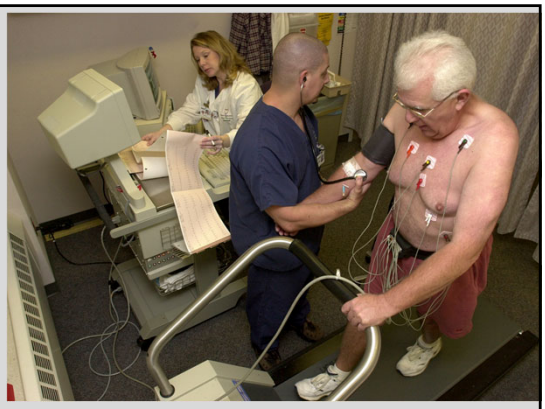


31 Mar 2008https://doi.org/10.1161/CIRCULATIONAHA.107.726711Circulation. 2008;117:1832–1841

Stress Echocardiogram

Objective

- Detection of reversible regional wall motion abnormalities unmasked during stress
  - Exercise: Images must be collected within 60 to 90 sec of exercise termination
  - With pharmacologic (dobutamine) studies, atropine may be used to augment heart rate (~50% of tests)



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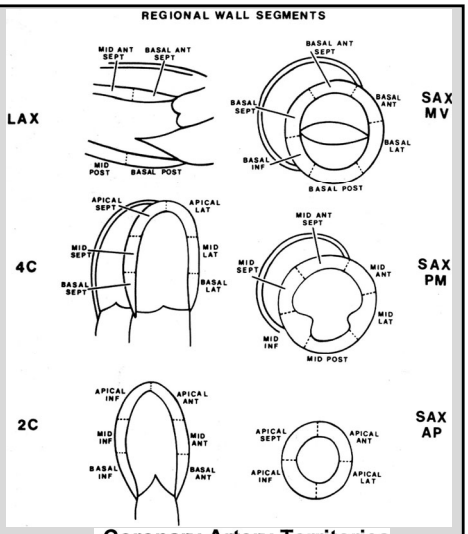
Stress Echocardiogram

Results

- Normal response: hyperdynamic
- Abnormal, "positive" responses
  - Typical findings
    - New WMAs
    - Worsening WMAs
  - More specific for severe CAD
    - LV cavity dilation
    - Decrease in global systolic function
  - Wall motion score index > 1.4 or exercise EF <50% are associated with poor prognosis



29 Jan 2002https://doi.org/10.1161/hc0402.102975Circulation. 2002;105:539–542

Stress Echocardiogram

Performance/Limitations

- Performance
  - Sensitivity: 79%
  - Specificity: 87%
- Advanced echocardiographic techniques
  - Tissue doppler imaging, strain
  - Microbubble myocardial contrast
- Limited endocardial visualization
  - Obese
  - Chronic lung disease

Guidelines

Exercise ECG/Echo/MPI

Table 11. Stress Testing and Advanced Imaging for Initial Diagnosis in Patients With Suspected SIHD Who Require Noninvasive Testing

	Exercise Status		ECG Interpretable		Pretest Probability of IHD					
Test	Able	Unable	Yes	No	Low	Intermediate	High	COR	LOE	References
Patients able to exercise*										
Exercise ECG	X		X			X		I	A	(114, 145–147)
Exercise with nuclear MPI or Echo	X			X		X	X	I	B	(91, 132, 148–156)
Exercise ECG	X		X		X			IIa	C	N/A
Exercise with nuclear MPI or Echo	X		X			X	X	IIa	B	(91, 132, 148–156)
Exercise Echo	X		X			X		IIb	C	N/A
Pharmacological stress with nuclear MPI, Echo, or CMR	X		X			Any		III: No Benefit	C	(155, 167, 168)
Exercise stress with nuclear MPI	X		X		X			III: No Benefit	C	N/A

Source: https://www.ahajournals.org/doi/pdf/10.1161/cir.0b013e318277d6a0

Guidelines

Exercise ECG/Echo/MPI

Table 11. Stress Testing and Advanced Imaging for Initial Diagnosis in Patients With Suspected SIHD Who Require Noninvasive Testing

	Exercise Status		ECG Interpretable		Pretest Probability of IHD					
Test	Able	Unable	Yes	No	Low	Intermediate	High	COR	LOE	References
Patients unable to exercise										
Pharmacological stress with nuclear MPI or Echo		X	Any			X	X	I	B	(148–150, 152–156)
Pharmacological stress Echo		X	Any		X			IIa	C	N/A
Exercise ECG		X		X		Any		III: No Benefit	C	(91, 132, 148–156, 161)

Source: https://www.ahajournals.org/doi/pdf/10.1161/cir.0b013e318277d6a0

Coronary CT Angiogram

Salman K. Bhatti, MD
Assistant Professor – Clinical
Division of Cardiovascular Medicine
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

The Ohio State University
Wexner Medical Center

CONTENTS

ASYMPTOMATIC

Appropriate Use Key: A ¼ Appropriate; M ¼ May Be Appropriate; R ¼ Rarely Appropriate. A ¼ Appropriate; CAD ¼ coronary artery disease; CCTA ¼ coronary computed tomography angiography; CHD ¼ coronary heart disease; CMR ¼ cardiac magnetic resonance; ECG ¼ electrocardiogram;
Echo ¼ echocardiography; M ¼ May Be Appropriate; R ¼ Rarely Appropriate; RNI ¼ radionuclide imaging.

Table 1.2. Asymptomatic (Without Symptoms or Ischemic Equivalent)

Refer to pages 17 and 18 for relevant definitions

	Indication Text	Exercise ECG	Stress RNI	Stress Echo	Stress CMR	Calcium Scoring	CCTA	Invasive Coronary Angiography
7.	• Low global CHD risk • Regardless of ECGinterpretability and ability to exercise	R	R	R	R	R	R	R
8.	• Intermediate global CHD risk • ECG interpretable and able to exercise	M	R	R	R	M	R	R
9.	• Intermediate global CHD risk ECG uninterpretable OR unable to exercise		M	M	R	M	R	R
10.	• High global CAD Risk • ECG interpretable and able to exercise	A	M	M	M	M	M	R
11.	• High global CAD Risk • ECG uninterpretable OR unable to exercise		M	M	M	M	M	R

Wolk, et al. JACC 2013 63(4) p 380-406

SYMPTOMATIC

Table 1.1. Symptomatic

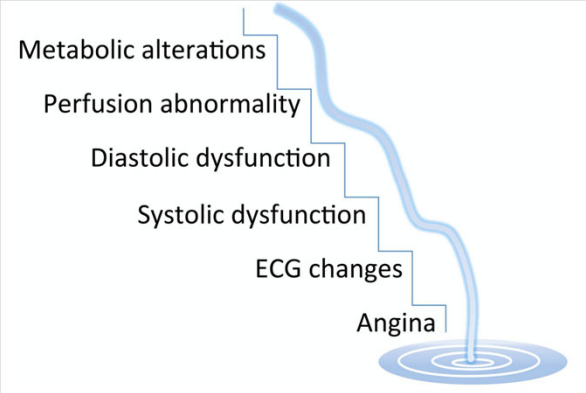
Appropriate Use Key: A ¼ Appropriate; M ¼ May Be Appropriate; R ¼ Rarely Appropriate. A ¼ Appropriate; CAD ¼ coronary artery disease; CCTA ¼ coronary computed tomography angiography; CMR ¼ cardiac magnetic resonance; ECG ¼ electrocardiogram; Echo ¼ echocardiography;
M ¼ May Be Appropriate; R ¼ Rarely Appropriate; RNI ¼ radionuclide imaging.

Refer to pages 16 and 17 for relevant definitions, in particular Table A and text for age, sex, symptom presentation, and risk factors relevant to each pre-test probability category

	Indication Text	Exercise ECG	Stress RNI	Stress Echo	Stress CMR	Calcium Scoring	CCTA	Invasive Coronary Angiography
1.	• Low pre-test probability of CAD • ECG interpretable AND able to exercise	A	R	M	R	R	R	R
2.	• Low pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	M	R	M	R
3.	• Intermediate pre-test probability of CAD • ECG interpretable AND able to exercise	A	A	A	M	R	M	R
4.	• Intermediate pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	A	R	A	M
5.	• High pre-test probability of CAD • ECG interpretable AND able to exercise	M	A	A	A	R	M	A
6.	• High pre-test probability of CAD • ECG uninterpretable OR unable to exercise		A	A	A	R	M	A

Wolk, et al. JACC 2013 63(4) p 380-406

WATERFALL ANALOGY OF ISCHEMIC CASCADE

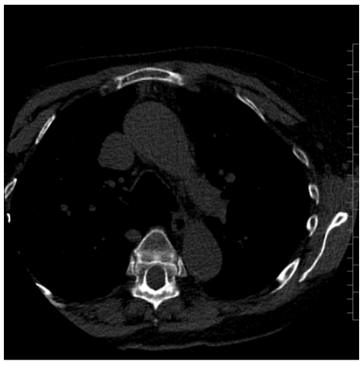


Maznyczka et al. Open Heart 2015;2:e000178

CARDIAC CT INTRODUCTION

- Cardiac CT is performed as contrast enhanced coronary CT angiography (CCTA) to evaluate for the presence and extent of coronary artery disease (CAD).
- Cardiac CT comprise of non contrast series and contrast series. Non contrast series is for the evaluation and quantification of coronary calcium. Contrast series is for the evaluation of soft plaques and degree of stenosis.

NON-CONTRAST SERIES (CALCIUM SCORE)



Introduced in 1990. Highly specific feature of coronary atherosclerosis.

Especially useful in asymptomatic patients for planning primary prevention.

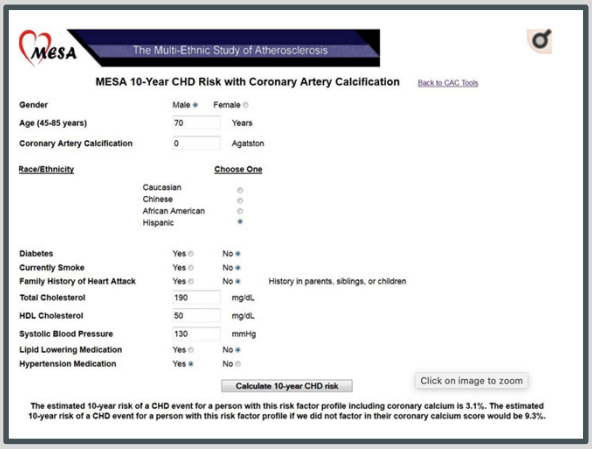
Usually done in patients between the ages of 40 – 65 who have strong family history of heart disease or one of the risk factors: Hypertension, DM, High cholesterol, Smoking or Obesity.

Modern CT scan: 1 mSy

Strongly association between Calcium score and major adverse cardiovascular event (MACE)

CT-CAC is a reasonable option to risk stratify patients.

CALCIUM SCORE



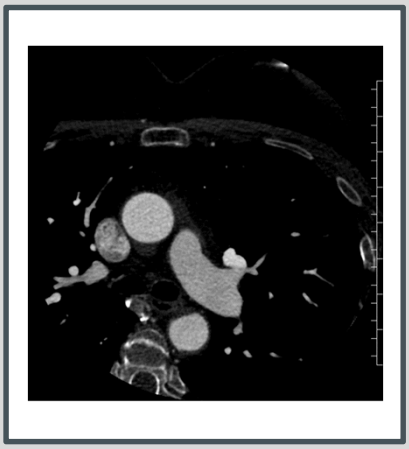
MESA studies also provide the percentile scores based on age, gender, ethnicity and calcium score.

McClelland et al. used MESA data to drive and validate a risk score to estimate 10 year CHD risk using CAC plus traditional risk factors.

Miedenna et al. studied the potential net benefit of aspirin in 4229 individuals free of diabetes. Net harm with aspirin when CAC = 0; Net benefit when CAC >100.

Net favorable change in patients who underwent CAC in BP, LDL, cholesterol and waist circumference who underwent CAC score when compared to patients in the control group.

CT CORONARY ANGIOGRAM (IMAGING PROTOCOL)



- 64 slice scanner is considered a minimum standard.
- Image acquisition is synchronized to ECG.
- A bolus of iodinated contrast is administered intravenously the acquisition is timed when the contrast reaches the coronaries.
- Sublingual nitroglycerin (or spray) is given immediately prior to the exam to dilate the coronary arteries and facilitate assessment.
- Beta blockers and/or ivabradine is administered to slow the heart rates to less than 60 – 70 beats/min.

CT CORONARY ANGIOGRAM

- Diagnosis – Detection of CAD

Among available non-invasive tests, CCTA has the highest diagnostic accuracy for detection of obstructive CAD.

The ideal patient would be an intermediate pretest probability (10 – 90 percent) for significant CAD.

- Prognosis- Coronary atherosclerosis

Absence of any CAD carries a very low risk (< 0.2 percent) of major adverse cardiovascular event (MACE)

Presence of non obstructive and obstructive CAD carries three- and six fold increased risk of future MACE over the next 5 years.

- Acute coronary syndrome

In patients with intermediate and low probability of ACS, early CCTA is an effective test to exclude the diagnosis.

CONTRAINDICATIONS AND ACCURACY

CONTRAINDICATIONS:

- Severe renal insufficiency (estimated GFR <30 ml/min/1.73 sq m)
- History of allergy to iodinated contrast
- Patient cooperation (able to hold breath for 5 – 10 seconds)
- Atrial fibrillation and excessive motion (especially with 64 slice scanner)

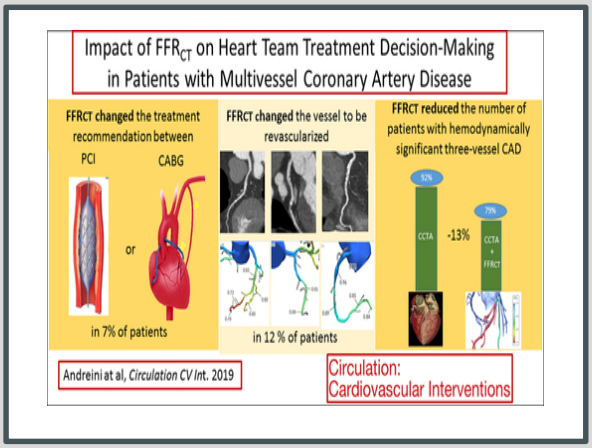
ACCURACY[1]

- Sensitivity of 95 – 99 percent.
- Specificity of 64 – 90 percent, based on image quality, calcified lesions and underlying artifacts.

In patients with high calcium score, specificity can be as low as 53 percent.

1. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. AUBudoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, Scherer M, Bellinger R, Martin A, Benton R, Delago A, Min JK SOJ Am Coll Cardiol. 2008;52(21):1724.

FRACTIONAL FLOW RESERVE



Fractional flow reserve (FFR) is a technique used in coronary catheterization to measure pressure differences across a coronary artery stenosis.

Emerging technology to improve the specificity for CCTA.

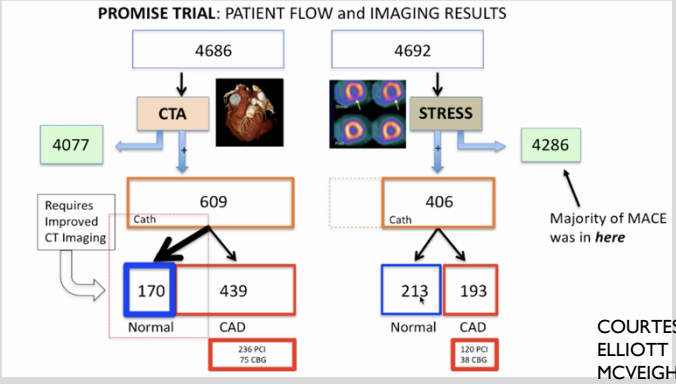
The CT images are segmented to delineate coronary lumen and myocardium and mathematical models are applied to simulate pharmacological stress across a stenotic segment.

FFR-CT is not universally available and is performed only by sending the CT image dataset to a commercial entity that provides the results.

Daniele Andreini. Circulation: Cardiovascular Interventions. Impact of Fractional Flow Reserve Derived From Coronary Computed Tomography Angiography on Heart Team Treatment Decision-Making in Patients With Multivessel Coronary Artery Disease, Volume: 12, Issue: 12, DOI: (10.1161/CIRCINTERVENTIONS.118.007607)

OUTCOMES OF ANATOMICAL VS FUNCTIONAL TESTING FOR CAD PROMISE TRIAL

- 10,003 patients
- Randomized 1:1 to a strategy of anatomic testing with use of coronary CTA or to functional testing (exercise ECG, nuclear stress test, stress echocardiography)
- Primary Endpoint: Composite of death, MI, hospitalization for unstable angina or major procedural complication.
- No significant difference in primary endpoint.



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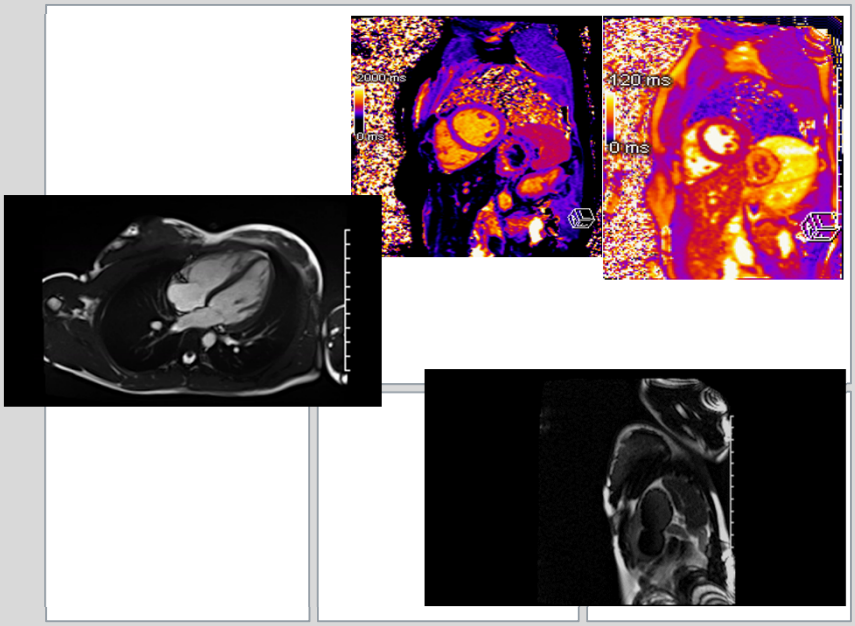
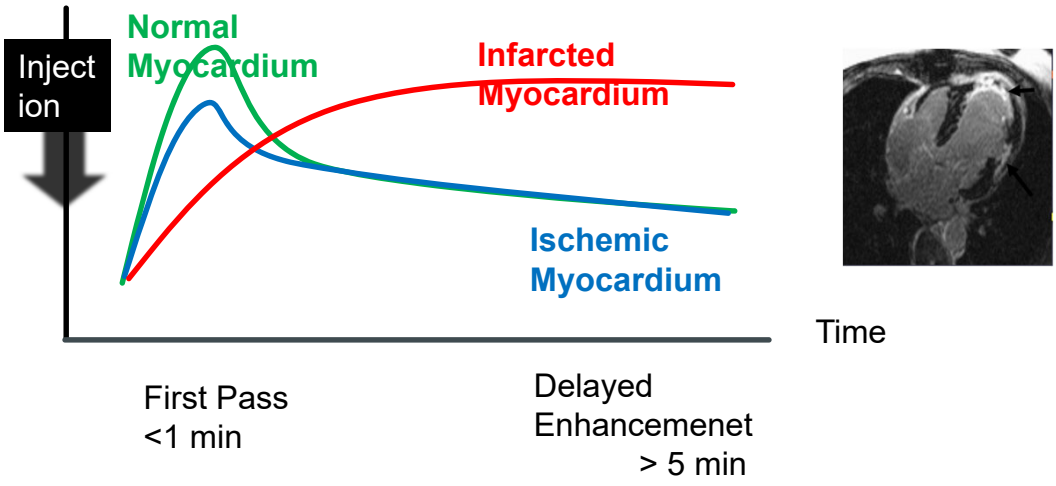
Douglas P et al. Outcomes of Anatomical Versus Functional Testing for Coronary Artery Disease. N Engl J Med 2015; 372:1291-1300

CARDIAC MRI

- Cardiac MRI provides superior assessment for the cardiac structure and function.
- It also provides myocardial characterization and assessment of scar/fibrosis burden.

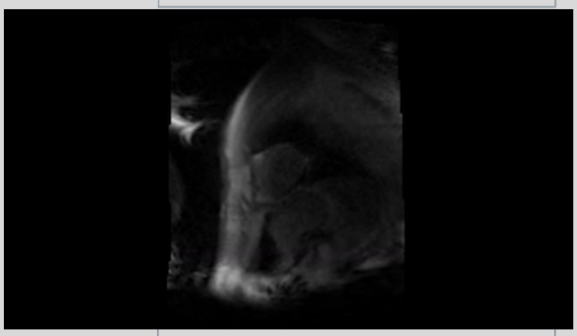


LATE GADOLINIUM ENHANCEMENT KINETICS

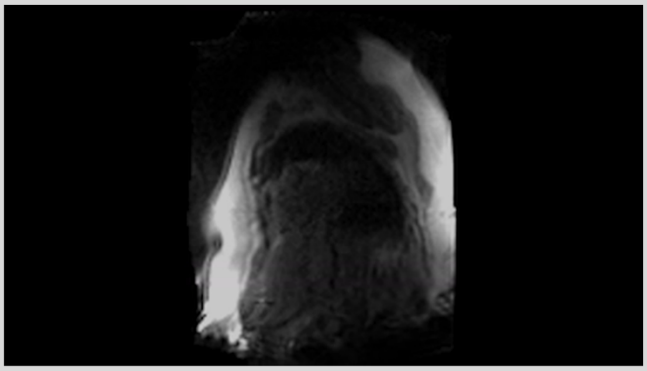


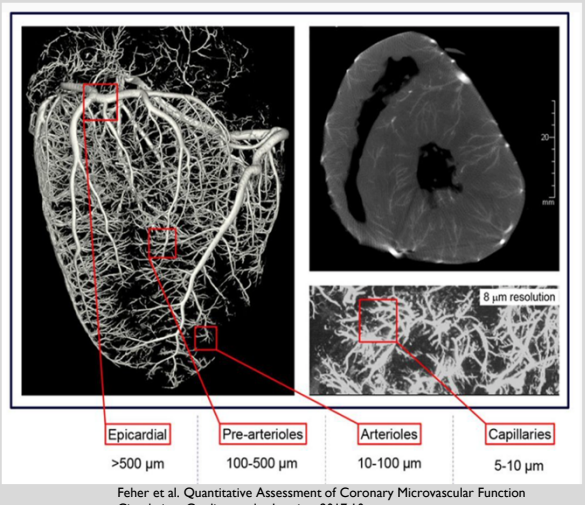
STRESS MODALITIES AND CONTRAINDICATIONS

- Dobutamine
  - AV peak gradient >50 mmHg, AVA <1cm2, BP >220/120 mmHg
  - Uncontrolled atrial fibrillation, complex arrhythmia
  - Obstructive cardiomyopathy
  - Myocarditis, pericarditis, endocarditis
  - Uncontrolled congestive heart failure
- Adenosine/Regadenoson
  - Advanced AV block or sinus node dysfunction without pacemaker
  - SBP < 90 mmHg
  - Sinus bradycardia < 40 bpm
  - Active bronchospastic disease
  - Allergies to stress/contrast agents
- Exercise
  MRI compatible treadmill



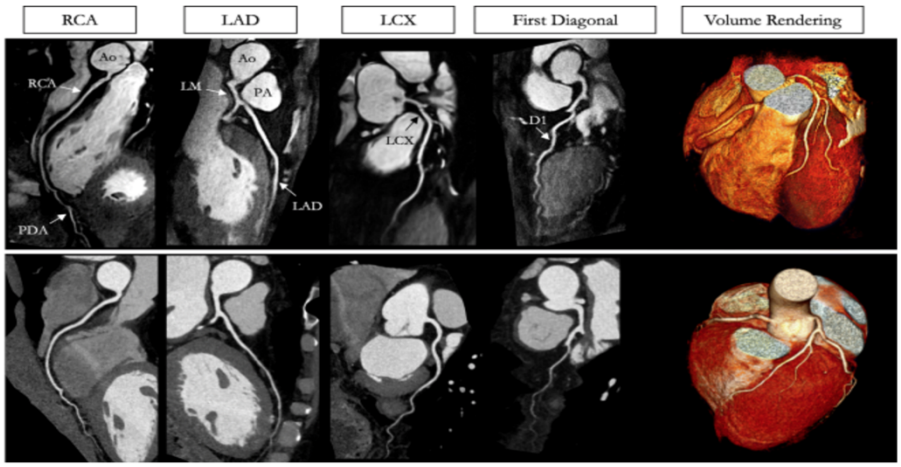
MICROVASCULAR DISEASE





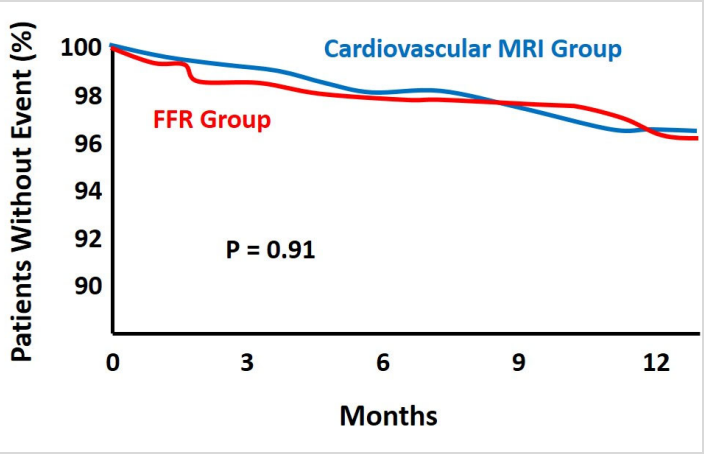
Feher et al. Quantitative Assessment of Coronary Microvascular Function
Circulation: Cardiovascular Imaging. 2017;10

CONTRAST FREE, FREE BREATHING CORONARY MRI AND CT



Bustin, A., Rashid, I., Cruz, G. *et al.* 3D whole-heart isotropic sub-millimeter resolution coronary magnetic resonance angiography with non-rigid motion-compensated PROST.*J Cardiovasc Magn Reson* **22,** 24 (2020).

INFORM TRIAL



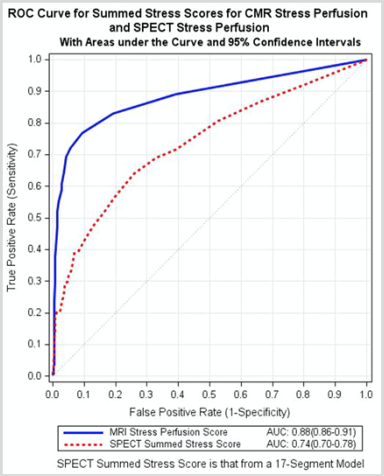
E NAGEL ET AL. N ENGL J MED 2019;380:2418-2428.

- To test whether a cardiovascular MRI based strategy is non inferior to an FFR based strategy with respect to major adverse cardiovascular events in patients with stable angina.
- Primary outcome was death, non-fatal MI or target vessel revascularization within 1 year.
- A total of 184 of 454 patients (40.5%) in the cardiovascular-MRI group and 213 of 464 patients (45.9%) in the FFR group met criteria to recommend revascularization (P=0.11).
- Fewer patients in the cardiovascular-MRI group than in the FFR group underwent index revascularization (162 [35.7%] vs. 209 [45.0%], P=0.005).
- Among patients with stable angina and risk factors for coronary artery disease, myocardial-perfusion cardiovascular MRI was associated with a lower incidence of coronary revascularization than FFR and was noninferior to FFR with respect to major adverse cardiac events.

CMR VS SPECT

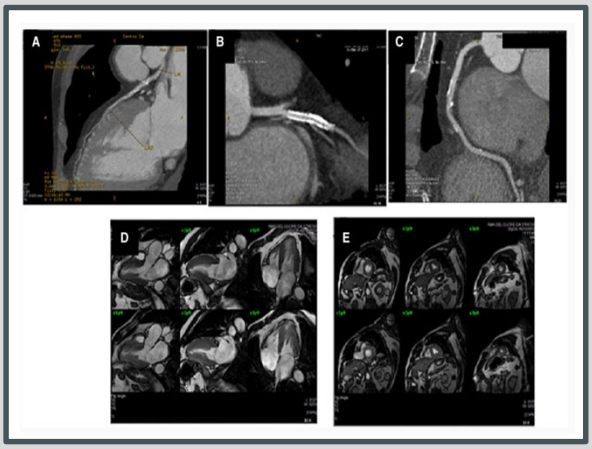
- CE-MARC study
- Prospective randomized single center trial
- Primary outcome: Diagnostic accuracy of stress CMR
- Gold standard: Coronary angiography (>50% LM; >70% other vessels >2mm)

	Sensitivity	Specificity	PPV	NPV
CMR	86.5%	83.4%	77.2%	90.5%
SPECT	66.5%	82.6%	71.4%	79.1%



Greenwood J et al. Clinical Evaluation of Magnetic Resonance Imaging in Coronary Heart Disease (The CE-MARC Study): A Prospective Evaluation of 750 Patients. Circulation. 2010;122:A21797

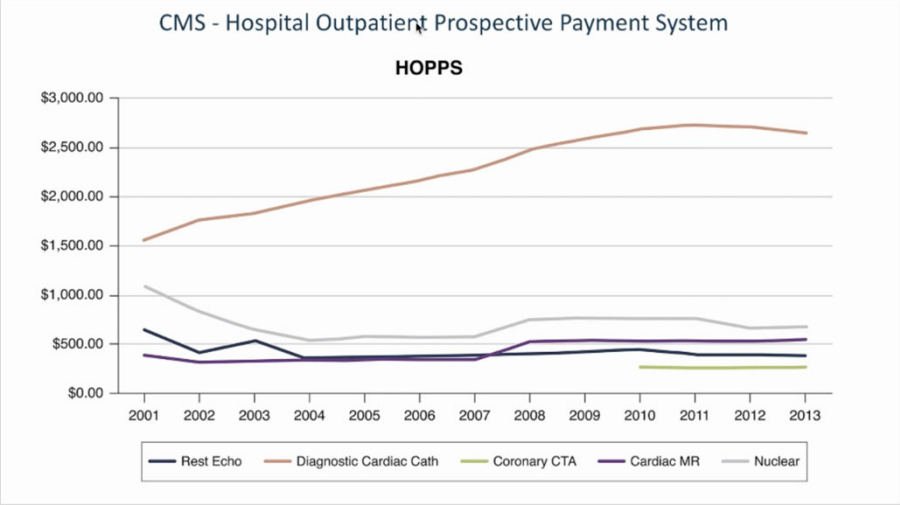
STRATEGY STUDY



Pontone et al. Circulation: Cardiovascular Imaging. 2016;9

- STRATEGY compared an anatomic CT coronary angiography versus a functional CMR strategy in symptomatic patients with prior myocardial revascularization procedures.
- 600 patients were enrolled (divided in 1:1 to the two groups) and followed in terms of subsequent noninvasive tests, invasive coronary angiography, revascularization procedures, cumulative effective radiation dose, major adverse cardiovascular events defined as nonfatal MI and cardiac death and medical costs.
- Stress-CMR strategy was associated with a significant reduction of radiation exposure and cumulative costs (59% and 24%, respectively; $P<0.001$). Patients undergoing stress-CMR showed a lower rate of major adverse cardiac events (5% versus 10%; $P<0.010$) and cost-effectiveness ratio (119.98±250.92 versus 218.12±298.45 Euro/y; $P<0.001$).
- Compared with CT, stress-CMR was more cost-effective in symptomatic revascularized patients.

RELATIVE COSTS



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	Stress ECG	Stress Echo	MPI	CT	Stress MRI
Advantages	Low cost, availability, acceptability and convenience Exercise tolerance determined Provide prognostic information Correlate symptoms with activity Assess rhythm rate, BP, response to activity	Safe No radiation Faster Widely available Relatively low cost Structural information (valvular, EF)	Detects abnormal flow reserve Peak exercise images acquired Most studies complete Quantified LVEF and volumes	Cost saving Combination of functional and anatomic data Amount of calcium correlates with plaque burden. Information on non obstructive CAD May avoid invasive procedures May identify other causes of chest pain	No radiation Structural information Also assesses for microvascular disease. Better modality Potentially can assess for both perfusion and wall motion

	Stress ECG	Stress Echo	MPI	CT	Stress MRI
Disadvantages	Limited sensitivity and specificity Does not localize ischemia No assessment of LV function Requires cooperation and ability to walk	Peak exercise images difficult to acquire False negative with rapid recovery Limited by windows and body habitus Technician dependent Afib, LBBB	Longer times Radiation Lower spatial resolution Relatively expensive Artifacts Isotope availability Balanced ischemia missed	Radiation Iodinated contrast dye Artifacts Excessive calcium – blooming artifact FFR expensive and requires offsite analysis. Afib Low heart rates required	Long examination Confinement and noise of the MR scanner Patient cooperation Frequent breath holds. Device artifacts. Lack of availability and expertise.