E·QUAL | EMERGENCY QUALITY NETWORK

Chest Pain Wave I

Making Dollars and Sense Out of Stress Testing

TCPi | Transforming Clinical Practices Initiative

American College of Emergency Physicians®
ADVANCING EMERGENCY CARE

E·QUAL EMERGENCY QUALITY NETWORK

Presenters

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Disclosures

Dr. Newby:

- None specifically related to this activity
- All RWI are available at https://www.dcri.org/about-us/conflict-of-interest

Dr. Kontos:

Consultant--Roche

Defining Low-Risk

- Normal/near-normal ECG
- Negative baseline cardiac injury markers
- Low-risk score (e.g., TIMI [0/1], GRACE [<109], HEART [<3])
- But low risk is not no risk

Amsterdam EA, et al. *J Am Coll Cardiol.*2014;64(24):e139-228.

The ADAPT ADP

All parameters had to be negative for the ADP to be considered negative and for the patient to be considered low risk

1. cTnl level at 0 and 2 hours below institutional cutoff for an elevated troponin concentration
2. No new ischemic changes on the initial ECG
3. TIMI score = 0
    a. Age ≥65 years
    b. Three or more risk factors for CAD
    c. Use of aspirin in last 7 days
    d. Significant coronary stenosis (e.g., previous coronary stenosis 50%)
    e. Severe angina (e.g., 2 angina events in past 24 hours or persisting discomfort)
    f. ST-segment deviation of ≥0.05mV on first ECG
    g. Increased troponin and/or creatinine kinase-MB blood tests (during assessment)

Proportion of patients safely discharged within 6 hours of ED arrival increased by 8%.

Outpatient stress testing within 72 hours of discharge.

Than M, et al. *J Am Coll Cardiol.* 2012;59(23):2091-2098.
Than M, et al. *JAMA Intern Med.* 2014;174(1):51-58.

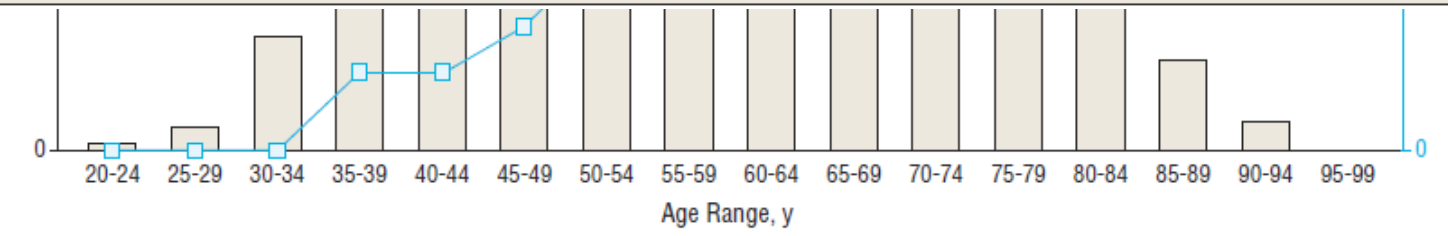
Challenges of Current State of Stress Testing in Low Risk Chest Pain Patients

- 80-90% of patients evaluated in the ED will not have ACS
- But, approximately 50% of chest pain patients will have stress testing, other noninvasive testing, or angiography
- Among low risk patients (ACS risk <2%) yield of stress testing is low and false positive tests are increased without improved outcomes
  - Prevalence of CAD is only approximately 5% in this population

Use and Results of Stress Testing in Low-Moderate Risk Chest Pain Patients

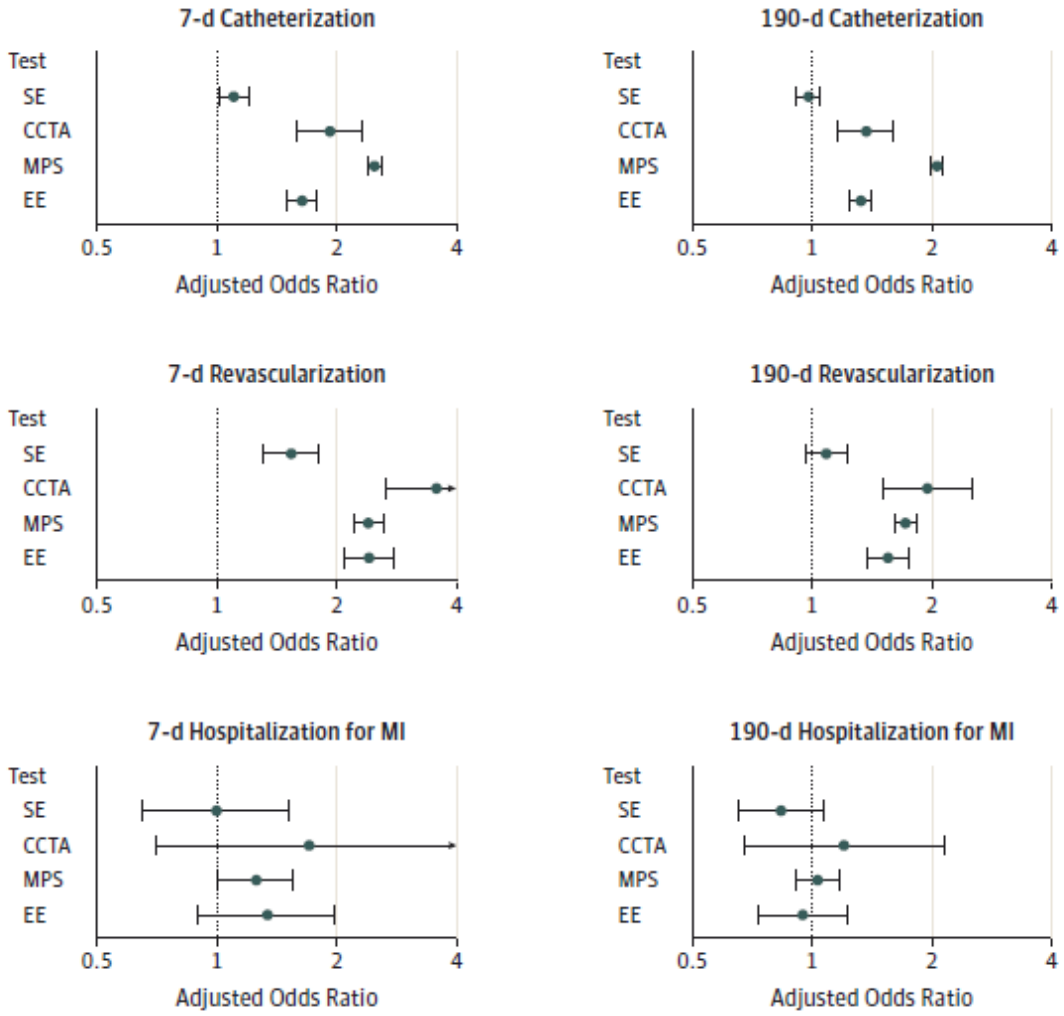
Table 4. Yield of Routine Provocative Cardiac Testing Before Discharge Among Patients in the Emergency Department–Based Chest Pain Unit

Variable	No./Total No. (%)
Positive provocative study result	470/4181 (11.2)
Confirmed true positive by angiography	63/123 (51.2)
Confirmed false positive by angiography	60/123 (48.8)
Angiography results	
New diagnosis of obstructive CAD	63/4181 (1.5)
Anatomic disease classified as having potential for benefit via revascularization, AHA class I or IIa	28/4181 (0.7)
Disease classified as AHA class I or IIa if coronary artery bypass graft performed	28/4181 (0.7)
Disease classified as AHA class I or IIa if percutaneous coronary intervention performed	7/4181 (0.2)



Hermann SK, et al. JAMA Int Med 2013:1128-1133.

Cost-effectiveness of Non-invasive Testing in ED Chest Pain Patients without MI



N=421,774
Claims data, primary or secondary diagnosis of chest pain

Overall MI rates:

7 days	0.11%
190 days	0.33%

Tested vs Not Tested

Foy AJ, et al. 2015;175:428-436.

VIEWPOINT

Defensive Medicine—Legally Necessary but Ethically Wrong?

Inpatient Stress Testing for Chest Pain in Low-Risk Patients

Allen Kachalia, MD, JD
Michelle M. Mello, JD, PhD

JAMA INTERN MED/VOL 173 (NO. 12), JUNE 24, 2013

Editor's Note

Stress Testing in the Emergency Department: Not Which Test but Whether Any Test Should Be Done

Rita F. Redberg, MD, MSc

JAMA Internal Medicine March 2015 Volume 175, Number 3

Bayes Theorem

$$P(A|B) = \frac{P(B|A)P(A)}{P(B)}$$

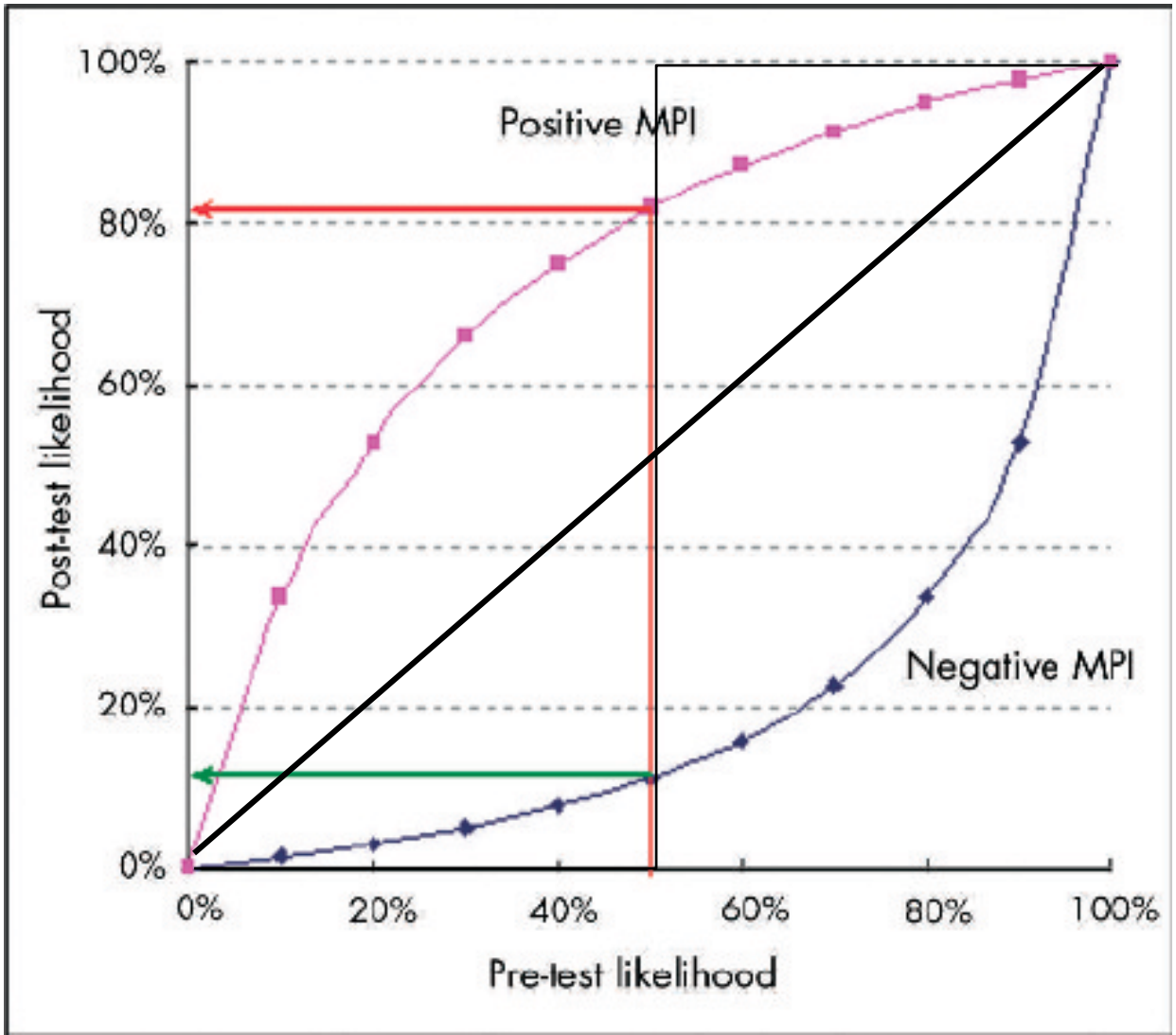
The ability of a test to predict the presence or absence of disease is dependent not only on the sensitivity and specificity of the test, but also the pretest probability of disease

Bayes Theorem

- An abnormal test is more likely to be a false positive in a patient with a low pretest likelihood of disease

- A negative test is more likely to be false negative in a patient with a high pretest likelihood of disease

Bayes Theorem
Effect of Disease Prevalence on Predictive Ability
Test with 90% SN and 80% SP



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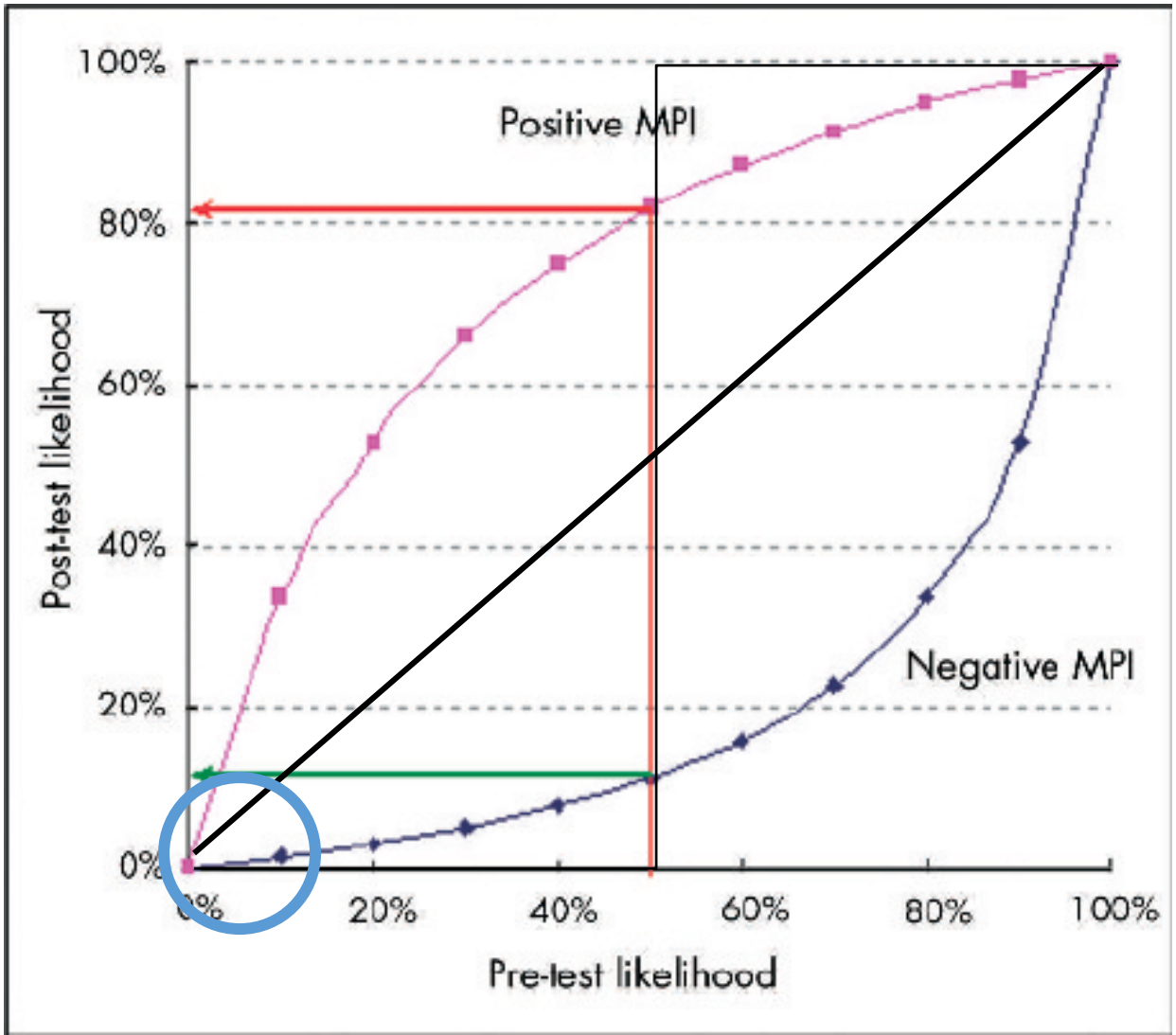
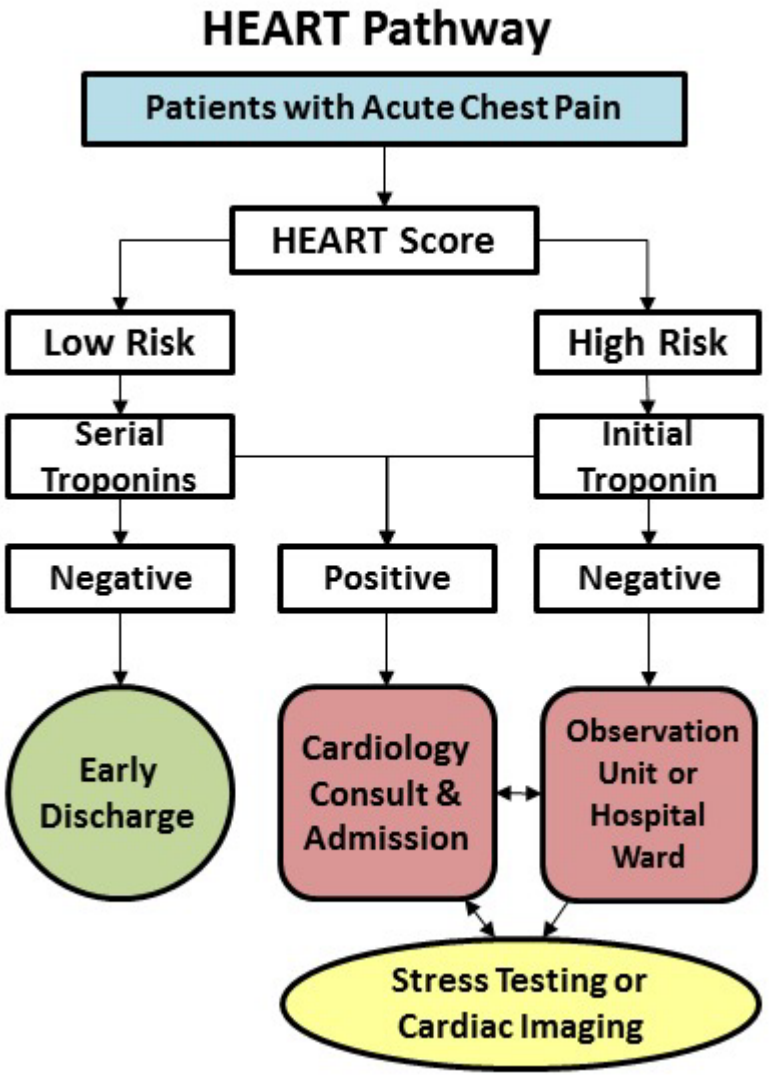


Bayes Theorem

- When the pretest likelihood of disease is <10% or >90%, the test has limited diagnostic ability
- However, it still may still have prognostic value

History
EKG
Age
Risk factors
Troponin

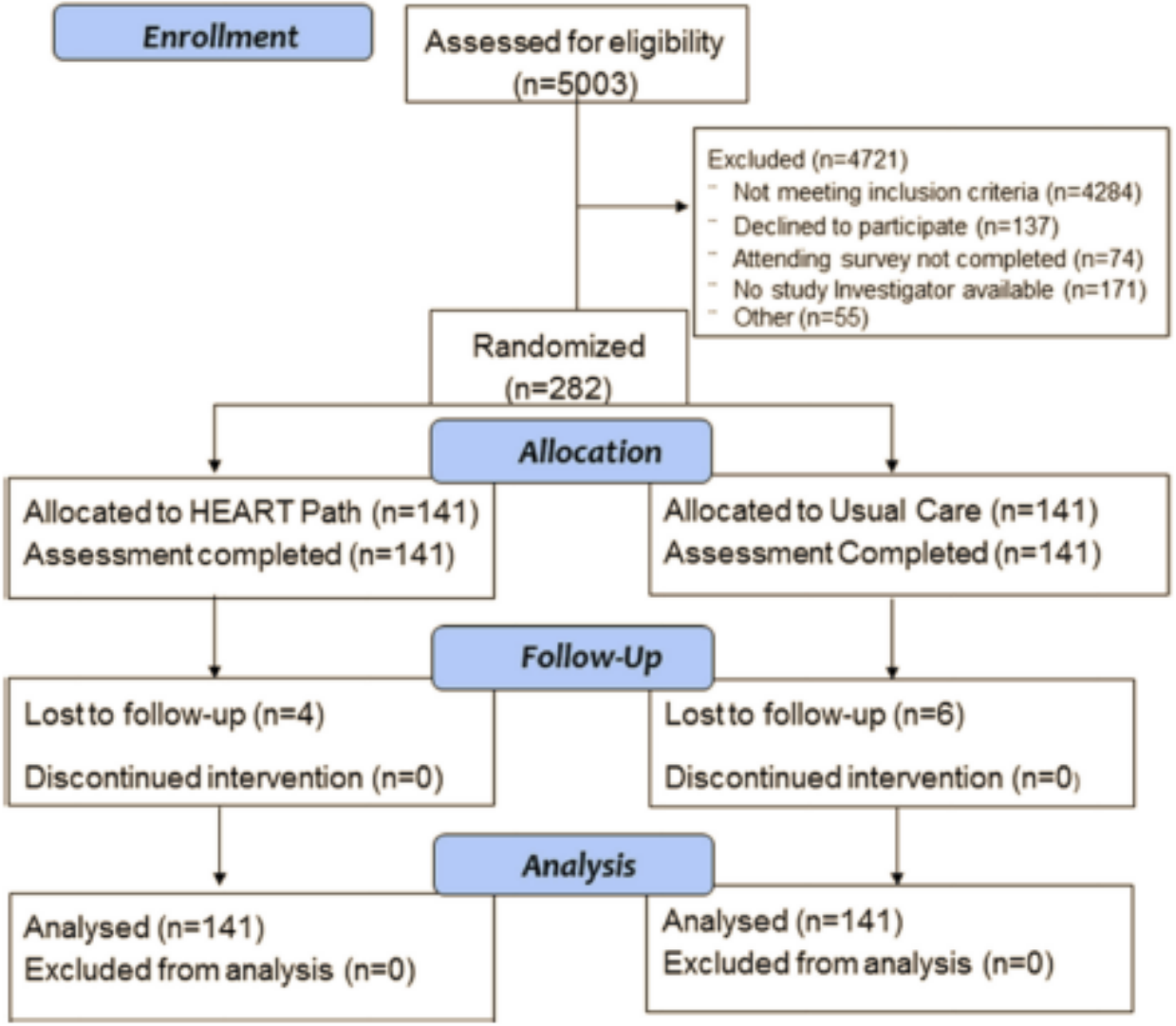


Low score ≤3 = low risk

High score ≥4 = high risk

Mahler SA, et al. *Crit Pathw Cardiol.* 2011;10(3):128-133.
Backus BE, et al. *Int J Cardiol.* 2013;168(3):2153-2158.
Mahler SA, et al. Circ Cardiovasc Qual Outcomes 2015;8:195-203.

RCT of HEART Pathway vs Usual Care

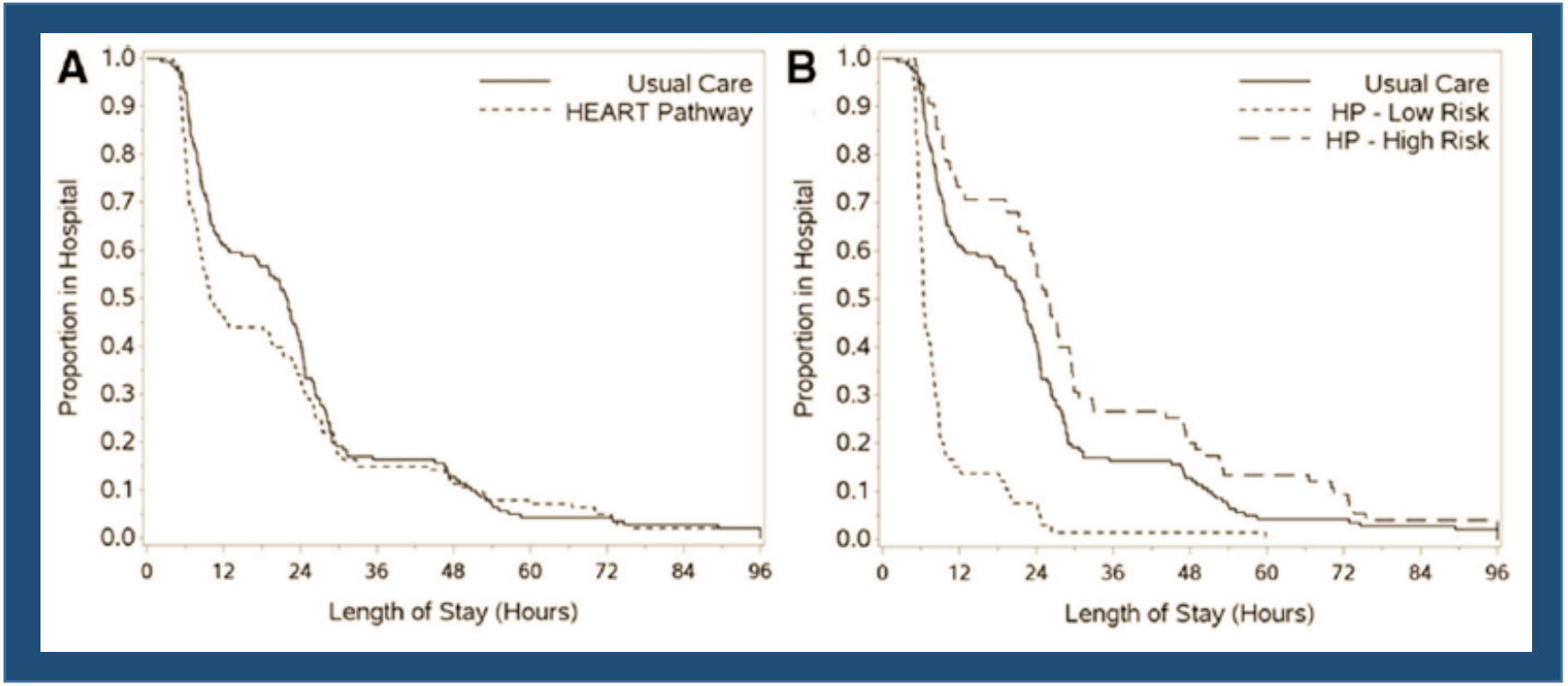


Mahler SA, et al. *Crit Pathw Cardiol.* 2011;10(3):128-133.
Mahler SA, et al. Circ Cardiovasc Qual Outcomes 2015;8:195-203.

RCT of HEART Pathway vs. Usual Care
Results

Objective testing	-12.1% (68.8% vs. 56.7%)
LOS	-12 hrs (9.9 vs. 21.9)
Early DC	+21.3% (39.7% vs. 18.4%)

No increase 30-day MACE in early DC group (6% overall)



ACC/AHA Guidelines on Stress Testing in Patients with Possible ACS

Class IIa (*Level of Evidence B*)

It is reasonable for patients with possible ACS who have normal serial ECGs and cardiac troponins to have a treadmill ECG*, stress myocardial perfusion imaging of stress echocardiography before discharge or within 72 hours after discharge.

*Level of evidence A

Amsterdam EA, et al. *J Am Coll Cardiol.*2014;64(24):e139-228.

Appropriate Use of Stress Modalities

Table 1.1. Symptomatic

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 MJ, et al. *J Am Coll Cardiol.*2014;63:380-406.

	Appropriate	Inappropriate/rarely appropriate
Stress echo	53%	28.4% (8-44% symptomatic)
Stress MPI	72%	15.7% (5-52% symptomatic)

Ladapo JA, et al. *PloS One.* 2016;11(8):e0161153.

Exercise Treadmill Testing
Bruce Protocol
NOT YOUR REGULAR GYM WORKOUT!

- Up to seven 3 minute stages
- Each stage increases in speed and grade
  - Initial: 1.7 mph and 10% grade
  - Maximum: 6.6 mph and 22% grade
- Each minute exercised is approx 1 MET
- If not able to go up 2 flights of steps without stopping, unlikely to be able to adequately perform an ETT

What Do I Learn from an Exercise Stress Test?

- Allows assessment of functional capacity in individuals who are able to exercise
- High negative predictive value of the exercise ECG for obstructive CAD (major epicardial lesions)
- Prognostic and diagnostic information (Duke treadmill score)
  - DTS=Exercise time (min) – (5 x ST deviation) – (4 x Angina Score Index*)
    - Range -25 to +15
    - Low risk (≥ +5) 3% 5-year mortality 60% no sig CAD
    - Intermediate risk (+4 to -10) 10% 5-year mortality
    - High risk (≤ -11) 35% 5-year mortality 74% 3V/LM CAD

*0=no angina; 1=nonlimiting angina; 2=exercise-limiting angina

Shaw LJ, et al. Circulation 1998;98:1622-1630.

What Do I Learn from an Exercise Stress Test?

Protocol: Treadmill Baseline 20 MET
Drugs: None
Target Heart Rate: 154 Maximum Predicted Heart Rate: 182
Resting ECG: Normal

TYPE	STAGE	TIME	HR	BP	COMMENTS
Baseline			53	105/ 76	
Stress	1	120 sec.	67	110/ 68	
Stress	2	120 sec.	80	120/ 70	
Stress	3	120 sec.	96	120/ 82	
Stress	4	120 sec.	137	142/ 88	PT RUNNING
Stress	5	120 sec.	164	/	
Stress	6	11 sec.	166	/	
Recovery	1	1 min.	127	130/ 60	
Recovery	2	2 min.	105	/	PVC'S IN RECOVERY
Recovery	3	4 min.	83	126/ 60	
Recovery	4	6 min.	86	110/ 60	
Recovery	5	8 min.	90	/	
Recovery	6	10 min.	84	/	

Stress Duration: 10.18 minutes. Max Stress H.R: 166
Target Heart Rate (154) Achieved: Yes
Max. workload of 19.10 METs was achieved during exercise.
BP Response: Normal resting BP - appropriate response

What Do I Learn from an Exercise Stress Test?

- Inability to achieve 85% of age-predicted maximum HR
  - Roughly 220-age
  - Do not stop ETT solely for achievement of 85% of age-predicted HR; continued to point of volitional fatigue, unless significant ischemia or sx
- Abnormal heart rate recovery
  - Decrease HR of <12 beats per minute from peak at 1 minute of recovery
- Hypotensive response with exercise
  - Fall in systolic BP >10 mmHg or a peak SBP of <110-120 mmHg
- Significant ST-segment depression
  - ≥1.0 mm of horizontal/downsloping depression 60 msec after J point (diagnostic sensitivity 47% and specificity 78%)
  - ≥2 mm ST-segment depression or ≥1 mm of ST segment elevation in non-q wave lead occurring at <5 METs or persisting >5 min into recovery

Types of Stress Modalities

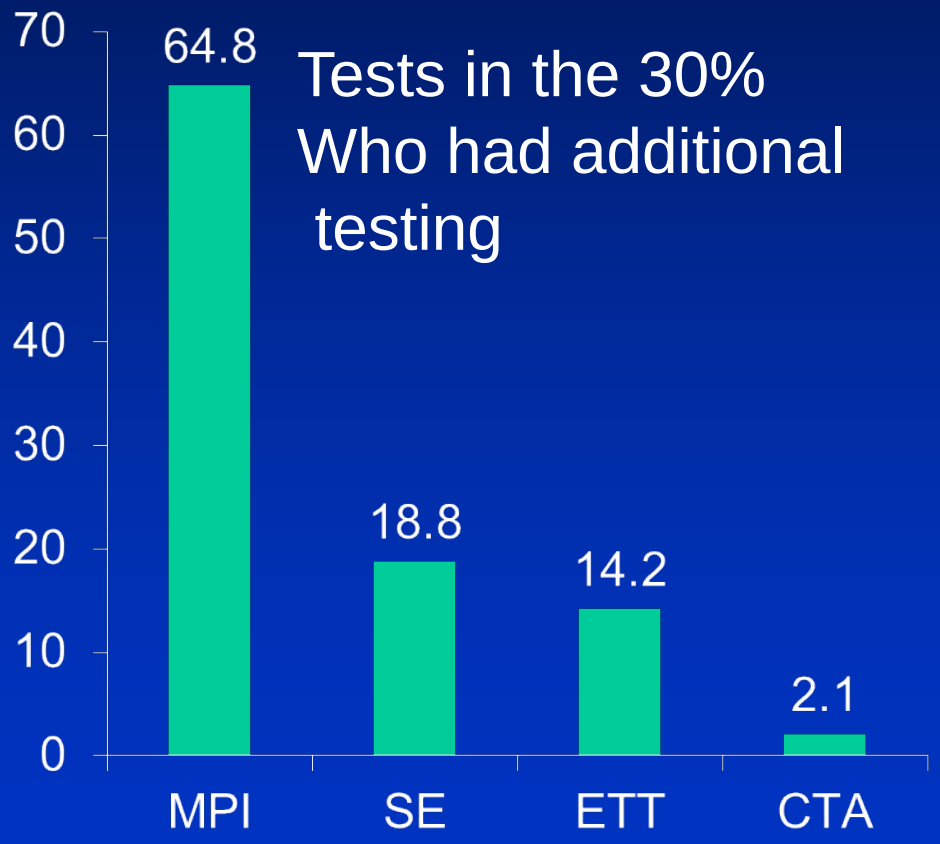
- Exercise
  - Treadmill
  - Bicycle
- Pharmacological
  - Vasodilator
    - Dipyridamole
    - Adenosine
    - Regadenoson
  - Inotrope/Chronotrope
    - Dobutamine

Imaging Techniques

- None (ETT alone)
- Nuclear
  - Thallium
  - Sestamibi
  - Tetrofosmin
- PET—requires rubidium generator
- Echocardiography
  - Transthoracic—with or without Contrast
- CT angiography
- Coronary Calcium scorging
- MRI
  - Stress--Dobutamine or adenosine

How Are ED CP Patients Being Evaluated Currently?

- Insurance claim data from 421,774 ED visits for CP in 2011
- 70% of patients did not undergo further diagnostic testing



Foy AJ et al JAMA Int Med 2015;online

Imaging Techniques

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- PET—requires rubidium generator
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- CT angiography
- Coronary Calcium scorging
- MRI
  - Stress--Dobutamine or adenosine

Different Types of Non-Invasive Evaluation

Absolute and Relative Contraindications to Stress Testing

- ECG not interpretable (LBBB, paced, LVH with strain)
- Moderate or severe stenotic valvular disease (eg, Aortic Stenosis)
- Electrolyte abnormalities (eg, hypokalemia)
- Severe hypertension
- Uncontrolled tachyarrhythmias (AF, PVCs)
- Hypertrophic stenosis or LVOT obstruction

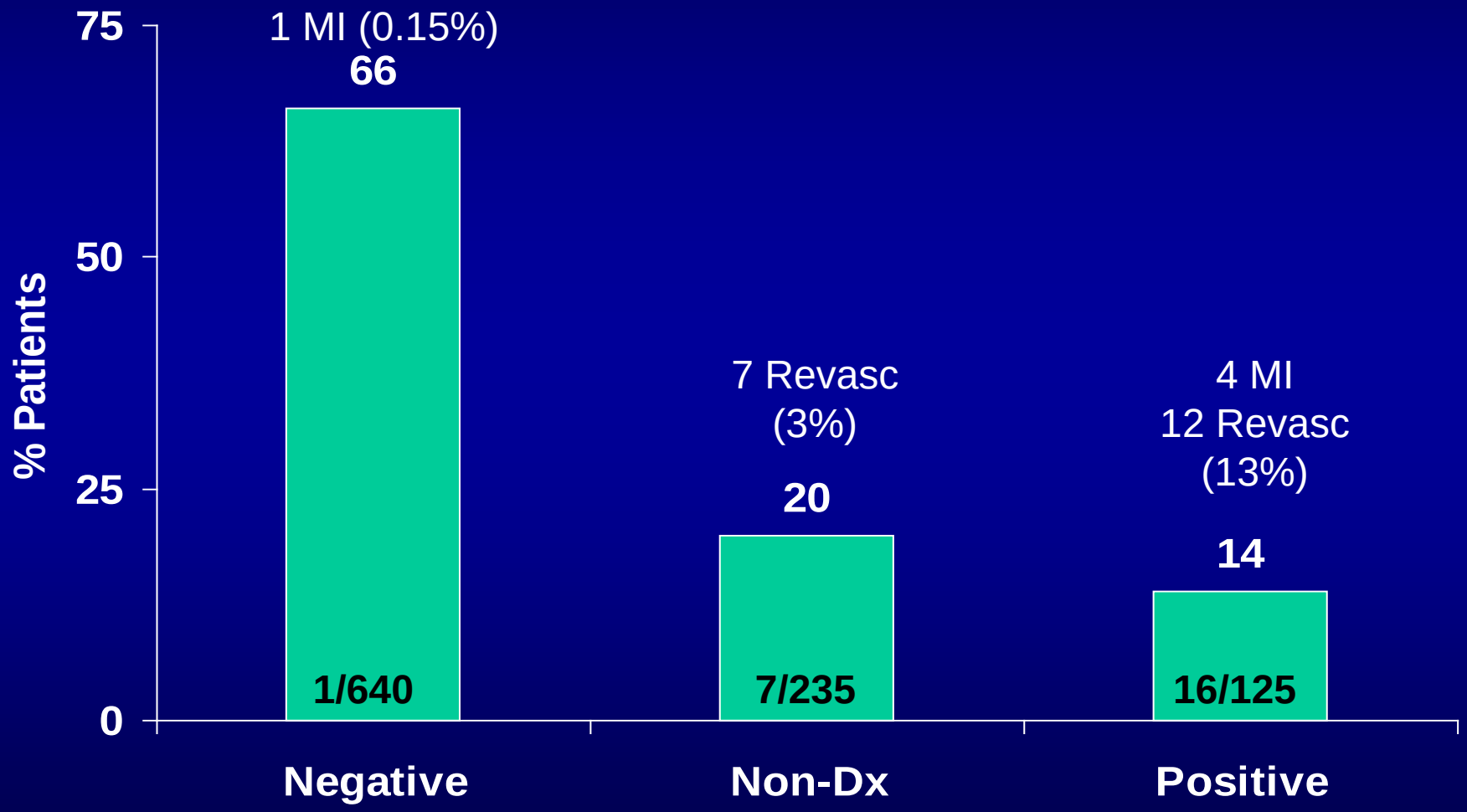
Ex-ECG: Advantage/Disadvantages

- Advantages
  - Reasonable specificity (90%)
  - Lower cost
  - Availability
  - Less than 1 hr
  - Convenience
  - Measure exercise capacity
  - Logistically easier than adding imaging
- Disadvantages
  - Lower sensitivity (50%)
  - No ischemic localization (ST↓)
  - No LV function measure (EF)
  - Not suitable for certain groups
    - Abnormal ECG (LBBB, ST depression)
    - Unable to exercise

When Should You Consider Stress ETT Alone

- Good exercise tolerance
- Normal (or near normal) ECG
- Low pre-test probability of CAD
  - Young age
  - Atypical symptoms

Immediate Exercise Test
UC Davis CPER



Amsterdam et al JACC 2002;40:251

Myocardial Perfusion Imaging

Ischemic Cascade

Stenosis

↓

Hypoperfusion

↓

Diastolic Dysfunction

↓

Systolic Dysfunction

↓

ST Depression

↓

Chest Pain

Types of Stress Protocols

- Sestamibi or tetrofosmin--same day
- Sestamibi or tetrofosmin--two day
- Dual isotope (Thallium rest, technetium stress)

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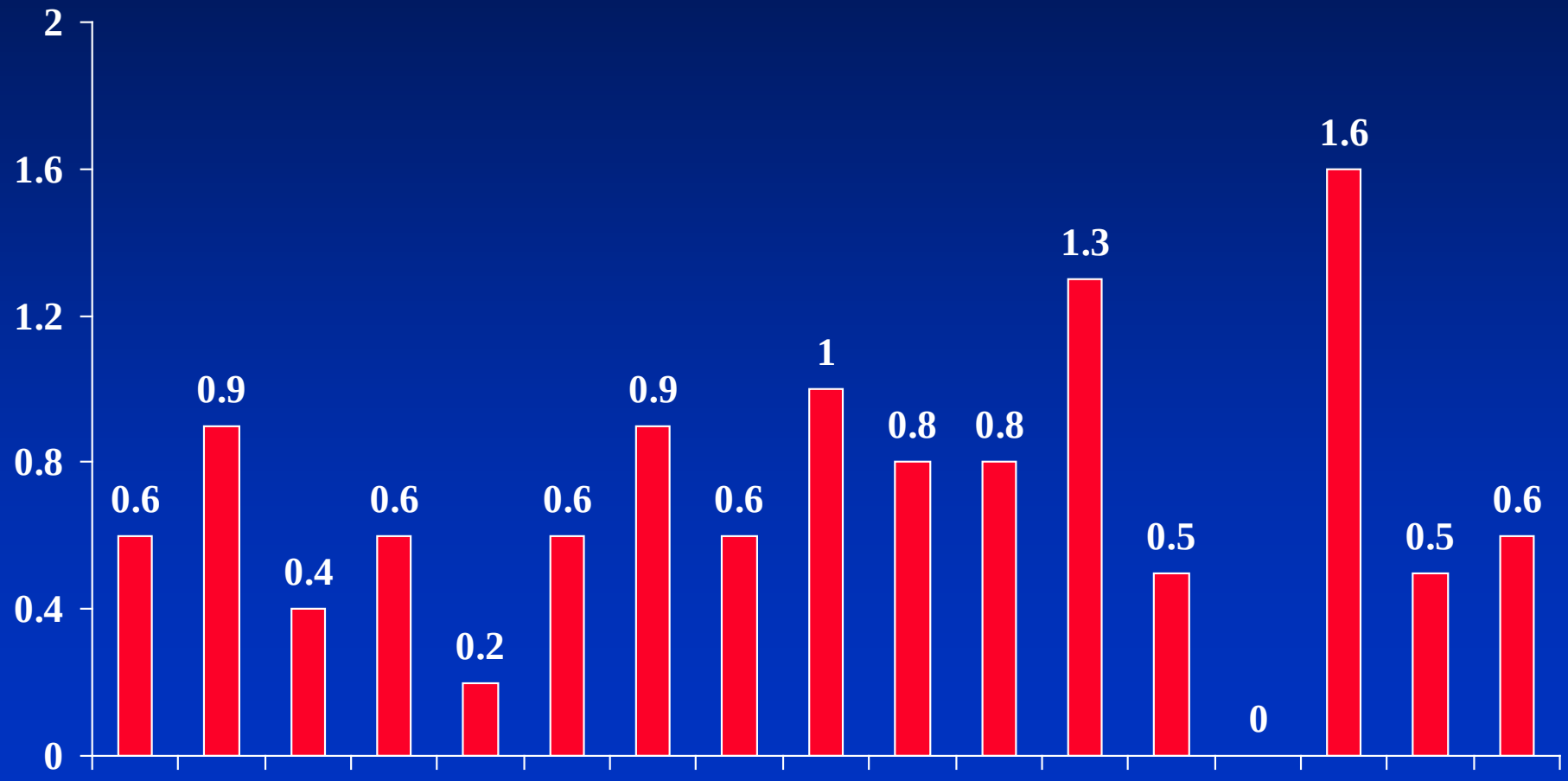
Myocardial Perfusion Imaging
Attenuations Artifacts (False Positive Defects)

- Women
  - anterior, breast
- Men
  - inferior, diaphragmatic
- Obese
  - overall decrease in photon counts secondary to soft tissue attenuation

Indications for Imaging (Echo or Nuclear)

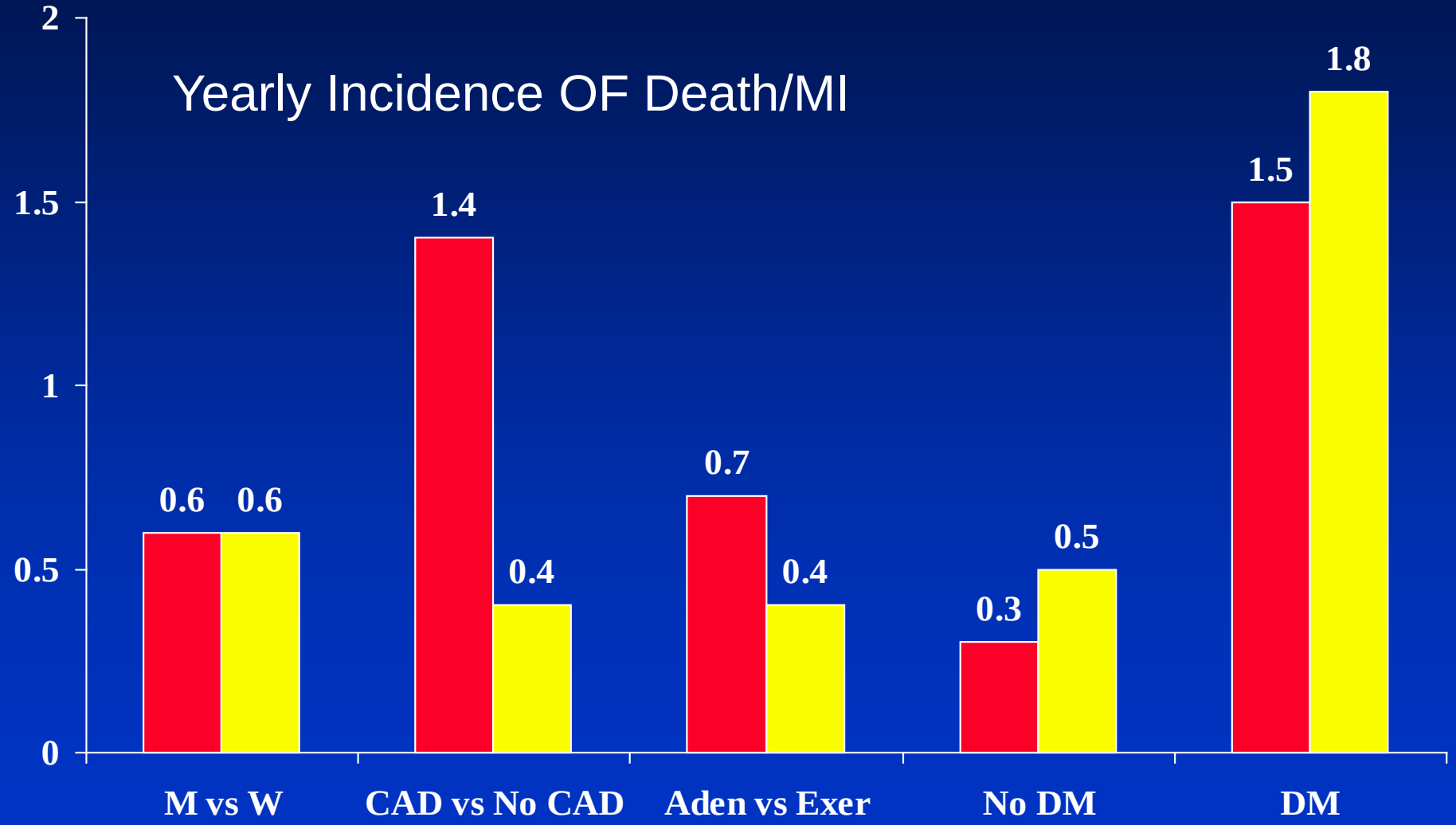
- Unable to exercise
- LBBB
- Paced rhythm
- Patient taking Digoxin
- LVH with ST -segment depression
- Pre-excitation (WPW)

Annual Event Rate Death/MI In patients with Normal Scan
16 Studies, 27,855 Patients



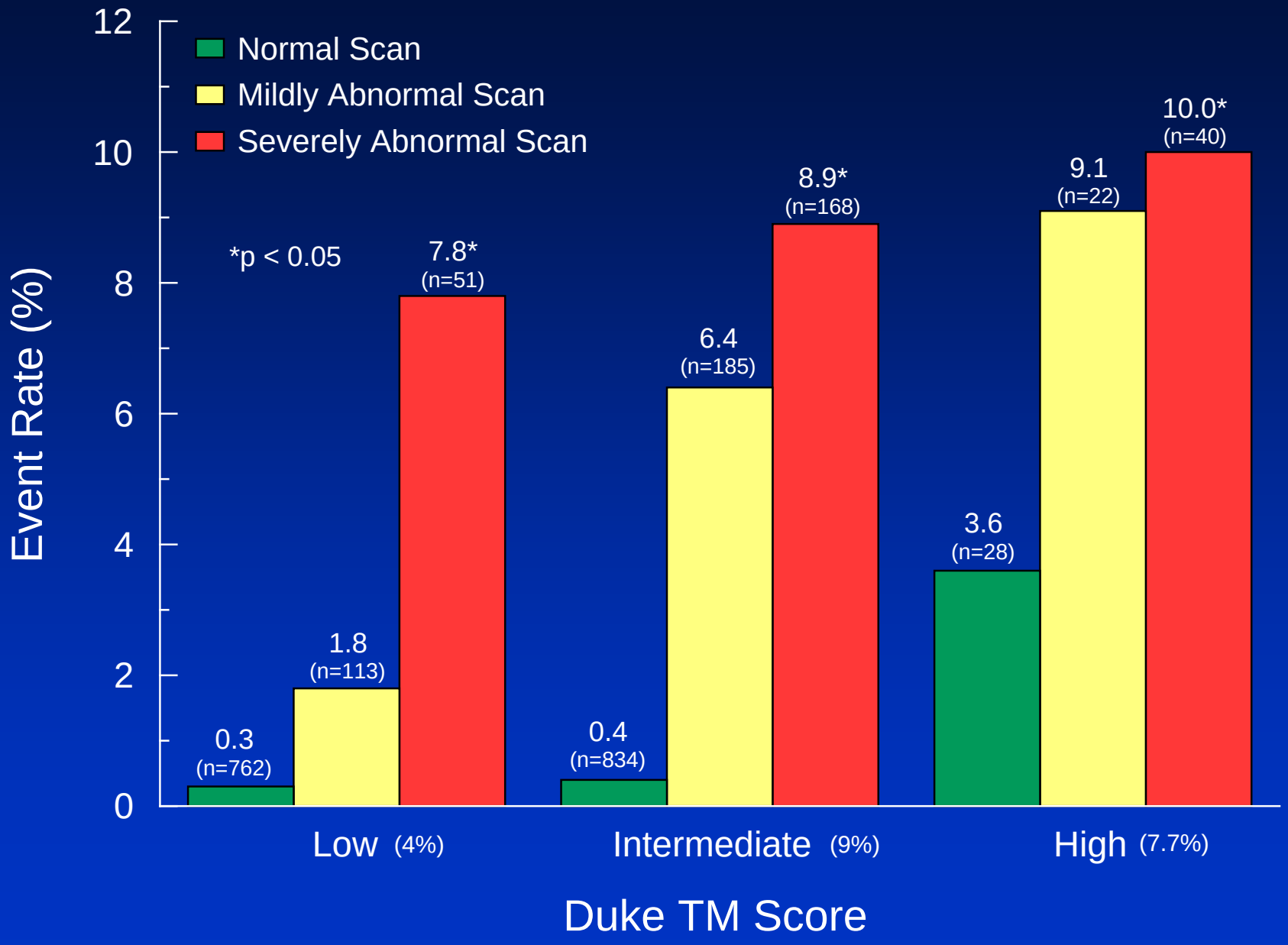
ACC/AHA/ASNC Guidelines for Clinical use of Cardiac Radionuclide Imaging

What is the Warranty Period of A Normal Stress MPI?



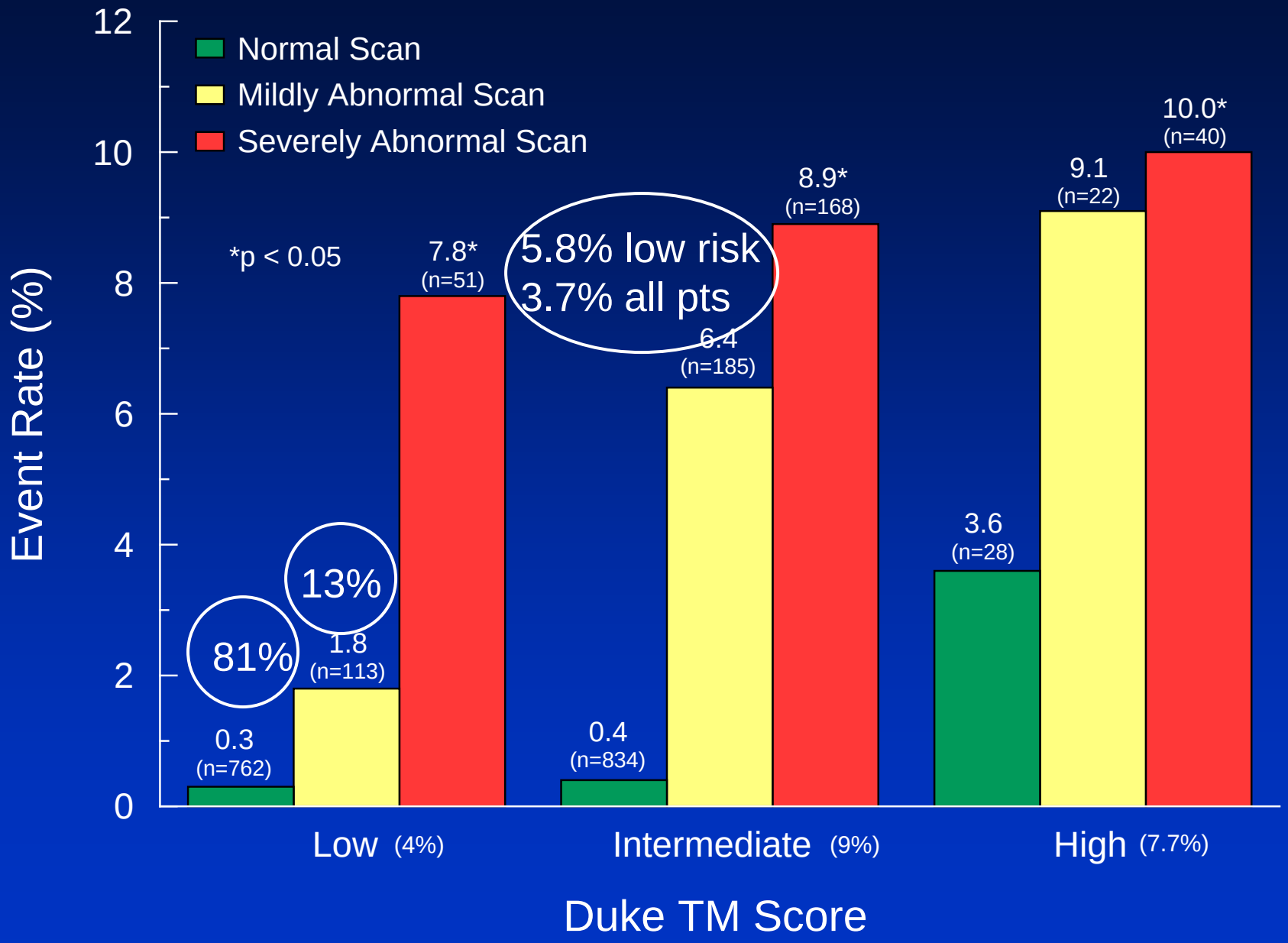
Hachamovitch JACC 2003;41:1329

Incremental Risk Stratification with SPECT MIBI



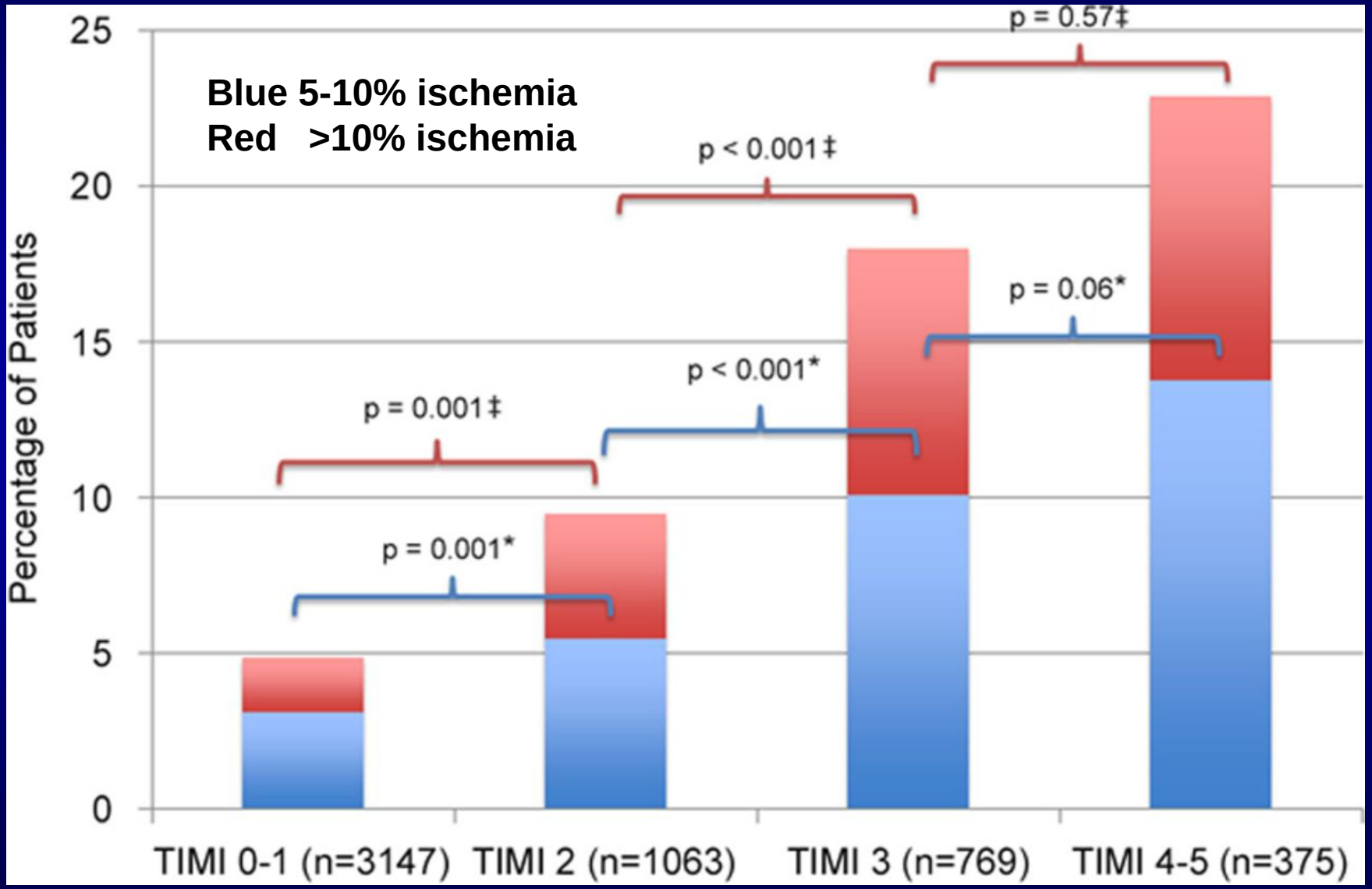
Hachamovitch Circ 1996:93:910

Incremental Risk Stratification with SPECT MIBI



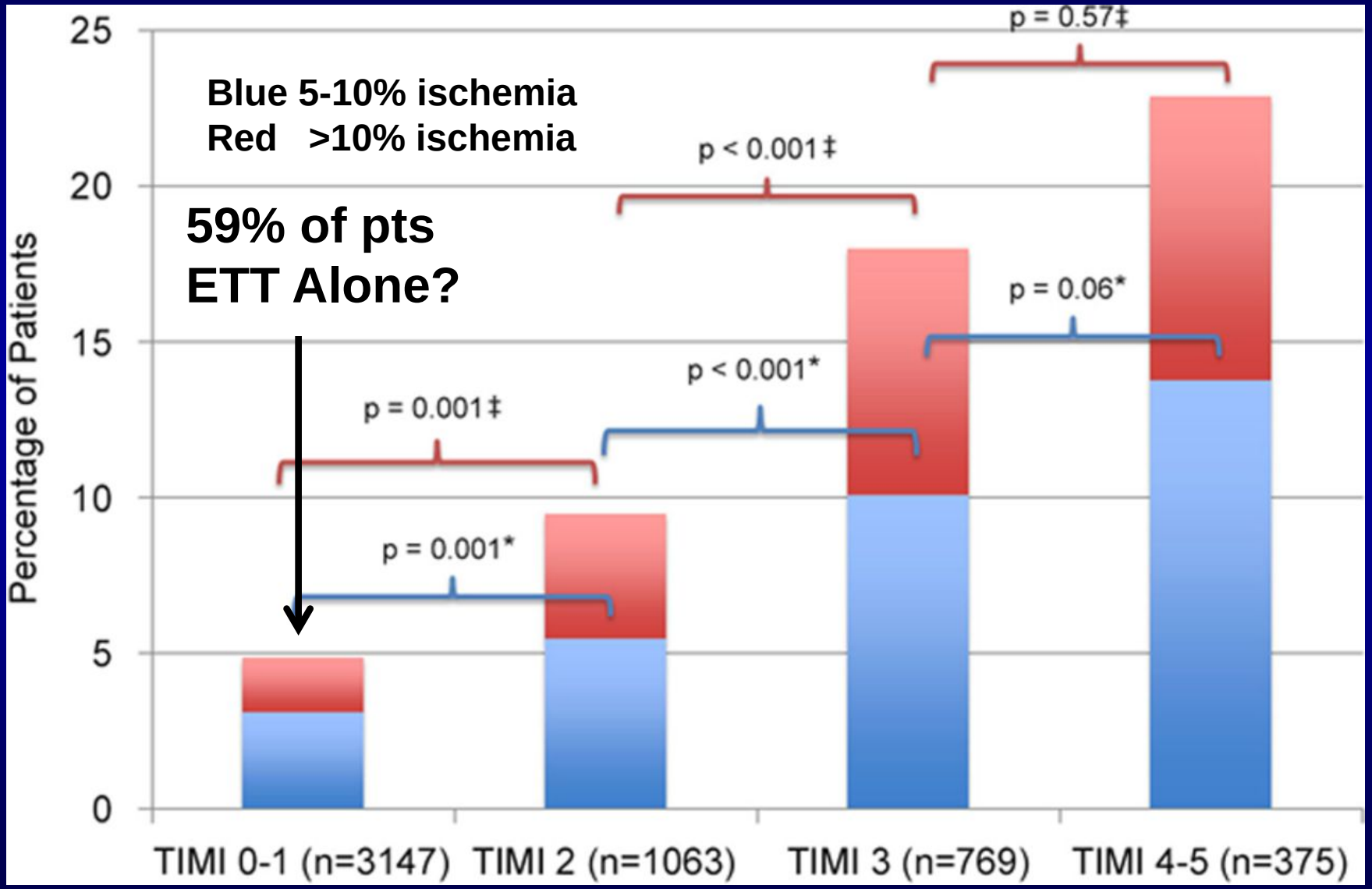
Hachamovitch Circ 1996:93:910

Ischemia Stratified by TIMI Scores



Cremer P C et al. Circ CV Imaging. 2014;7:912-919

Ischemia Stratified by TIMI Scores



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Stress Echocardiography

Stress Echocardiography
Protocols

Stress Echocardiography

- Suitable candidate; suitable window
- Bruce protocol
- Images acquired and recorded at base-line and within 30-60 sec of stress termination

Dobutamine stress echo (DSE)

- Suitable candidate; suitable window
- Dobutamine delivered by continuous IV
  - (up to 40 ug/kg)
  - Atropine added if target heart rate not reached
- Images acquired at base-line and within 30 sec of each infusion stage

Left Ventricular Opacification with Echo Contrast

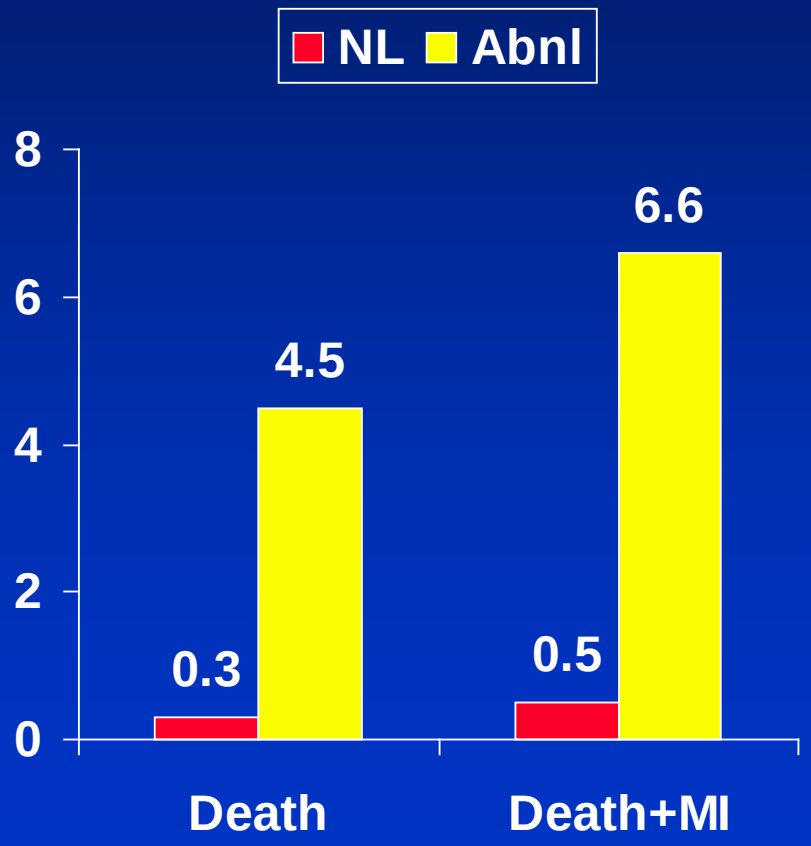
Without contrast

With contrast

Images courtesy of Duke University.

Stress Echo in ED patients

- 839 patients admitted with acute chest pain non-diagnostic ECG, and (-) 12-hour troponin
- 811 (97%) had diagnostic SE results (78% DSE, 22% Ex)
- Event rate lower in NL versus abnormal SE groups
- Abnormal SE (HR, 4.1; P<0.001) and age (HR, 1.8; P<0.001) predicted hard events



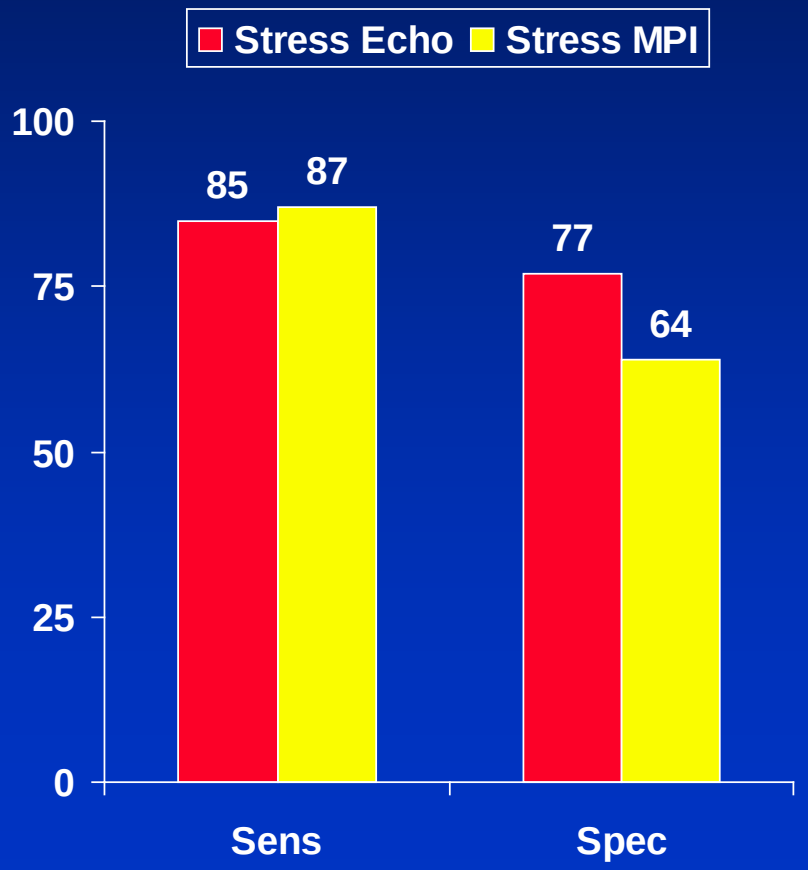
Shah B, Circ CV Imaging 2013;6:202

Stress Echocardiography

- In general, indications for stress echo are the same as stress MPI
- Normal findings identify low risk patients (< 1% events)
- More segments or territories abnormal, the higher the risk
- Patient characteristics more likely to limit study quality and interpretation

Stress Echo vs Stress SPECT Meta-Analysis

- Meta-analysis comparing stress echo and stress SPECT imaging for diagnosing CAD
- 44 studies from Jan 1990 to Oct 1997
  - 24 studies reported stress echo results on 2637 pts
  - 27 studies reported stress SPECT results on 3237 pts
- When adjusted for age and CAD, stress echo higher discriminatory power (1.18; 95% CI, 0.71-1.65)(although not significant)



Fleischmann KE et al: JAMA 280, 913, 1998

Stress Echo and MPI: Comparison

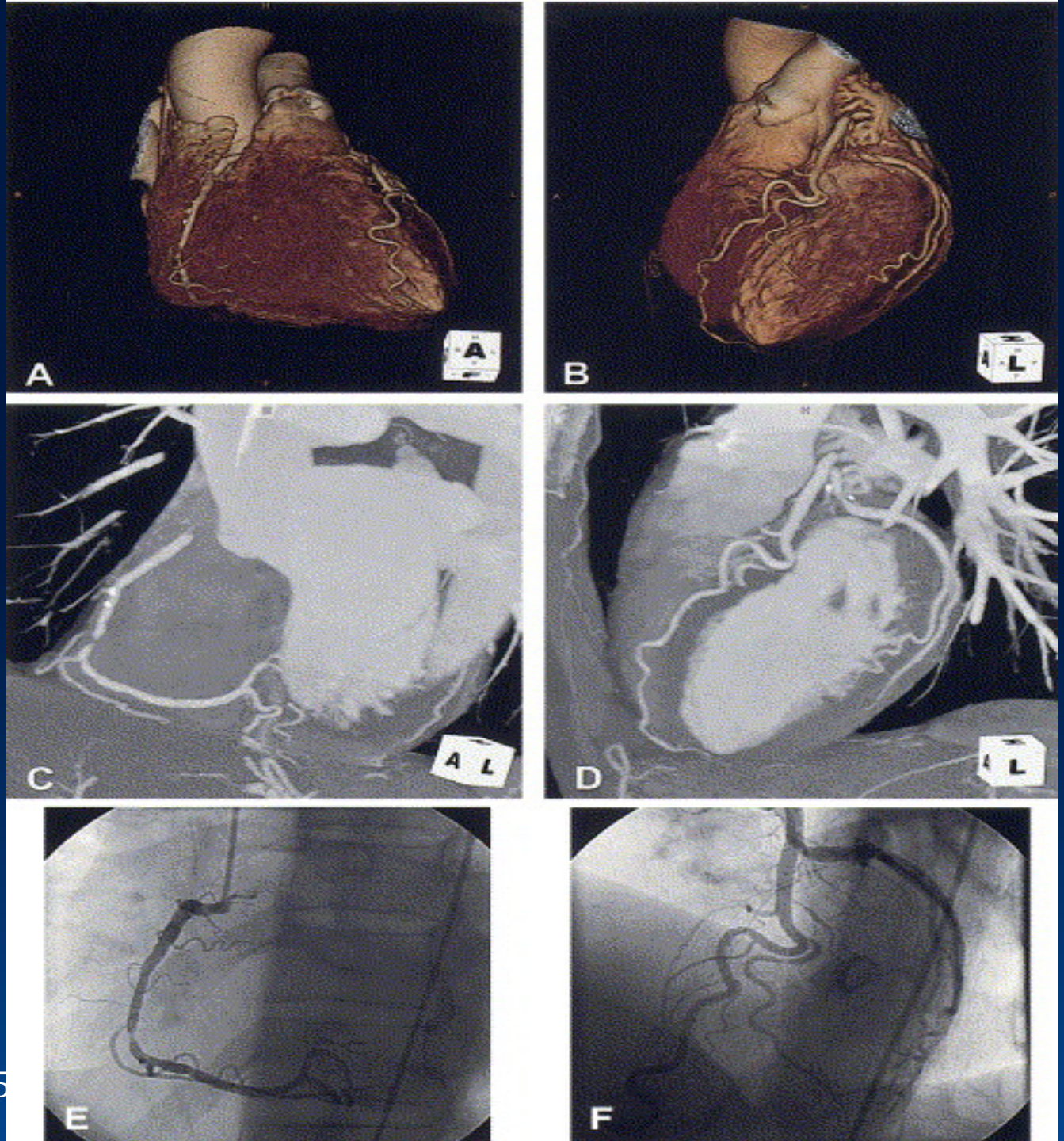
Stress Echo	MPI
Less expensive	More expensive
No radiation	Radiation
Shorter test time	Time consuming
Function	Perfusion/Function
Qualitative	Quantitative
Variable windows	Tissue attenuation

How to Choose Between the Two

- Expertise of the institution performing the test
- Convenience
- Cost
- Patient factors limiting study interpretability

CT Angiography

Time Magazine, Sept 2005



Raff JACC 2005

Advantages of CTA

- Accelerate diagnostic ED CP evaluation
- Improved accuracy with each new generation]
  - Sensitivity 99%, Specificity 89%
  - Standard is 64 slices; newer generation up to 512
- Identify pts with non-obstructive disease
  - Candidates for aggressive secondary prevention measures
  - Motivate patients to adopt life-style changes
- Identify other causes of chest pain
- Accelerate the ED diagnostic evaluation

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Randomized CTA Trials

Study	CT-STAT		ACRIN		ROMICAT II	
Year	2011		2012		2012	
Population	699		1370		985	
	TIMI RS 0-4		TIMI RS 0-2		Low-inter Risk	
MI rate	0.9%		1%		2.5%	
Control group	MPI		usual care		usual care	
	CTA	Stand	CTA	Stand	CTA	Stand
ACS dx	1.1%	2.4%	1%	1%	9%	6%
Cath Rate	8.0%	7.4%	5%	4%	12%	8%
Revasc	3.6%	2.4%	2.7%	1.3%	6.4%	4.2%
Time to dx/LOS	2.9	6.3	18.0	24.8	23.2	30.2
Cost	2137	3458			4028	3874

Comparing CTA vs Functional Imaging

- Upside
  - Faster ED throughput
- Downside:
  - Significantly more exclusions
  - Increased costs
  - Higher rates of cath, revascularization
  - No difference in mortality

Jorgensen ME et al. JACC 2017;69;1761;ShreibatiJB et al JAMA 2011;306;2138
Williams MC et al JACC 2016;67;1759; Bittencourt MS, et al Circ Imaging 2016;9;e004419

NSTE-ACS Guidelines 2014

- ETT alone remains the preferred testing:
- In the absence baseline changes
  - Able to adequately exercise
- Add imaging if there are baseline ECG abnormalities precluding interpretation
- Pharmacologic stress testing with imaging if cannot adequately exercise

2015 Appropriate CV Imaging in the ED Suspected STE-ACS; Observational Pathway After Serial Troponin Assessment

Indication	ETT	Echo	SPECT	CMR	CTA	Cath
Dx (+) for ACS	M	M	M	M	M	A
ECG/Tn (-) for ACS	A	A	A	A	A	R
ECG/Tn Equiv for ACS	M	A	A	A	A	M

Rybick FJ et al JACC 2016;67;853

What Do the Guidelines Say About CTA?

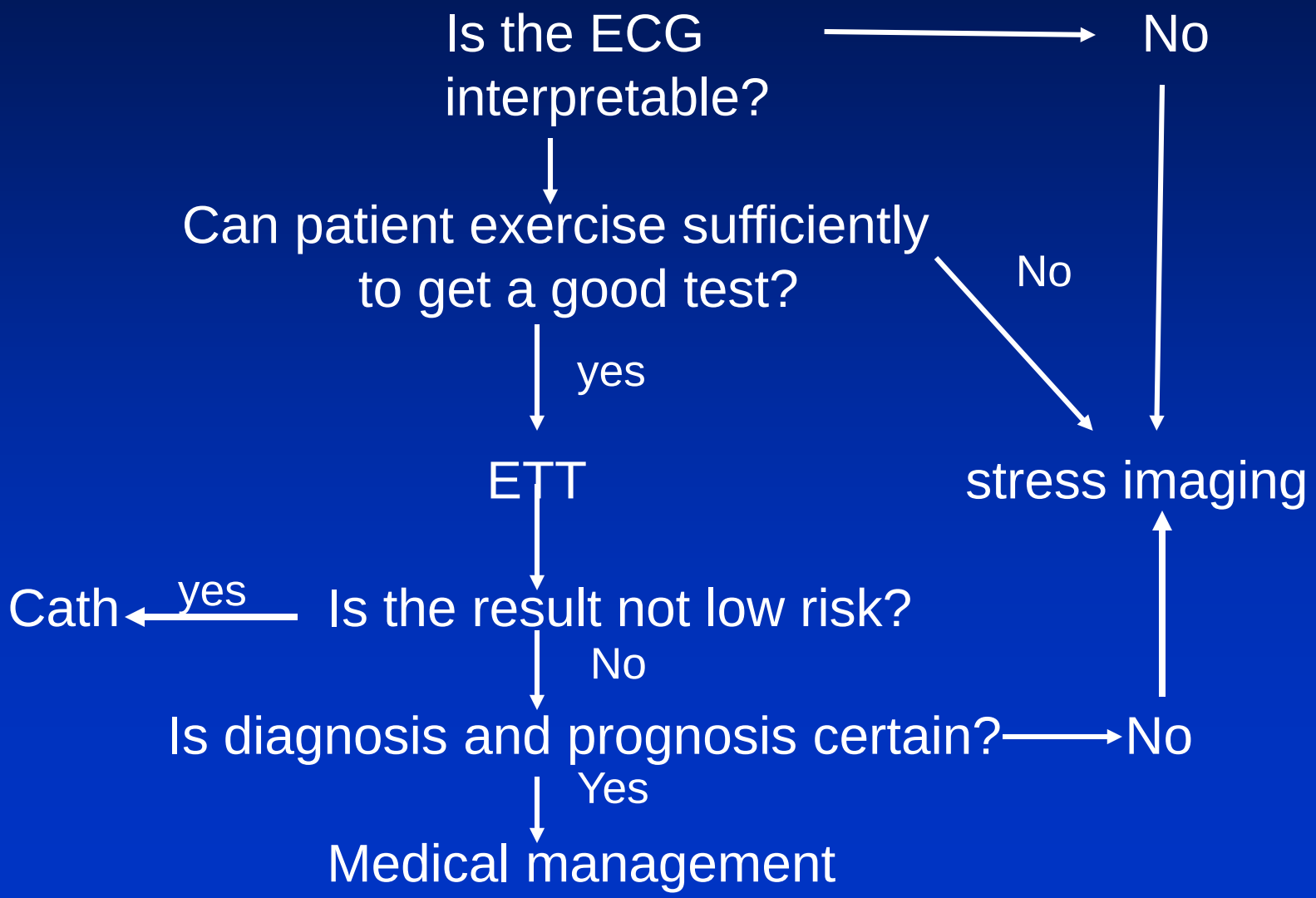
- Patients with an intermediate pretest probability of IHD who have:
  - Continued symptoms with prior normal test findings
  - Inconclusive results from prior exercise or pharmacological stress testing
  - Are unable to undergo stress MPI or echocardiography
- Appropriateness Guidelines:
  - Similar to those for Stress MPI and Echo
  - Intermediate pre-test probability of CAD, unable to exercise, or ECG not interpretable
  - Discordant stress ECG and imaging results
  - Caveats—known CAD, severe coronary calcium

Circulation 2008;118;586; JACC 2006;48:1475

Variables That Go Into the Decision Making Process

- Baseline ECG
- Patient characteristics
  - Ability to exercise
  - Known coronary disease
- Availability
- Local expertise
- Cost/reimbursement

Stress Pathway



Stress Testing--High Risk Predictors

- Duration of exercise <6 METS (Stage 2)
- ST-depression--High risk
  - ≥ 2 mm
  - Early onset
  - involving ≥ 5 leads
  - persistence ≥5 min into recovery
- Ischemic ST-elevation
- BP response:
  - failure to obtain SBP ≥120 mmHg
  - fall in SBP ≥ 10 mmHg
  - fall in SBP below rest values
- Sustained or symptomatic VT

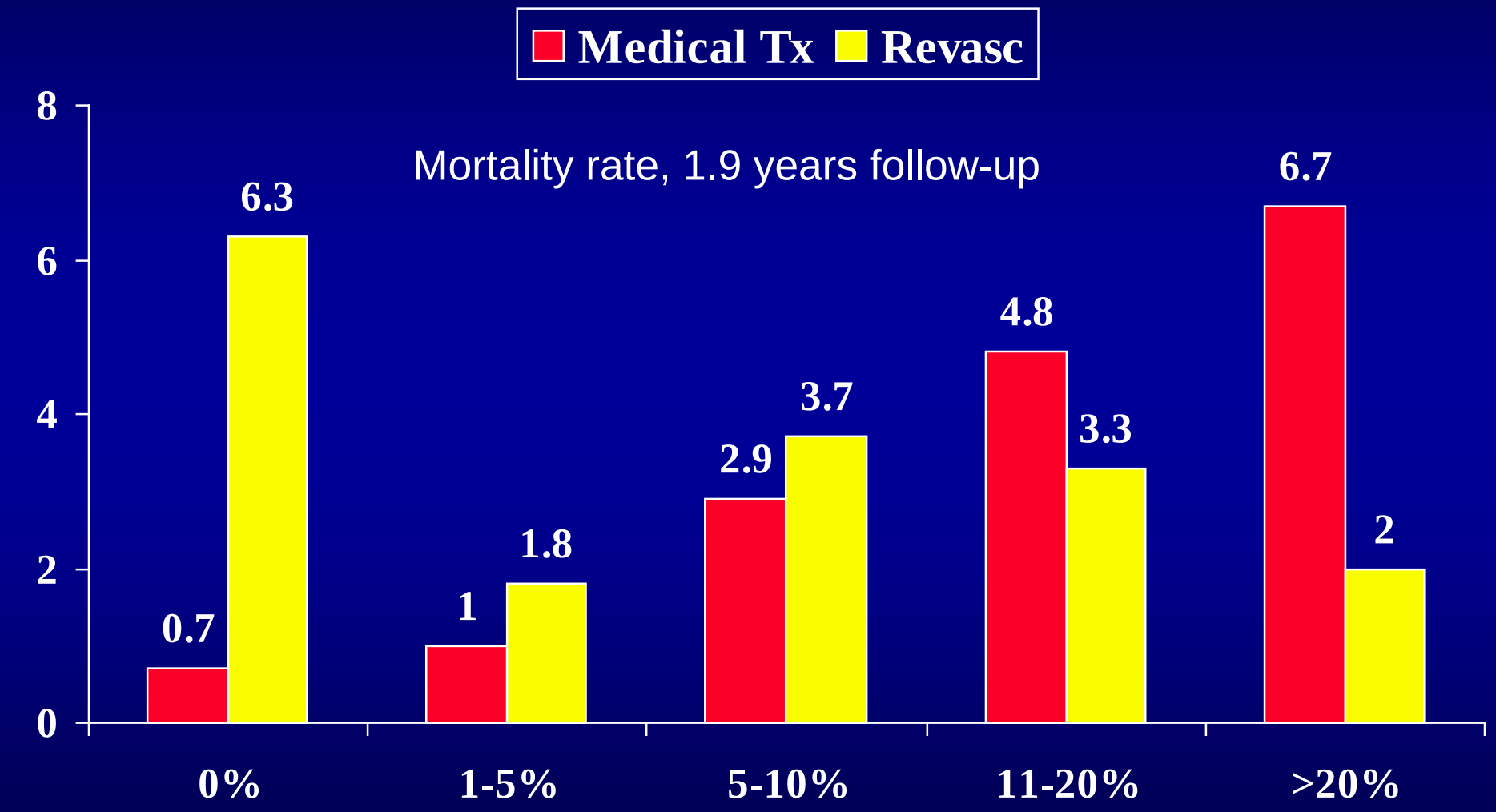
Clues that the ETT is a False Positive

- Rapid resolution of ischemic ST↓
- Absence of chest pain on Ex Test
- High functional capacity (>10 METS)
- High double product (>25,000)

Outcomes with Normal Stress MPI and (+) ETT

Study	# Pts	Annual Cardiac Death or MI
Fagan	70	0.7 %
Schalet (2 mm)	154	0.0 %
Krishnan (2 mm)	32	0.0 %

Revascularization vs Medical Treatment



Hachamovitch Circulation 2003;107;2899

Risk Stratification
High Risk (>3% annual mortality)
(Probably should be referred for cathed)

- Severe resting LV dysfunction (EF<35%0
- High risk treadmill score
- Stress induced large perfusion defect (especially anterior)
- Stress induced multiple defects of moderate size
- Large fixed perfusion defect with LV dilation or increased lung uptake

Risk Stratification
Low (<1%) and Intermediate (1-3% annual mortality)

- Intermediate (medical management)
  - Mild/moderate LV dysfunction (EF35-49%)
  - Intermediate risk treadmill score
  - Stress induced moderate perfusion defect without LV dysfunction or increased lung uptake

- Low (not likely to be cardiac)
  - Low risk treadmill score
  - Normal or small perfusion defect at rest or with exercise (probably not low risk if has EF < 35%)

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Take Home Points . . .

- Stress testing and imaging should be used selectively based on - disease probability, patient characteristics, test characteristics, test availability, and cost.

- If you will be ordering these tests - work with your Cardiology and Radiology colleagues to develop an evidence based algorithm to order the right test on the right patient at the right time.

- Know the strengths, limitations, and outcomes of the tests that you will be working with.

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Questions? Contact the E-QUAL team at equal@acep.org

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