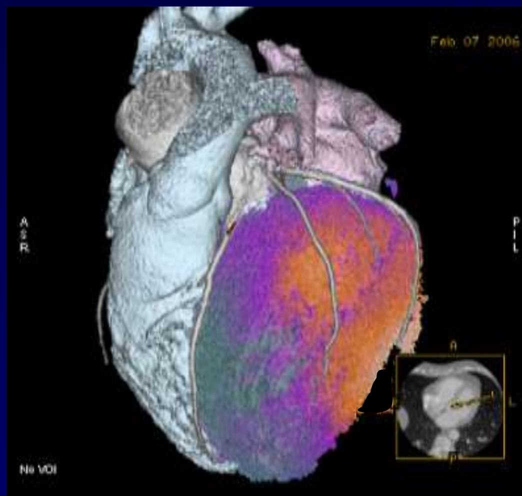
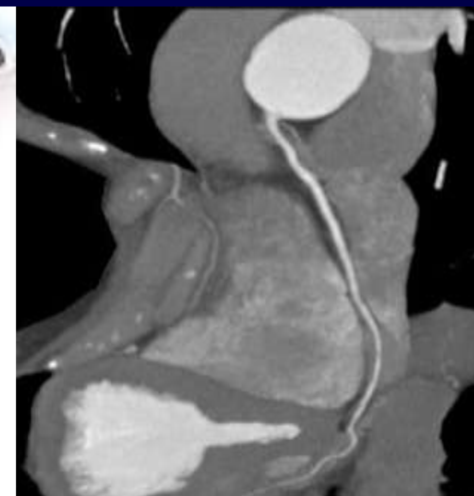
Prognosis of CAD



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Zurich

Clinical validity of diagnostic procedures

Cornerstones

- Diagnosis
- Prognosis
- Outcome

CORE Elements of a Clinical Trial

- Enroll representative inception cohort
- Compare interventions or strategies
- Follow over time for "big 4" outcomes
  - Length of life (deaths)
  - Quality of life (morbidity)
  - Discrete negative events (harms)
  - Costs

ROBUST trial
Detection of CAD by SPECT

	Total		Thallium		MIBI		Tetrofosmin		*P*
Studies	2,523		903		760		860		0.04
Age (years)	62	SD 12.9	63	SD 12.8	62	SD 12.9	61	SD 12.7	ns
Male (%)	1,460	58%	539	60%	436	57%	485	56%	ns
Weight (kg)	76	SD 16.0	76	SD 15.3	76	SD 16.5	76	SD 15.9	ns
BMI (kg/m^2)	27	SD 5.3	27	SD 5.0	27	SD 5.7	27	SD 5.2	ns
Risk factors (mean *n*)[a]	1.8	SD 1.2	1.8	SD 1.2	1.8	SD 1.2	1.8	SD 1.2	ns
Diagnosis (%)[b]	1,451	58%	485	54%	465	61%	501	58%	ns
Infarction (%)	813	32%	329	36%	227	30%	257	30%	0.003
CABG (%)	383	15%	151	17%	111	15%	121	14%	ns
PTCA (%)	277	11%	118	13%	67	9%	92	11%	0.02
Heart failure (%)	168	7%	63	7%	52	7%	53	6%	ns
Stress type									
Adenosine + exercise	2,036	81%	723	80%	619	81%	694	81%	ns
Adenosine	211	8%	84	9%	63	8%	64	7%	ns
Dobutamine	259	10%	92	10%	74	10%	93	11%	ns
Exercise	13	1%	3	0%	3	0%	7	1%	ns
Stress dose (MBq)			78	SD 5	261	SD 63	253	SD 42	ns*
Rest dose (MBq)					744	SD 45	741	SD 39	ns*
Re-injection number (%)			159	18%					
Stress image time (min)			10	SD 6	50	SD 39	40	SD 16	<0.0001*
Rest image time (min)			197	SD 30	49	SD 21	40	SD 17	<0.0001*

Eur J Nucl Med (2002) 29:1608–1616

ROBUST trial
Detection of CAD by SPECT

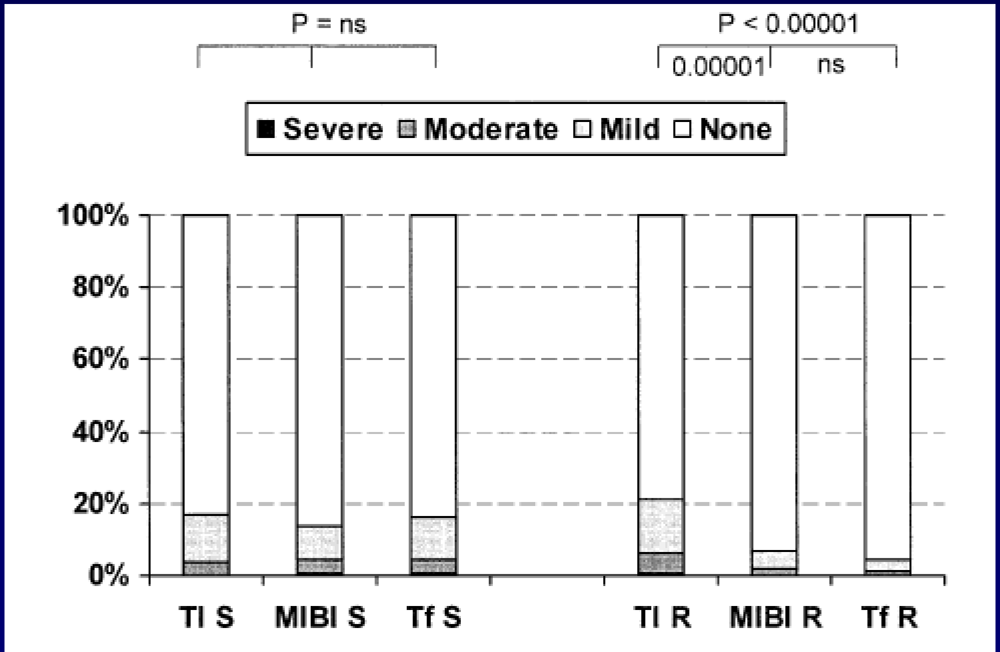
	Overall		Thallium		MIBI		Tetrofosmin	
Sensitivity	86/94	91%	25/27	93%	35/37	95%	26/30	87%
Specificity	33/43	87%	13/15	87%	9/10	90%	16/18	89%

The differences between tracers are not statistically significant

Eur J Nucl Med (2002) 29:1608–1616

ROBUST trial
Detection of CAD by SPECT

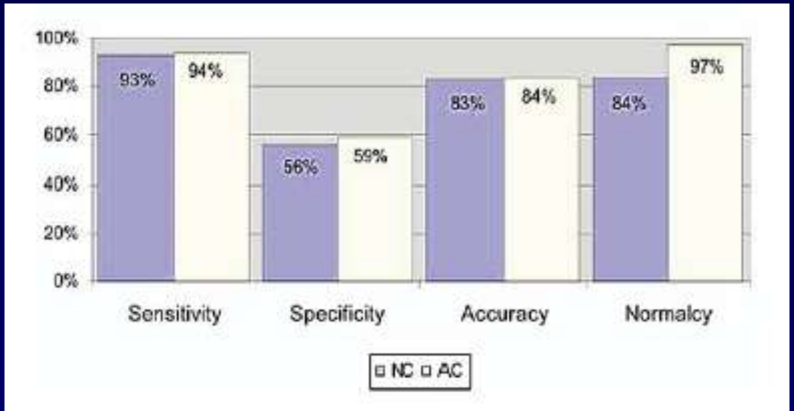
Drawbacks: low count artefacts

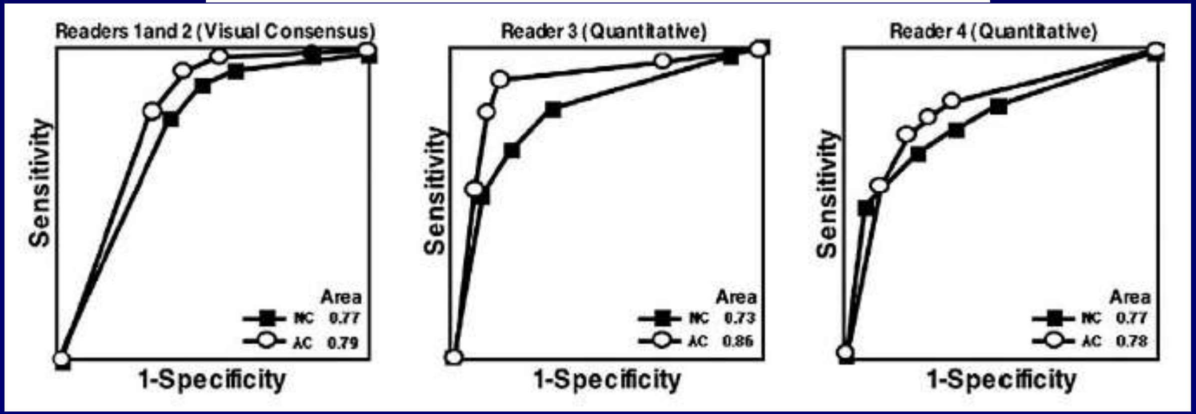


Eur J Nucl Med (2002) 29:1608–1616

Multicenter X-ray attenuation correction trial
Detection of CAD by SPECT

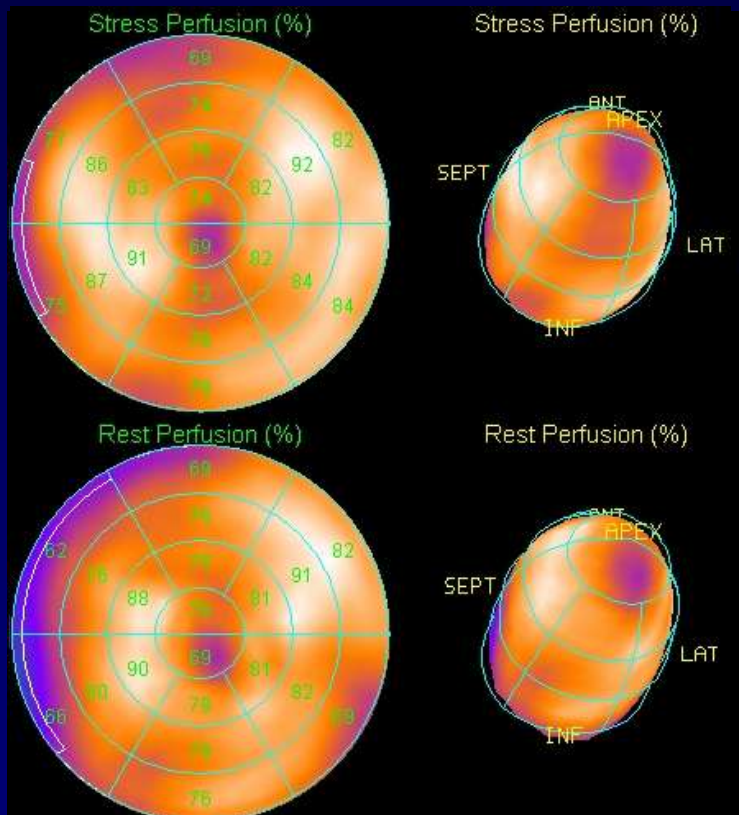
Possible solution: X-ray attenuation correction



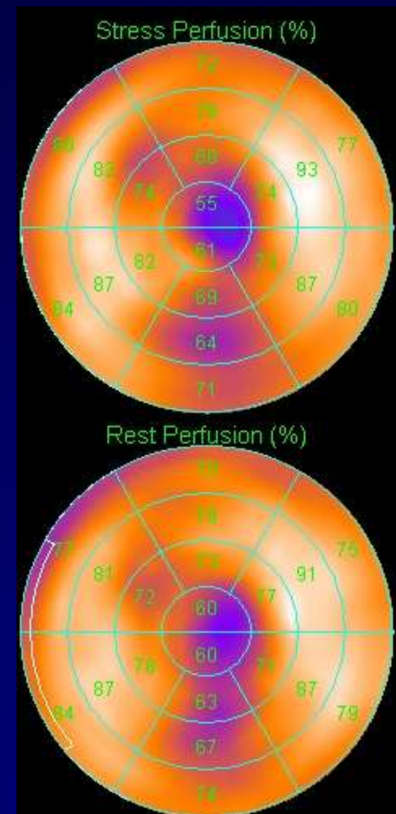


J Nucl Cardiol 2005;12:676-86.

SPECT MPI:
(CT) AC recommended in high BMI patients



BMI 31



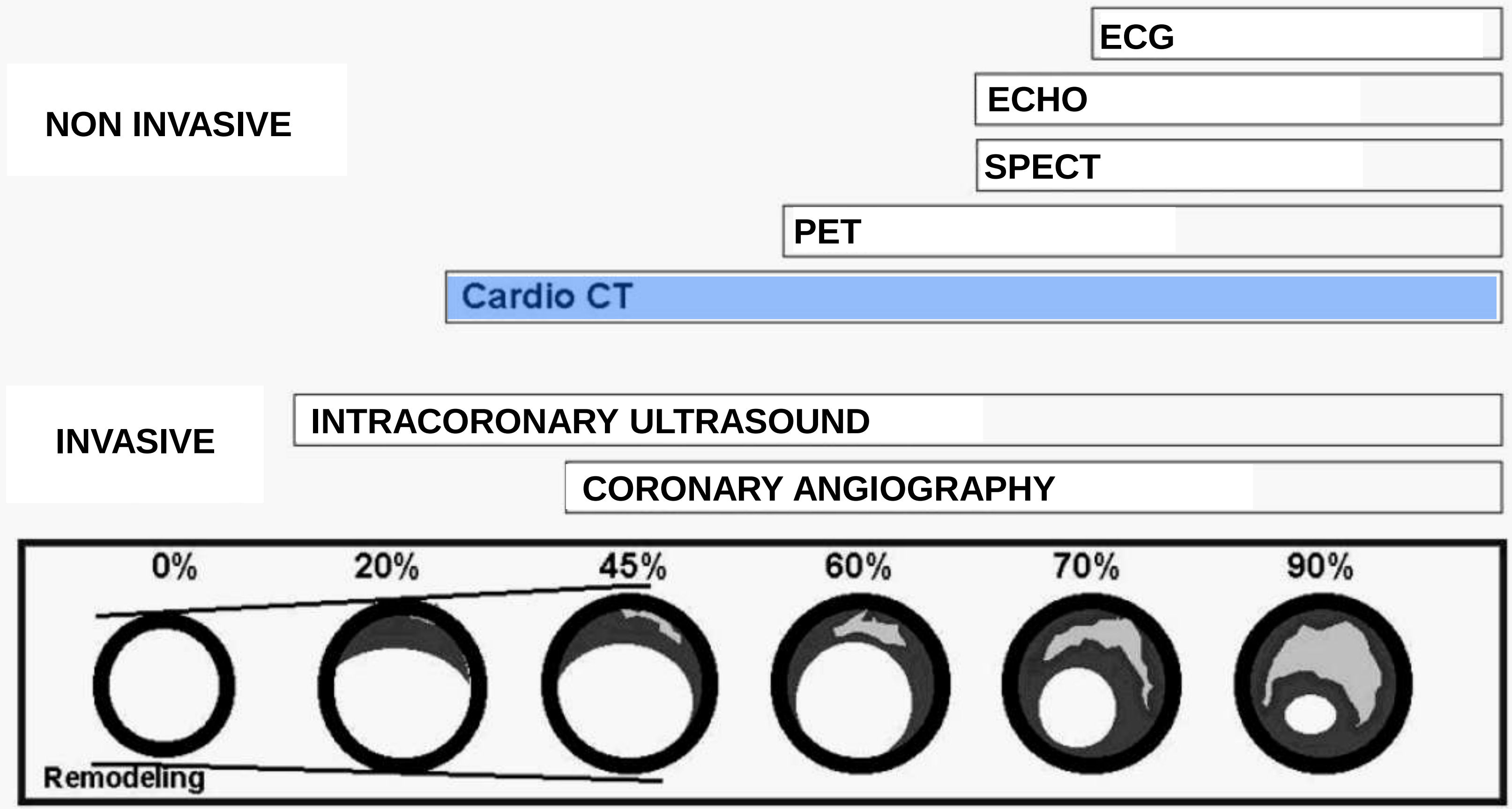
BMI 38

Accuracy 64-slice CT: segment based

Author	year	n	Not evaluable	Sensitivity	Specificity	Diam	Comment
Leschka	2005	67	0%	94%	97%	≥ 1,5	suspected / known CAD
Raff	2005	70	0%	86%	95%	Alle	suspected CAD
Leber	2005	59	4%	73%	97%	Alle	Stable angina
Mollet	2005	52	3%	99%	95%	Alle	angina, MI
Pugliese	2006	35	3%	99%	96%	Alle	Stable angina
Nikolaou	2006	72	10%	82%	93%	Alle	suspected / known CAD including Stents
Ong	2006	134	6,4%	85%	98%	≥ 1,5	suspected / known CAD
Ehara	2006	69	8%	90%	94%	11 Seg	suspected / known CAD including Stents
Ropers	2006	84	4%	93%	97%	≥ 1,5	suspected CAD
Leschka	2006	115	1,5%	91%	97%	≥ 1,5	suspected / known CAD

Overall	**554**	**21,2%**	**79,3%**	**94,8%**	***4-slice CT***
Overall	**707**	**9,6%**	**88,2%**	**96,5%**	***16-slice CT***
Overall	**787**	**3,1%**	**88,6%**	**96,6%**	***64-slice CT***

Diagnosis of coronary atherosclerosis



ACC/AHA Practice Guidelines

ACC/AHA Guidelines for Coronary Angiography: Executive Summary and Recommendations

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Coronary Angiography)

Developed in collaboration with the Society for Cardiac Angiography and Interventions

Recommendations for Coronary Angiography in Patients With Known or Suspected CAD Who Are Currently Asymptomatic or Have Stable Angina

Class I

1. **CCS class III and IV angina on medical treatment.** *(Level of Evidence: B)*
2. **High-risk criteria on noninvasive testing regardless of anginal severity (Table 1).** *(Level of Evidence: A)*
3. **Patients who have been successfully resuscitated from sudden cardiac death or have sustained (>30 seconds) monomorphic ventricular tachycardia or nonsustained (<30 seconds) polymorphic ventricular tachycardia.** *(Level of Evidence: B)*

(*Circulation*. 1999;99:2345-2357.)

Guidelines for Percutaneous Coronary Interventions

The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology

Authors/Task Force Members: Sigmund Silber, Chairperson* (Germany), Per Albertsson (Sweden), Francisco F. Avilés (Spain), Paolo G. Camici (UK), Antonio Colombo (Italy), Christian Hamm (Germany), Erik Jørgensen (Denmark), Jean Marco (France), Jan-Erik Nordrehaug (Norway), Witold Ruzyllo (Poland), Philip Urban (Switzerland), Gregg W. Stone (USA), William Wijns (Belgium)

2. Indications for PCI

2.1. Indications for PCI in stable coronary artery disease

Table 1 Recommendations of PCI indications in stable CAD

Indication	Classes of recommendations and levels of evidence	Randomized studies for levels A or B
Objective large ischaemia	I A	ACME[a] ACIP[b]
Chronic total occlusion	IIa C	—
High surgical risk, including LV-EF $< 35\%$	IIa B	AWESOME
Multi-vessel disease/diabetics	IIb C	—
Unprotected LM in the absence of other revascularization options	IIb C	—
Routine stenting of *de novo* lesions in native coronary arteries	I A	BENESTENT-I STRESS
Routine stenting of *de novo* lesions in venous bypass grafts	I A	SAVED VENESTENT

Assuming that the lesions considered most significant are technically suited for dilatation and stenting, the levels of recommendation refer to the use of stainless steel stents.

[a]The benefit was limited to symptom improvement and exercise capacity.

[b]ACIP is not a pure trial of PCI vs. medical treatment as half of the revascularization patients were treated with bypass graft surgery. Drug-eluting stents are discussed subsequently.

European Heart Journal (2005) **26**, 804–847

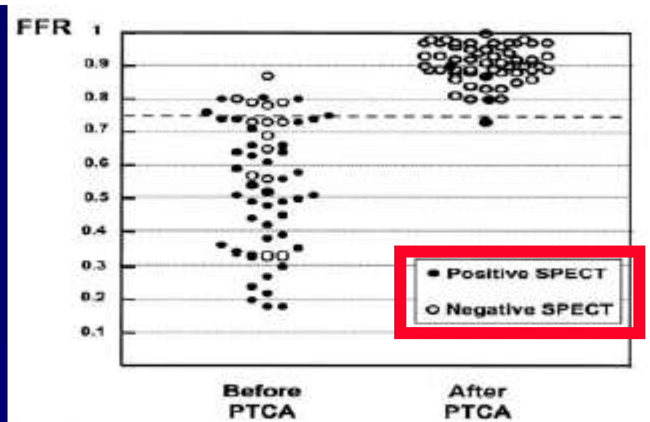
AHA Scientific Statement

Physiological Assessment of Coronary Artery Disease in the Cardiac Catheterization Laboratory

A Scientific Statement From the American Heart Association Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology

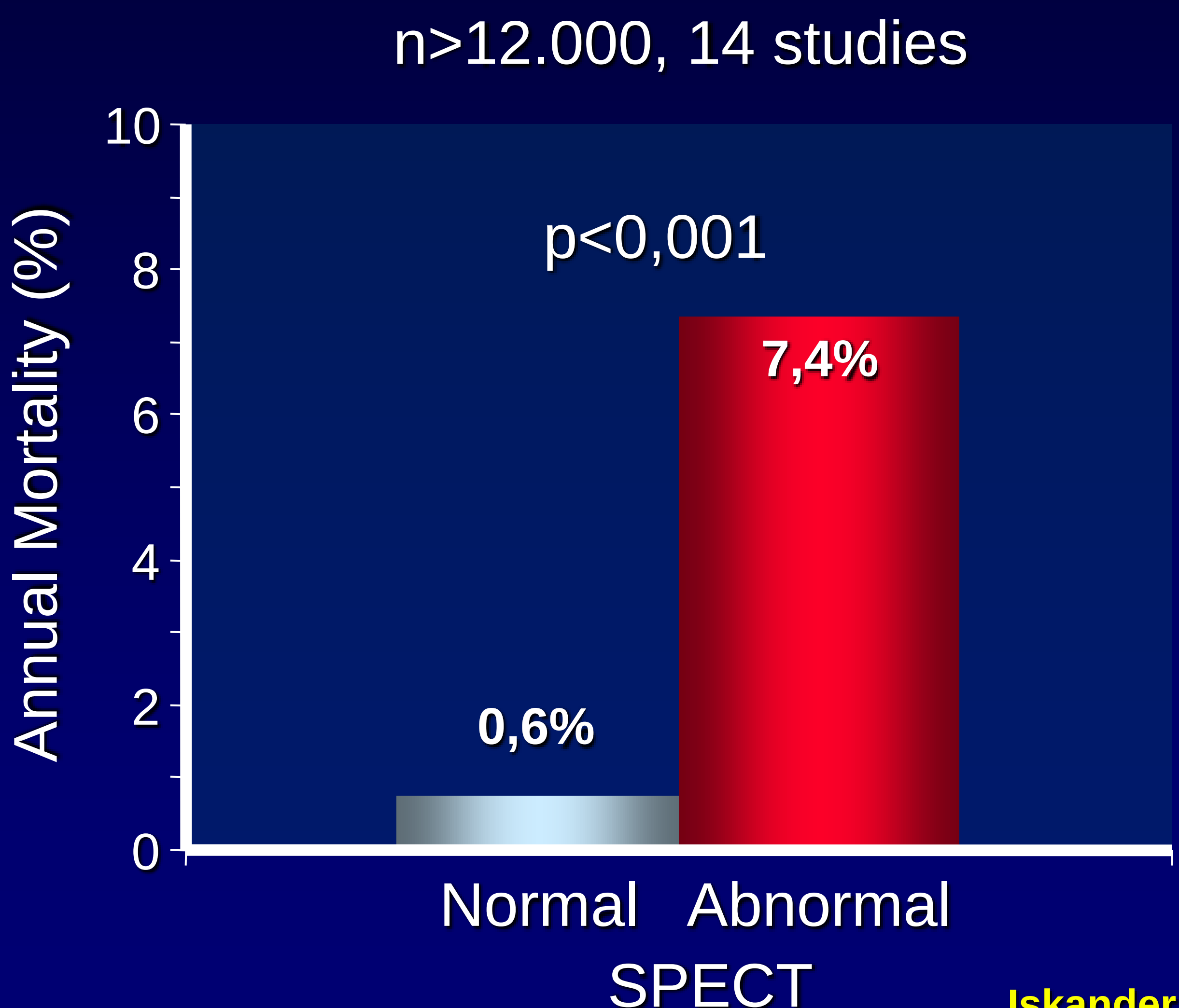
Recommendations and Summary

physiology in the cardiac catheterization laboratory. Best clinical practice suggests that the addition of coronary physiological measurements complements traditional angiographic information and is essential for accurate clinical decision-making. The current applications of coronary



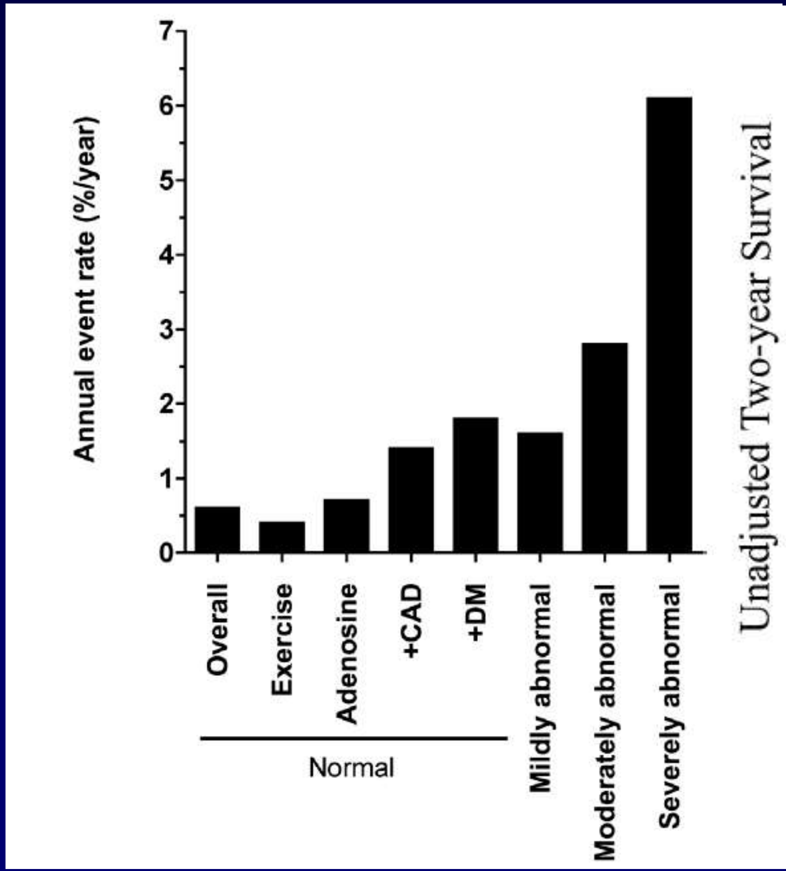
(*Circulation*. 2006;114:1321-1341.)

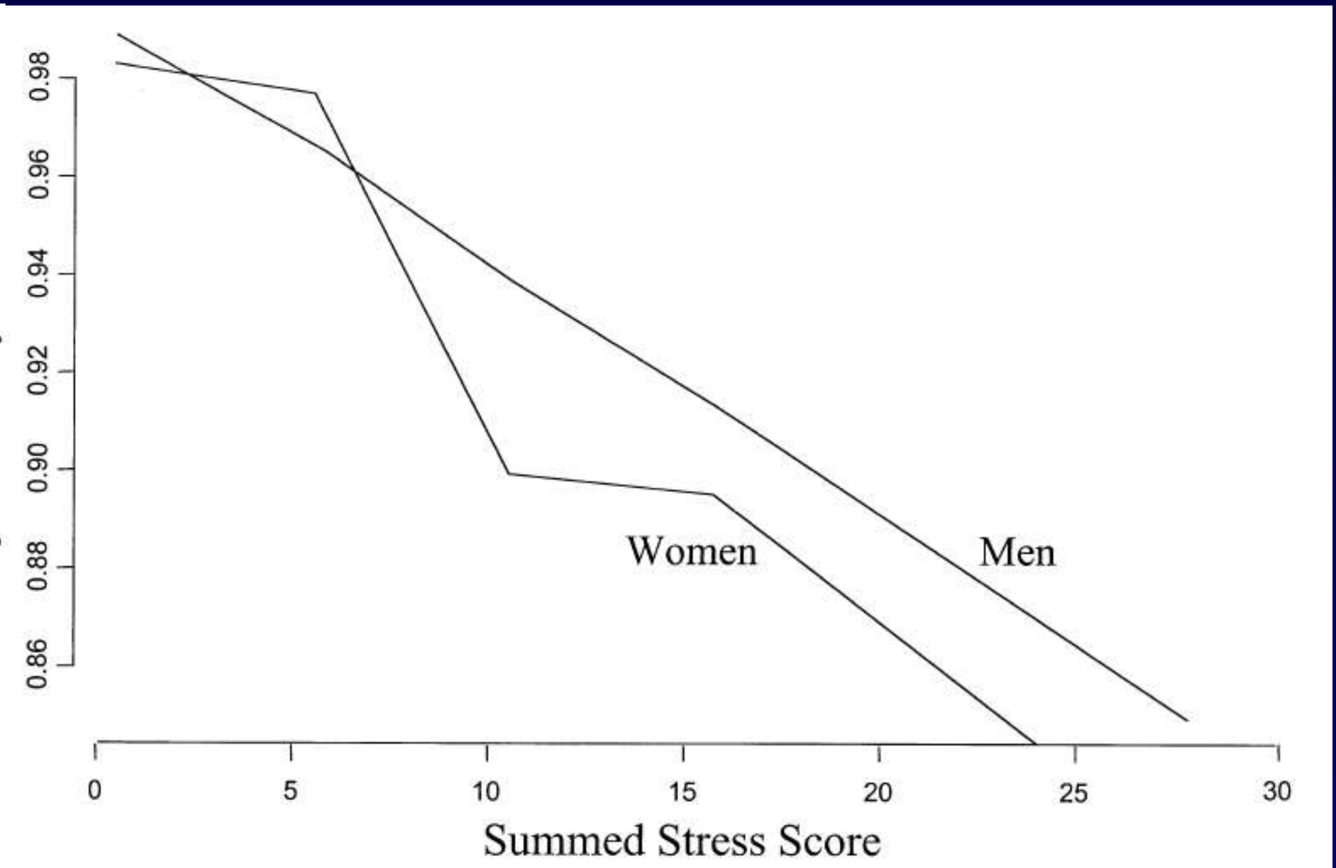
SPECT: Prognostic impact



Iskander, JACC 1998; 32: 57-62

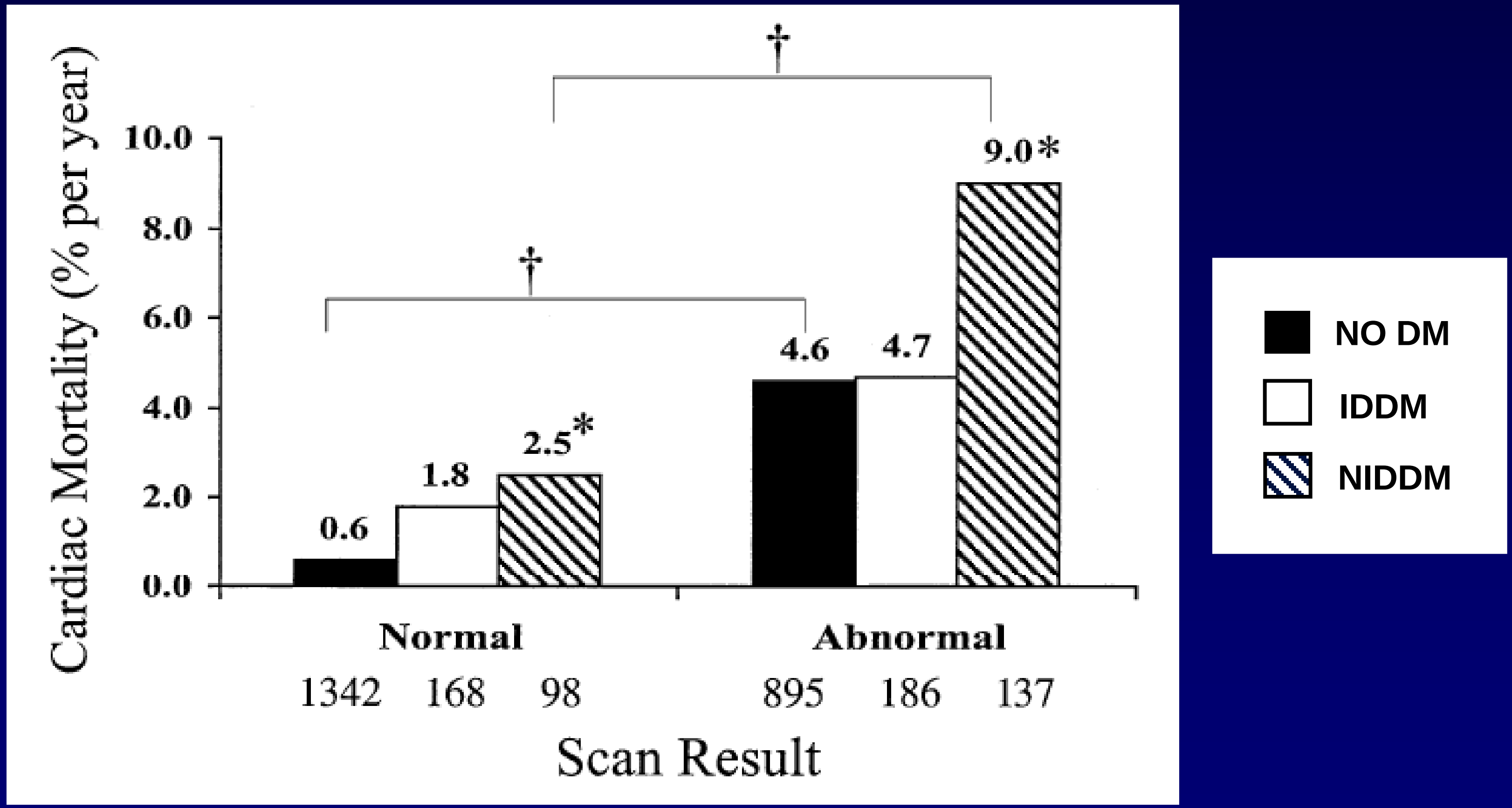
Prognostic value of SPECT





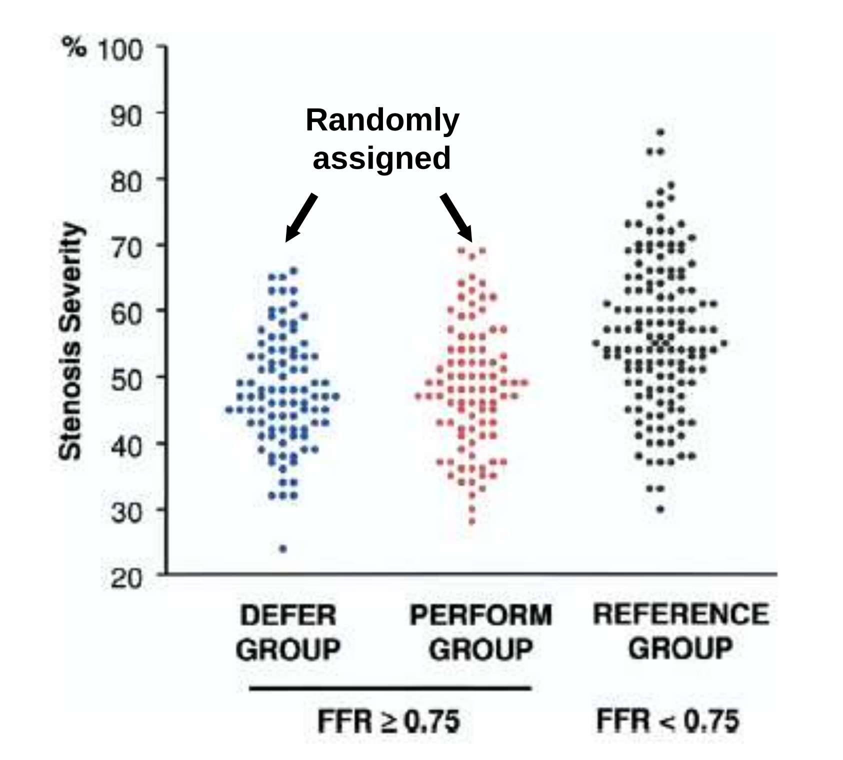
JACC Vol. 41, No. 7, 2003
April 2, 2003:1125–33

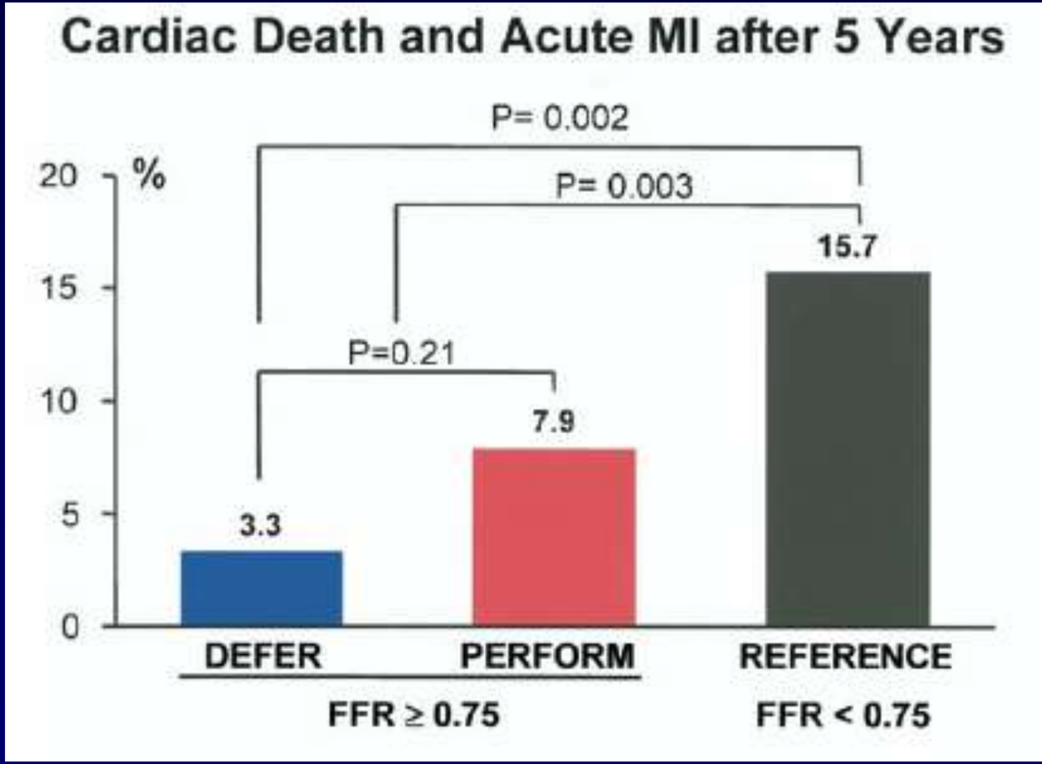
Prognostic value of SPECT:
Incremental value of clinical information



Percutaneous Coronary Intervention of Functionally Nonsignificant Stenosis

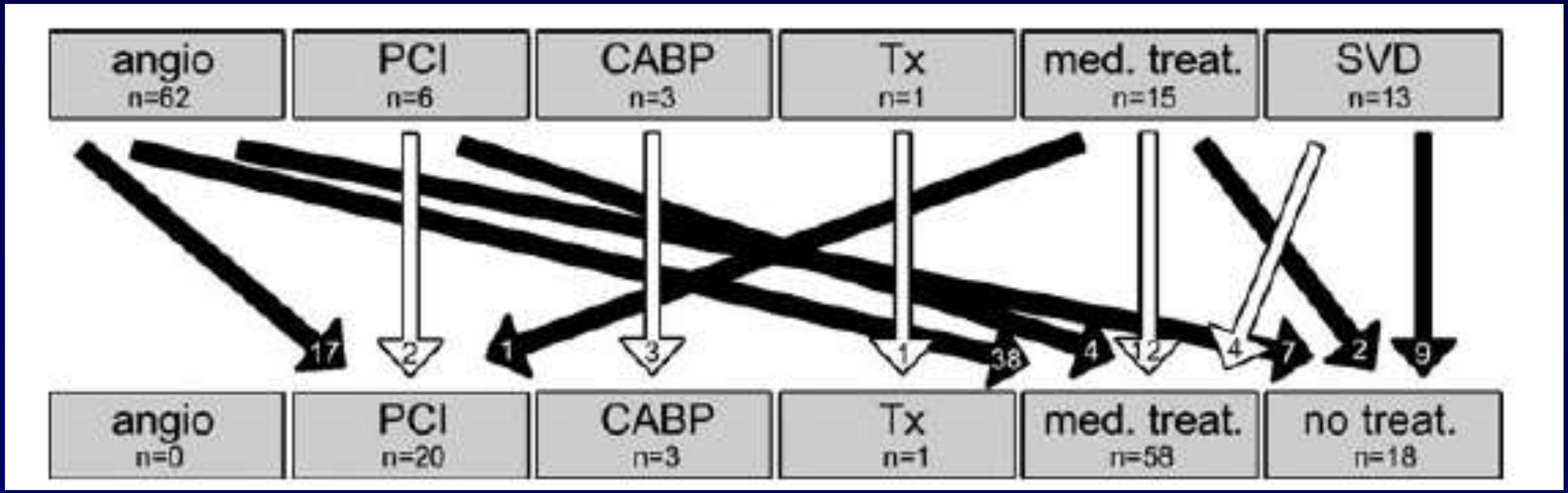
5-Year Follow-Up of the DEFER Study





Pijls N et al. JACC 2007;49:2105-11

Impact of PET perfusion scanning on pts management



Treatment was altered by PET in 78% of patients

Recommendations from PET were followed in 97% of patients

Siegrist, EJNMMI 2008;35:889-95

Impact of FDG PET on outcome – Mission impossible if clinicians do not follow recommendations from scan results

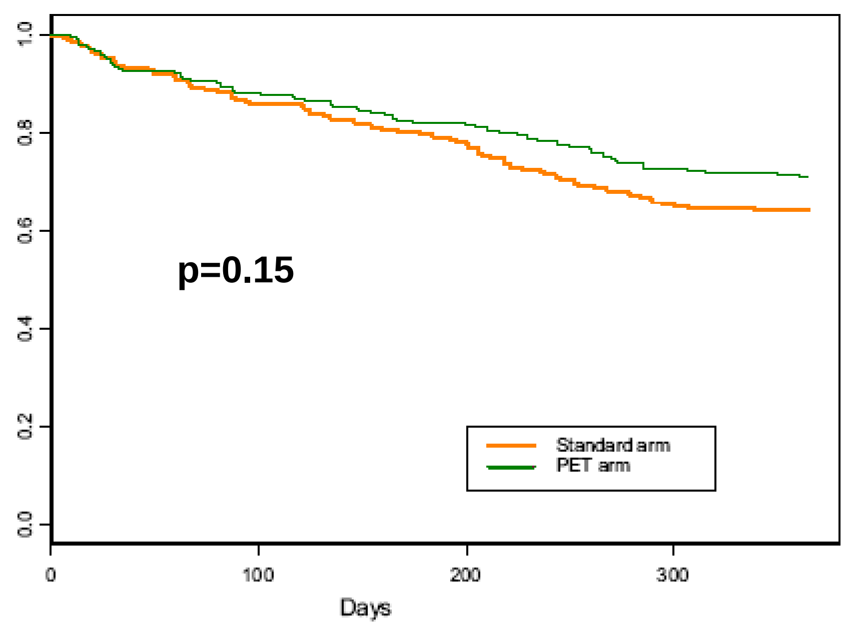


Figure 3 "Survival Curves" (on the Basis of Time to First Occurring Outcome of the Composite Event)

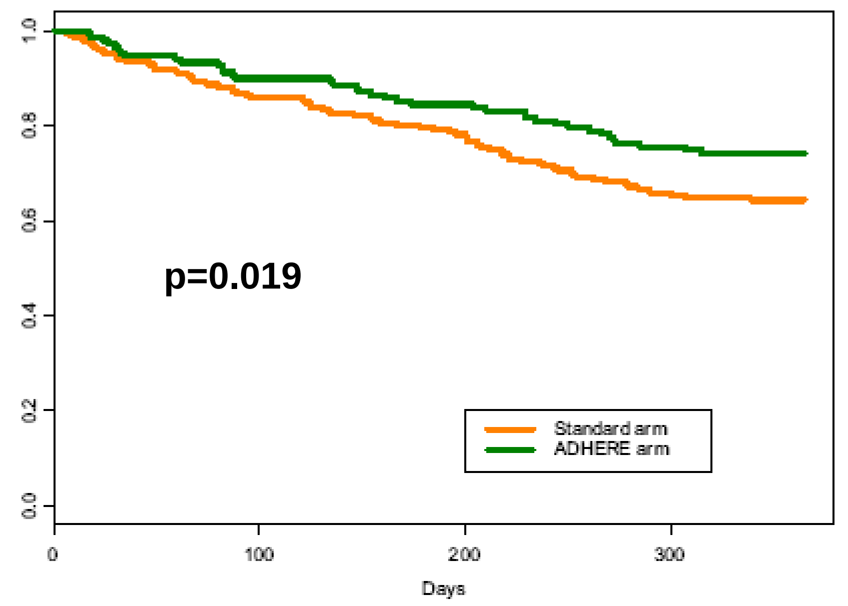
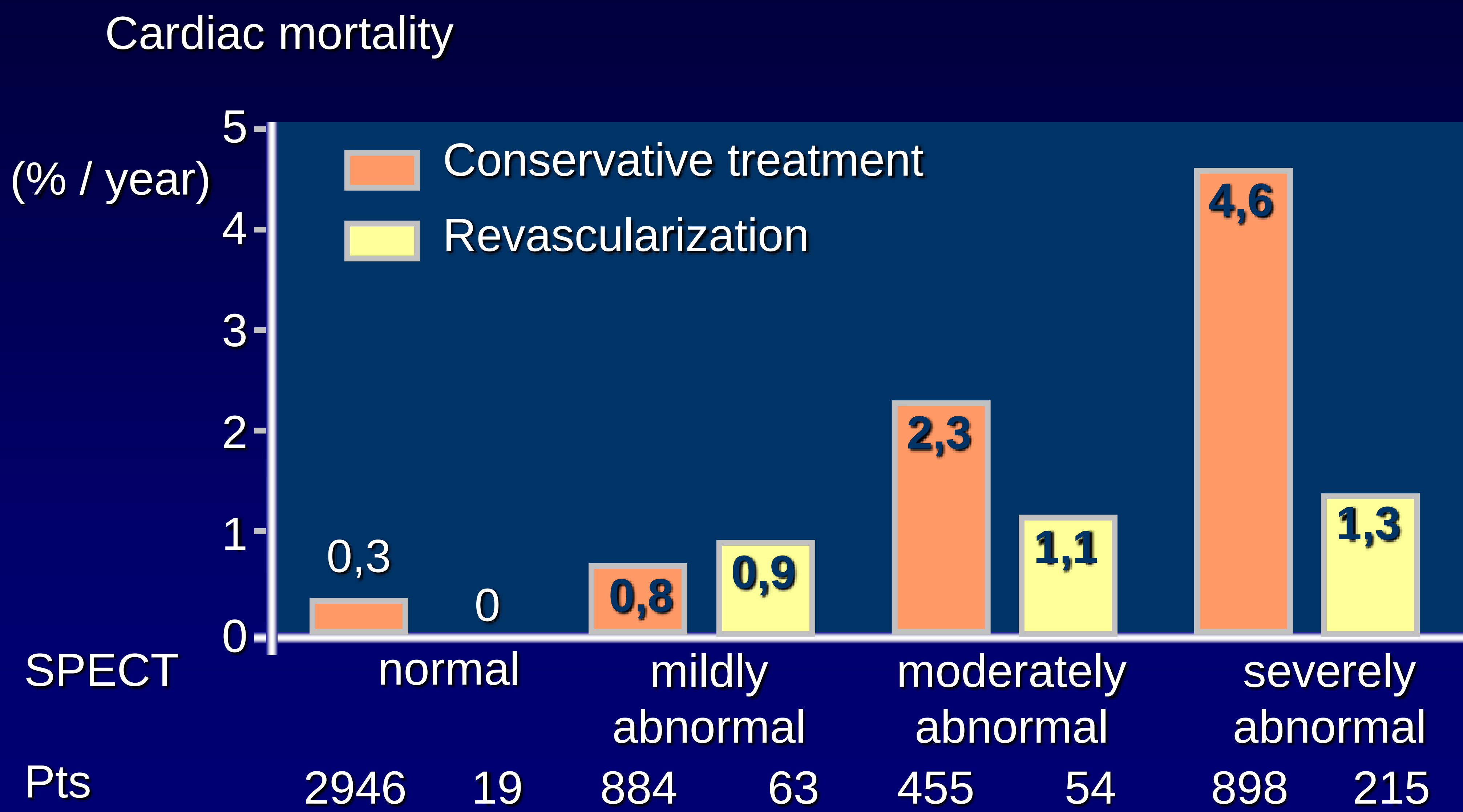


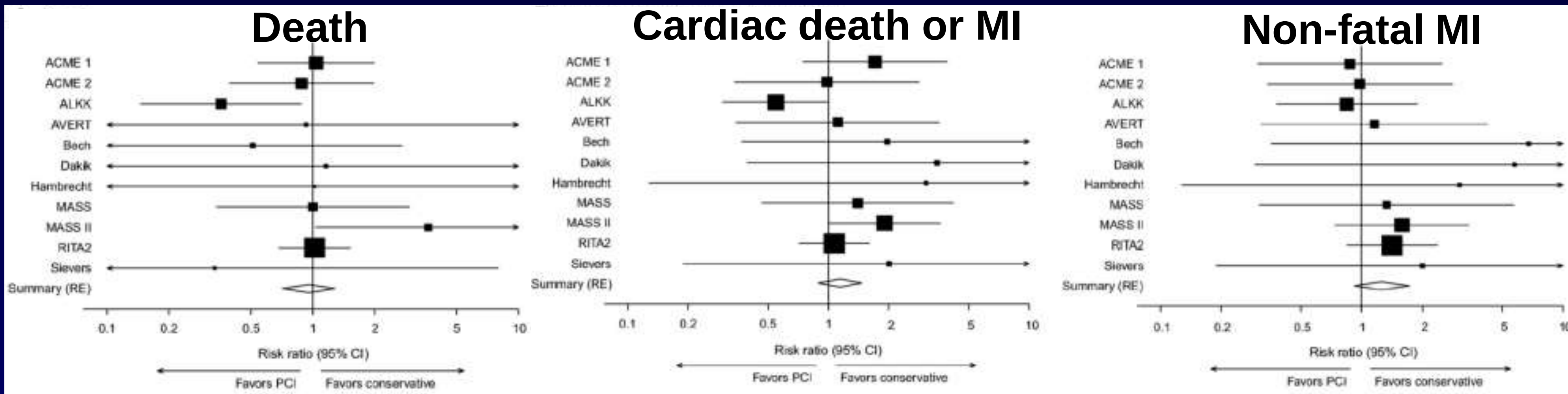
Figure 7 "Survival Curves" (on the Basis of Time to First Occurring Outcome Out of the Composite Event)

Impact of SPECT on pts outcome

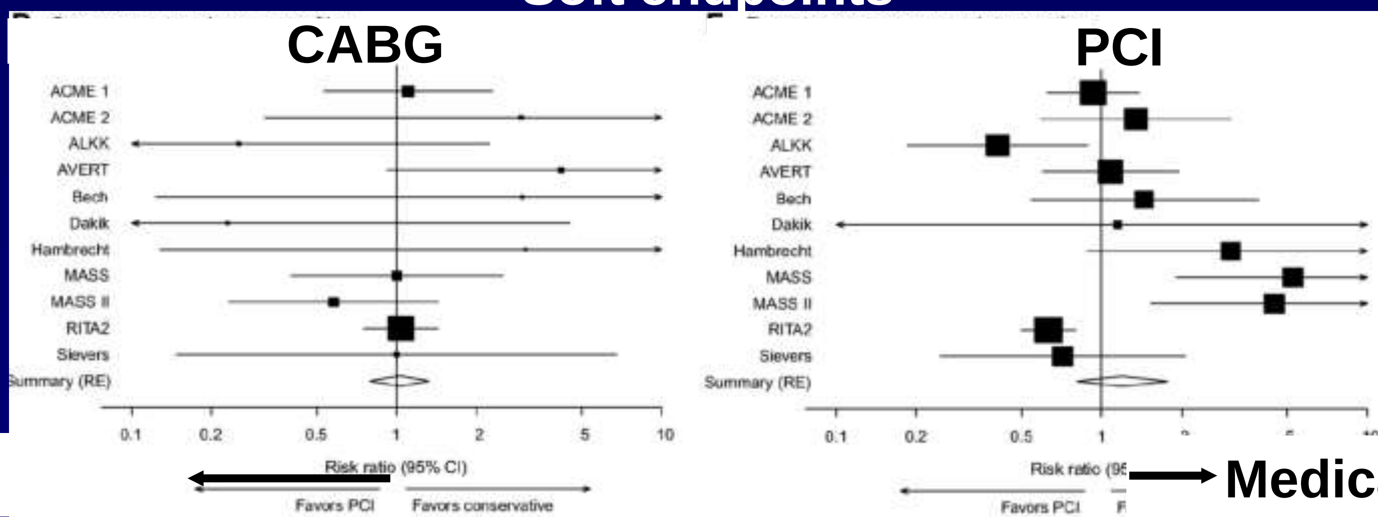


Hachamovitch, Circulation 1998; 97:535-43

PCI vs medical treatment for chronic stable CAD



Soft endpoints



PCI better ← → **Medication better**

(*Circulation*. 2005;111:2906-2912.)

COURAGE trial

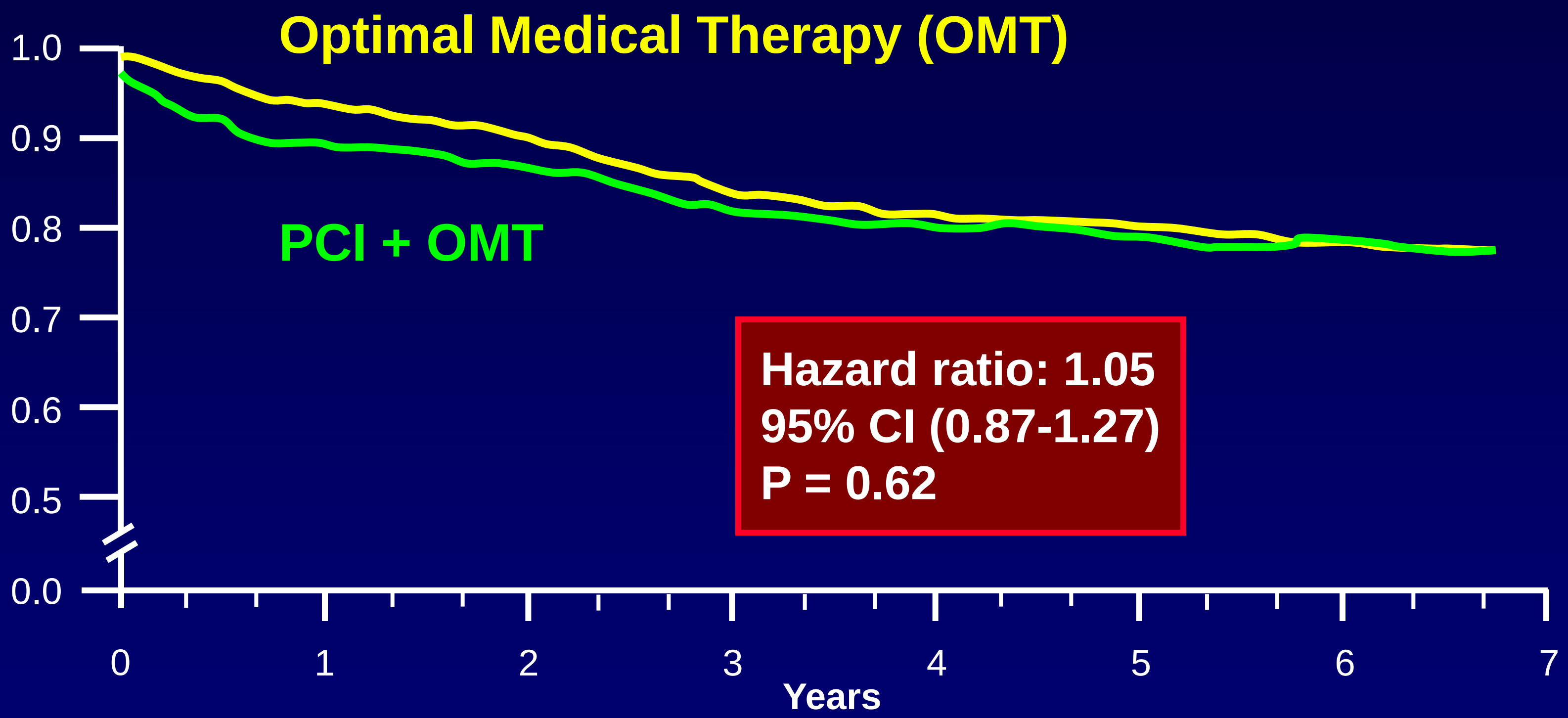
Clinical **O**utcomes **U**tilizing

Revascularization and

Aggressive **G**uideline-Driven

Drug **E**valuation

Survival Free of Death from Any Cause and Myocardial Infarction

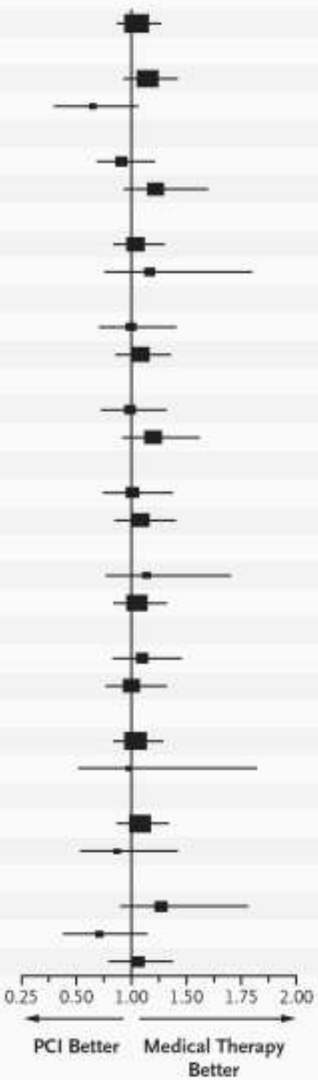


Number at Risk

	0	1	2	3	4	5	6	7
Medical Therapy	1138	1017	959	834	638	408	192	30
PCI	1149	1013	952	833	637	417	200	35

PCI vs conservative therapy - COURAGE trial

Baseline Characteristics	No. of Patients	Hazard Ratio (95% CI)	Event Rate for the Primary Outcome PCI	Event Rate for the Primary Outcome Medical Therapy	P Value
Overall	2287	1.05 (0.87–1.27)	0.19	0.19	
Sex					0.03
Male	1947	1.15 (0.93–1.42)	0.19	0.18	
Female	338	0.65 (0.40–1.06)	0.18	0.26	
Myocardial infarction					0.15
Yes	876	0.91 (0.69–1.21)	0.23	0.25	
No	1371	1.22 (0.93–1.60)	0.17	0.14	
Extent of CAD					0.65
Multivessel disease	1581	1.04 (0.84–1.30)	0.21	0.21	
Single-vessel disease	700	1.17 (0.76–1.80)	0.15	0.12	
Smoking					0.71
Current	653	1.00 (0.71–1.41)	0.20	0.21	
Not current	1631	1.08 (0.86–1.36)	0.19	0.18	
Diabetes					0.33
Yes	766	0.99 (0.73–1.32)	0.25	0.24	
No	1468	1.20 (0.92–1.56)	0.17	0.15	
CCS angina class					0.73
0 or I	964	1.01 (0.75–1.38)	0.17	0.20	
II or III	1371	1.09 (0.85–1.40)	0.20	0.18	
Ejection fraction					0.72
≤50%	406	1.14 (0.77–1.70)	0.28	0.26	
>50%	1848	1.05 (0.84–1.32)	0.17	0.16	
Age					0.62
>65 yr	904	1.10 (0.83–1.46)	0.24	0.22	
≤65 yr	1381	1.00 (0.77–1.32)	0.16	0.16	
Previous CABG					0.81
No	2039	1.04 (0.84–1.29)	0.17	0.17	
Yes	248	0.98 (0.52–1.82)	0.34	0.29	
Race					0.43
White	1963	1.08 (0.87–1.34)	0.19	0.18	
Nonwhite	322	0.87 (0.54–1.42)	0.19	0.24	
Health care system					0.17
Canadian	932	1.27 (0.90–1.78)	0.17	0.14	
U.S. non-VA	387	0.71 (0.44–1.14)	0.15	0.21	
U.S. VA	968	1.06 (0.80–1.38)	0.22	0.22	



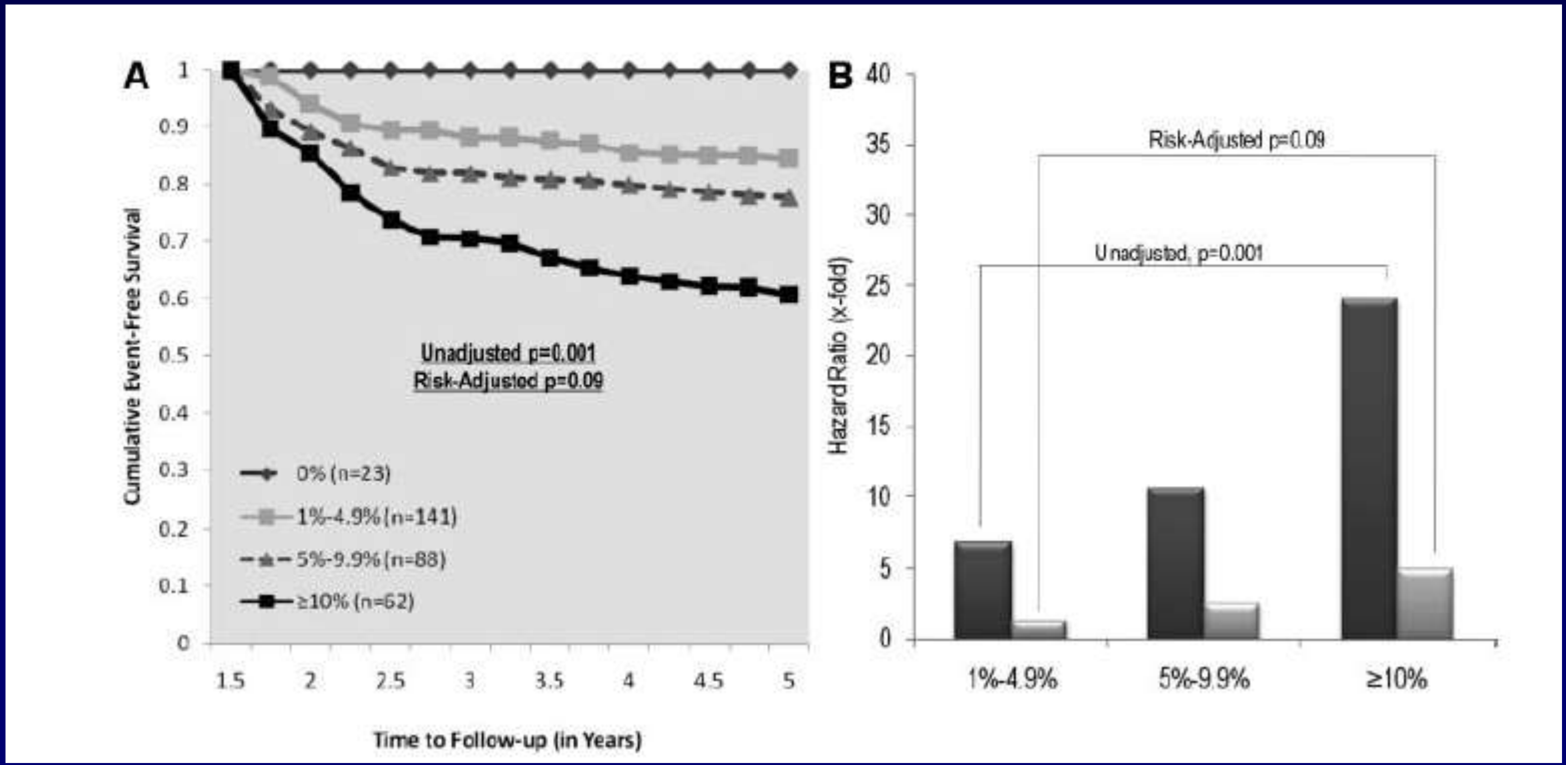
PCI better ←

→ **Medication better**

N Engl J Med 2007;356:1503-16.

COURAGE trial – nuclear substudy

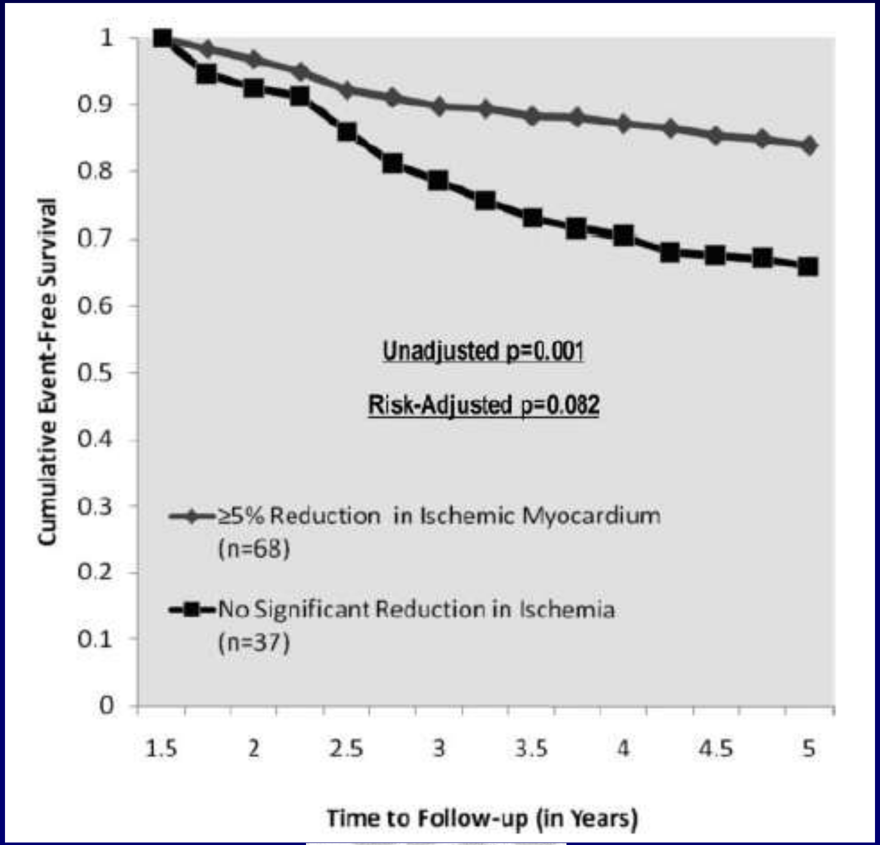
Residual ischemia affects outcome



Circulation. 2008;117

COURAGE trial – nuclear substudy

Reduction of ischemia improves outcome
Treatment target – 5% ischemia reduction



Circulation. 2008;117

INSPIRE trial

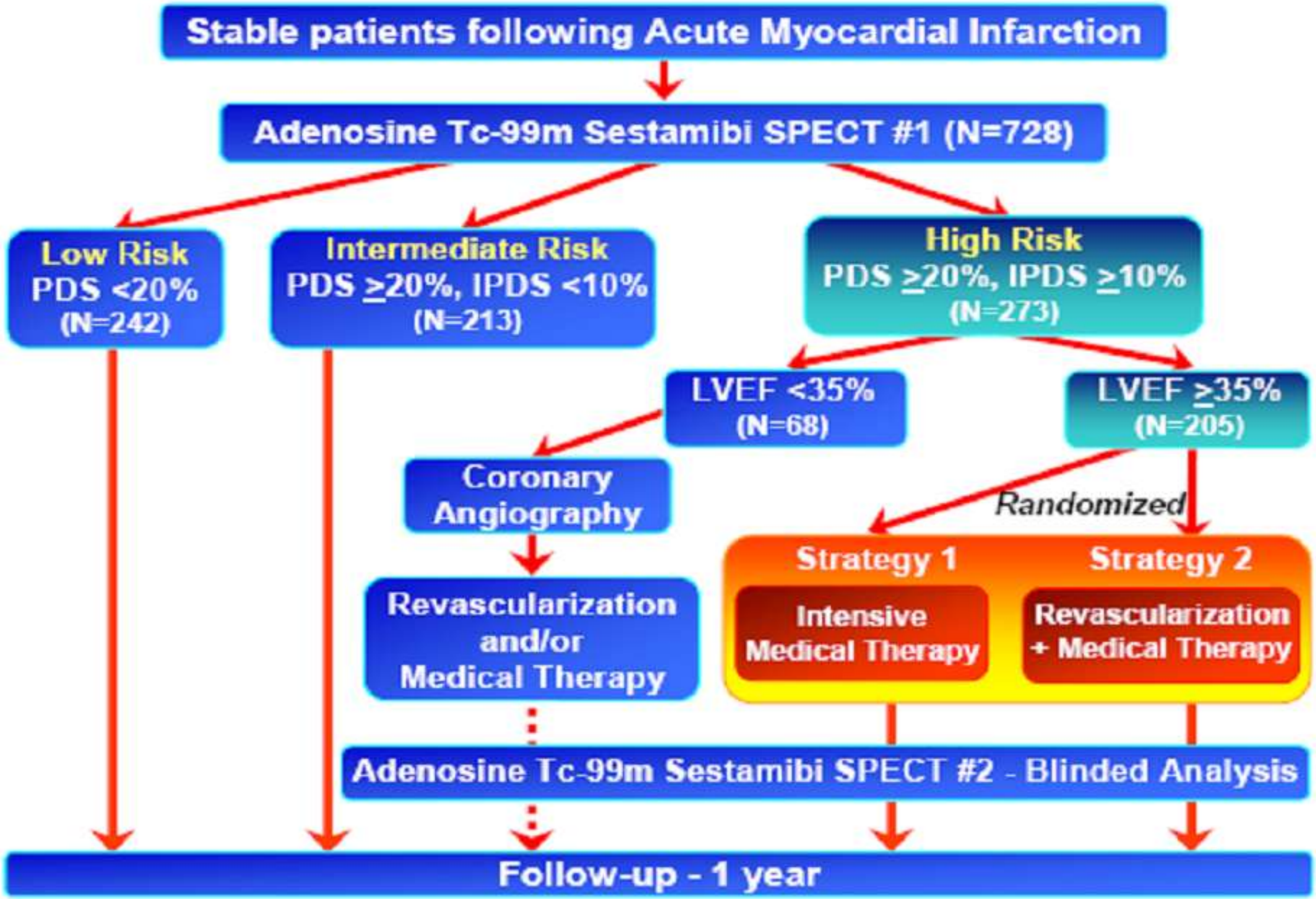
Journal of the American College of Cardiology
Vol. 48, No. 11, 2006

A Multinational Study to Establish the Value of Early Adenosine Technetium-99m Sestamibi Myocardial Perfusion Imaging in Identifying a Low-Risk Group for Early Hospital Discharge Following Acute Myocardial Infarction

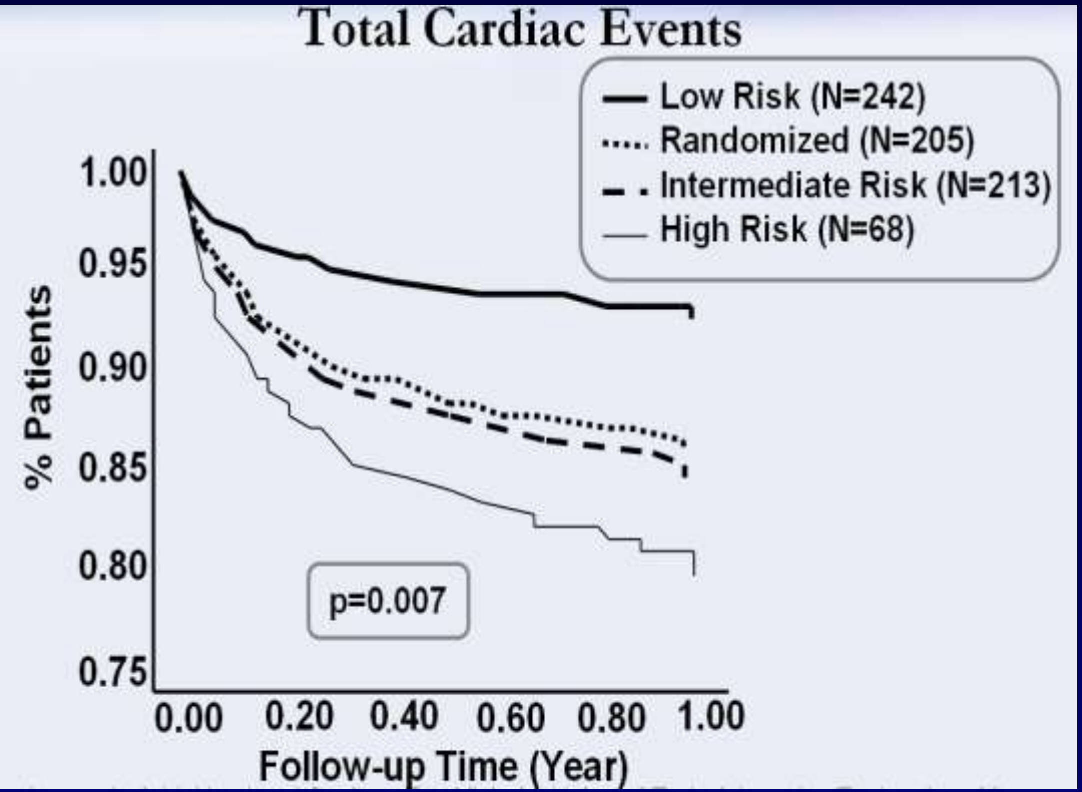
John J. Mahmarian, MD, Leslee J. Shaw, PhD, Neil G. Filipchuk, MD, Habib A Dakik, MD Sherif S. Iskander, MD, Terrence D. Ruddy, MD, Milena J. Henzlova, MD, Felix Keng, MD, Abel Allam, MD, Lemuel A. Moye, MD, PhD, and Craig M. Pratt, MD for the ADENOSINE SESTAMIBI SPECT POST-INFARCTION EVALUATION (INSPIRE) Investigators

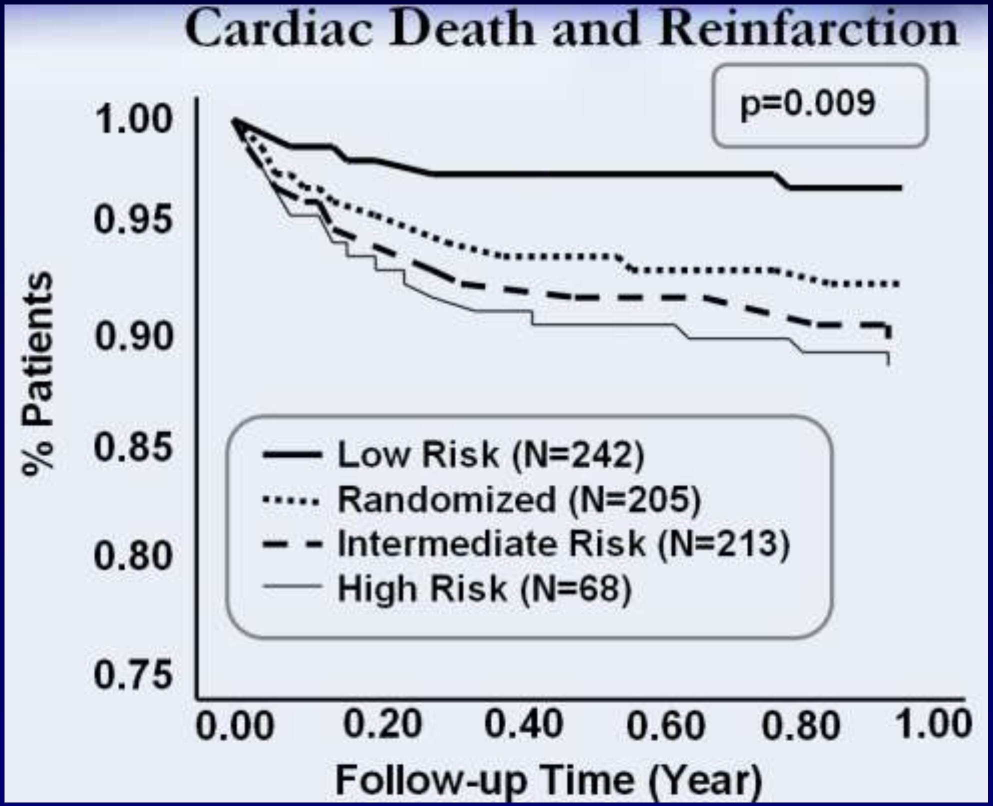
J Am Coll Cardiol 2006;48:2448–57

INSPIRE Study Design



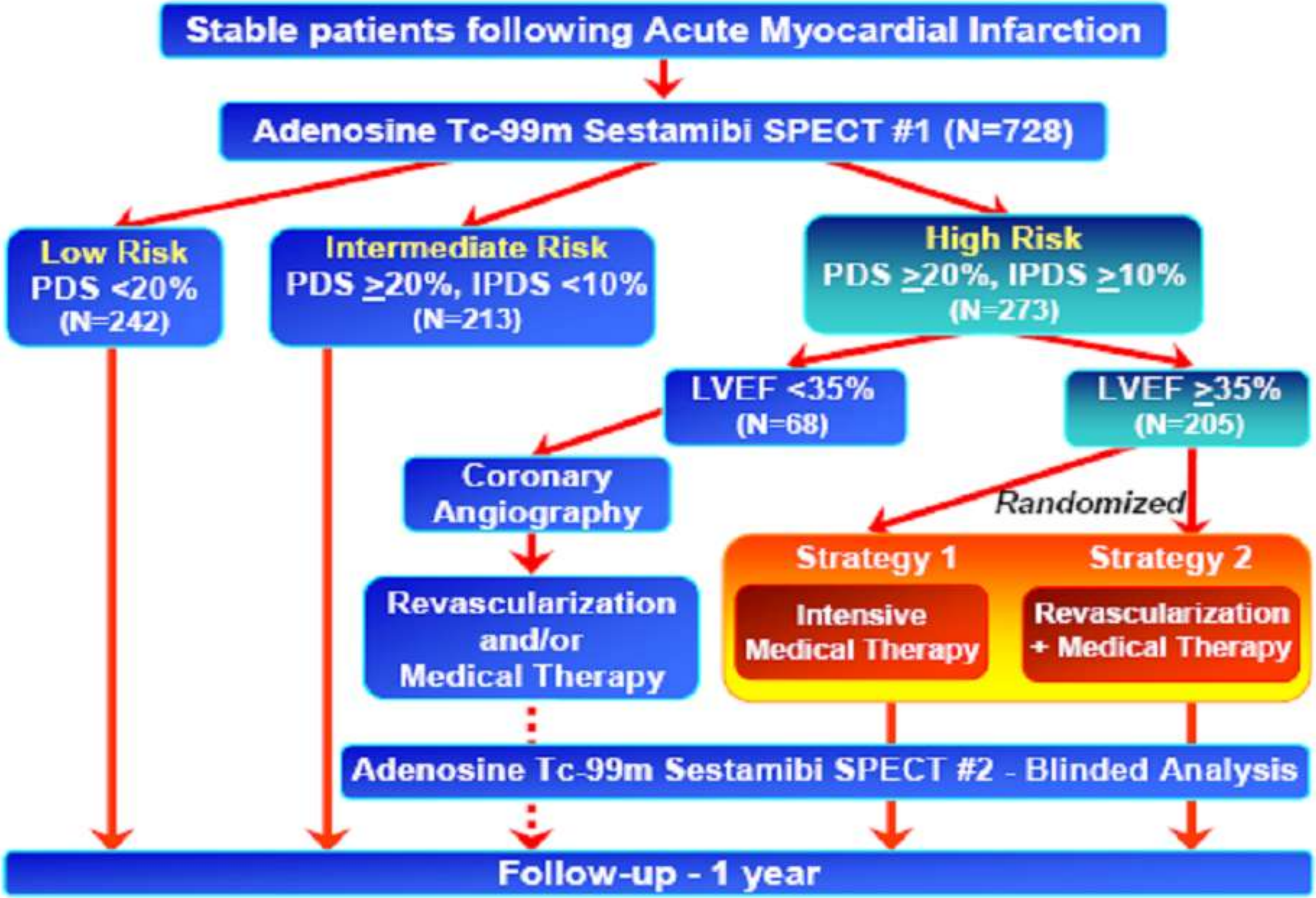
INSPIRE trial



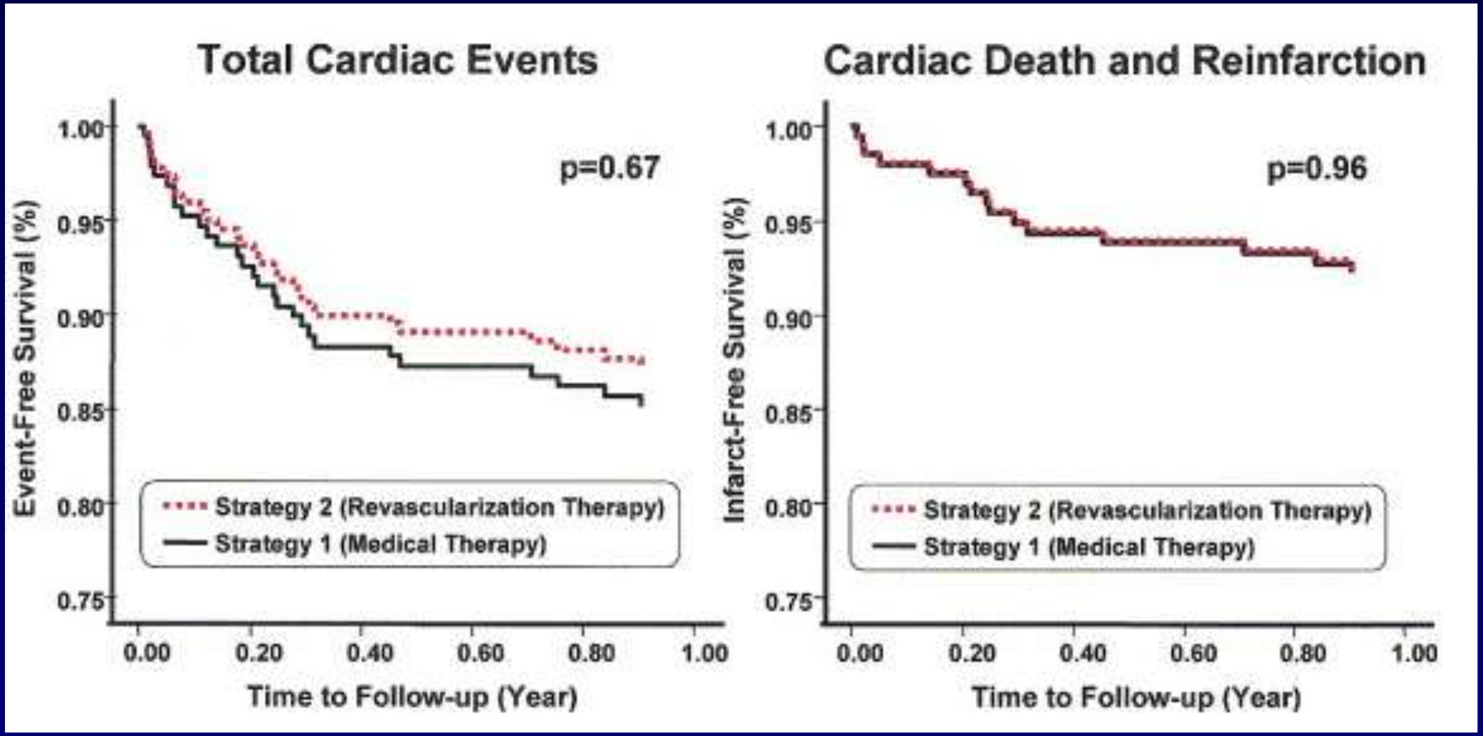


J Am Coll Cardiol 2006;48:2448–57

INSPIRE Study Design



INSPIRE intervention trial



J Am Coll Cardiol 2006;48:2458−67

Myocardial Perfusion Imaging for Evaluation and Triage of Patients With Suspected Acute Cardiac Ischemia

A Randomized Controlled Trial

James E. Udelson, MD
Joni R. Beshansky, RN, MPH
Daniel S. Ballin, MD
James A. Feldman, MD
John L. Griffith, PhD
Gary V. Heller, MD, PhD
Robert C. Hendel, MD
J. Hector Pope, MD
Robin Ruthazer, MPH
Ethan J. Spiegler, MD
Robert H. Woolard, MD
Jonathan Handler, MD
Harry P. Selker, MD, MSPH

Context Observational studies of acute myocardial perfusion imaging in emergency department (ED) patients with chest pain have suggested high sensitivity and negative predictive value for acute cardiac ischemia, but use of this method has not been prospectively tested.

Objective To assess whether incorporating acute resting perfusion imaging into an ED evaluation strategy for patients with suspected acute ischemia but no initial electrocardiogram (ECG) changes diagnostic of acute ischemia improves clinical decision making for initial ED triage.

Design, Setting, and Patients Prospective, randomized controlled trial conducted at 7 academic medical centers and community hospitals between July 1997 and May 1999 among 2475 adult ED patients with chest pain or other symptoms suggestive of acute cardiac ischemia and with normal or nondiagnostic initial ECG results.

Intervention Patients were randomly assigned to receive either the usual ED evaluation strategy (n=1260) or the usual strategy supplemented with results from acute resting myocardial perfusion imaging using single-photon emission computed tomography with injection of 20 to 30 mCi of Tc-99m sestamibi (n=1215), interpreted in real time by local staff physicians and with results provided to the ED physician for incorporation into clinical decision making.

Main Outcome Measure Appropriateness of triage decision either to admit to hospital/observation or to discharge directly home from the ED.

Results Among patients with acute cardiac ischemia (ie, acute myocardial infarction [MI] or unstable angina; n=329), there were no differences in ED triage decisions between those receiving standard evaluation and those whose evaluation was supplemented by a sestamibi scan. Among patients with acute MI (n=56), 97% vs 96% were hospitalized (relative risk [RR], 1.00; 95% confidence interval [CI], 0.89-1.12), and among those with unstable angina (n=273), 83% vs 81% were hospitalized (RR, 0.98; 95% CI, 0.87-1.10). However, among patients without acute cardiac ischemia (n=2146), hospitalization was 52% with usual care vs 42% with sestamibi imaging (RR, 0.84; 95% CI, 0.77-0.92).

Conclusions Sestamibi perfusion imaging improves ED triage decision making for patients with symptoms suggestive of acute cardiac ischemia without obvious abnormalities on initial ECG. In this study, unnecessary hospitalizations were reduced among patients without acute ischemia, without reducing appropriate admission for patients with acute ischemia.

JAMA. 2002;288:2693-2700 www.jama.com

EACH YEAR IN THE UNITED STATES, more than 6 million patients present to emergency departments (EDs) with chest pain or other symptoms suggestive of acute cardiac ischemia (ie, either acute myocardial infarction [MI] or unstable angina pectoris).[1] The majority of these patients are admitted to the hospital or to an observation unit, because the initial clinical examination, electrocardiogram (ECG) results, and initial cardiac enzyme levels are insufficient to eliminate the possibility of acute infarction or unstable angina.[1-4] Nevertheless, most patients without obvious ischemic ECG changes who are hospitalized or observed in special units ultimately prove

JAMA. 2002;288:2693-2700

Impact of sestamibi MPI on triage decision in acute cardiac ischemia

Patients with ischemia

Table 4. Effect of Sestamibi Imaging on ED Triage Decisions in Patients With ACI*

	No. (%) Scan Strategy	No. (%) Usual Care	RR (95% CI)	*P* Value
All patients with ACI	165	164†		
Hospital admission rate	138 (84)	140 (85)	0.98 (0.90-1.08)	.74
Triage disposition				
CCU	33 (20)	39 (24)		.71
Telemetry ward	86 (52)	86 (53)		
Chest pain unit	19 (12)	14 (9)		
Home from ED	27 (16)	24 (15)		
Acute myocardial infarction	26	30		
Hospital admission rate	25 (96)	29 (97)	1.00 (0.89-1.12)	>.99
Triage disposition				
CCU	15 (58)	17 (57)		.92
Telemetry ward	10 (39)	10 (33)		
Chest pain unit	0 (0)	2 (7)		
Home from ED	1 (4)	1 (3)		
Unstable angina	139	134		
Hospital admission rate	113 (81)	111 (83)	0.98 (0.87-1.10)	.68
Triage disposition				
CCU	18 (13)	22 (17)		.58
Telemetry ward	76 (55)	76 (57)		
Chest pain unit	19 (14)	12 (9)		
Home from ED	26 (19)	23 (17)		

*ED indicates emergency department; ACI, acute cardiac ischemia; RR, relative risk; CI, confidence interval; and CCU, coronary care unit.
†One patient missing data for triage disposition.

Patients without ischemia

Table 5. Effect of Sestamibi Imaging on ED Triage Decisions in Patients Without ACI*

	No. (%) Scan Strategy (n = 1050)†	No. (%) Usual Care (n = 1096)‡	RR (95% CI)	*P* Value
Hospital admission rate	438 (42)	567 (52)	0.84 (0.77-0.92)	<.001
Triage disposition				
CCU	43 (4)	27 (3)		.002
Telemetry ward	282 (27)	379 (35)		
Chest pain unit	112 (11)	160 (15)		
Home from ED	610 (58)	529 (48)		

*ED indicates emergency department; ACI, acute cardiac ischemia; RR, relative risk; CI, confidence interval; and CCU, coronary care unit.
†Two patients missing data for admission status; 3 patients missing data for triage disposition.
‡One patient missing data for triage disposition.

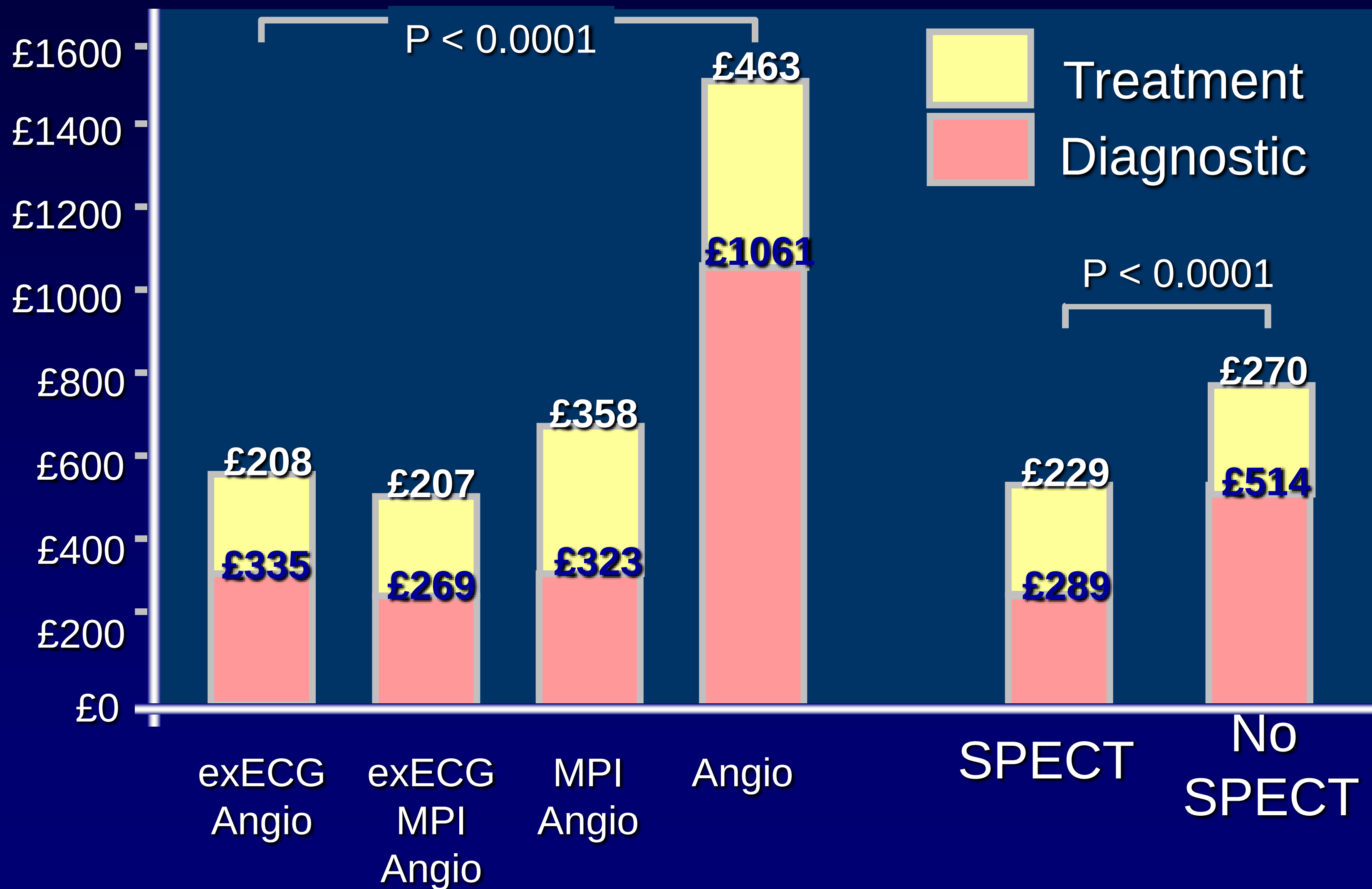
JAMA. 2002;288:2693-2700

Impact of sestamibi MPI on triage decision in acute cardiac ischemia

Conclusions Sestamibi perfusion imaging improves ED triage decision making for patients with symptoms suggestive of acute cardiac ischemia without obvious abnormalities on initial ECG. In this study, unnecessary hospitalizations were reduced among patients without acute ischemia, without reducing appropriate admission for patients with acute ischemia.

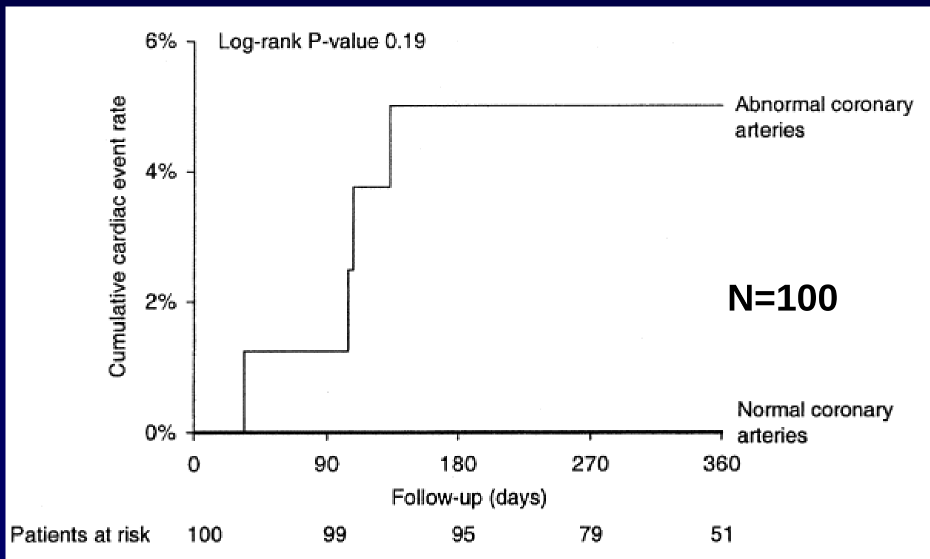
JAMA. 2002;288:2693-2700

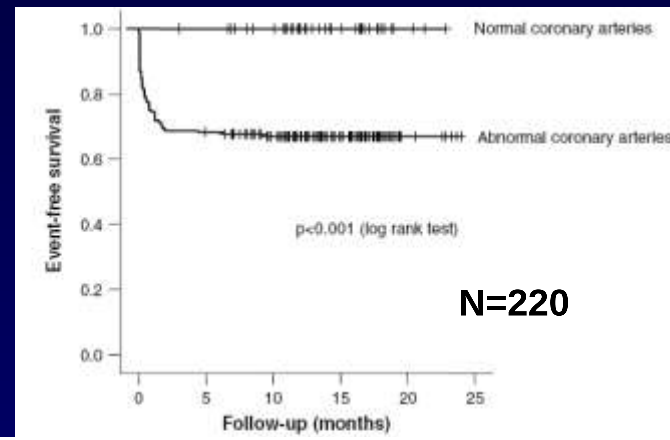
Economics of myocardial perfusion imaging in Europe – The EMPIRE study

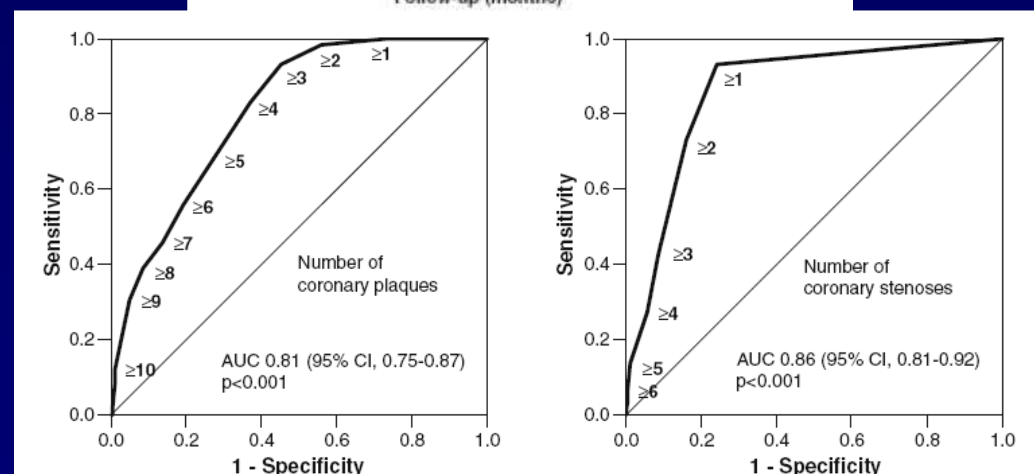


European Heart Journal (1999) **20**, 157–166

Predicting outcome using 64-slice CT coronary angiography







J Am Coll Cardiol 2007;49:62–70

Eur Radiol
DOI 10.1007/s00330-008-0871-7

Prognostic Value of Multidetector Coronary Computed Tomographic Angiography for Prediction of All-Cause Mortality

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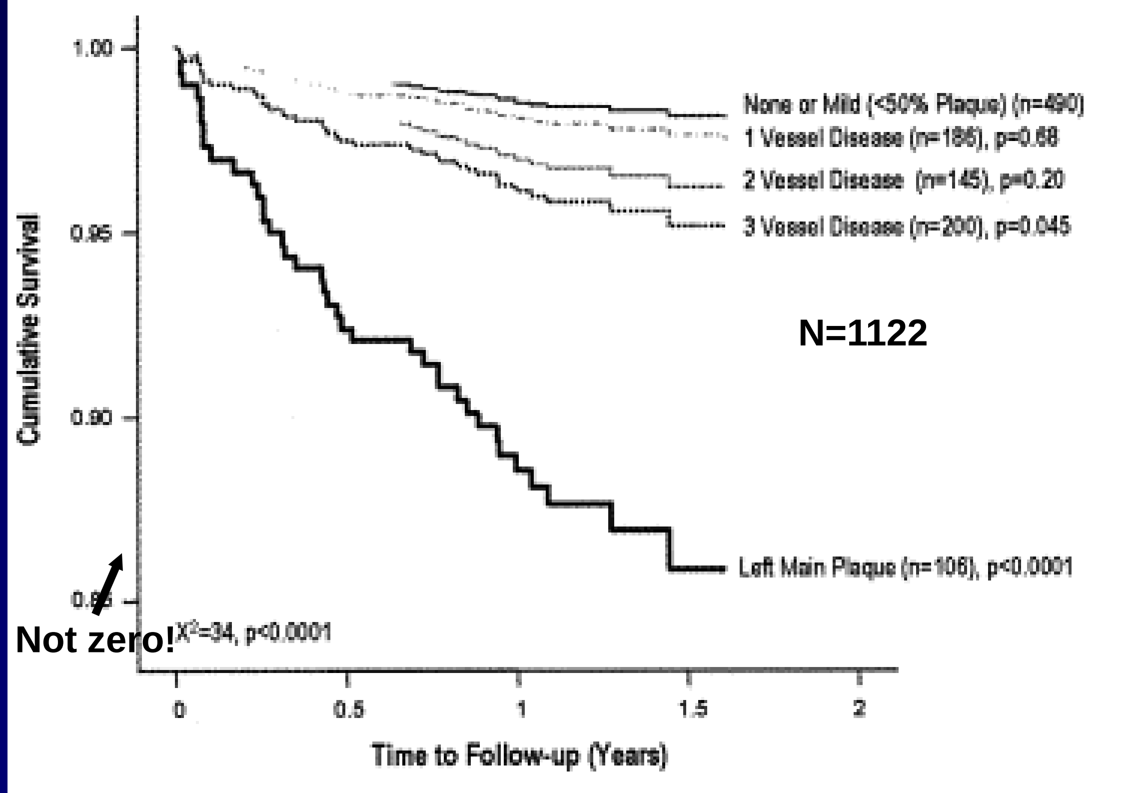
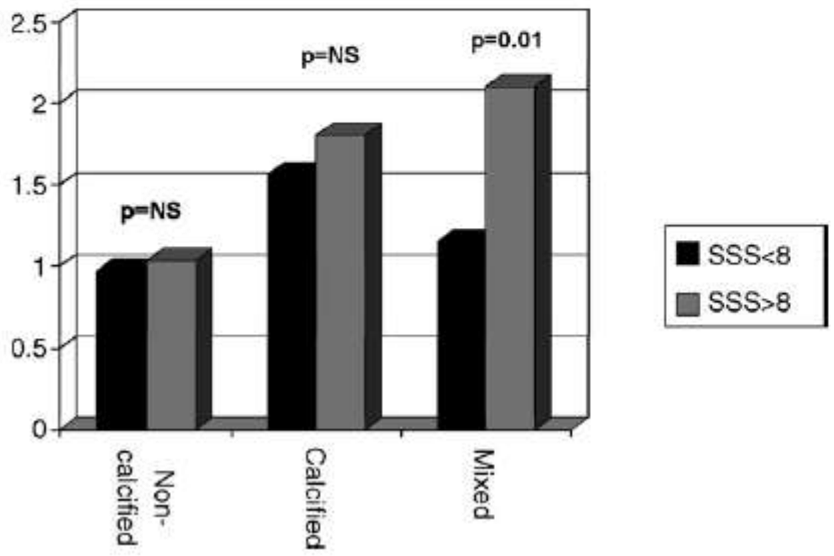
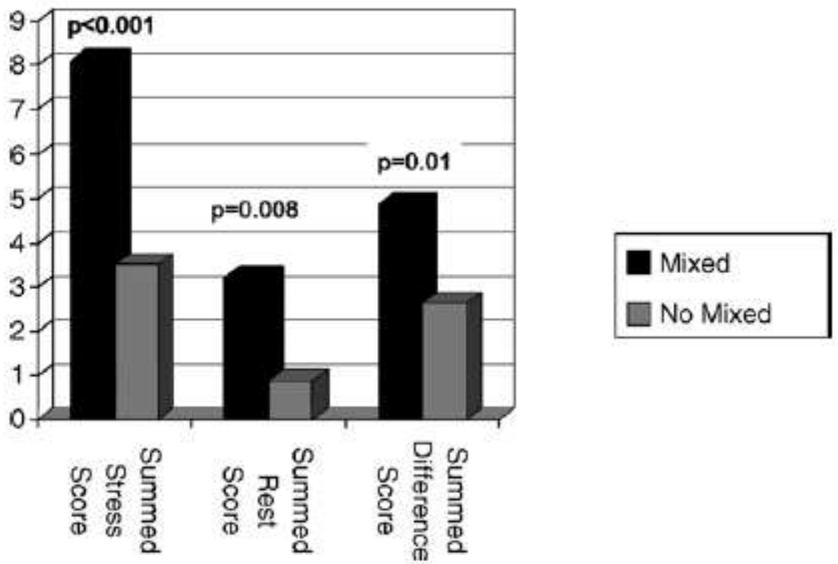


J Am Coll Cardiol 2007;50:1161–70

Multidetector computed tomography coronary artery plaque predictors of stress-induced myocardial ischemia by SPECT

Fay Lin [a], Leslee J. Shaw [b], Daniel S. Berman [b], Tracy Q. Callister [c], Jonathan W. Weinsaft [a], Franklin J. Wong [a], Massimiliano Szulc [a], Vishal Tandon [a], Peter M. Okin [a], Richard B. Devereux [a], James K. Min [a,*]





F. Lin et al. / Atherosclerosis 197 (2008) 700–709

Clinical validity of diagnostic procedures

Cornerstones

- Diagnosis
- Prognosis
- Outcome