

Clinical Results of Transmyocardial Laser Revascularization for Diffuse Coronary Artery Disease

Keith A. Horvath, MD

Associate Professor of Cardiothoracic Surgery

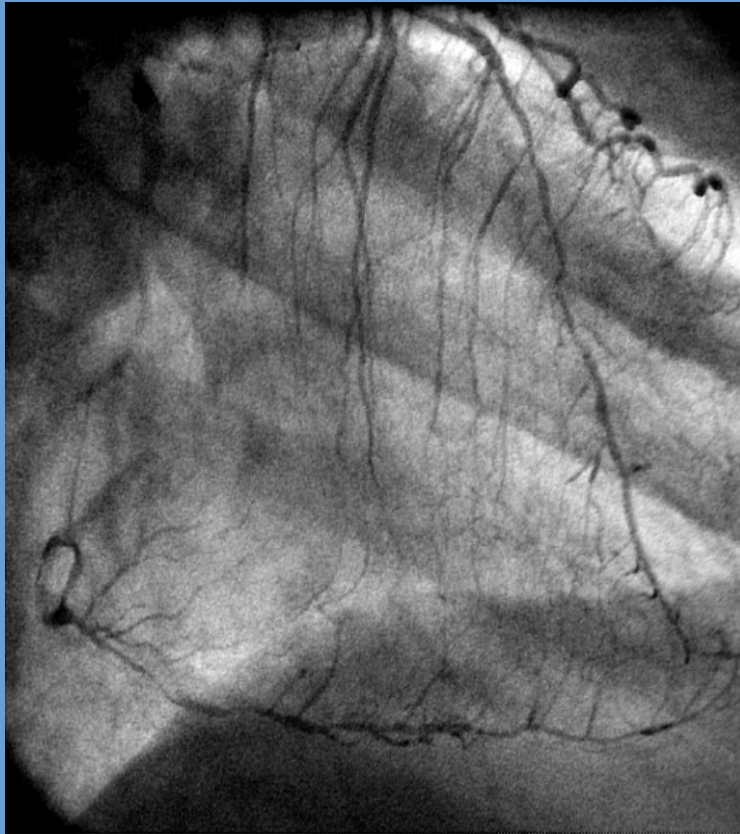
Northwestern University Medical School

Disclosure

- Member, Society of Thoracic Surgeons
 - Workforce on Coding & Nomenclature Committee
 - Workforce on National Databases
- TMR practitioner since 1989
- Consultant to Edwards Lifesciences
- Research funded by:
 - American College of Surgeons
 - American Heart Association
 - National Institute of Health
- Expenses for MCAC hearing: self-pay

Diffuse Coronary Artery Disease

Impact On Surgical Outcomes



When quantified, is a strong independent predictor of operative mortality, particularly in the elderly.

Graham, et al. JTCVS 1999;118:618-27.

Osswald, et al. Eur J Cardiothorac Surg 2001;20:120-26.

Incomplete revascularization due to small or diffusely diseased vessels significantly increases the risk of late cardiac events

Lawrie, et al. Circulation 1982;66:717-23.

Bell, et al. Circulation 1992;86:446-57.

Schaff, et al. Circulation 1983;68:II200-04.

Sole Therapy vs. MM

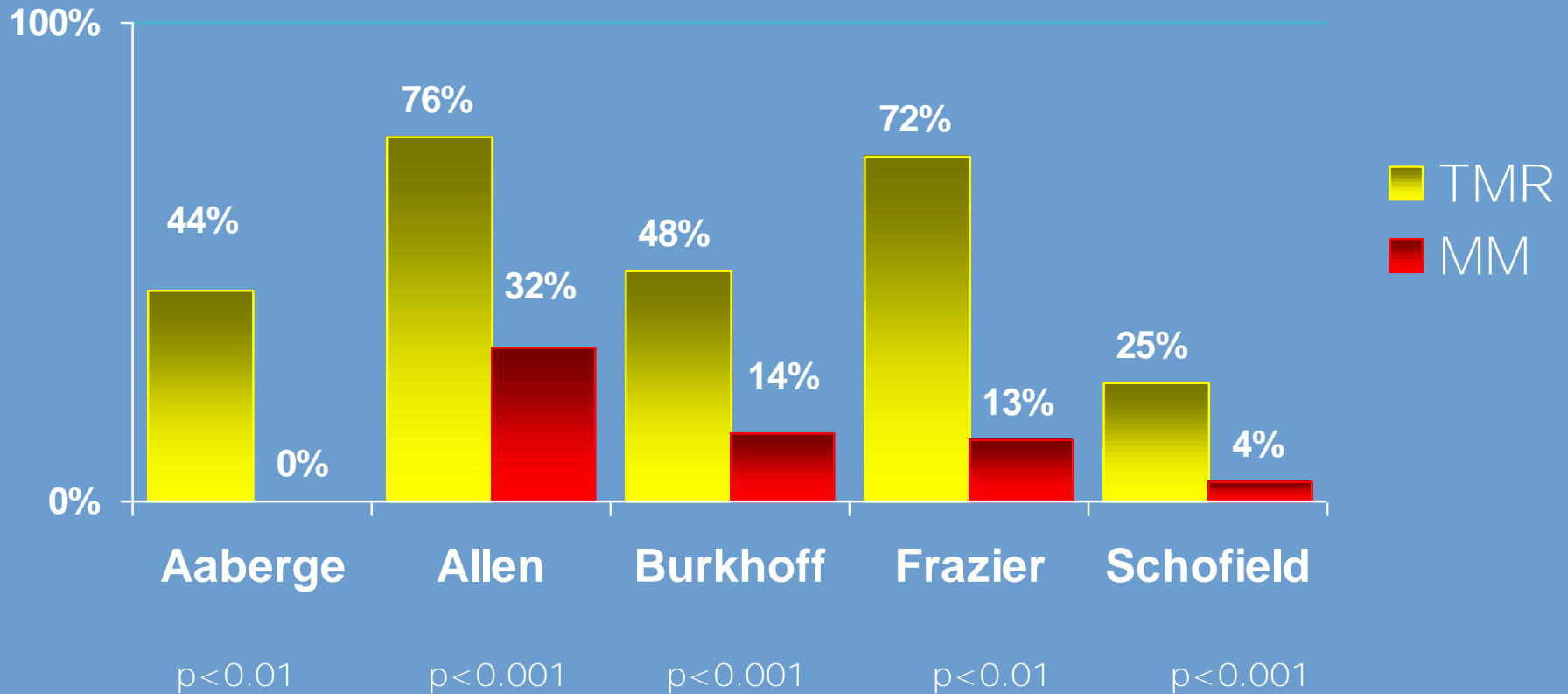
Randomized Controlled Trials

Patient Characteristics

	n	Mean Age	% Class IV	% Unstable angina	% Previous MI	% Previous CABG	% Previous PTCA	% Diabetes	% Heart failure
Aaberge	100	63	29	0	70	85	37	25	--
Allen	275	60	100	0	64	86	47	47	22
Burkhoff	182	64	62	0	70	88	59	35	--
Frazier	192	61	66	11	80	91	50	46	35
Schofield	188	61	27	0	74	93	28	17	8

Total 937

Angina Relief at 12 Months: TMR vs. MM



Meta Analysis for Angina Reduction

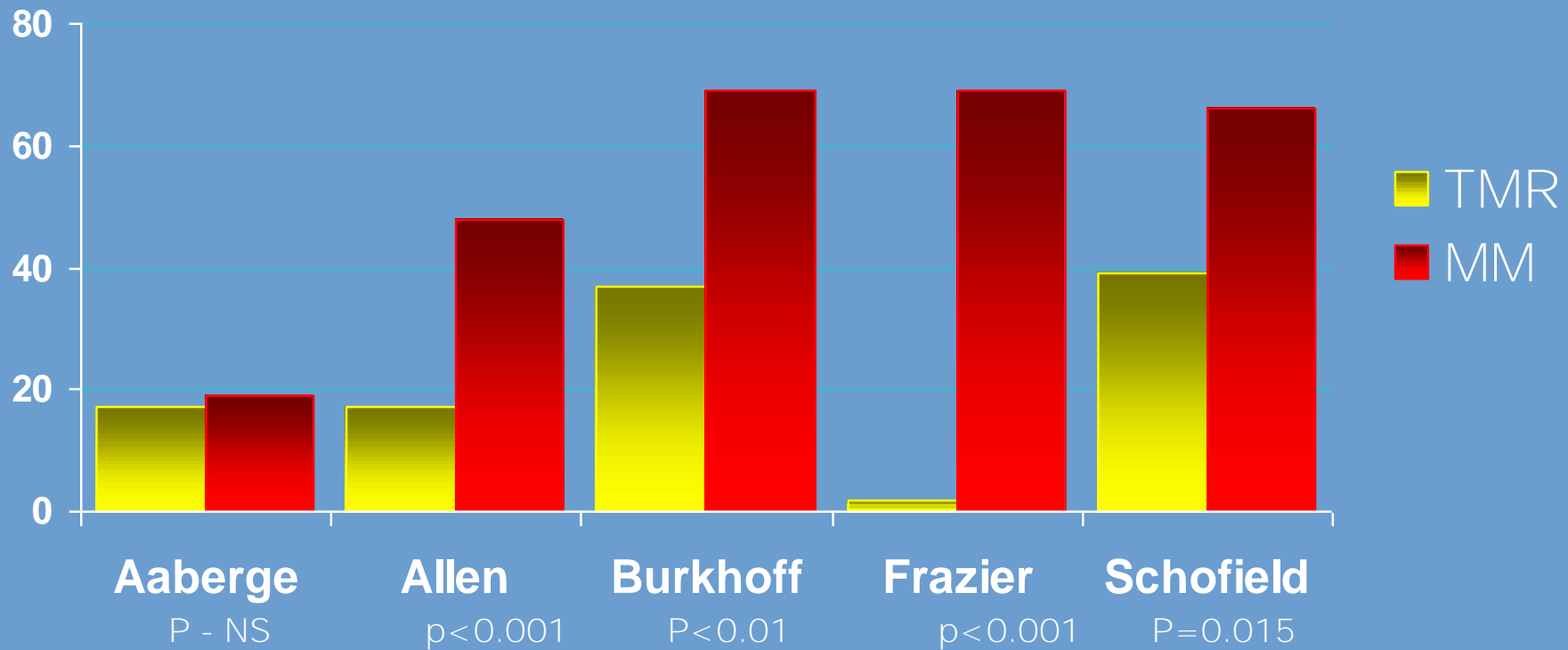
Summary Odds Ratio
9.3

95% CI
4.6 - 18.5

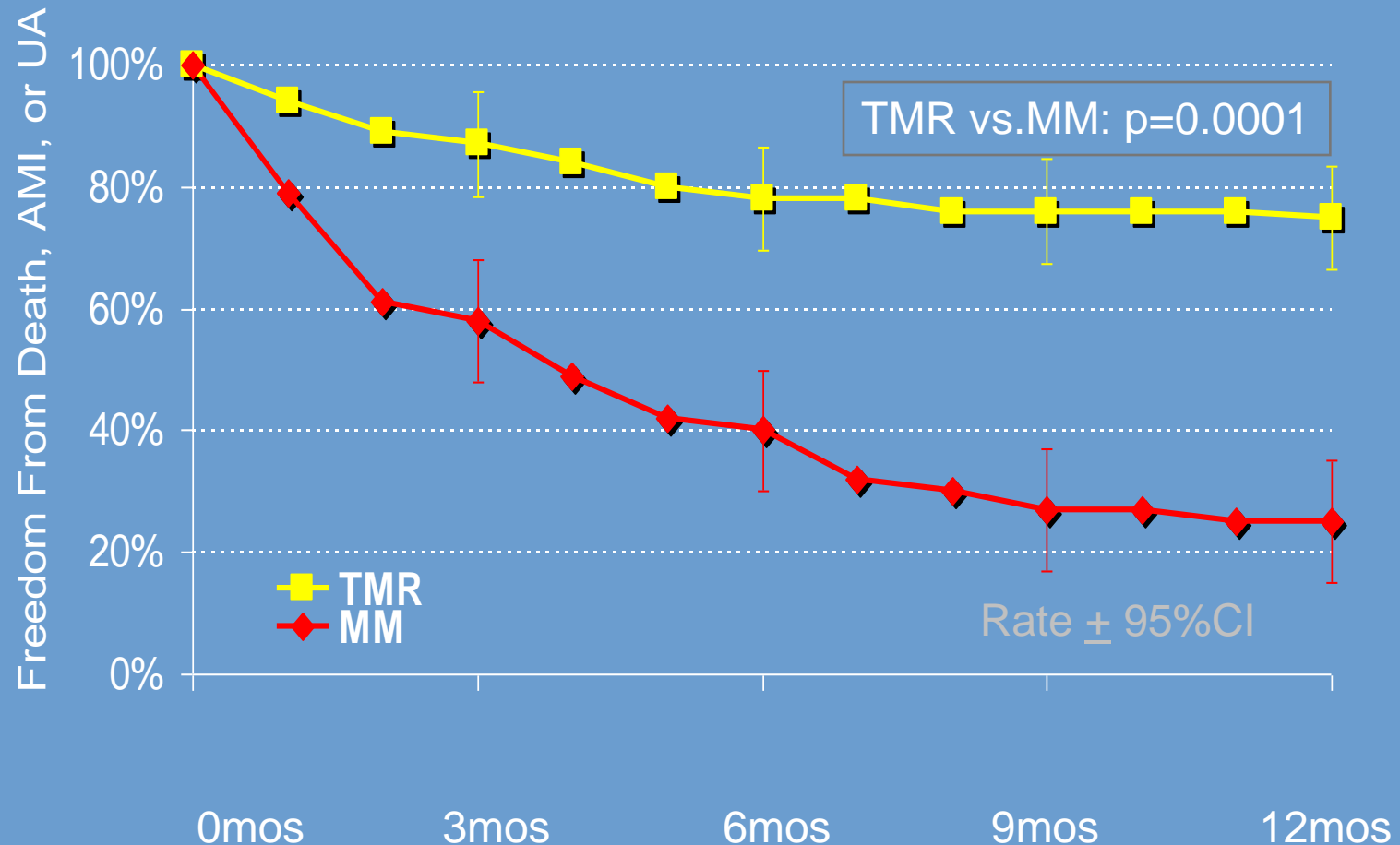
p-value
<0.0000001

Hospitalization Results:

% Patients Readmitted over 12 months



Freedom From Death, MI, or Unstable Angina



Frazier OH, et al. Transmyocardial Laser Revascularization with a CO₂ Laser in Patients with End-Stage Coronary Artery Disease. N Engl J Med 341:1021-8, 1999

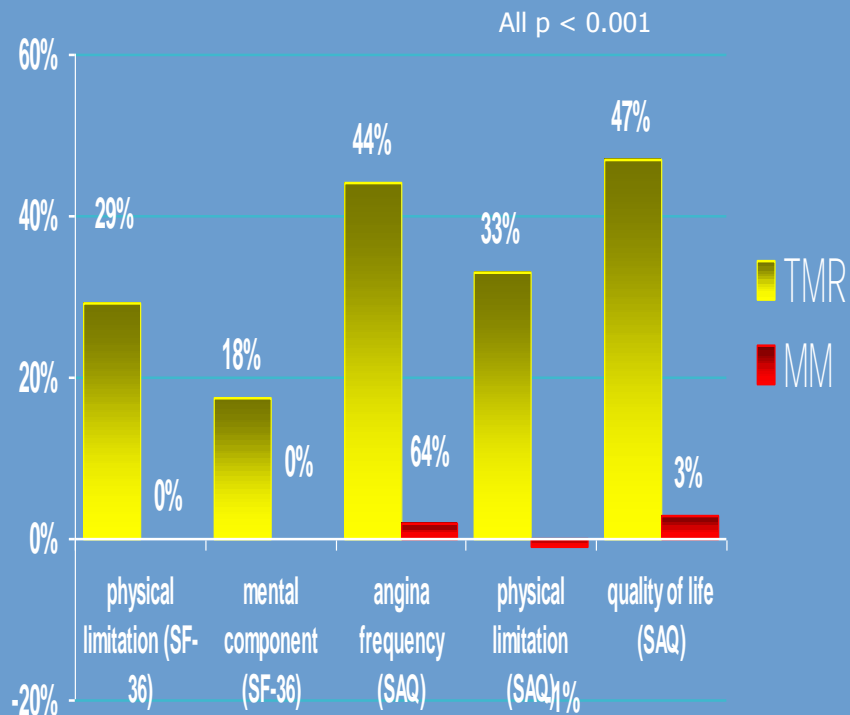
Quality of Life Improvement

- Validated instruments used
 - SF-36
 - Seattle Angina Questionnaire (SAQ)
 - Duke Activity Status Index (DASI)
- Significant improvements in quality of life at 1 year in TMR vs. MM patients
 - Allen ($p=0.003$)
 - Burkhoff ($p<0.001$)
 - Frazier ($p<0.001$)

Quality of Life Measures

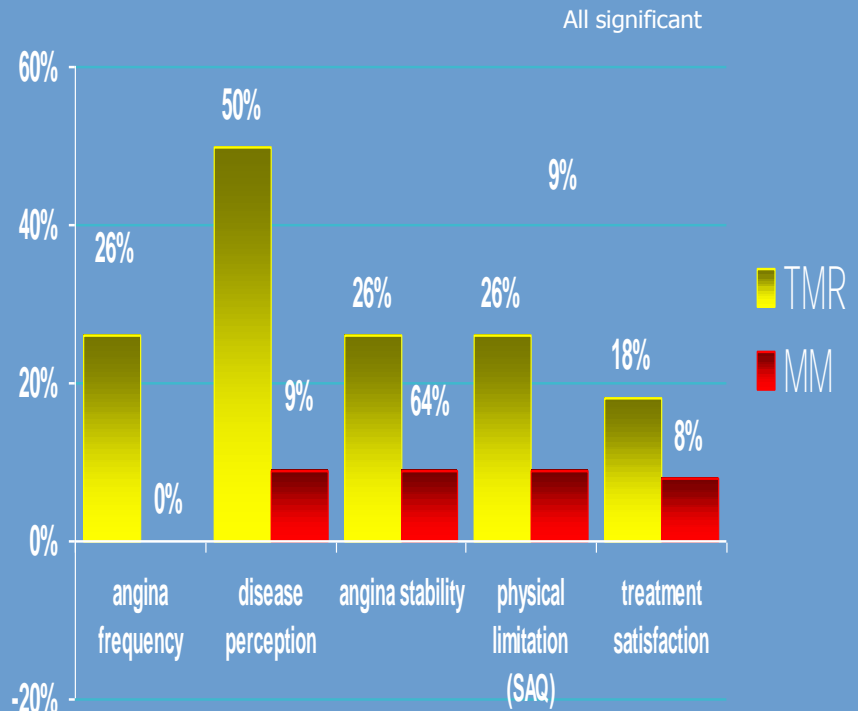
Frazier et. al., 1999

% improvements at 12 months vs. baseline



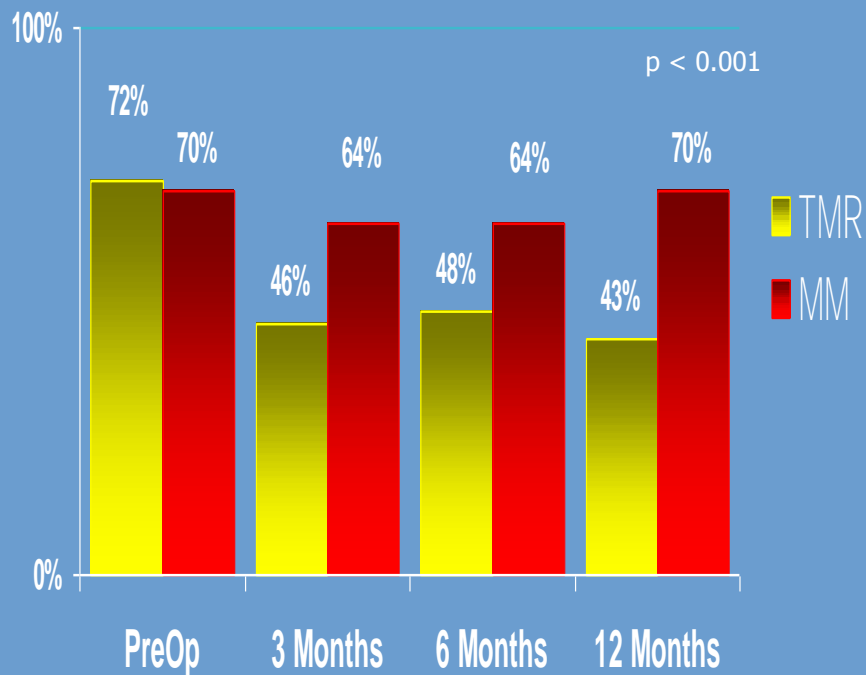
Burkhoff et. al., 1999

% median change at 12 months vs. baseline

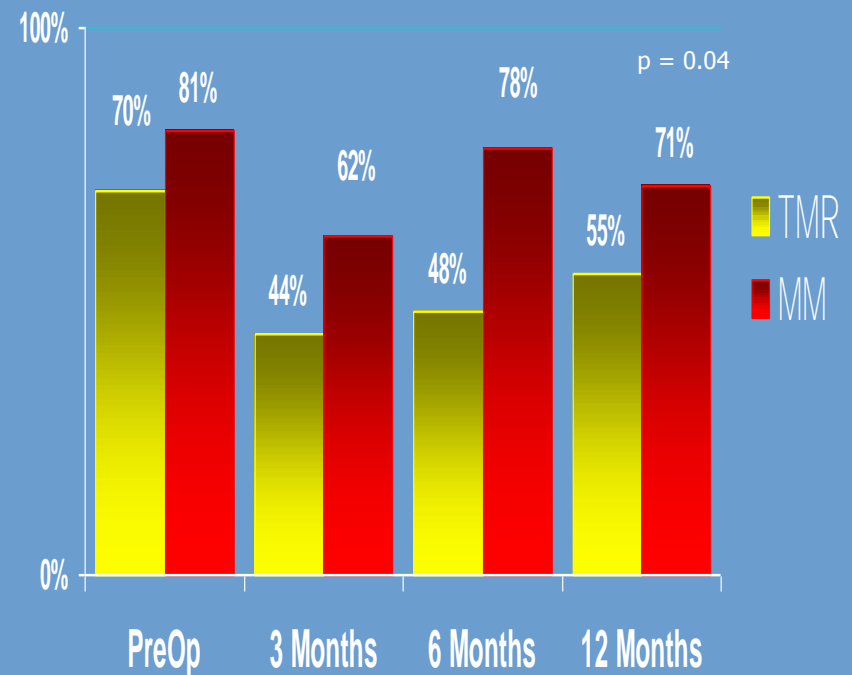


Improvement in Exercise Tolerance

Angina on treadmill %

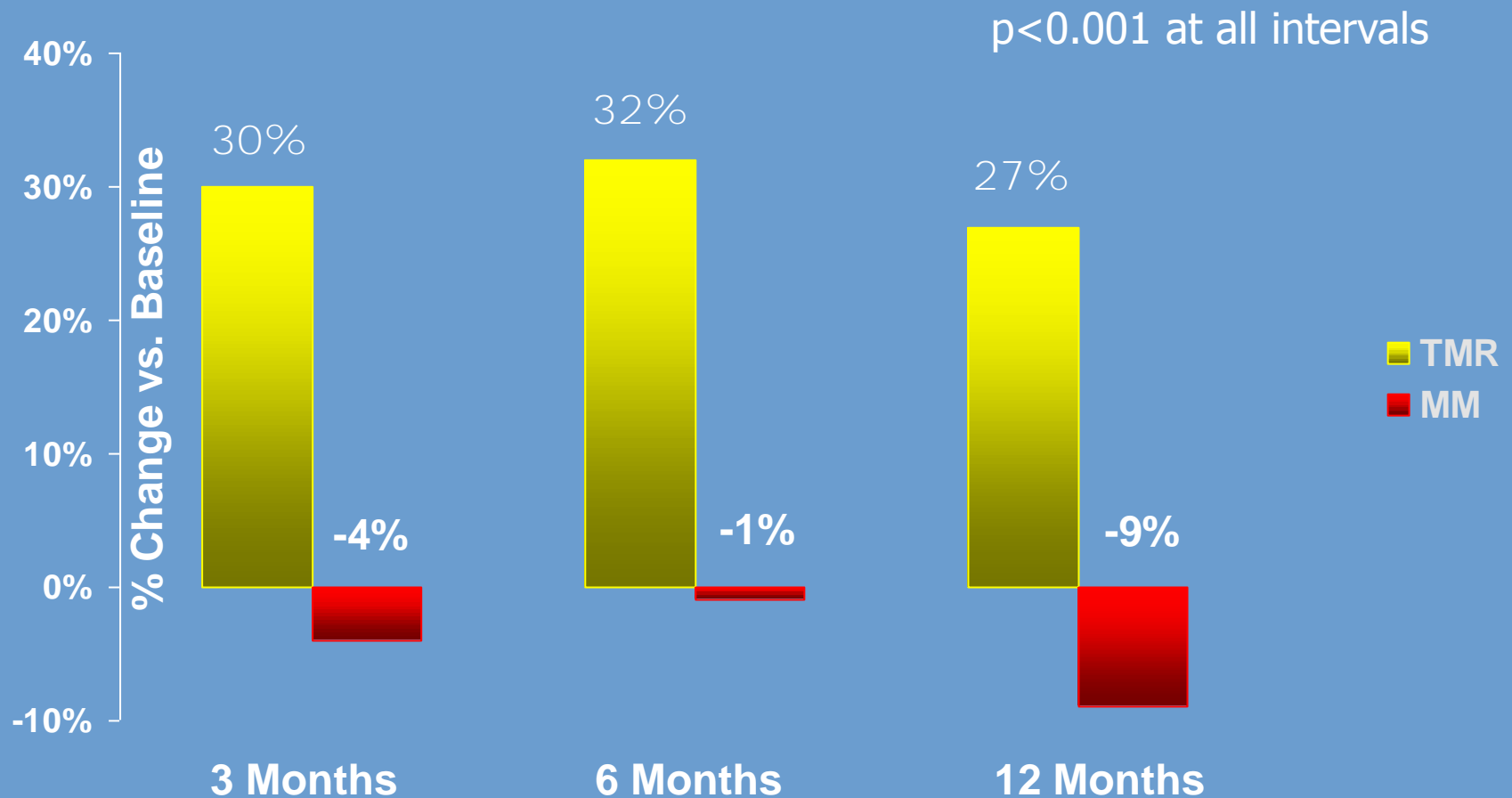


Angina during a 12 minute walk



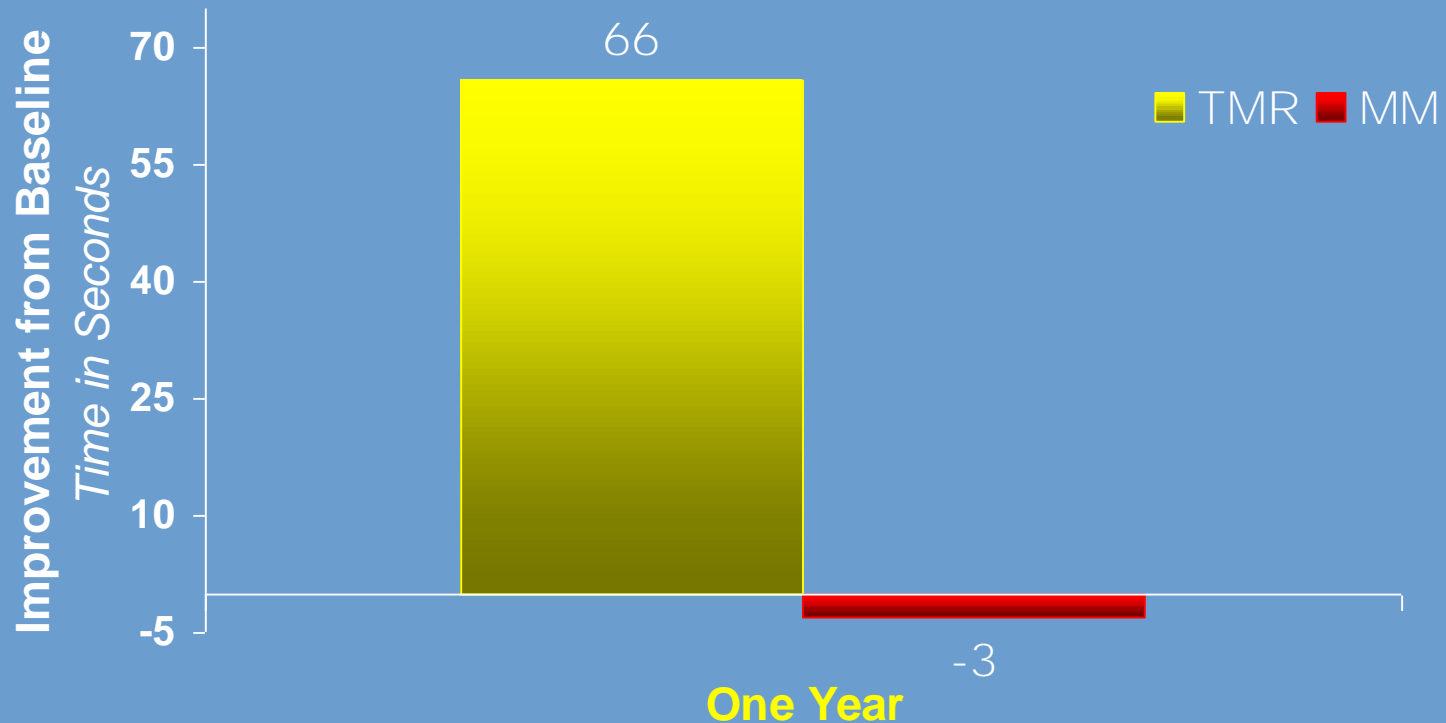
Schofield PM, et al. Transmyocardial Laser Revascularization in Patients with Refractory Angina Lancet 353:519-24, 1999

Improvement in Exercise Tolerance



Burkhoff et al, Transmyocardial Laser Revascularization Compared with Continued Medical Therapy for Treatment of Refractory Angina Pectoris: a Prospective Randomised Trial. ATLANTIC Trial. Lancet 1999; 354:885-890

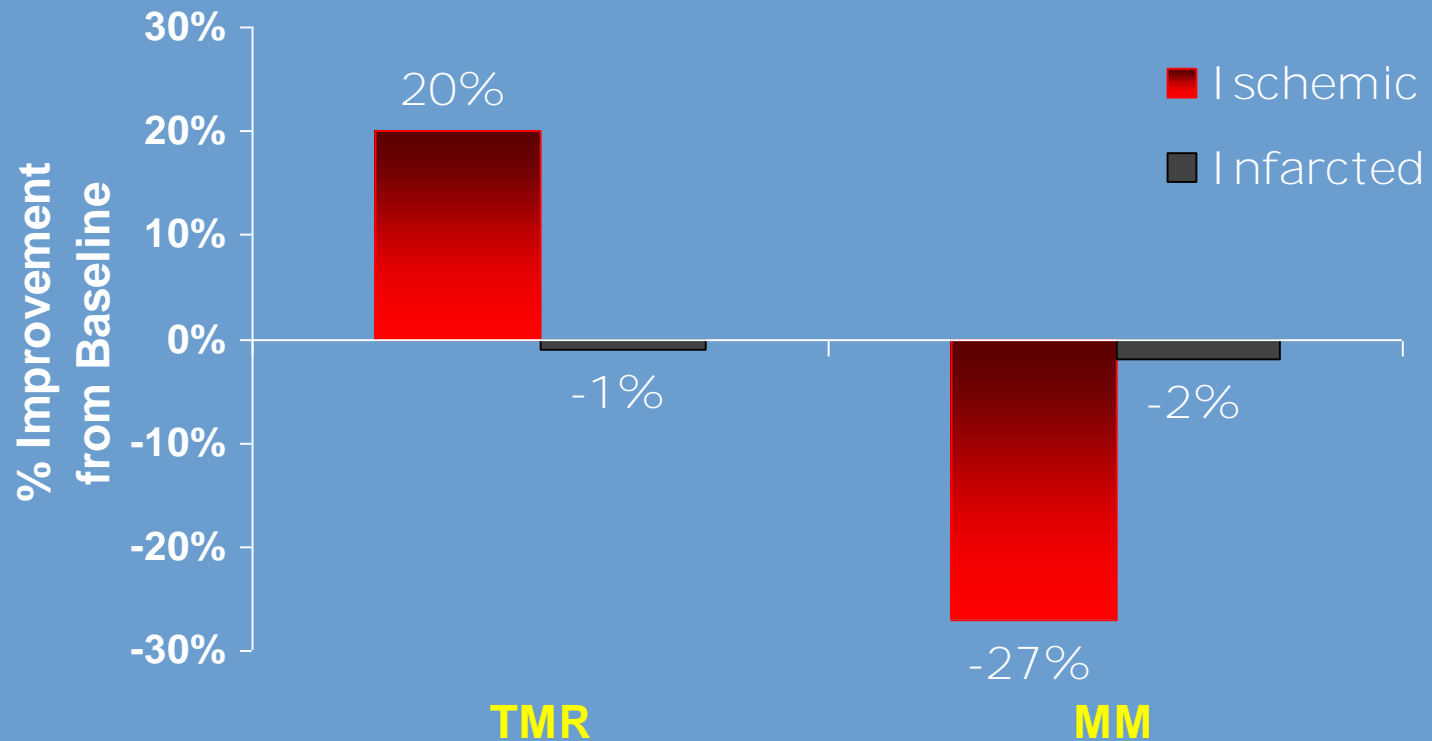
Improvement in Exercise Tolerance



Aaberge L, et al. Transmyocardial Revascularization with CO₂ Laser in Patients with Refractory Angina Pectoris, JACC, 200: 35:1170-7

Improvement in Myocardial Perfusion

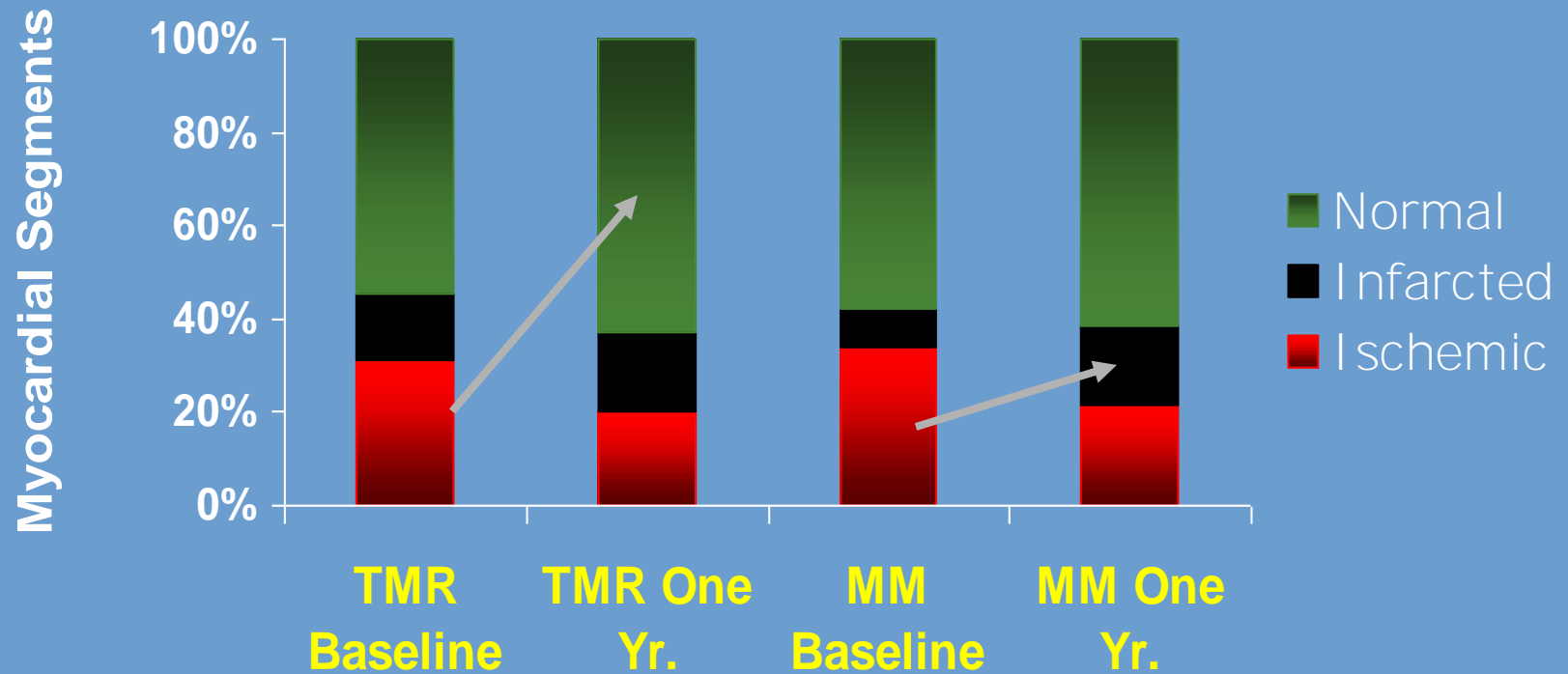
Results at One Year



Frazier OH, et al. Transmyocardial Laser Revascularization with a CO₂ Laser in Patients with End-Stage Coronary Artery Disease. N Engl J Med 341:1021-8, 1999

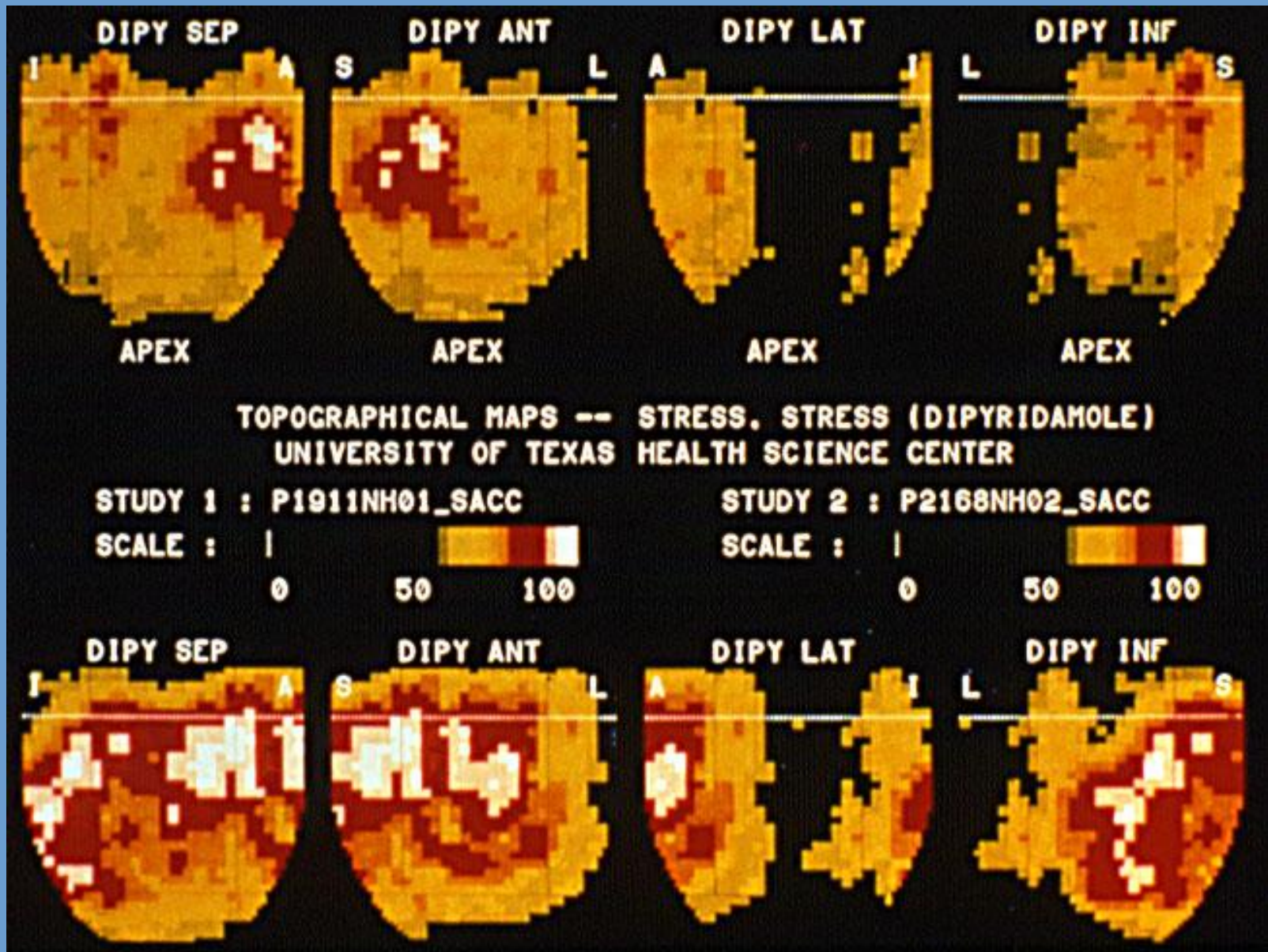
Improvement in Myocardial Perfusion

Results at One Year

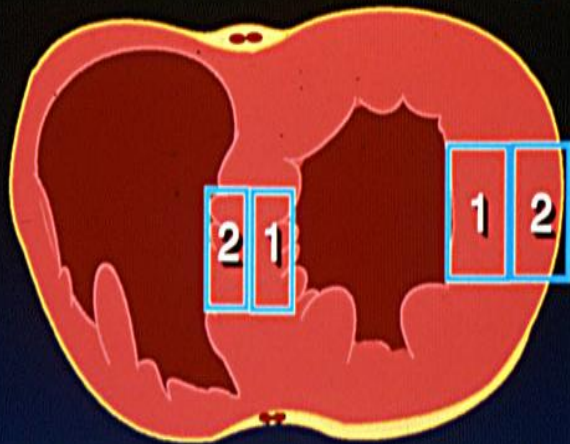


Schofield PM, et al. Transmyocardial Laser Revascularization in Patients with Refractory Angina Lancet 353:519-24, 1999

PET Perfusion Improvement with TMR



PET Improvement with TMR

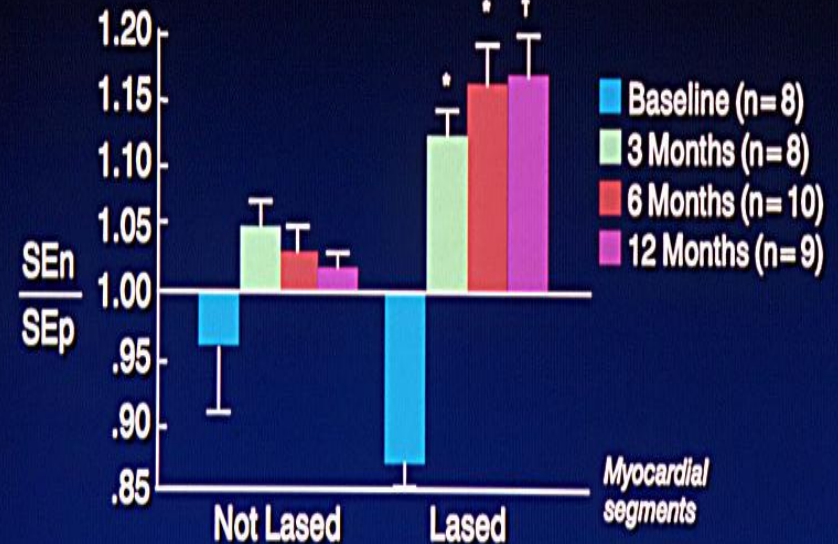


1. Tracer concentration [] measured in myocardial regions of interest

2. Regional perfusion ratios calculated from

$$\frac{SE_n}{SE_p} = \frac{[\text{Region 1}]}{[\text{Region 2}]}$$

Nov '94



SEn: subendocardial perfusion

SEp: subepicardial perfusion

* $p < 0.05$

† $p < 0.001$



$SE_n/SE_p > 1$ suggests sub-endocardial dominant myocardial perfusion

Frazier et al, Circulation 1995, 92 Suppl:1588

Functional Improvement with TMR

Dobutamine Stress Echo Pre & 6 months post CO₂ TMR

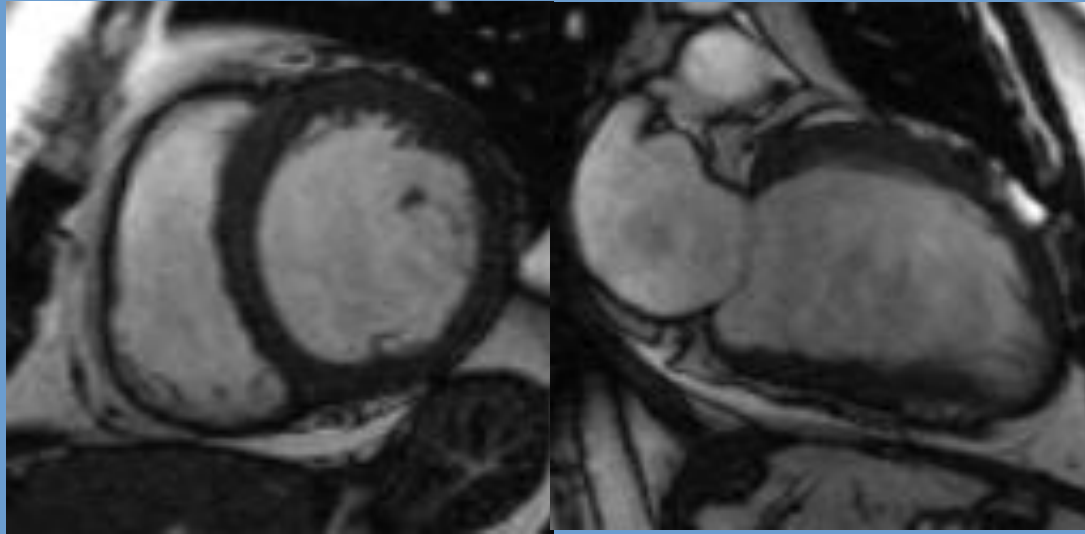
**Improvement in WMSI at rest
WMSI with stress markedly improved
Decrease in % of ischemic segments
No change in % of infarcted segments
Improved stress tolerance**

Donovan et al. Improvement in Inducible Ischemia During Dobutamine Stress

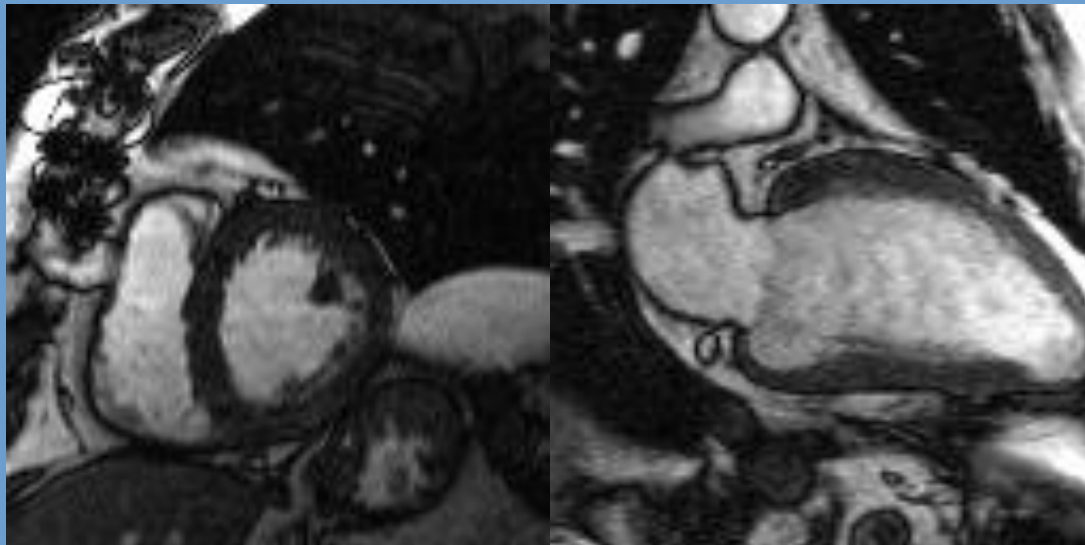
Echocardiography after TMR in Patients with Refractory Angina Pectoris. JACC 1997;30:607

Functional Improvement with TMR

Preop



Postop



Functional Improvement with TMR

Perfusion & Cine MRI

Pre & 8 weeks post CO₂ TMR

No change in number of infarcted segments

No extension of infarctions within segments

Improvement in segmental wall motion

No worsening of wall motion

Angina Class avg 4 pre → 0.6 post

Horvath KA, et al. Contrast Enhanced MRI Assessment of Microinfarction after Transmyocardial Laser Revascularization. Circulation 102:II-765-768, 2000

Long Term Angina Relief

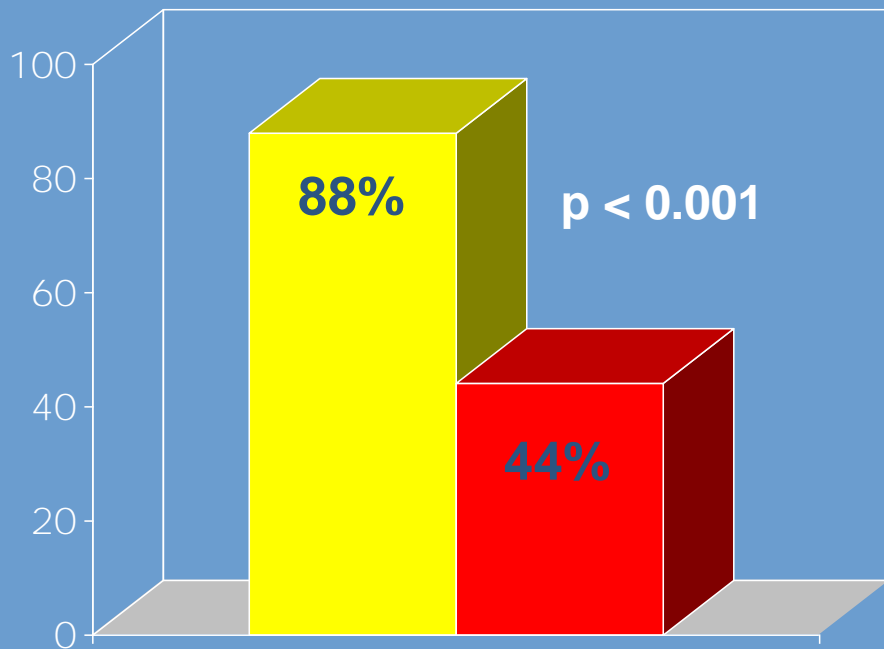
Mean Angina Class



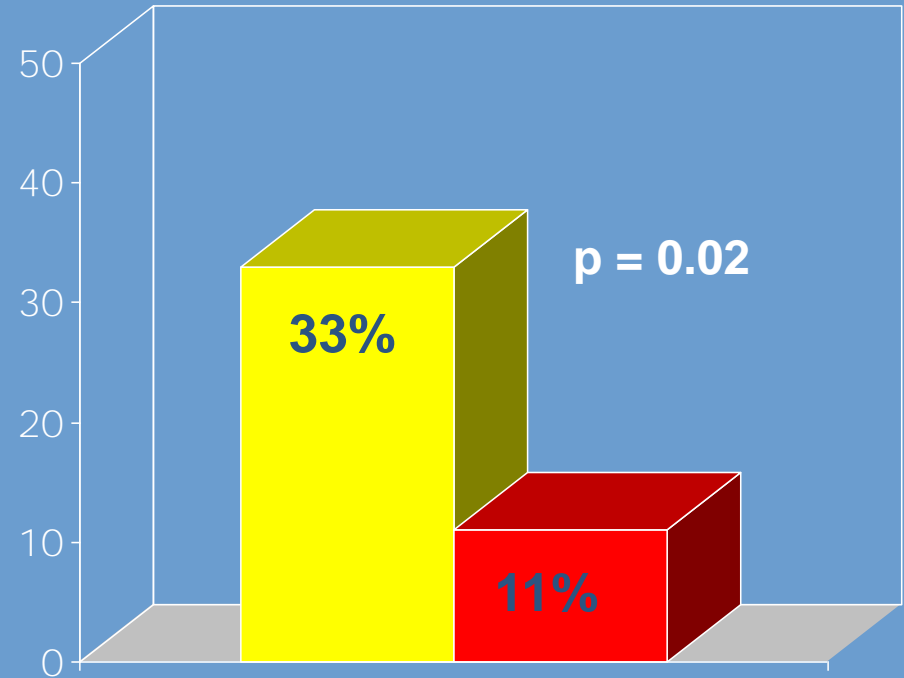
Allen KB, et al. Transmyocardial Revascularization: 5-Year Follow-up of a Prospective Randomized Trial Ann Thorac Surg 2004; 77:1228-34.

Long Term Angina Relief

■ TMR
■ Medical Management



% Patients with 2 Class Improvement

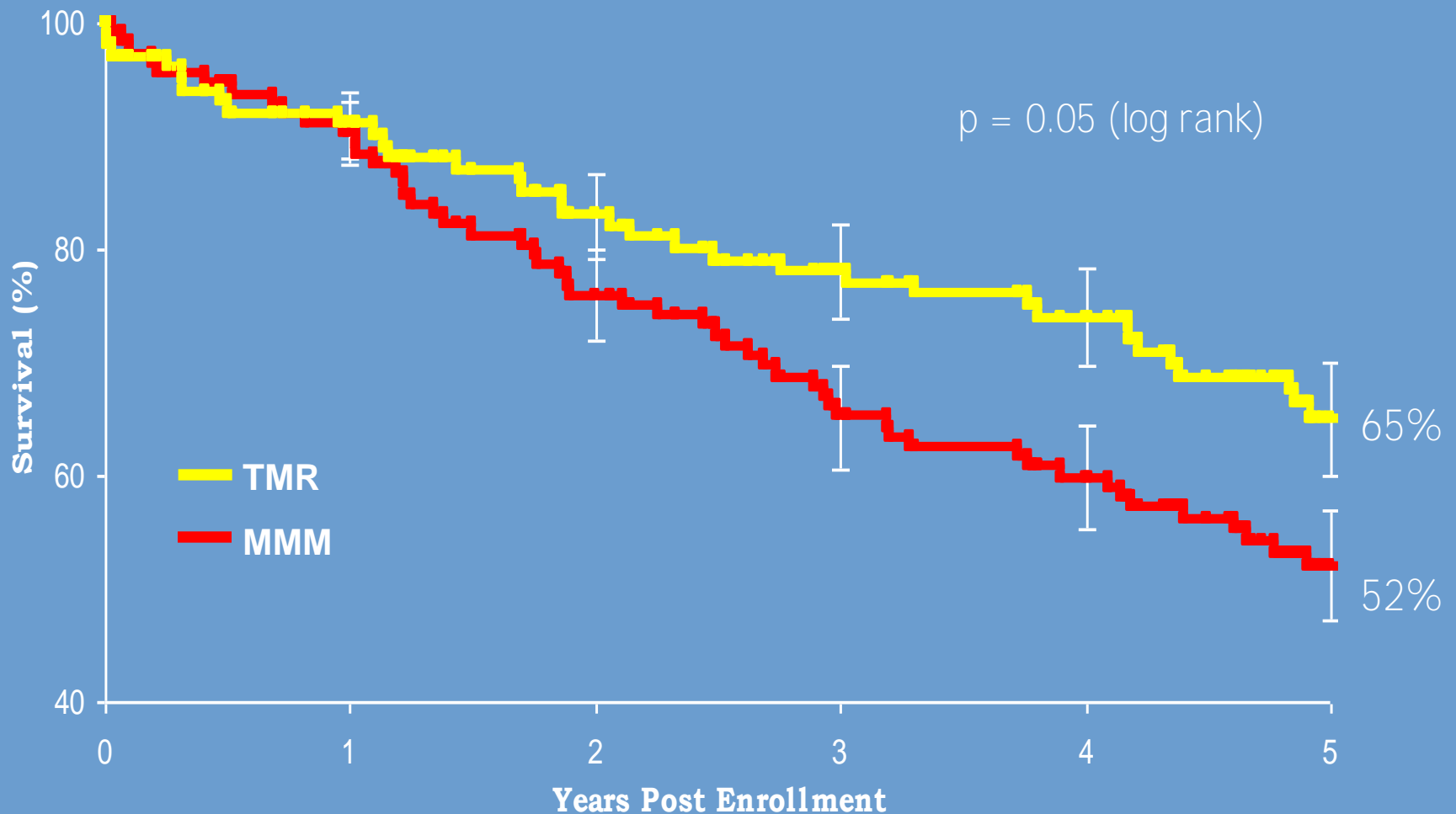


% Patients Angina Free

Allen et al, Transmyocardial Revascularization: 5-Year Follow-up of a Prospective Randomized Trial Ann Thorac Surg 2004; 77:1228-34

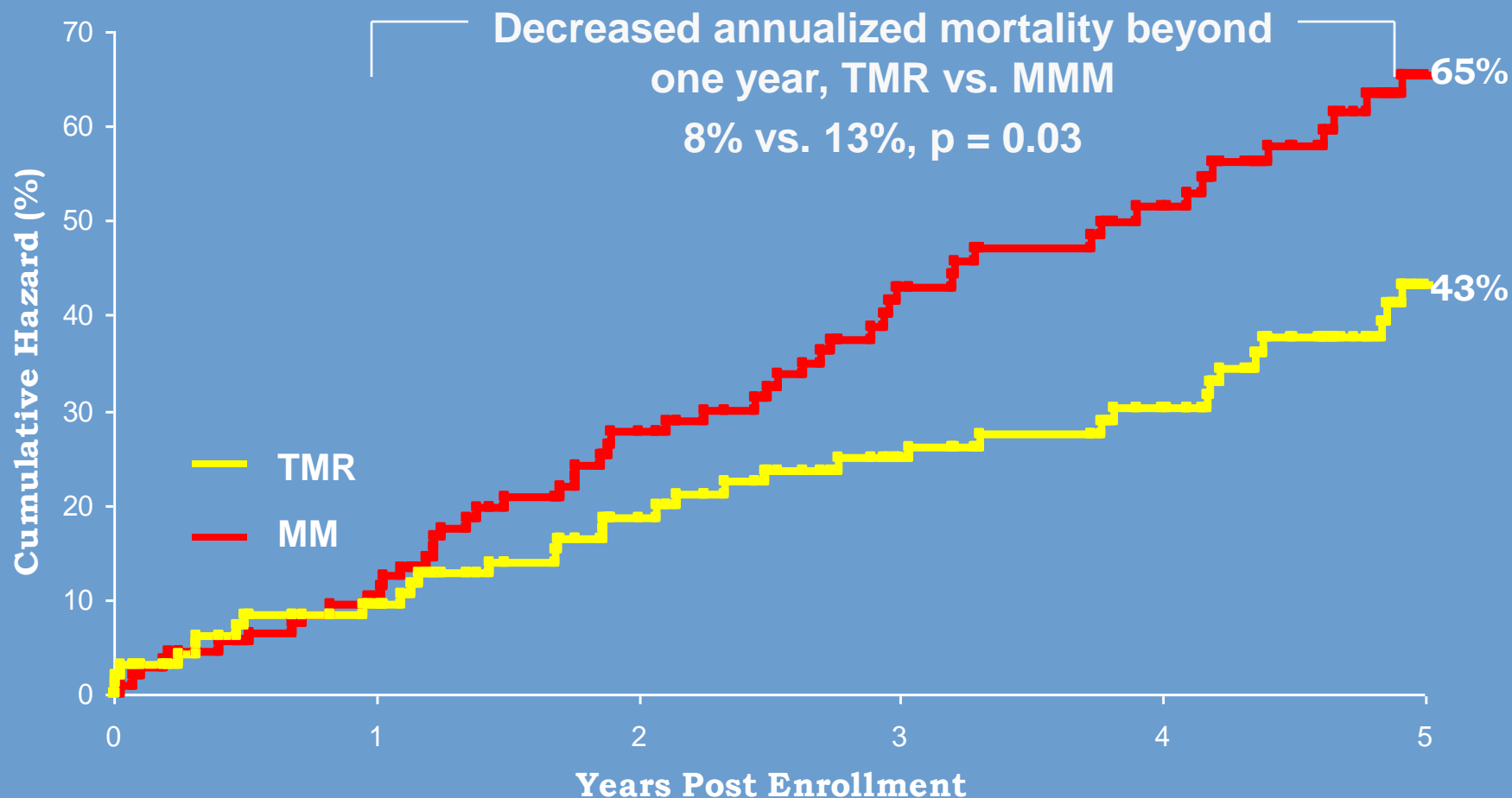
Five-Year Kaplan-Meier Survival

Intent-To-Treat Analysis



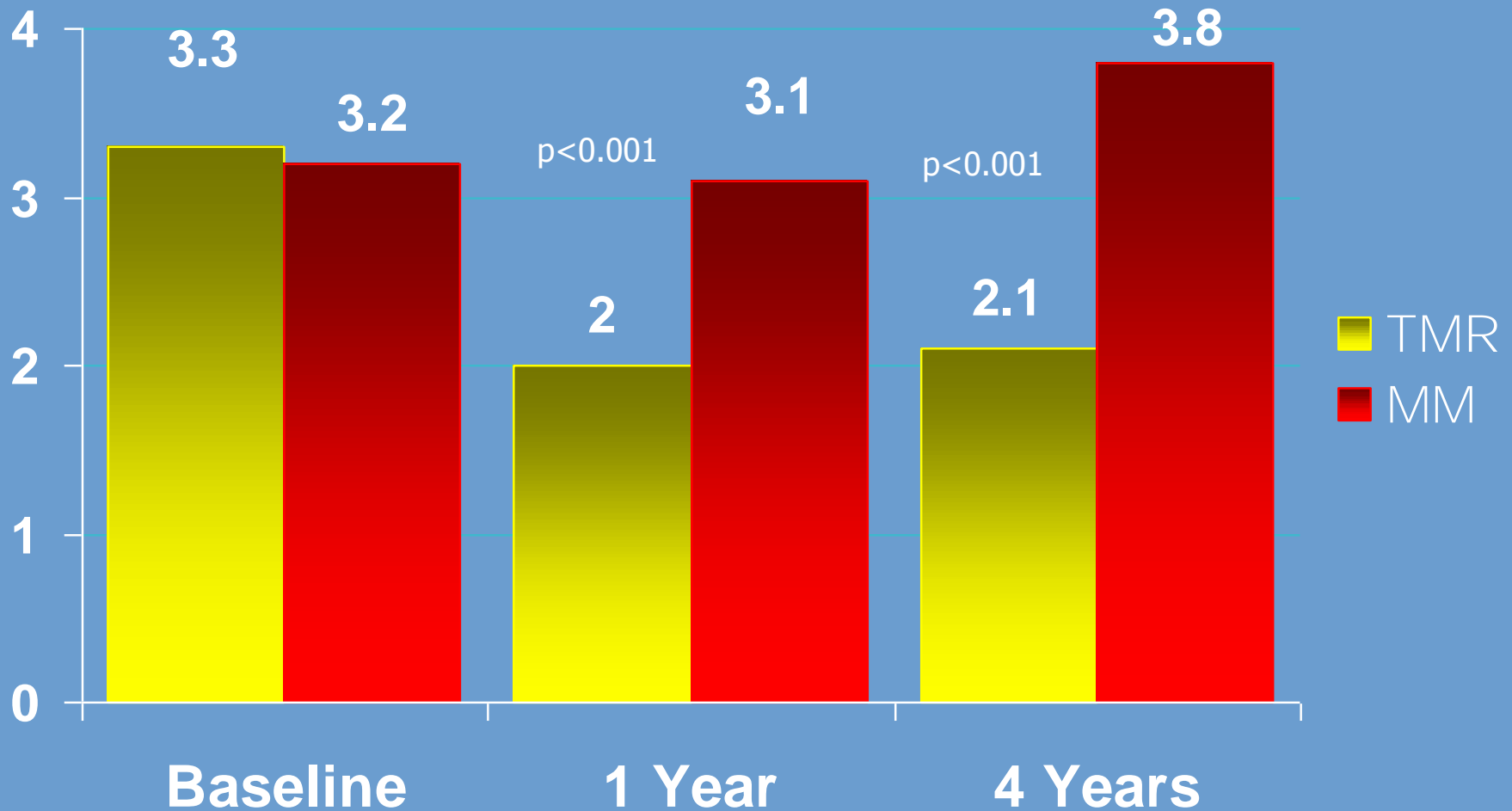
Allen KB, et al. Transmyocardial Revascularization: 5-Year Follow-up of a Prospective Randomized Trial Ann Thorac Surg 2004; 77:1228-34.

Five-Year Cumulative Hazard Analysis



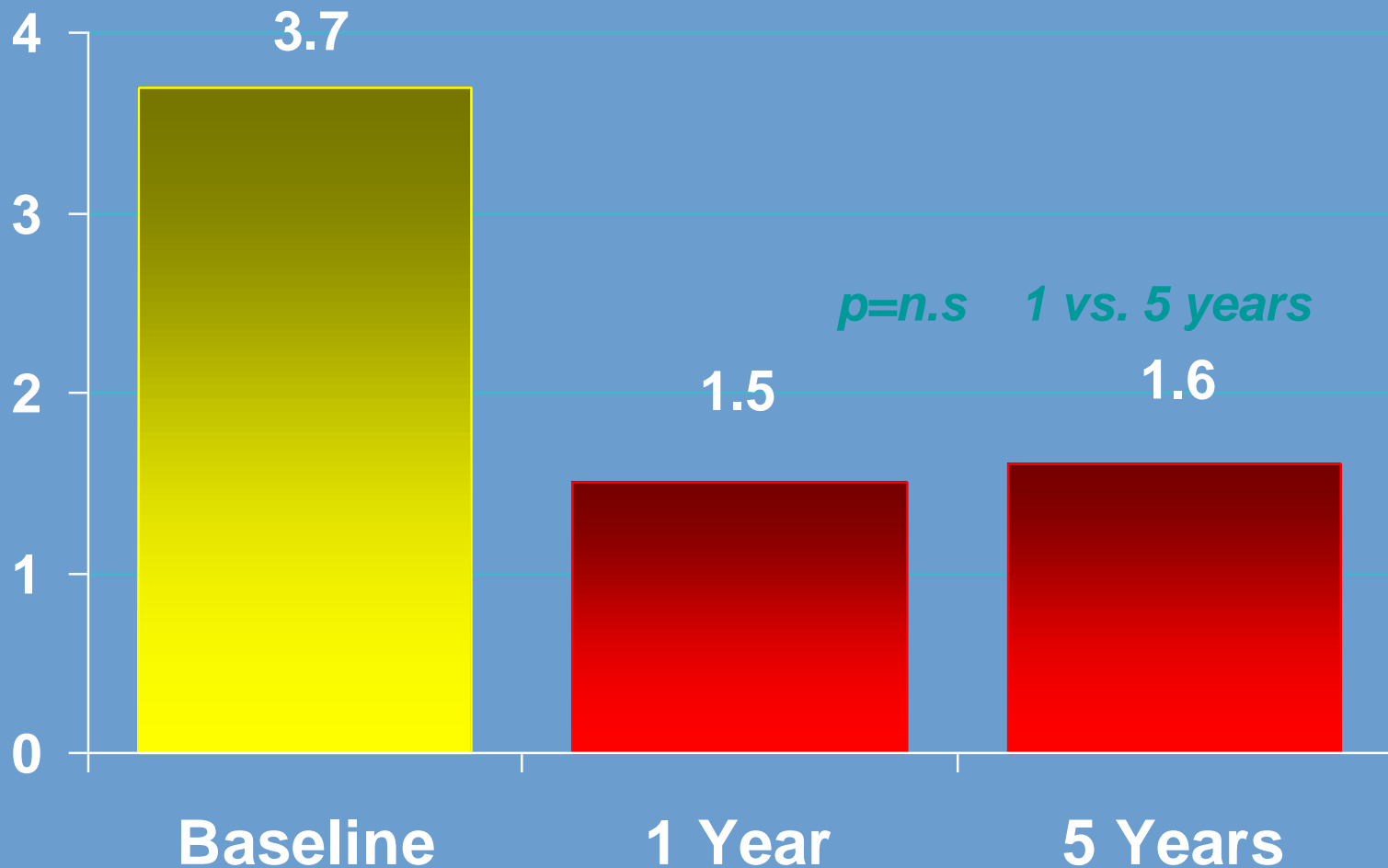
Allen et al, Transmyocardial Revascularization: 5-Year Follow-up of a Prospective Randomized Trial Ann Thorac Surg 2004; 77:1228-34

Long Term Angina Relief



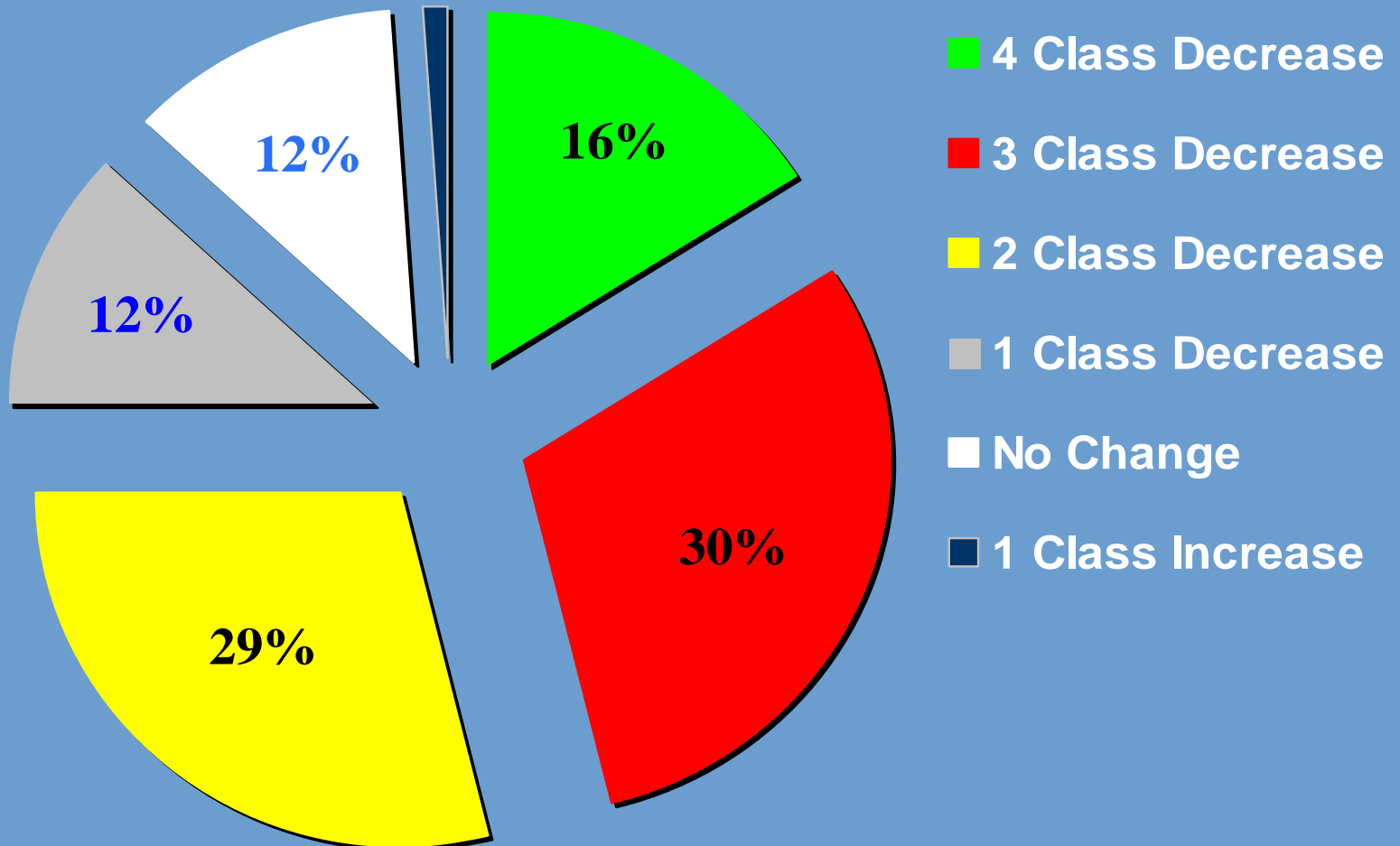
Aaberge L, et al. Continued Symptomatic Improvement 3 to 5 years after TMR with CO2 Laser, JACC, 2002: 39:1588-93

Long Term Angina Relief



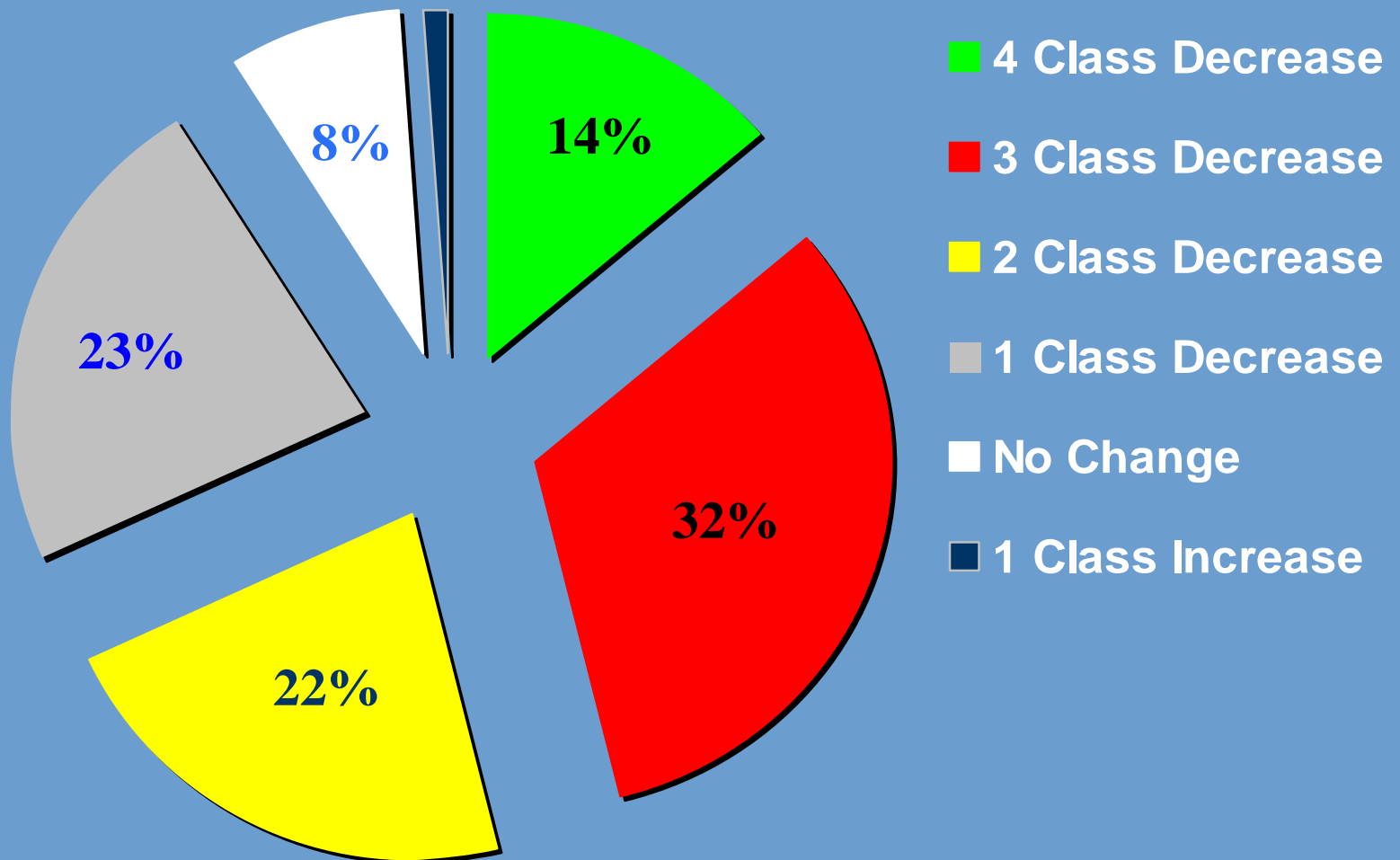
Horvath KA, et al. Sustained Angina Relief 5 Years After Transmyocardial Laser Revascularization with a CO₂ Laser. Circulation 104:I81-84, 2001

Angina Class Change: *From Baseline to 1 year*



Horvath KA, et al. Sustained Angina Relief 5 Years After Transmyocardial Laser
Revascularization with a CO2 Laser. Circulation 104:I81-84, 2001

Angina Class Change: *From Baseline to 5 years*



Horvath KA, et al. Sustained Angina Relief 5 Years After Transmyocardial Laser Revascularization with a CO2 Laser. *Circulation* 104:I81-84, 2001

TMR + CABG v. CABG

Randomized Controlled Trials

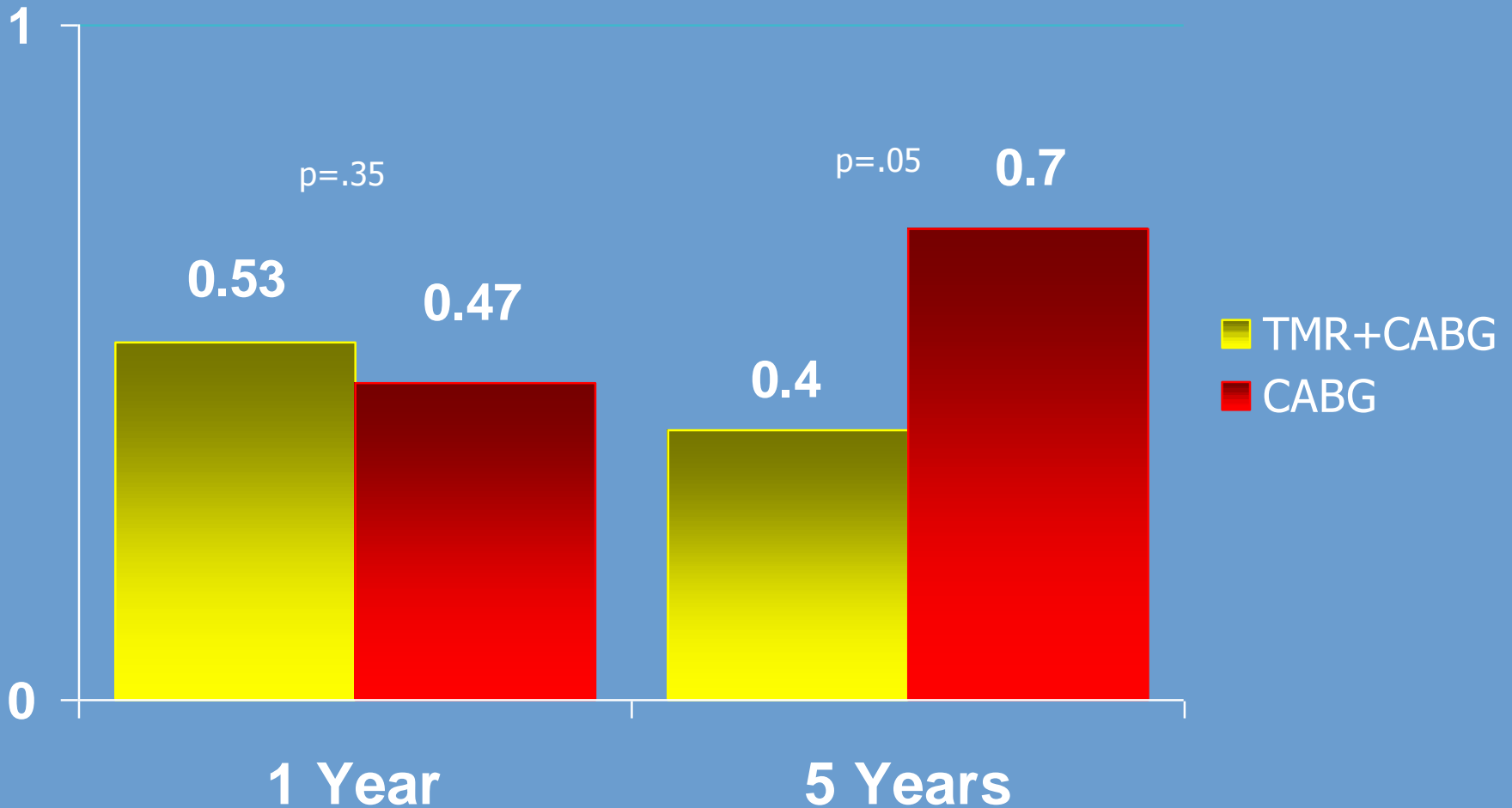
Patient Characteristics

	n	Mean Age	Mean Angina Class	% Unstable angina	% Previous MI	% Previous CABG	% Previous PTCA	% Diabetes	% Heart failure
Allen	263	64	2.8	--	45	20	--	44	0
Frazier	44	63	3.5	59	57	43	49	61	36

1. Allen et. al., TMR Combined with CABG: A Multicenter, Blinded, Prospective, Randomized, Controlled Trial. J Thorac Cardiovasc Surg 2000; 119:540-549
2. Frazier et. al., TMR as an Adjunct to CABG: A Randomized, Multicenter Study with 4 year Follow-up. Tex Heart Inst J, 2004 in press

Long Term Angina Relief

TMR+CABG v. CABG

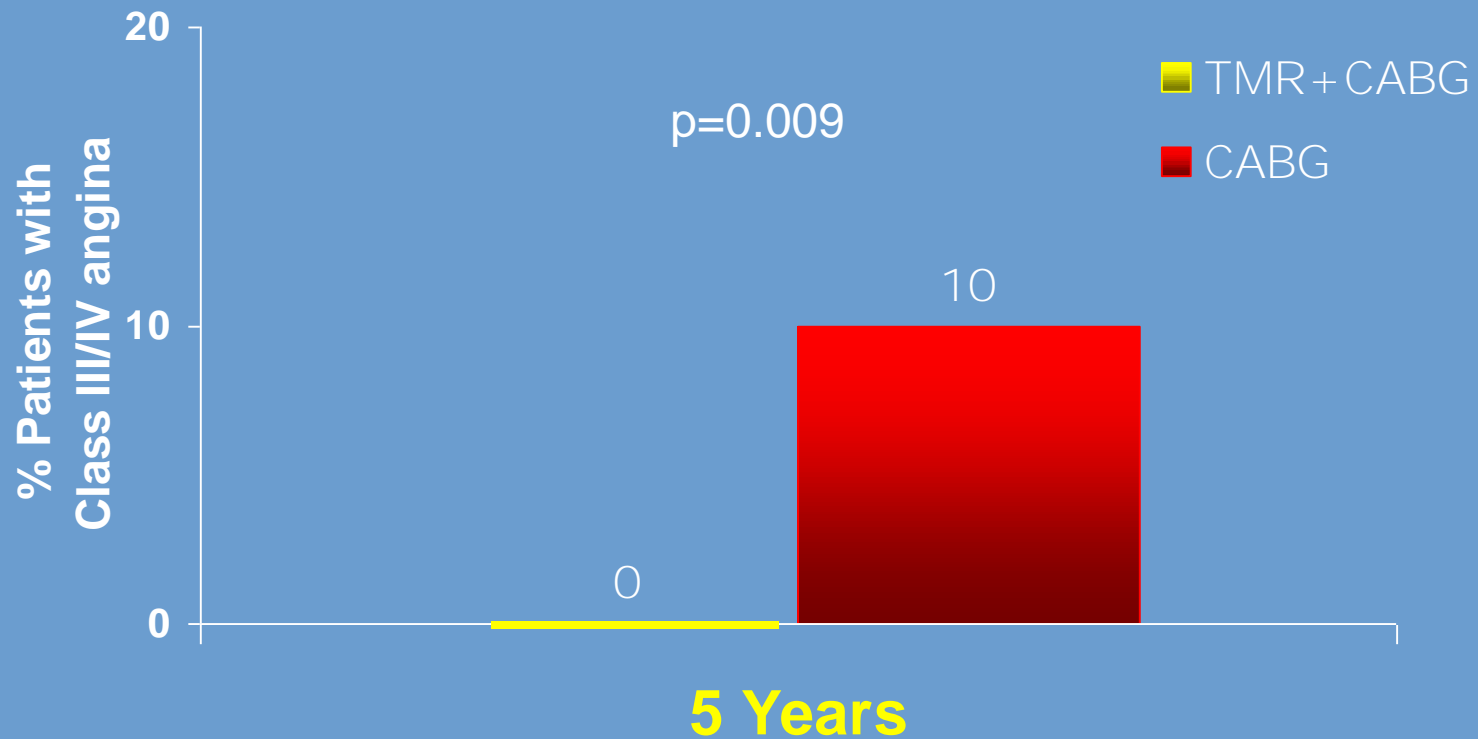


Allen K, et al. Adjunctive Transmyocardial Revascularization: 5 Year Follow-up of a Prospective Randomized Trial. Ann Thorac Surg, 2004 (in press)

Long Term Angina Relief

TMR+CABG v. CABG

% Patients with Class III/IV angina

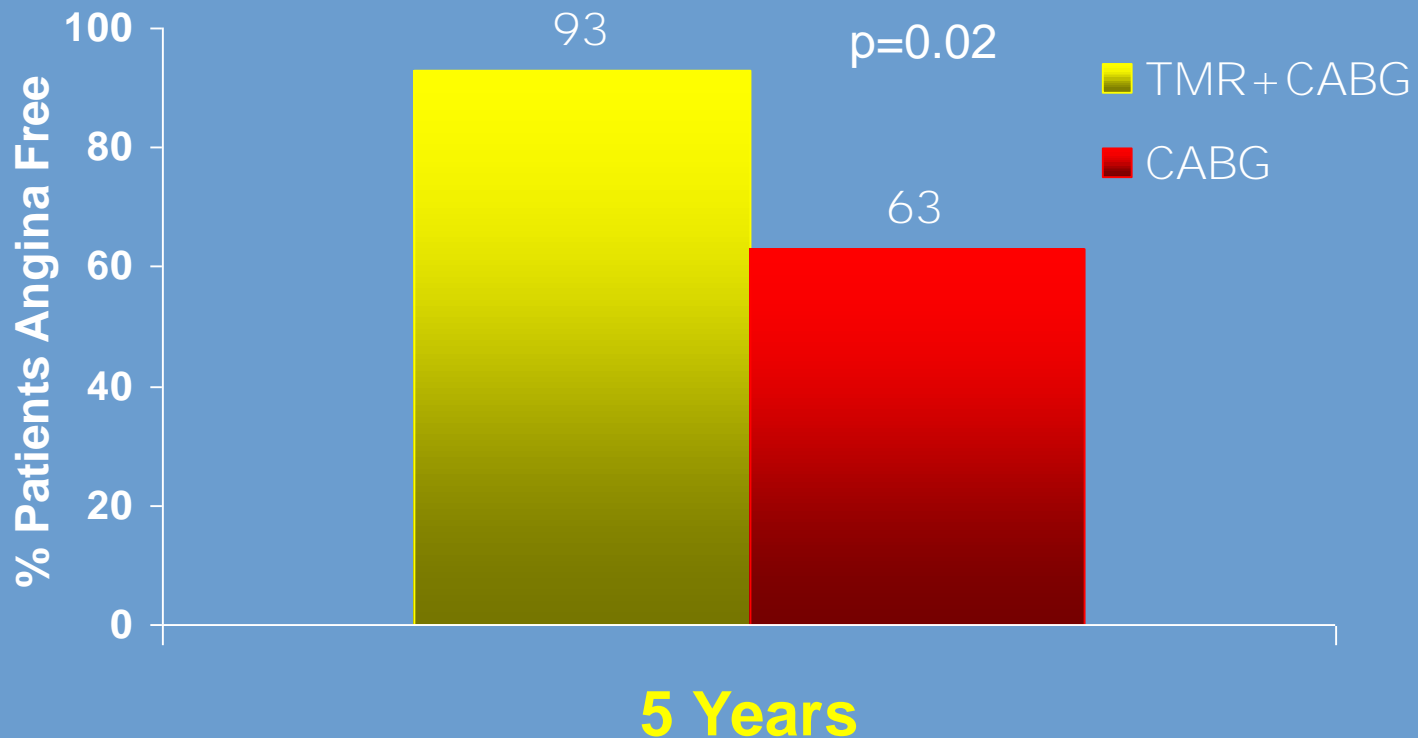


Allen K, et al. Adjunctive Transmyocardial Revascularization: 5 Year Follow-up of a Prospective Randomized Trial. Ann Thorac Surg, 2004 (in press)

Long Term Angina Relief

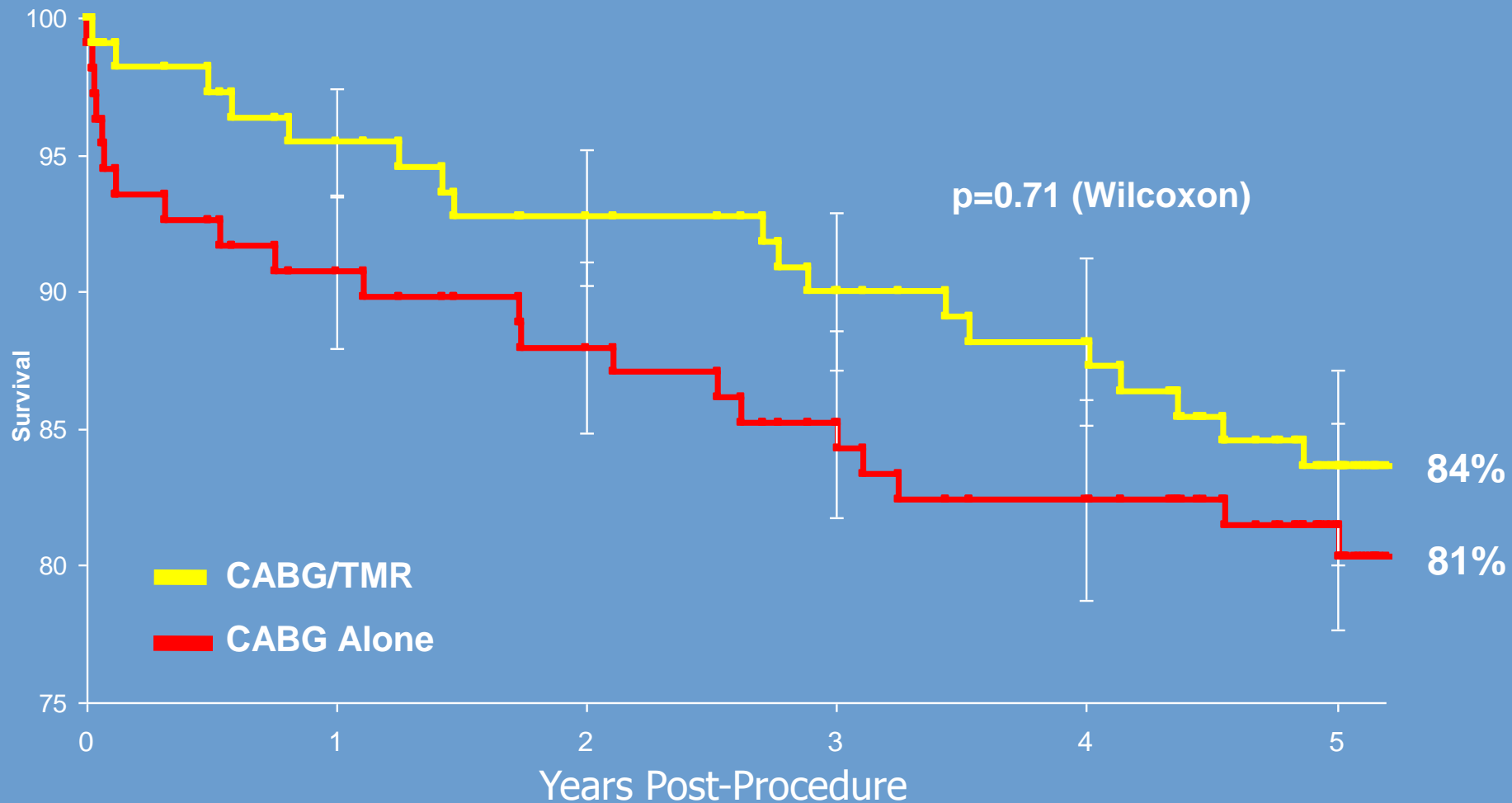
TMR+CABG v. CABG

% Diabetics Angina Free



Allen K, et al. Adjunctive Transmyocardial Revascularization: 5 Year Follow-up of a Prospective Randomized Trial. Ann Thorac Surg, 2004 (in press)

Five-Year Kaplan-Meier Survival

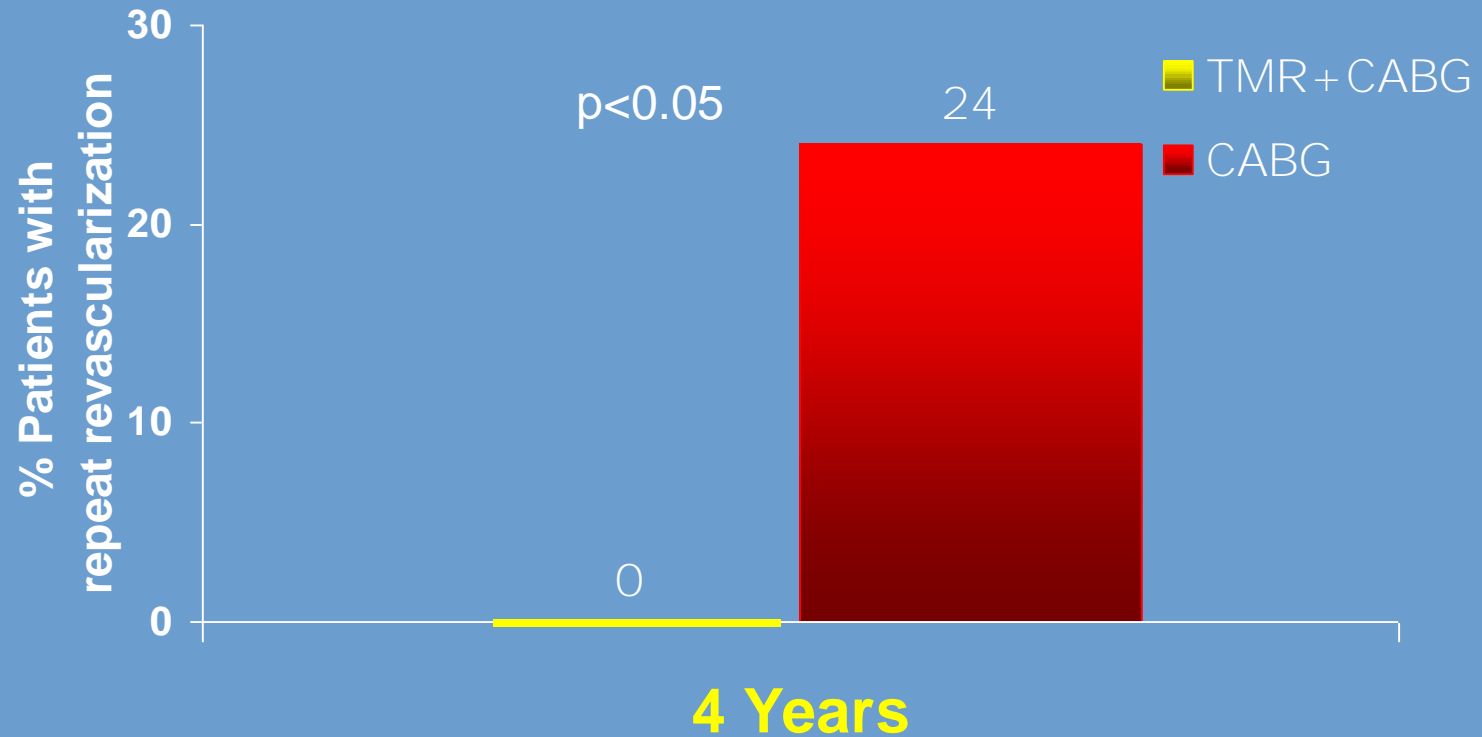


Allen K, et al. Adjunctive Transmyocardial Revascularization: 5 Year Follow-up of a Prospective Randomized Trial. Ann Thorac Surg, 2004 (in press)

Long Term Angina Relief

TMR+CABG v. CABG

% Patients with repeat revascularization

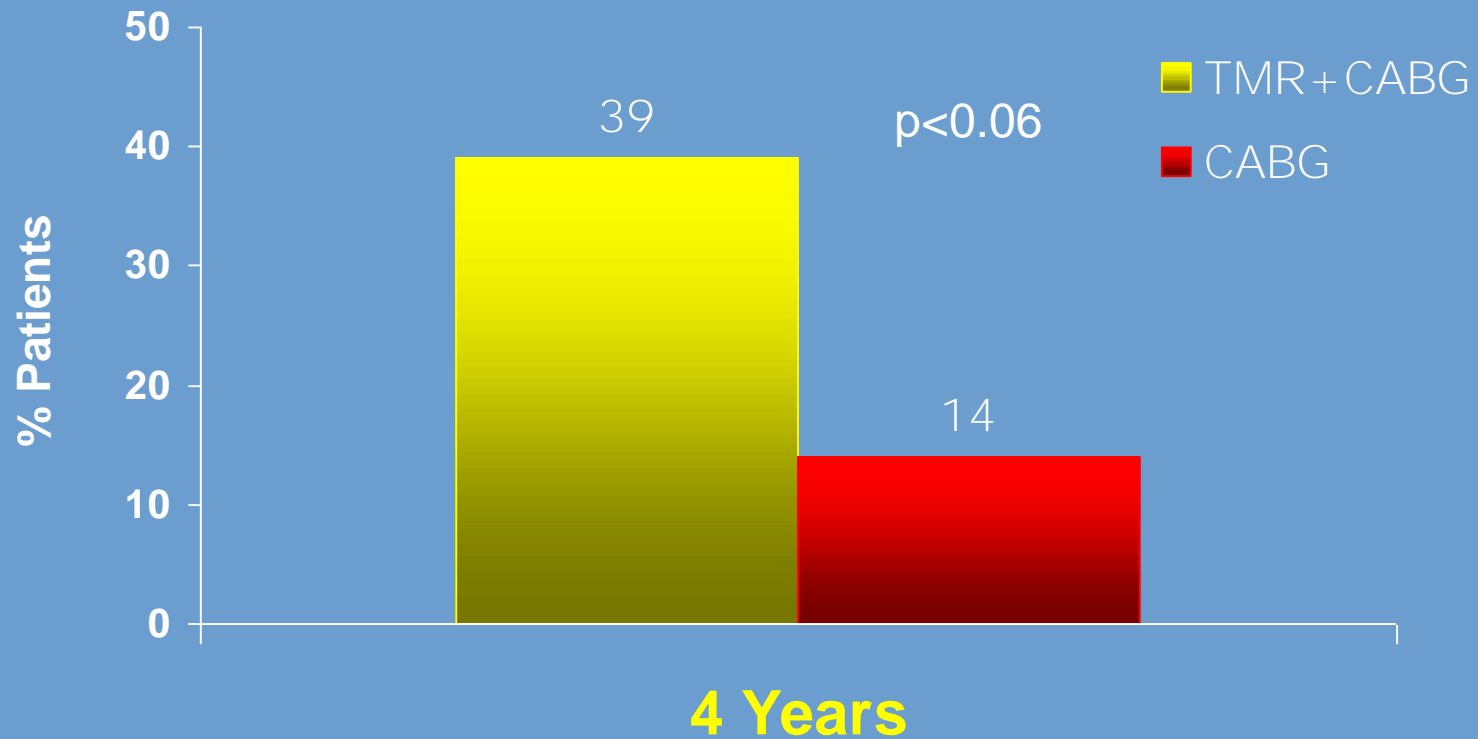


Frazier, et al. Transmyocardial Laser Revascularization as an Adjunct to CABG: A Randomized Multicenter Study with 4 yr. Follow-up. Journal THI, 2004 (in press)

Long Term Angina Relief

TMR+CABG v. CABG

*Event-Free Survival**



**Freedom from Death, Repeat Revascularization, Recurrent Angina*

Frazier, et al. Transmyocardial Laser Revascularization as an Adjunct to CABG: A Randomized Multicenter Study with 4 yr. Follow-up. Journal THI, 2004 (in press)

Demographically “Case-Matched” Patients

Same Predicted Risk



\neq



CABG x 2
Normal Targets

TMR+CABG x 2
Diffusely Diseased Targets

Comparison of CABG v. TMR+CABG patients *STS Adult Cardiac Database 1998-2003*

- As the TMR+CABG patients had more of the significant preoperative risk factors, predictably the overall raw mortality was higher at **3.8%** (vs. **2.7%** for CABG alone).
- A comparison of patients with three vessel disease but received fewer than three bypass grafts reveals TMR+CABG mortality of 5.2% vs. 4.3% for CABG alone (p=.13).
- Removing unstable angina patients lowered observed mortality for TMR+CABG was decreased to **2.7%** and the O/E ratio was 0.87.

Mortality Facts About Patients with Coronary Artery Disease

30 day mortality:

- for CABG alone : 2.4% *STS Database*
- for TMR plus CABG : 2.6 - 4.2% *Peterson et al Am Coll Cardiol 2003*
- for CABG alone w/unstable angina : 5.8% *Rodriguez et al J Am Coll Cardiol 2001*
- for Re-Op CABG alone : 3-7% *ibid*

One year mortality:

- after CABG alone in diabetics : 10% *Weintraub et al. J Am Coll Cardiol 1998*
- after Re-Op CABG alone : 10-15% *ibid*

Diffuse Disease Patients *from Marks et al., J of Clinical Hypertension 2004*

- One year mortality of patients with microvascular disease : 8%
- One year mortality of the same patients with diabetes : 33%
- "At one year, those with microvascular coronary disease are six times as likely to die as those without"

RCT Summary

	TMR Use	n	Mean follow- up, months	Number of Centers	Angina relief	Improvement in objective measure
<i>Aaberge (2000)</i>	Sole	100	12	1	Yes	Yes
<i>Aaberge (2002)</i>	Sole	100	43	1	Yes	Yes
<i>Allen (1999)</i>	Sole	275	12	18	Yes	Yes
<i>Allen (2004)</i>	Sole	212	60	18	Yes	Yes
<i>Allen (2000)</i>	+ CABG	263	12	24	N/A	Yes
<i>Allen (2004)</i>	+ CABG	218	60	13	Yes	Yes
<i>Burkhoff (1999)</i>	Sole	182	12	16	Yes	Yes
<i>Frazier (1999)</i>	Sole	192	12	12	Yes	Yes
<i>Frazier (2004)</i>	+ CABG	44	48	4	N/A	Yes
<i>Horvath (2001)</i>	Sole	78	60	12	Yes	Yes
<i>Schofield (1999)</i>	Sole	188	12	1	Yes	Yes

Observational Study Summary

	TMR Use	n	Mean follow-up, months	Number of Participating Centers	Significant angina relief, <u>YES</u> or <u>NO</u>	Significant improvement in objective measure, <u>YES</u> or <u>NO</u>
<i>Horvath (1997)</i>	Sole	200	12	8	Yes	Yes
<i>Argarwal (1999)</i>	Sole	102	12	1	Yes	Yes
<i>Schnieder (2001)</i>	Sole/Combined	41	12	1	Yes	Yes
<i>DeCarlo (2000)</i>	Sole	34	12/36	1	Yes	Yes
<i>Allen (1998)</i>	Sole	42	6	1	Yes	No
<i>Burkhoff (1999)</i>	Sole	132	1	1	Yes	Yes
<i>Hattler (1999)</i>	Sole	167	12	13	Yes	NR
<i>Guleserian (2003)</i>	Sole/Combined	81	18	4	NS	Yes
<i>Gregoric (2003)</i>	Combined	17	12	1	Yes	NR
<i>Schofield (1999)</i>	Sole	188	12	1	Yes	Yes
<i>Stamou (2002)</i>	Combined	169	12	1	Yes	NR
<i>Trehan (1998)</i>	Combined	77	12	1	Yes	Yes
<i>Wheberg (2003)</i>	Combined	255	1	1	NR	Yes
<i>Peterson (2003)</i>	Sole/Combined	3136	1	173	NR	NR

TMR: Evidence-Based Recommendations

- Based on an accumulation of data from sole therapy and adjunctive trials:
 - ♦ 1999: CMS Coverage Policy
 - ♦ 2001: Blue Cross Blue Shield Association Technology Evaluation Center (re-assessed, 2004).
 - ♦ 2002: American College of Cardiology/American Heart Association Taskforce on practice guidelines: assessment
 - ♦ 2003: Emergency Care Research Institute (ECRI): technology assessment
 - ♦ 2004: Society of Thoracic Surgeons Workforce on evidence-based surgery: national practice guidelines