

# Clinical Results of Transmyocardial Laser Revascularization for Diffuse Coronary Artery Disease

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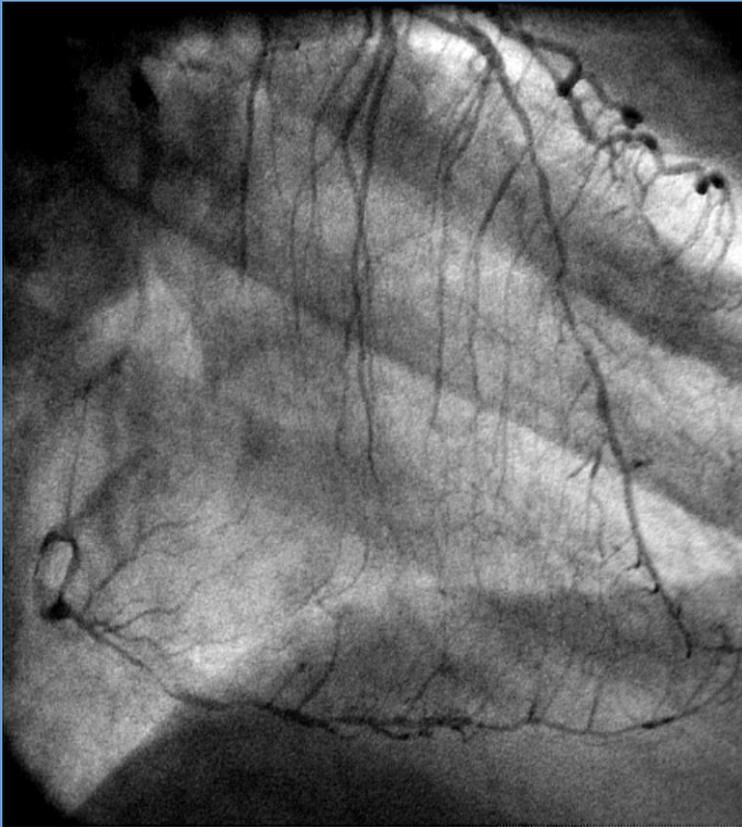
*Northwestern University Medical School*

# 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.

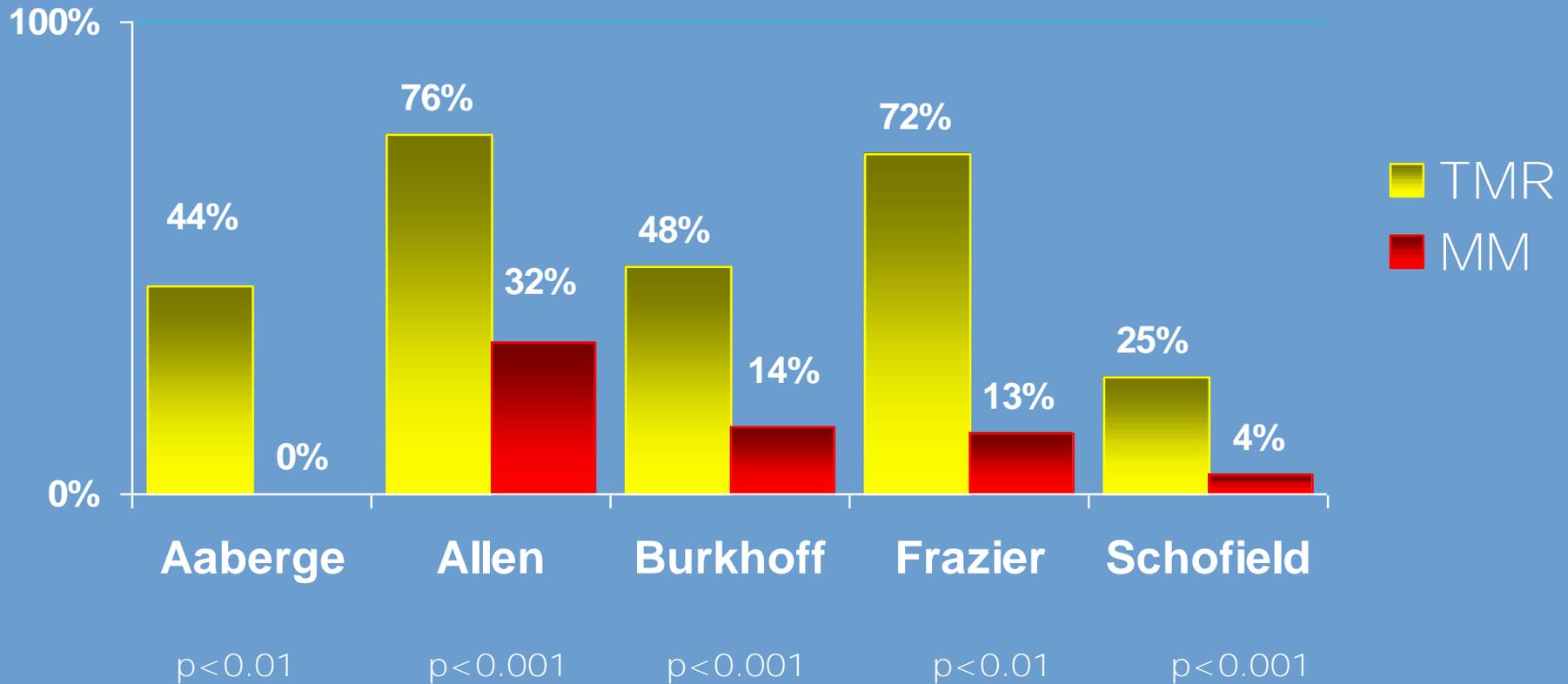
# Sole Therapy vs. MM Randomized Controlled Trials

## *Patient Characteristics*

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

Total 937

# Angina Relief at 12 Months: TMR vs. MM



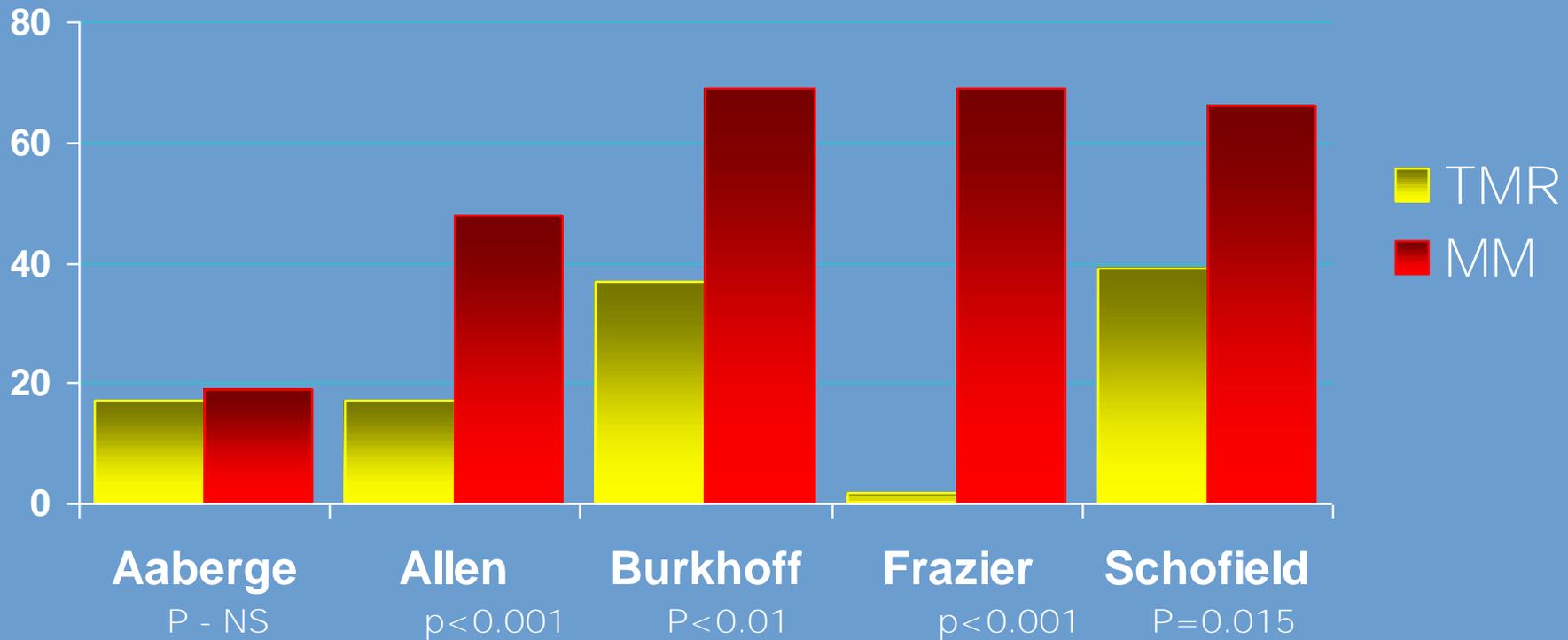
## Meta Analysis for Angina Reduction

Summary Odds Ratio  
9.3

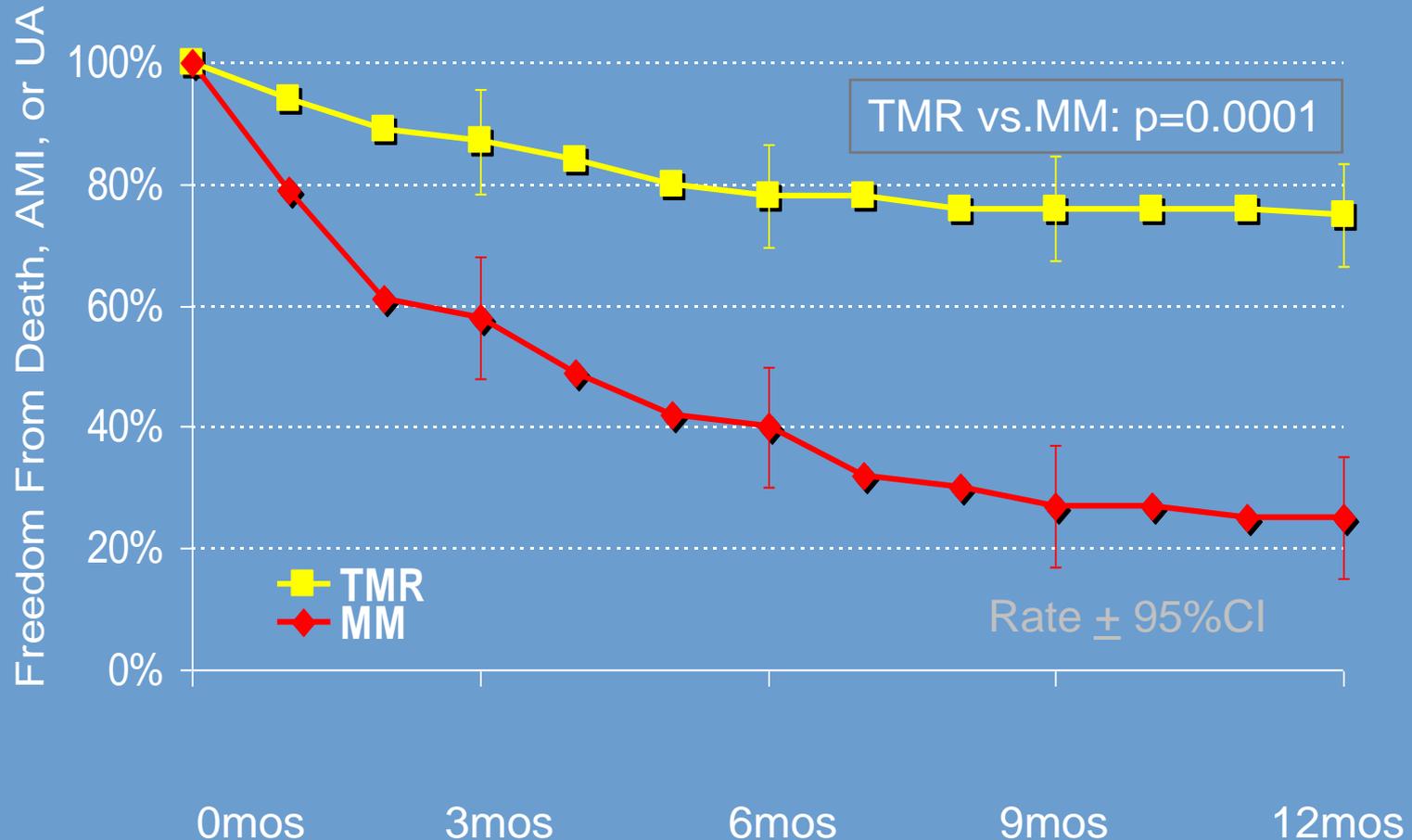
95% CI  
4.6 - 18.5

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 CO<sub>2</sub> Laser in Patients with End-Stage Coronary Artery Disease. N Engl J Med 341:1021-8, 1999

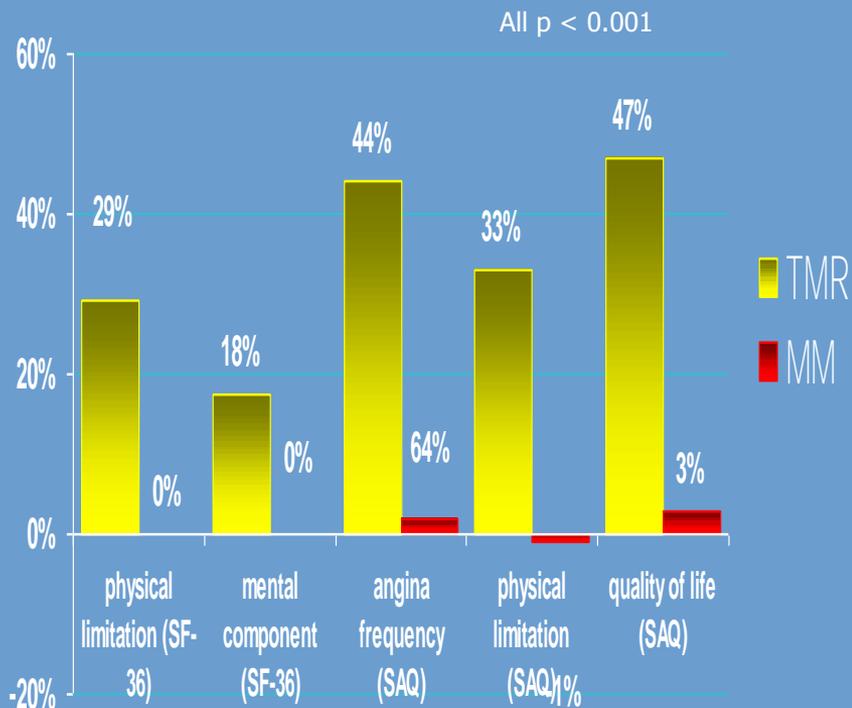
# Quality of Life Improvement

- 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

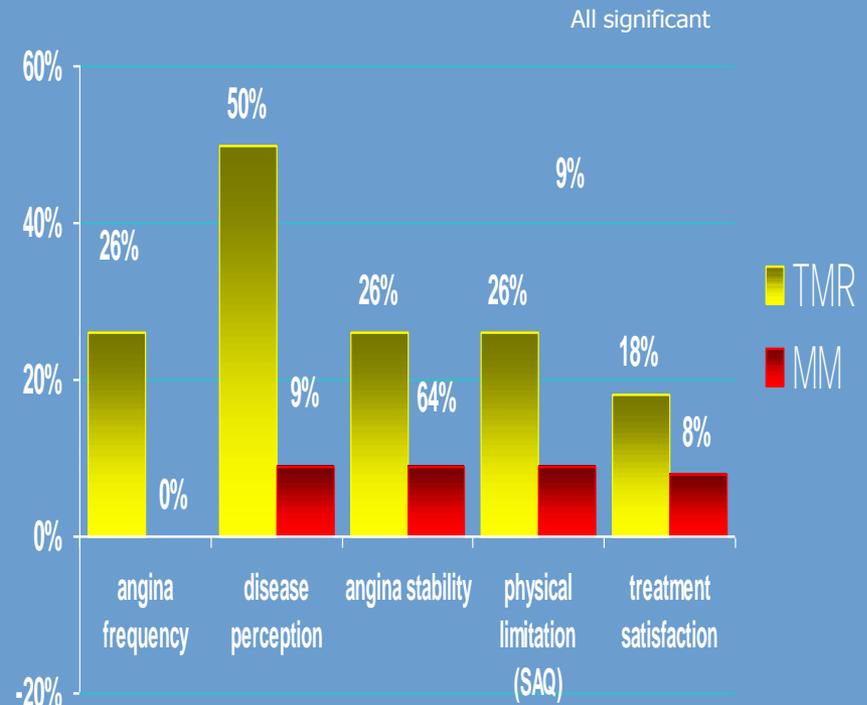
Frazier et. al., 1999

% improvements at 12 months vs. baseline



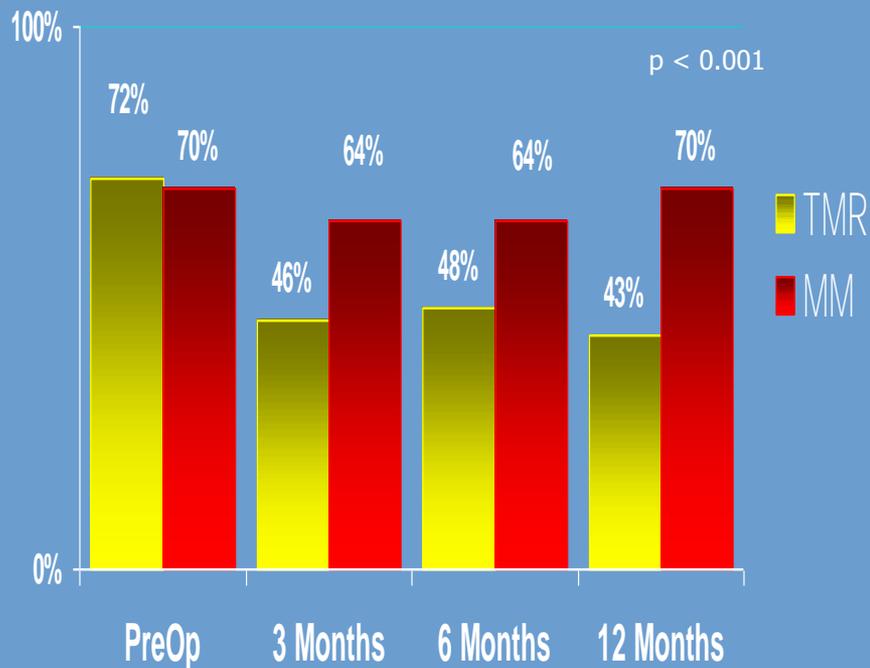
Burkhoff et. al., 1999

% median change at 12 months vs. baseline

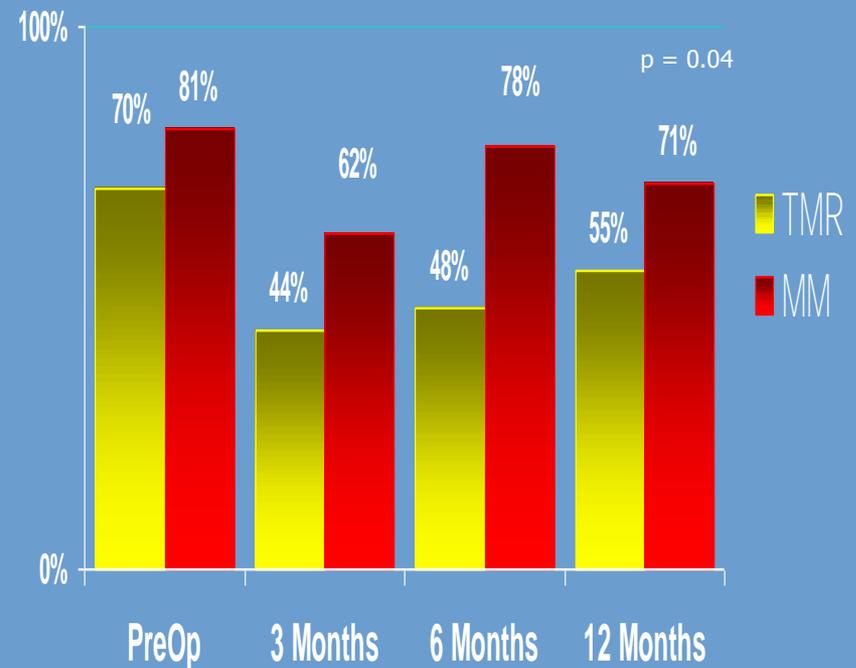


# Improvement in Exercise Tolerance

Angina on treadmill %

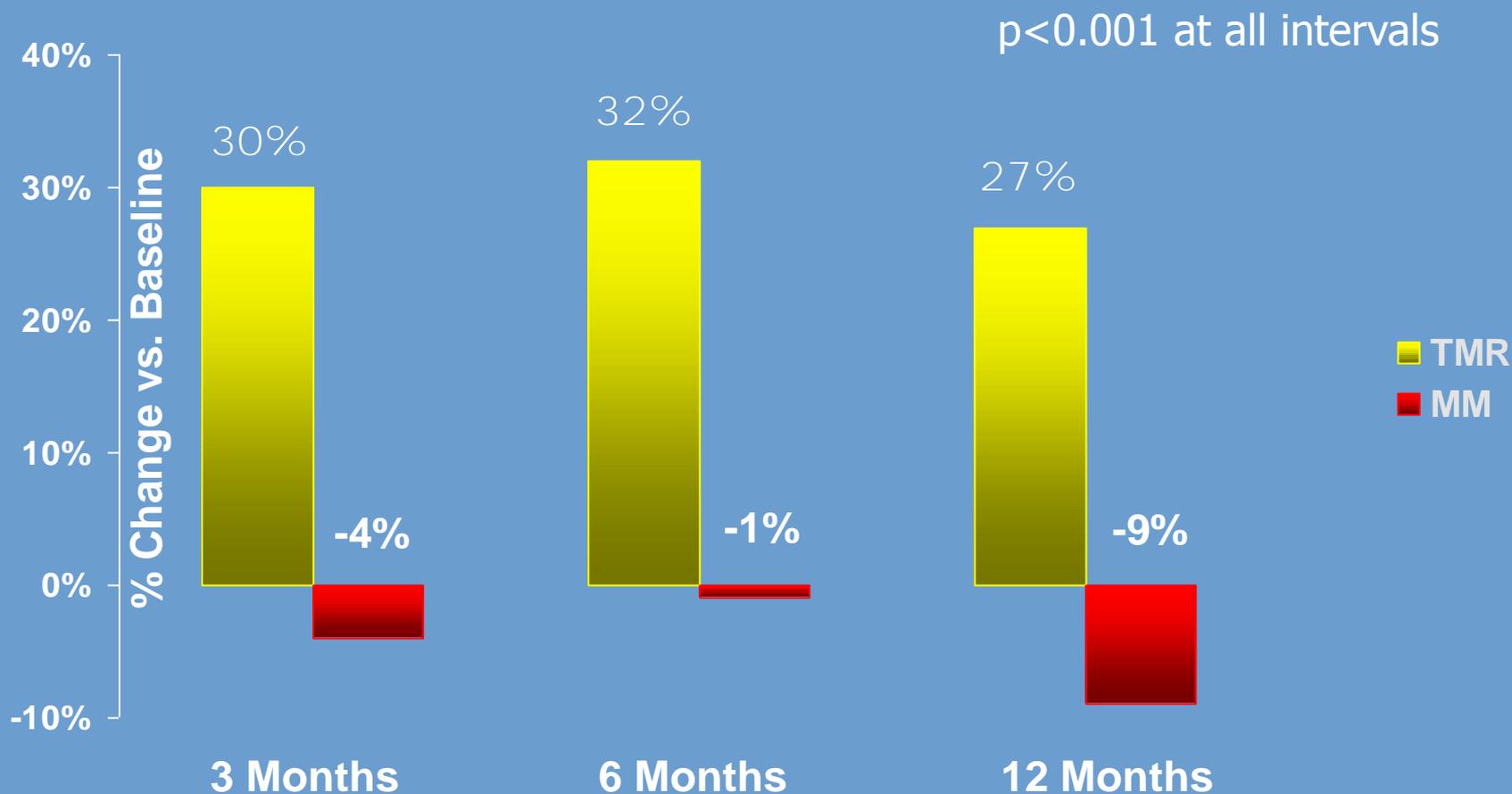


Angina during a 12 minute walk



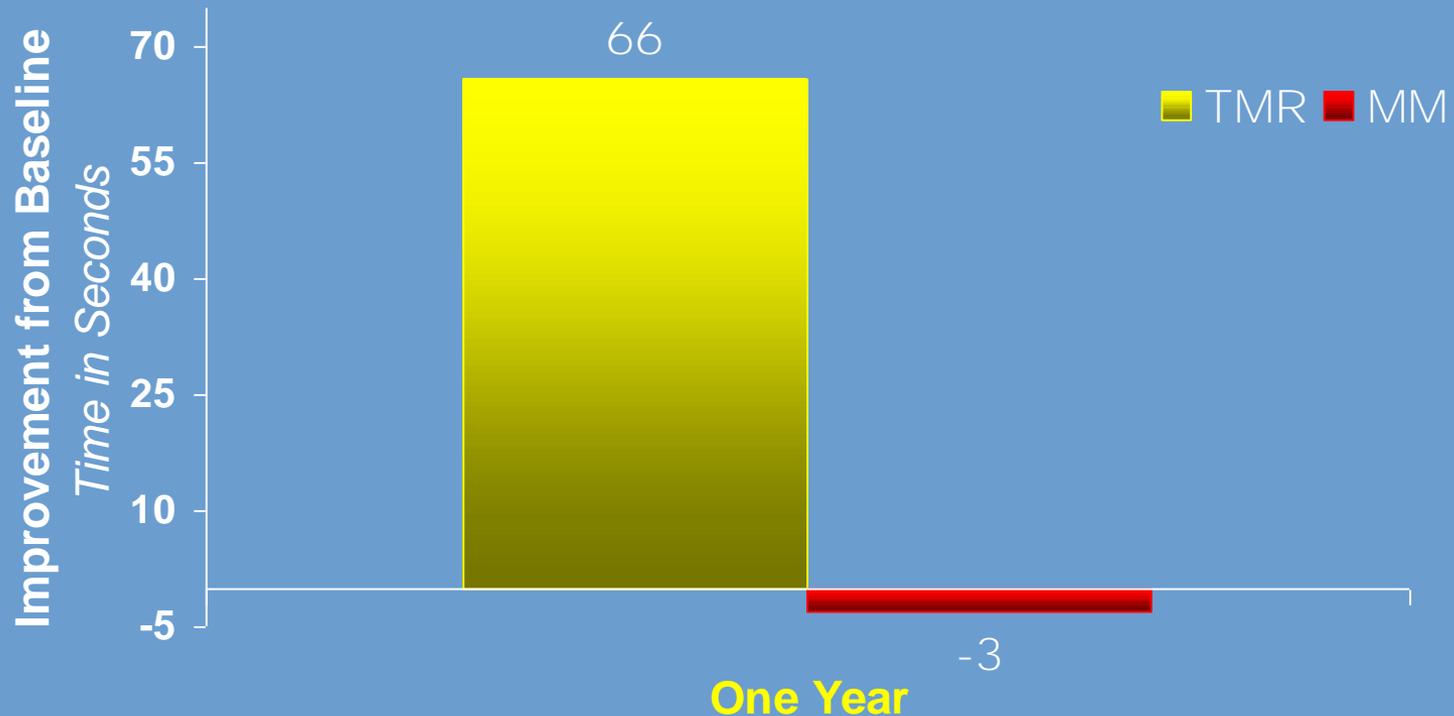
Schofield PM, et al. Transmyocardial Laser Revascularization in Patients with Refractory Angina Lancet 353:519-24, 1999

# 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

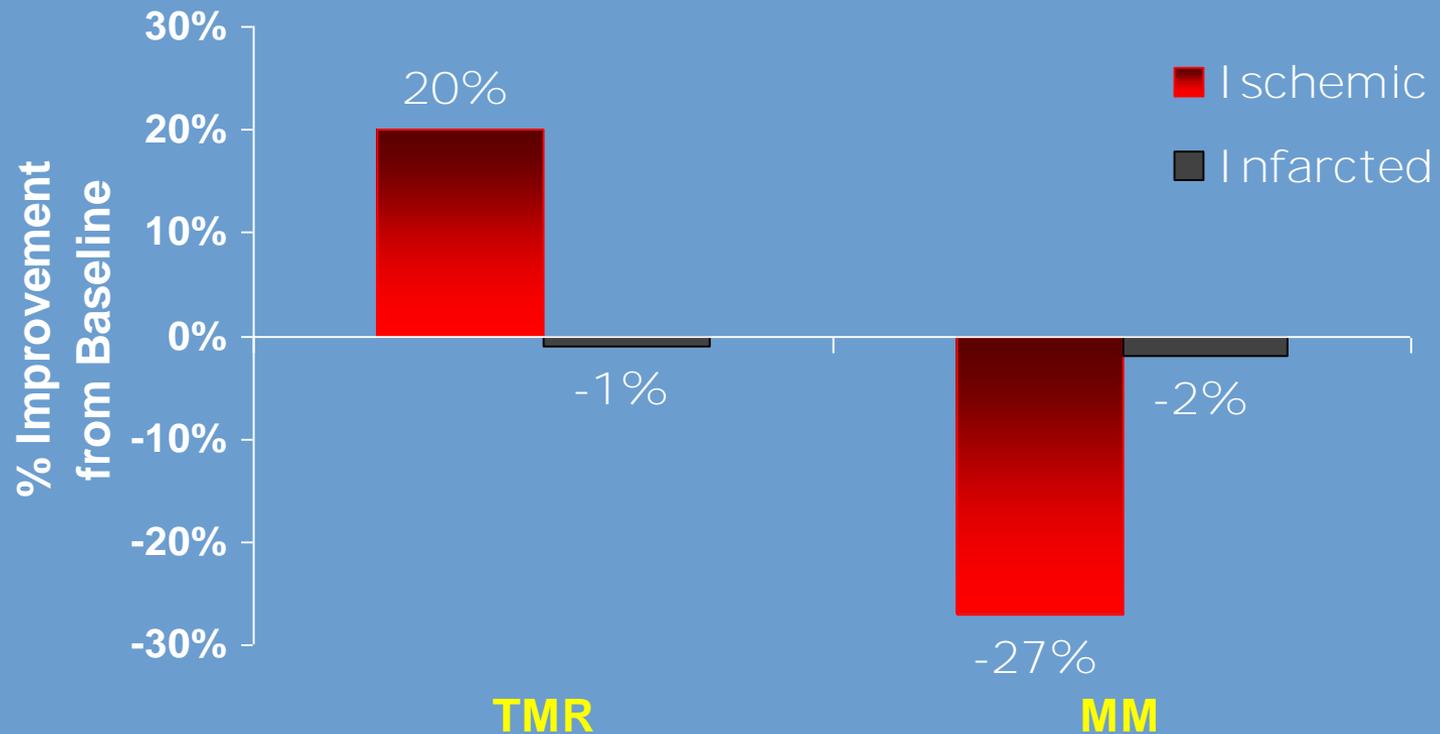
# Improvement in Exercise Tolerance



Aaberge L, et al. Transmyocardial Revascularization with CO<sub>2</sub> Laser in Patients with Refractory Angina Pectoris, JACC, 200; 35:1170-7

# Improvement in Myocardial Perfusion

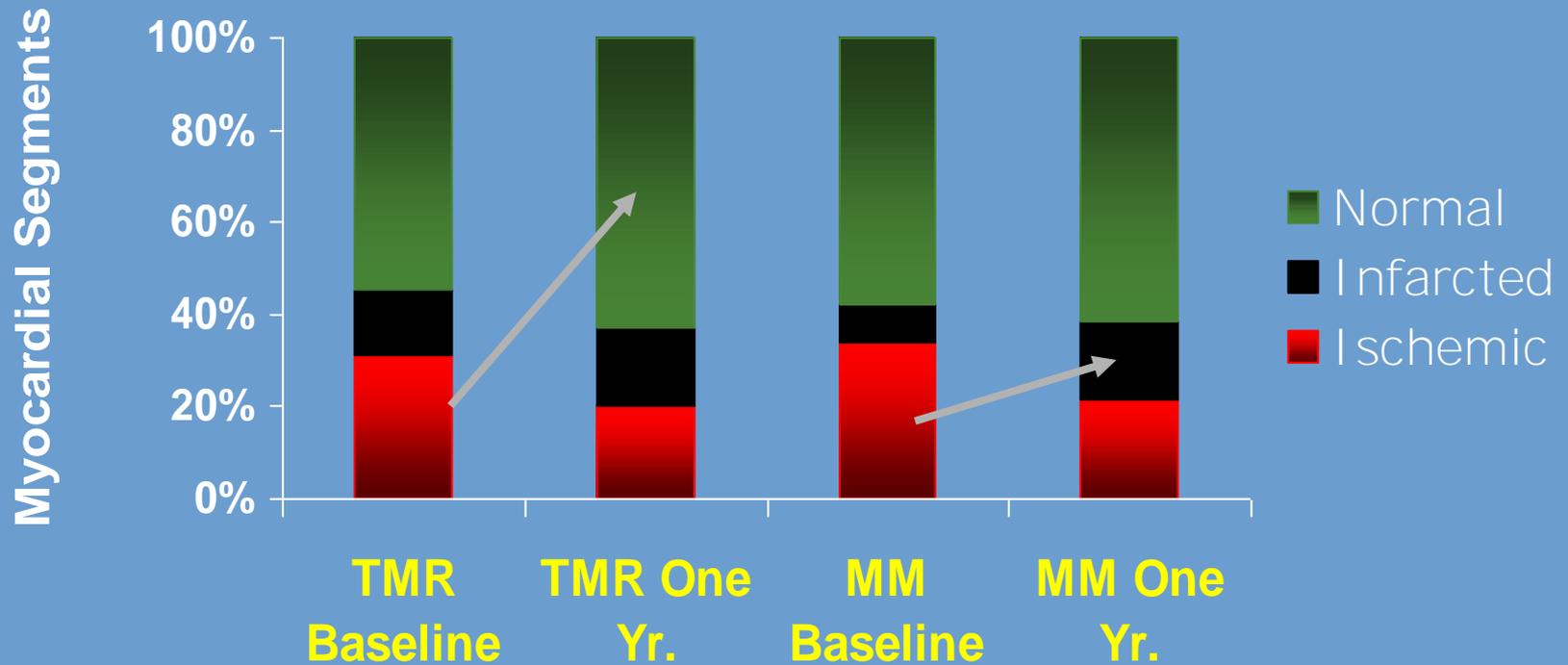
## *Results at One Year*



Frazier OH, et al. Transmyocardial Laser Revascularization with a CO<sub>2</sub> Laser in Patients with End-Stage Coronary Artery Disease. N Engl J Med 341:1021-8, 1999

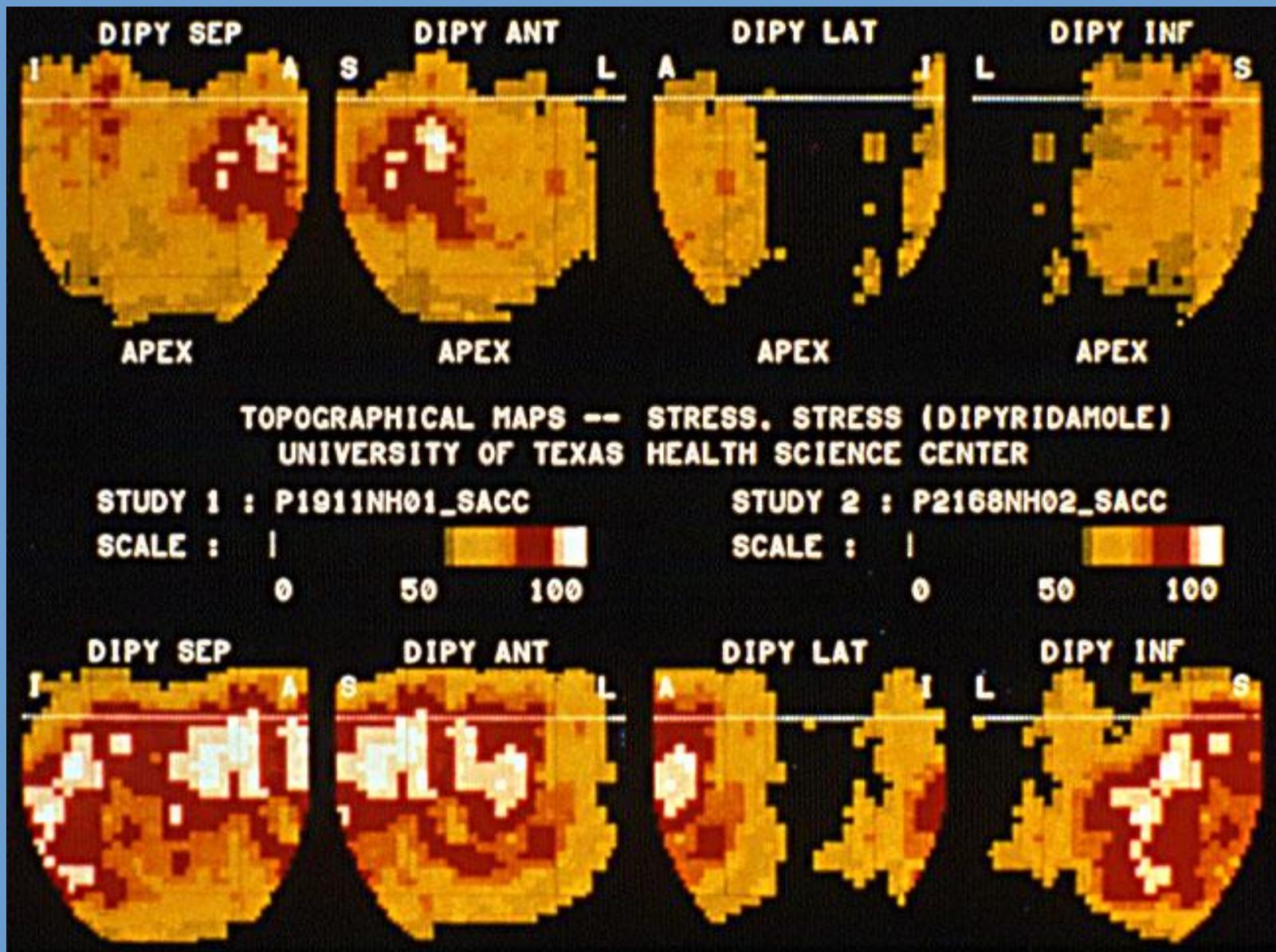
# Improvement in Myocardial Perfusion

## *Results at One Year*

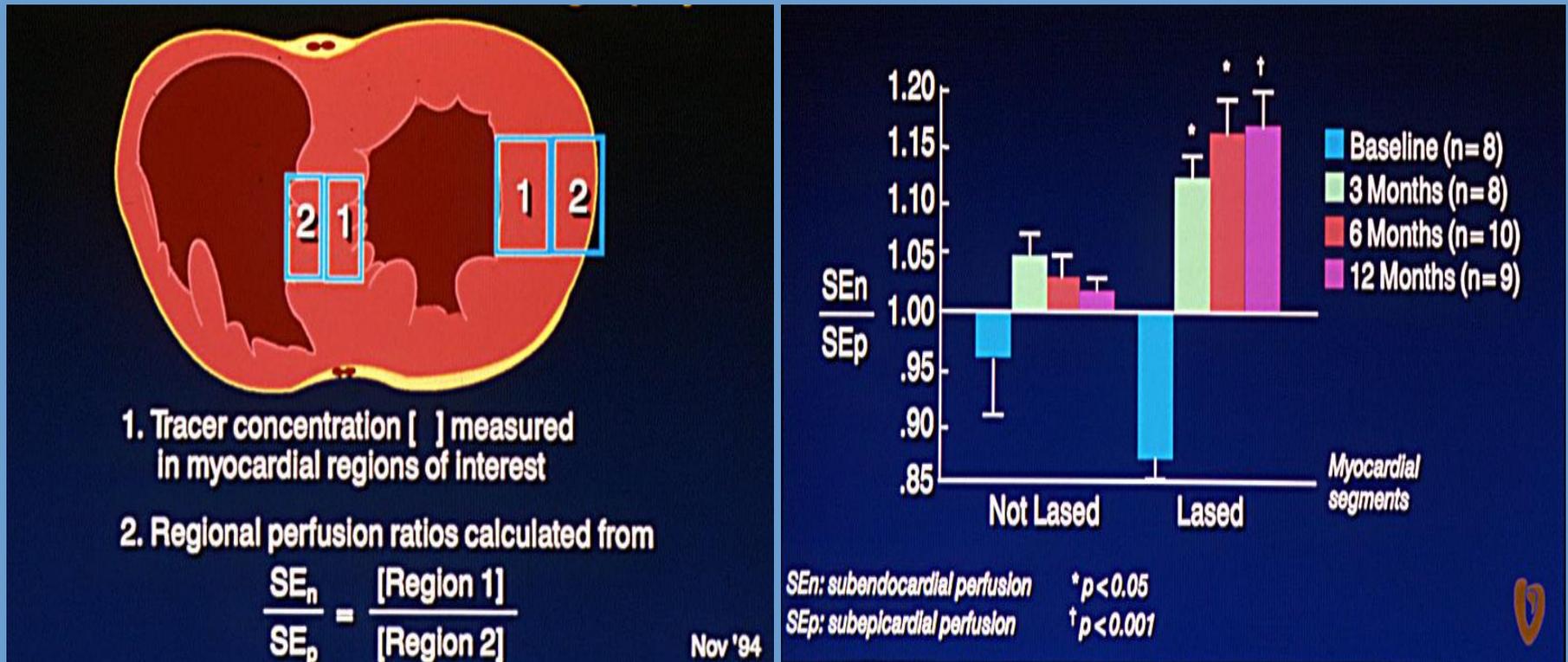


Schofield PM, et al. Transmyocardial Laser Revascularization in Patients with Refractory Angina Lancet 353:519-24, 1999

# PET Perfusion Improvement with TMR



# PET Improvement with TMR



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

Frazier et al, Circulation 1995, 92 Suppl:1588

# Functional Improvement with TMR

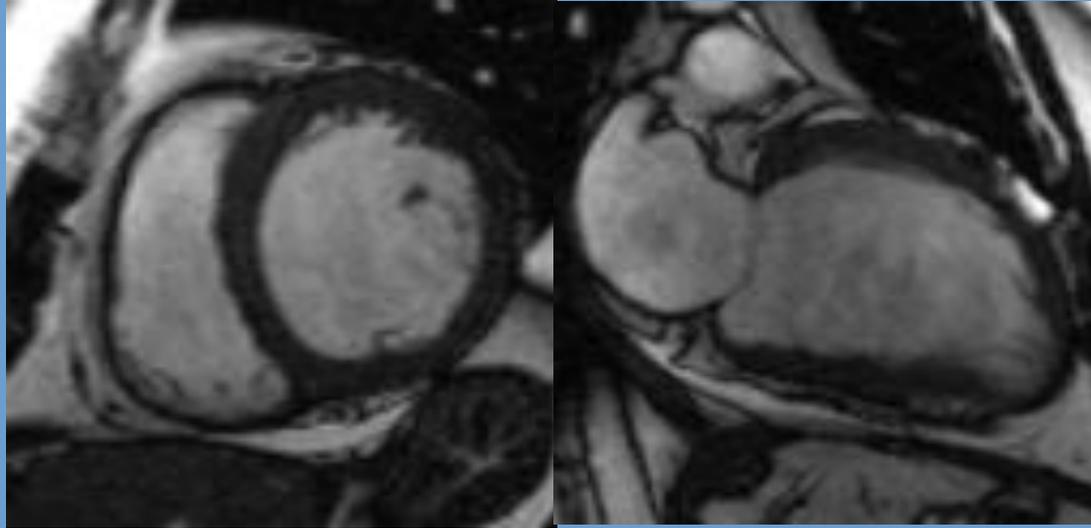
## **Dobutamine Stress Echo Pre & 6 months post CO<sub>2</sub> TMR**

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

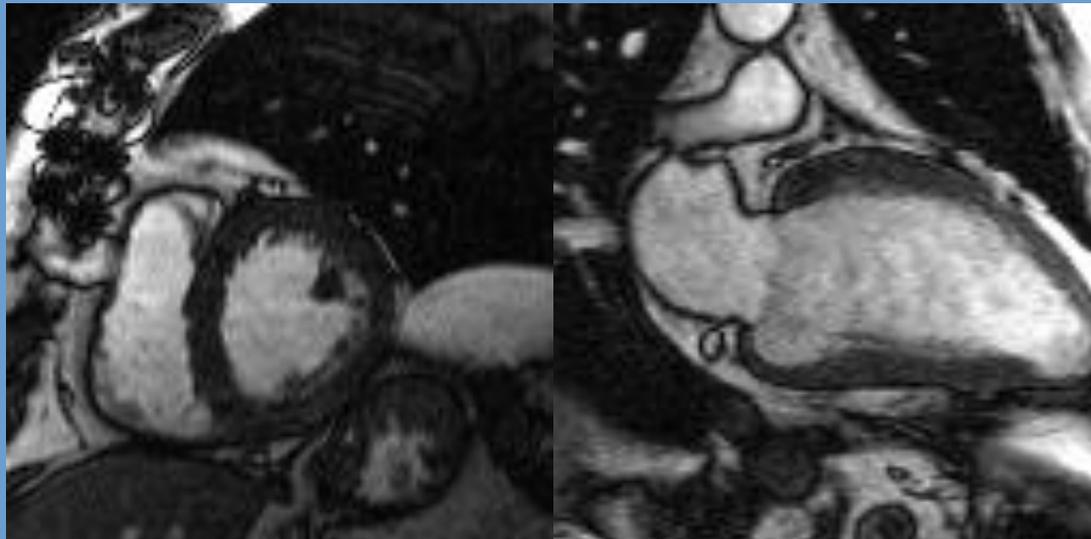
Donovan et al. Improvement in Inducible Ischemia During Dobutamine Stress  
Echocardiography after TMR in Patients with Refractory Angina Pectoris. JACC 1997;30:607

# Functional Improvement with TMR

Preop



Postop



# Functional Improvement with TMR

## Perfusion & Cine MRI

Pre & 8 weeks post CO<sub>2</sub> 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

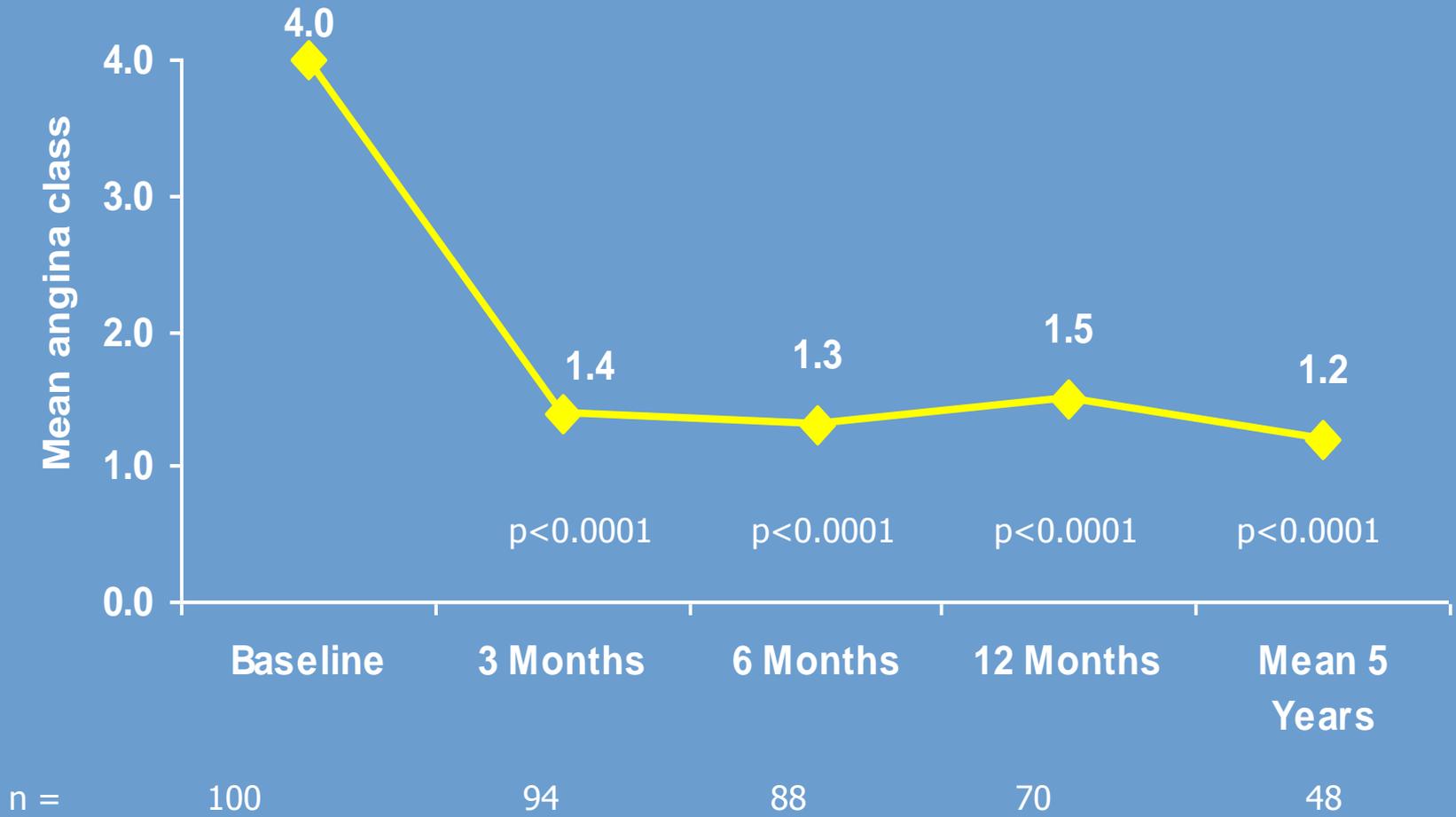
# Sole Therapy TMR Outcomes

## *Long-Term Follow-Up Studies*

Study	Mean Follow-up (years)	Patients (n)	
		TMR	MM
Allen, et al [ <i>Ann Thorac Surg</i> 2004;77:1228-34]	5.7	100	112
Aaberge, et al [ <i>JACC</i> 2002;39:1588-93]	3.6	50	50
Horvath, et al [ <i>Circ</i> 2001;104:181-184]	5.0	78	0

# Long Term Angina Relief

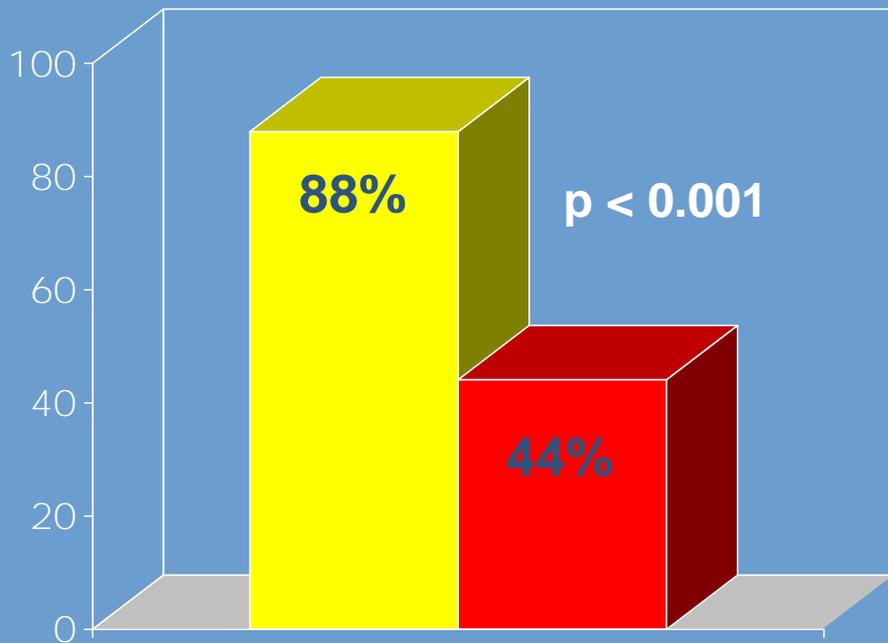
## *Mean Angina Class*



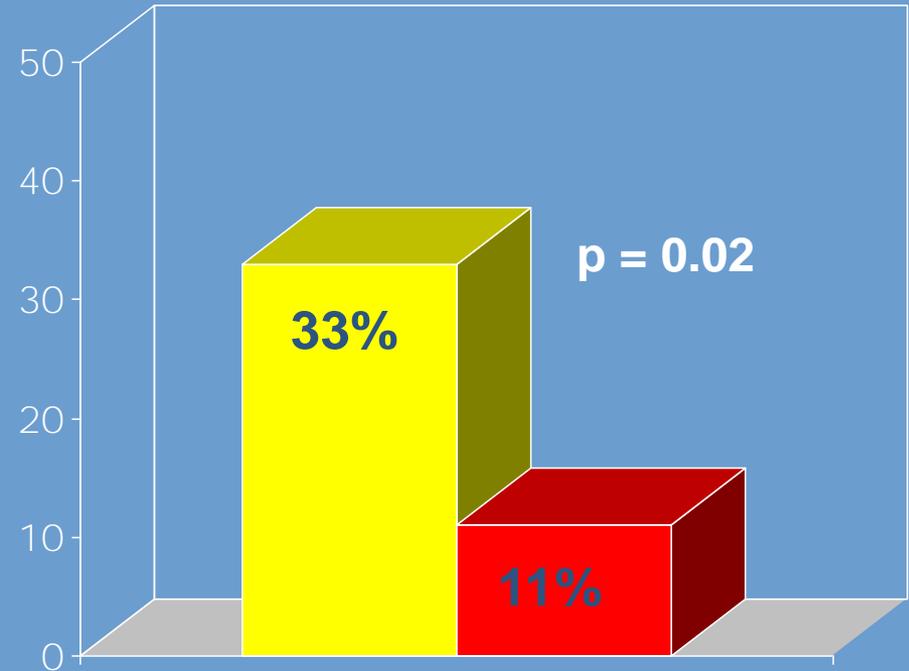
Allen KB, et al. Transmyocardial Revascularization: 5-Year Follow-up of a Prospective Randomized Trial *Ann Thorac Surg* 2004; 77:1228-34.

# Long Term Angina Relief

■ TMR  
■ Medical Management



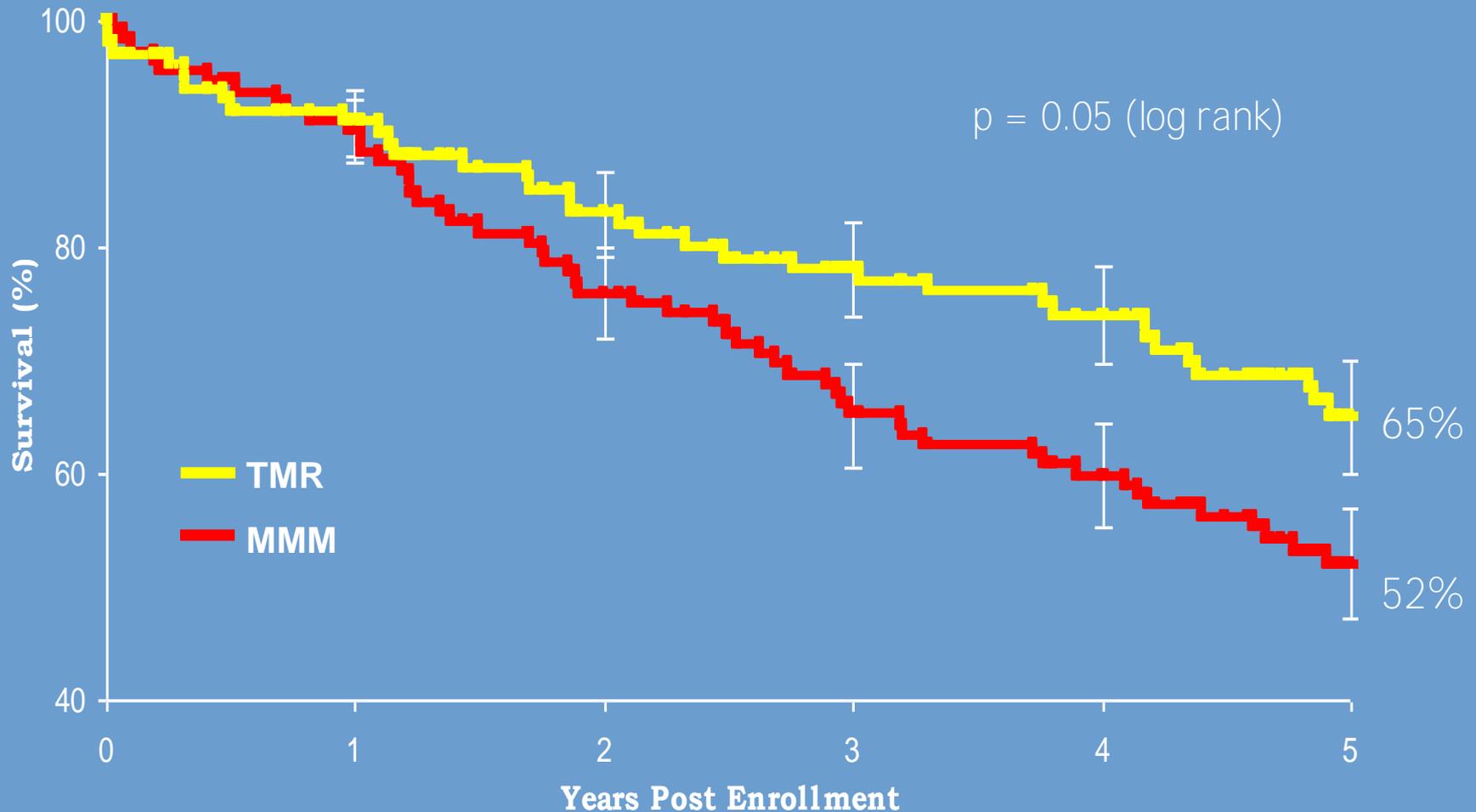
**% Patients with 2 Class Improvement**



**% Patients Angina Free**

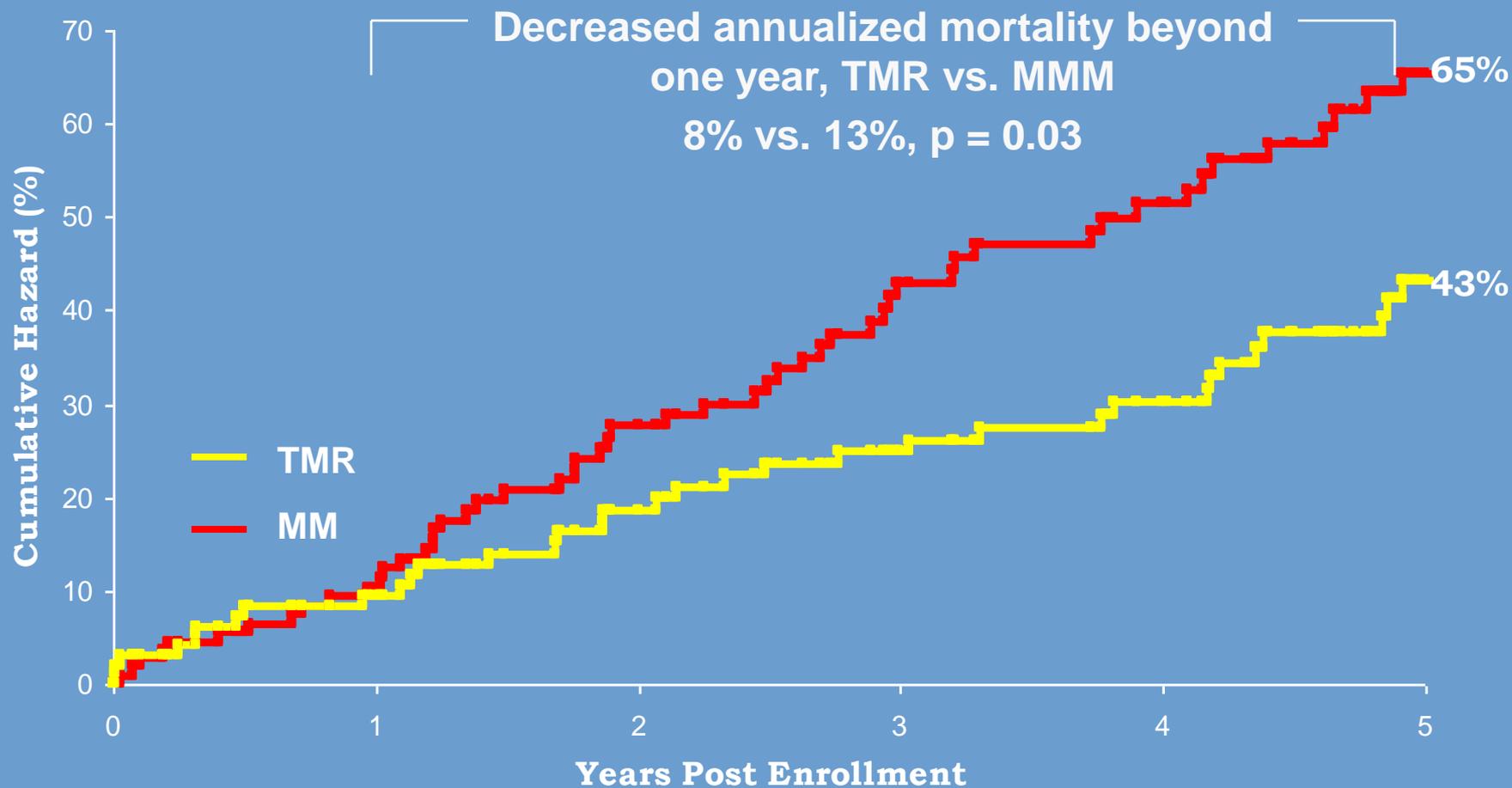
Allen et al, Transmyocardial Revascularization: 5-Year Follow-up of a Prospective Randomized Trial Ann Thorac Surg 2004; 77:1228-34

# Five-Year Kaplan-Meier Survival *Intent-To-Treat Analysis*



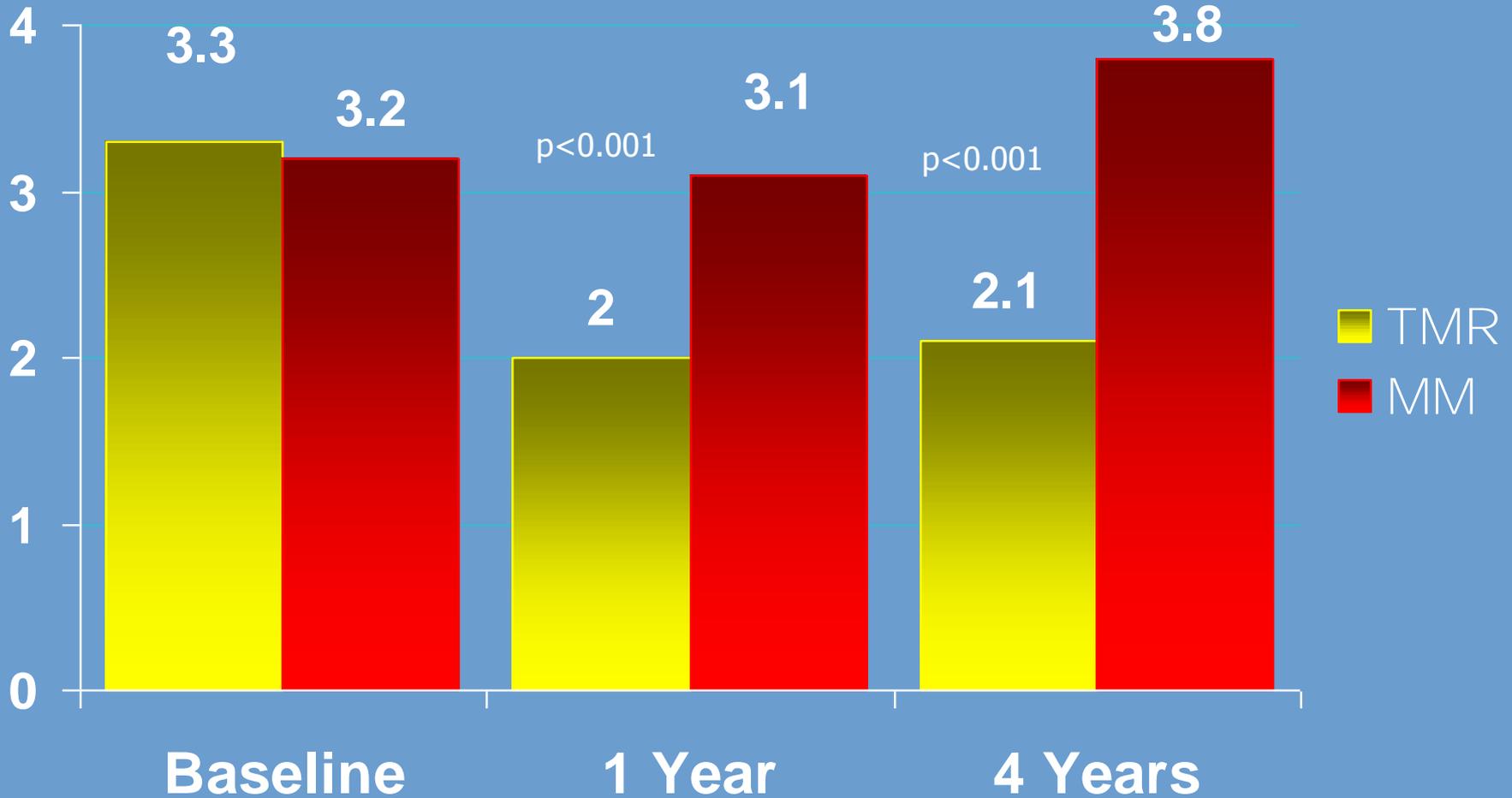
Allen KB, et al. Transmyocardial Revascularization: 5-Year Follow-up of a Prospective Randomized Trial *Ann Thorac Surg* 2004; 77:1228-34.

# Five-Year Cumulative Hazard Analysis



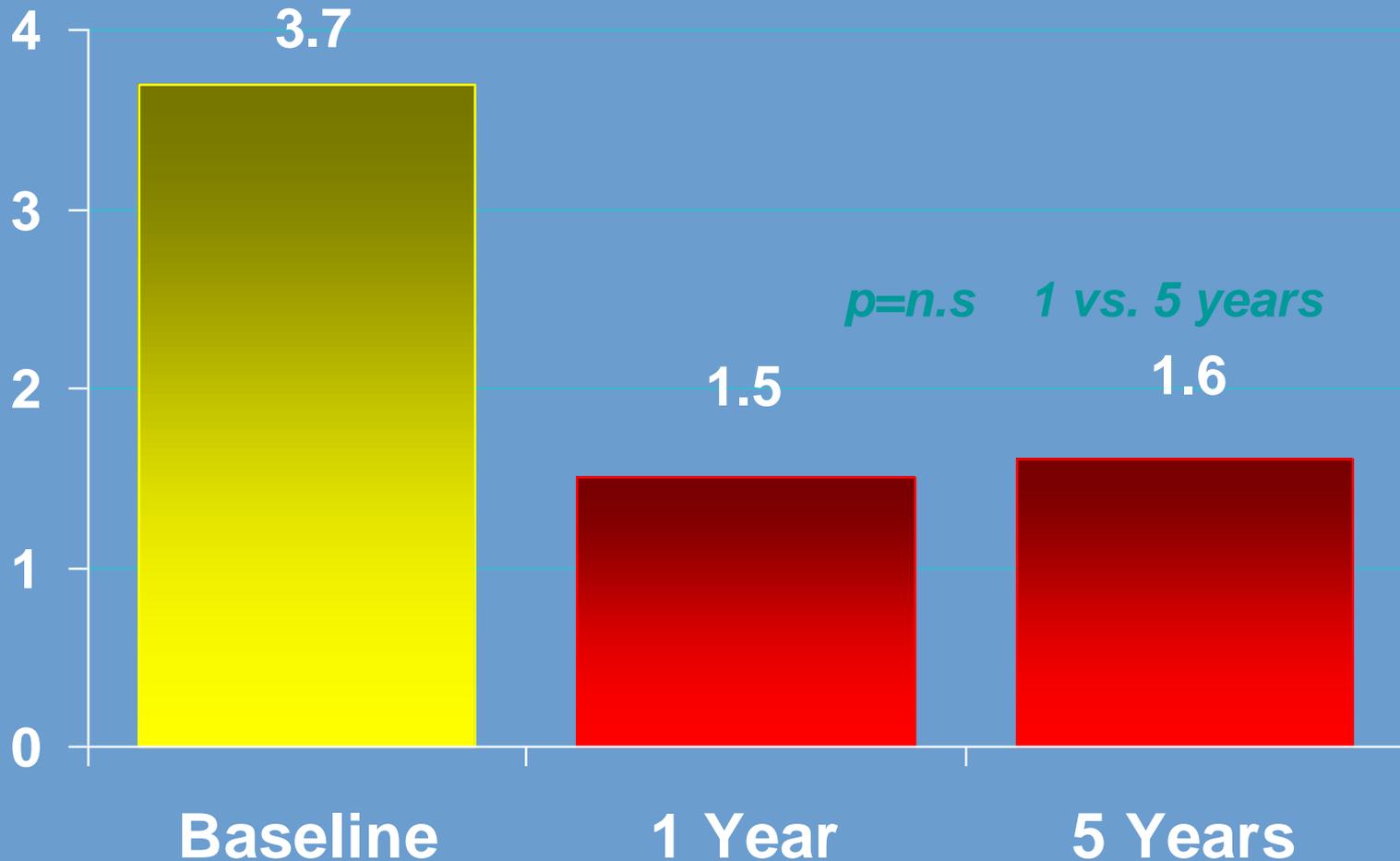
Allen et al, Transmyocardial Revascularization: 5-Year Follow-up of a Prospective Randomized Trial *Ann Thorac Surg* 2004; 77:1228-34

# Long Term Angina Relief

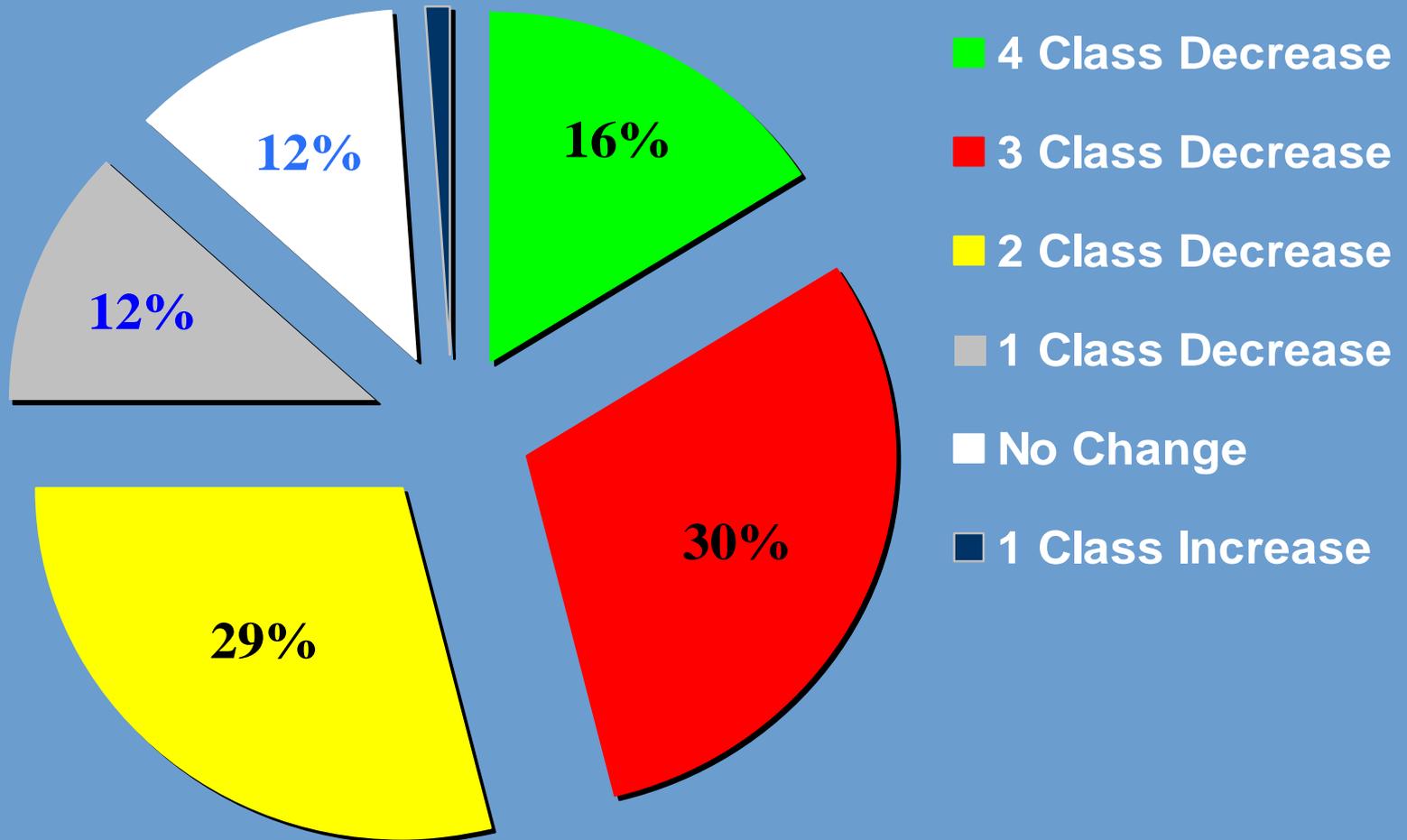


Aaberge L, et al. Continued Symptomatic Improvement 3 to 5 years after TMR with CO2 Laser, JACC, 2002: 39:1588-93

# Long Term Angina Relief

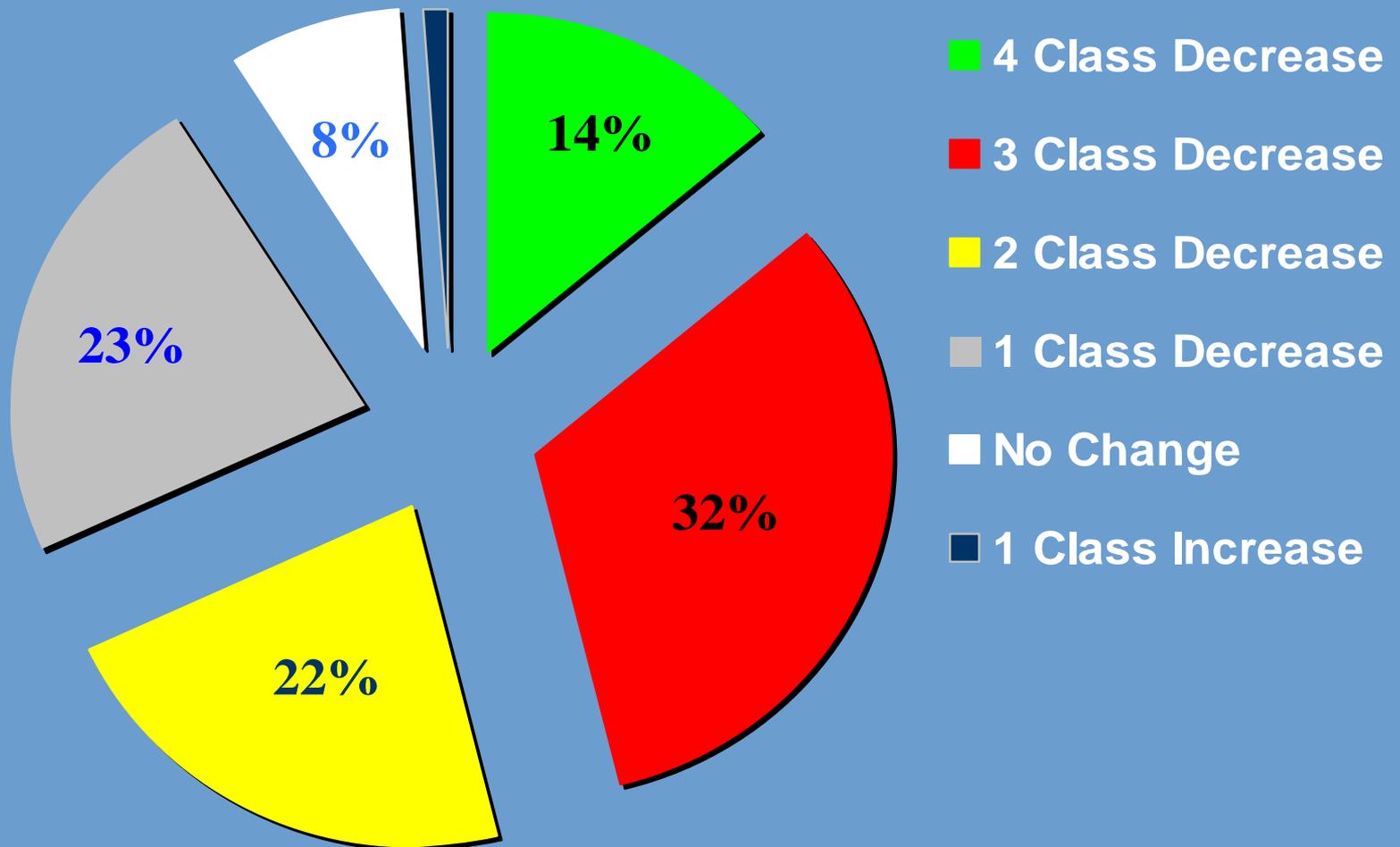


# Angina Class Change: *From Baseline to 1 year*



Horvath KA, et al. Sustained Angina Relief 5 Years After Transmyocardial Laser  
Revascularization with a CO2 Laser. *Circulation* 104:181-84, 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

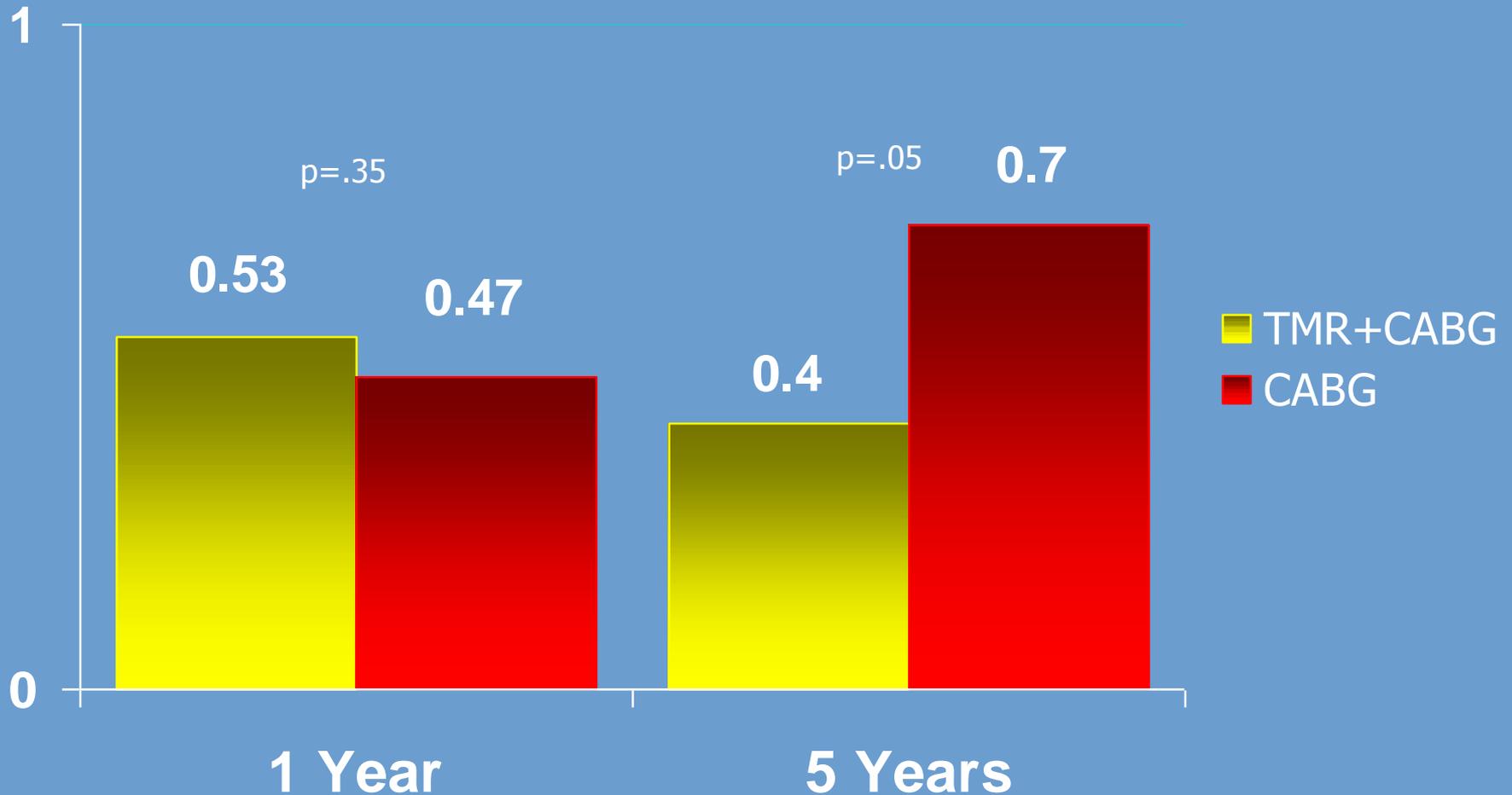
## Randomized Controlled Trials

### *Patient Characteristics*

	n	Mean Age	Mean Angina Class	% Unstable angina	% Previous MI	% Previous CABG	% Previous PTCA	% Diabetes	% Heart failure
<b>Allen</b>	263	64	2.8	--	45	20	--	44	0
<b>Frazier</b>	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

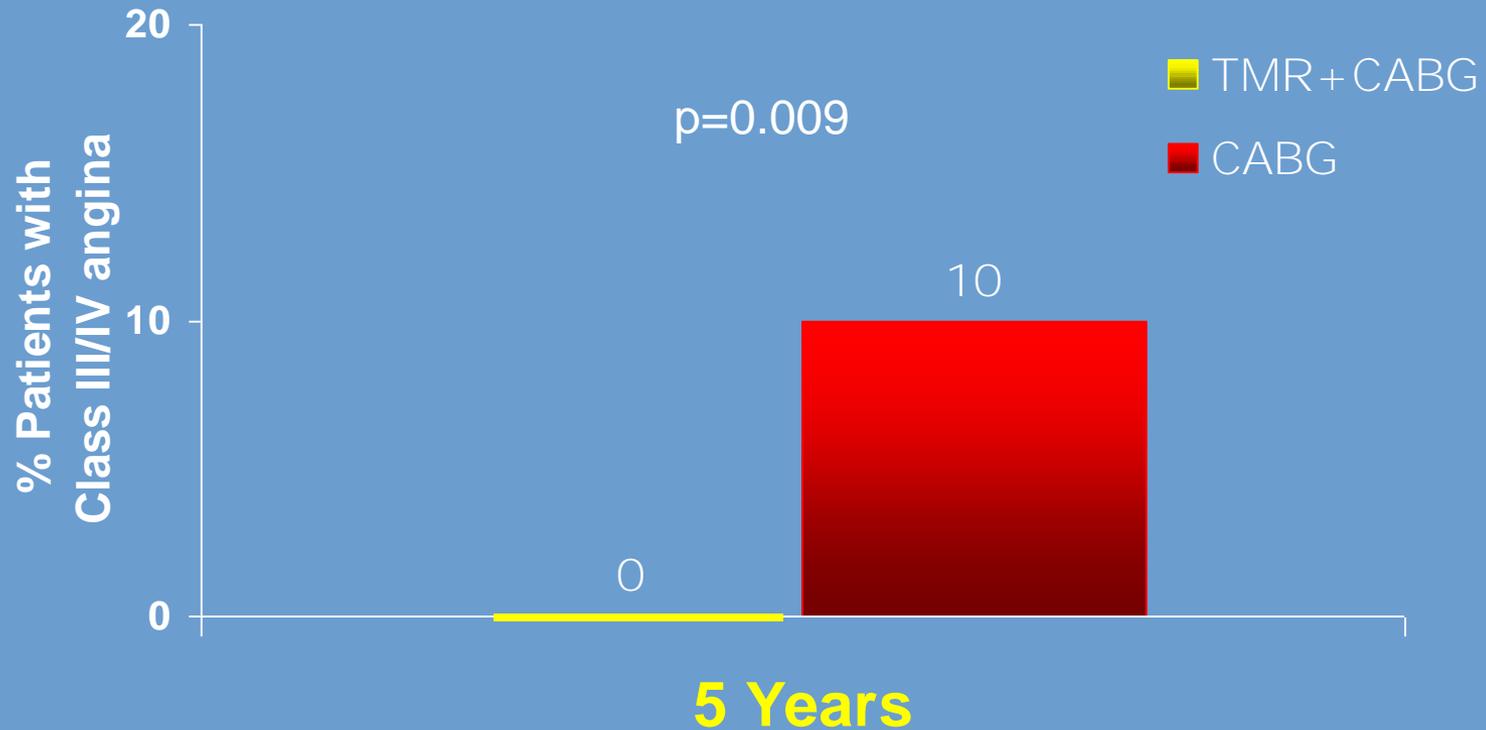
# Long Term Angina Relief TMR+CABG v. CABG



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*

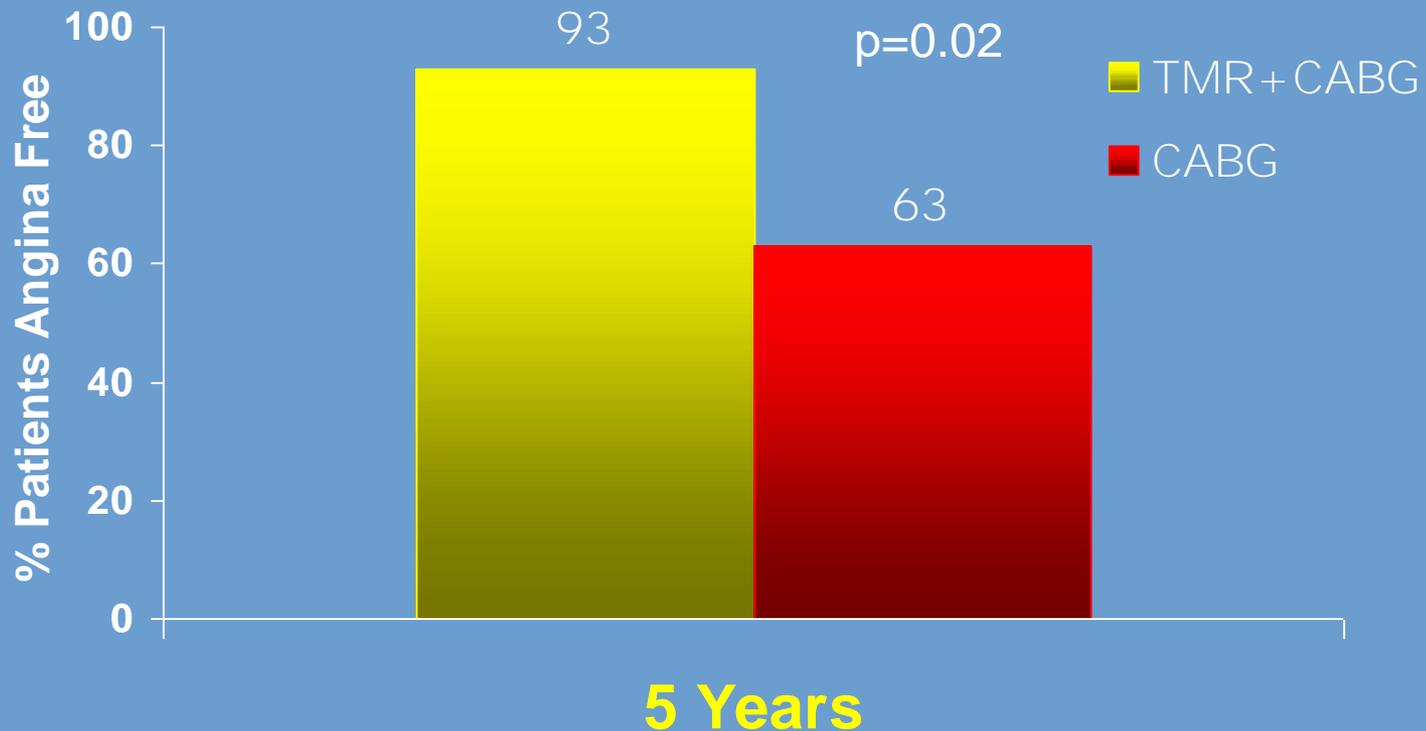


Allen K, et al. Adjunctive Transmyocardial Revascularization: 5 Year Follow-up of a Prospective Randomized Trial. Ann Thorac Surg, 2004 (in press)

# Long Term Angina Relief

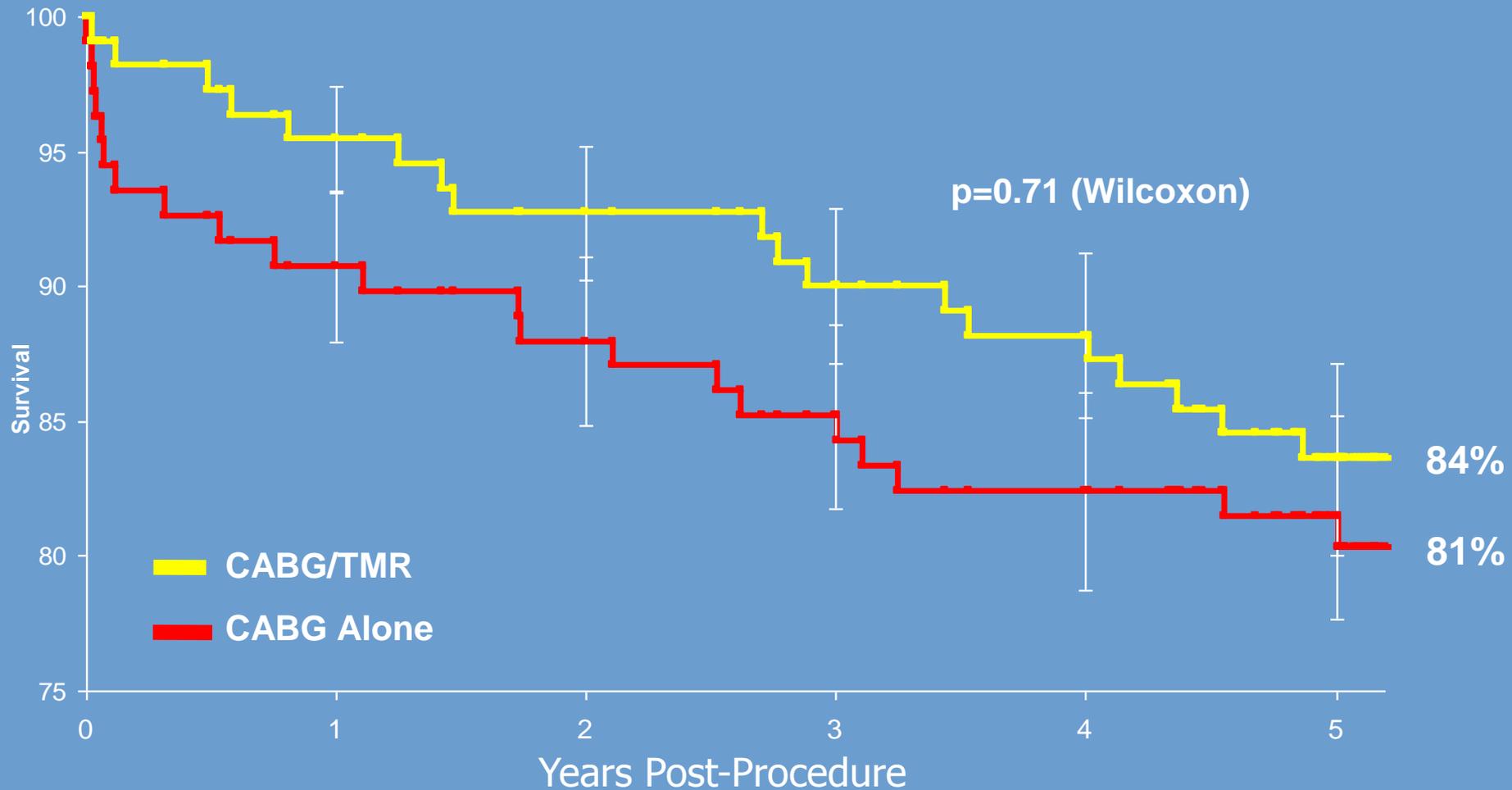
## TMR+CABG v. CABG

### *% 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)

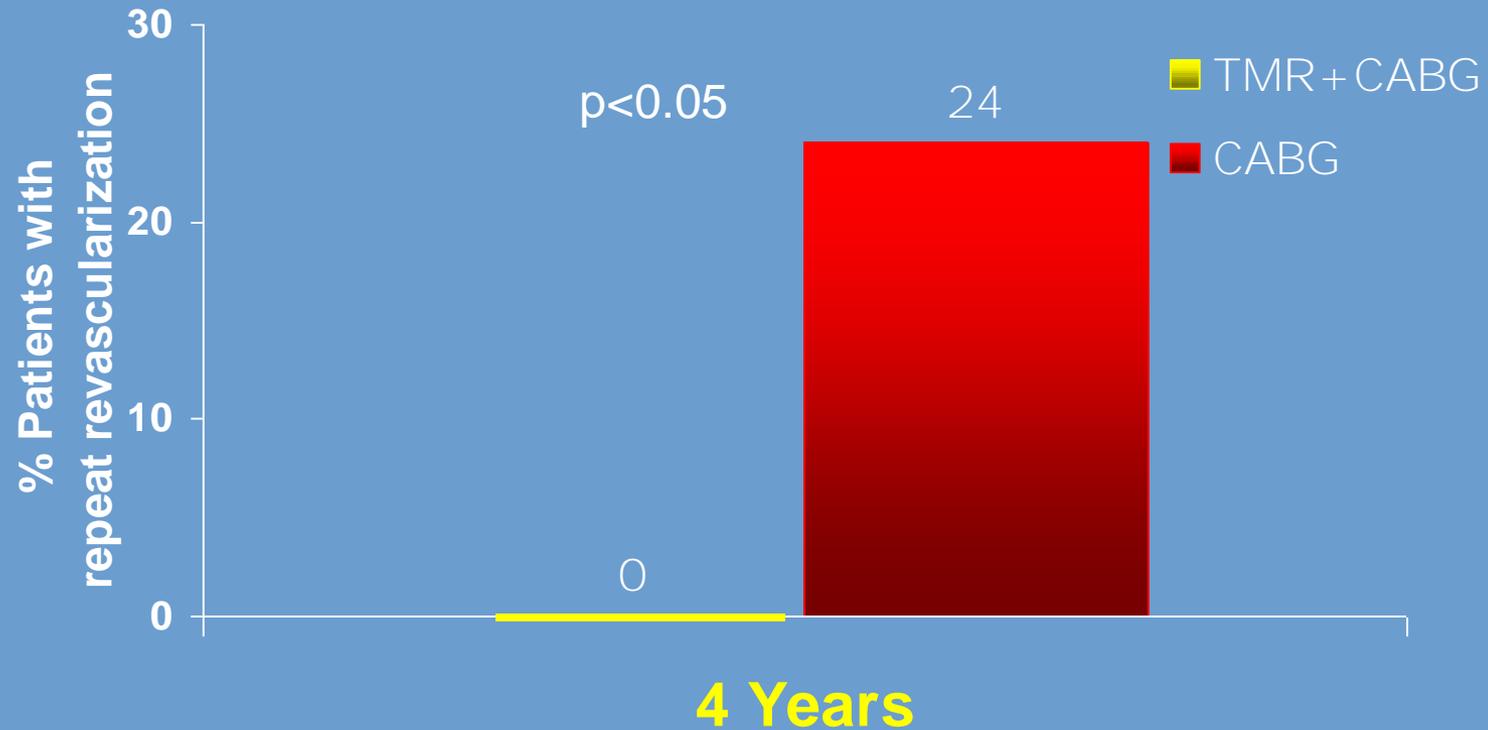
# Five-Year Kaplan-Meier Survival



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*

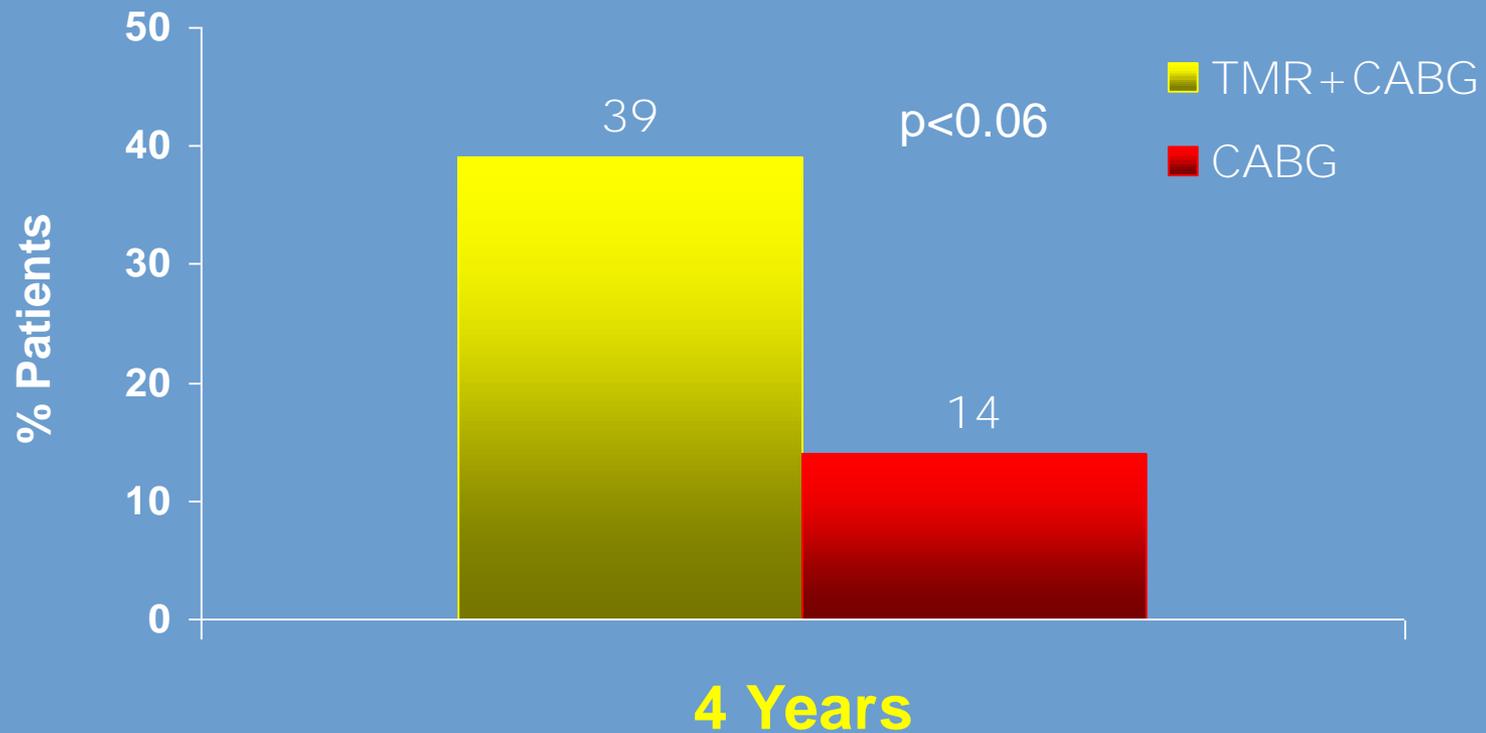


Frazier, et al. Transmyocardial Laser Revascularization as an Adjunct to CABG: A Randomized Multicenter Study with 4 yr. Follow-up. Journal THI, 2004 (in press)

# 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*



**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
<b><i>Aaberge (2000)</i></b>	Sole	<b>100</b>	<b>12</b>	<b>1</b>	<b>Yes</b>	<b>Yes</b>
<b><i>Aaberge (2002)</i></b>	Sole	<b>100</b>	<b>43</b>	<b>1</b>	<b>Yes</b>	<b>Yes</b>
<b><i>Allen (1999)</i></b>	Sole	<b>275</b>	<b>12</b>	<b>18</b>	<b>Yes</b>	<b>Yes</b>
<b><i>Allen (2004)</i></b>	Sole	<b>212</b>	<b>60</b>	<b>18</b>	<b>Yes</b>	<b>Yes</b>
<b><i>Allen (2000)</i></b>	+ CABG	<b>263</b>	<b>12</b>	<b>24</b>	<b>N/A</b>	<b>Yes</b>
<b><i>Allen (2004)</i></b>	+ CABG	<b>218</b>	<b>60</b>	<b>13</b>	<b>Yes</b>	<b>Yes</b>
<b><i>Burkhoff (1999)</i></b>	Sole	<b>182</b>	<b>12</b>	<b>16</b>	<b>Yes</b>	<b>Yes</b>
<b><i>Frazier (1999)</i></b>	Sole	<b>192</b>	<b>12</b>	<b>12</b>	<b>Yes</b>	<b>Yes</b>
<b><i>Frazier (2004 )</i></b>	+ CABG	<b>44</b>	<b>48</b>	<b>4</b>	<b>N/A</b>	<b>Yes</b>
<b><i>Horvath (2001)</i></b>	Sole	<b>78</b>	<b>60</b>	<b>12</b>	<b>Yes</b>	<b>Yes</b>
<b><i>Schofield (1999)</i></b>	Sole	<b>188</b>	<b>12</b>	<b>1</b>	<b>Yes</b>	<b>Yes</b>

# 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