CORSO AVANZATO DI ECOCARDIOGRAFIA DI "ECOCARDIOCHIRURGIA"

con uno sguardo all'imaging integrato

ECOCARDIOCHIRURGIA.it

Terapia medica della cardiopatia ischemica stabile: opzione terapeutica da valutare sempre prima di proporre il BP o l'angioplastica

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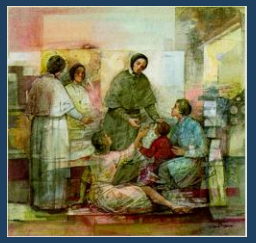
H. Valduce 1879



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CONFLITTI D'INTERESSI: NESSUNO

Terapia medica della cardiopatia ischemica stabile: opzione terapeutica da valutare sempre prima di proporre il BP o l'angioplastica

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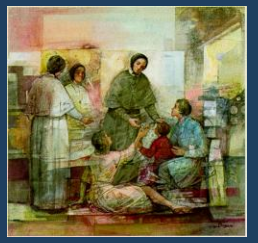
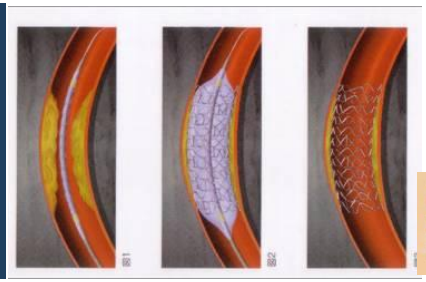


BACKGROUND I

- **Sin dalla sua introduzione nel 1977 la PCI ha rivoluzionato il trattamento della CAD permettendo una rivascolarizzazione meccanica su lesioni instabili**
- **La PCI nei pz con ACS ↓ l'incidenza di morte/IMA [1,2]**
- **Negli USA eseguite > 10^6 PCI nel 2006[3]**

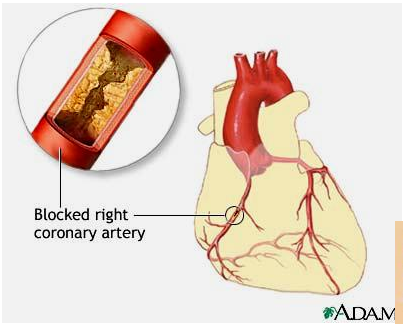
1. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003; 361: 13–20.
2. Mehta SR, Cannon CP, Fox KA, et al. Routine *vs* selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. *JAMA* 2005; 293: 2908–17.
3. Lloyd-Jones D et al. Heart disease and stroke statistics — 2010 update: a report from the American Heart Association. *Circulation* 2010;121:e46-e215.



BACKGROUND II

- ≈ 85% PCI eseguite su pz con CAD stabile[1]
- In questi pz la PCI ha ≤ 1% complicanze gravi (morte – IMA - BPAC) e ≥ 95% successo[2]
- Intuitivamente, una PCI efficace su una lesione stenosante dovrebbe ↓ l'incidenza di morte/IMA/ACS anche in pz con CAD stabile….. ma è così ?

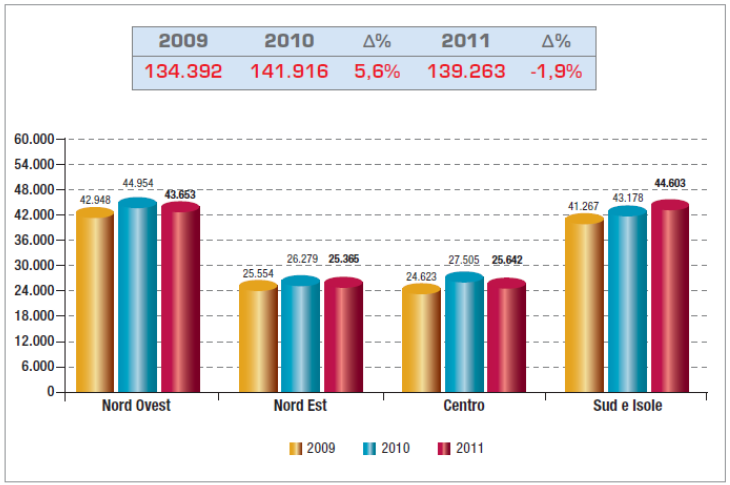
1. Feldman DN, Gade CL, Slotwiner AJ, et al. Comparison of outcomes of percutaneous coronary interventions in patients of three age groups (<60, 60 to 80, and >80 years) (from the New York State Angioplasty Registry). *Am J Cardiol* 2006;98:1334-9.
2. Kastrati A, Mehilli J, Schuhlen H, et al, for the Intracoronary Stenting and Antithrombotic Regimen–Rapid Early Action for Coronary Treatment (ISAR-REACT) Study Investigators. A clinical trial of abciximab in elective percutaneous coronary intervention after pretreatment with clopidogrel. *N Engl J Med* 2004; 350: 232–38.



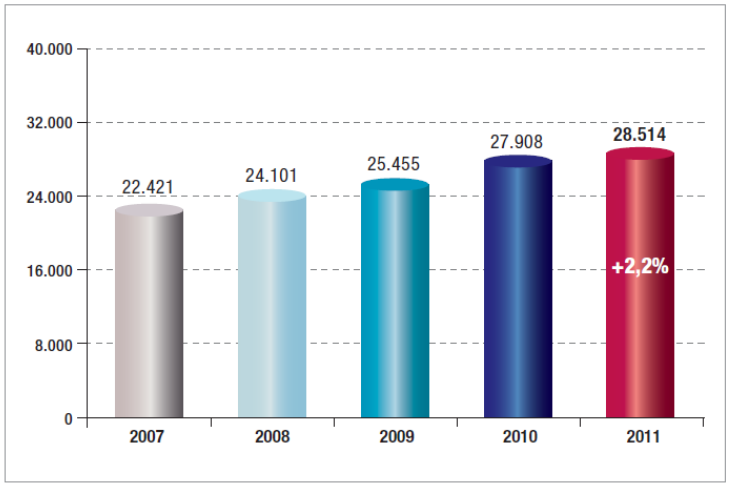
LA REALTA' ITALIANA

Angioplastica coronarica - PCI

2009	2010	Δ%	2011	Δ%
134.392	141.916	5,6%	139.263	-1,9%



PCI Primarie



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SCOPI DEL TRATTAMENTO

MALATTIA CRONICA STABILE:

1. Alleviare i sintomi e l'ischemia
2. Prevenire la progressione della malattia sino a IMA
3. Prevenire la morte CV prematura

In questo contesto tutti i trattamenti disponibili sono palliativi, ovvero non possono GURARIRE la malattia coronarica ma possono modificarne la storia naturale.

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2000

BMJ

Percutaneous transluminal coronary angioplasty versus medical treatment for non-acute coronary heart disease: meta-analysis of randomised controlled trials

Heiner C Bucher, Peter Hengstler, Christian Schindler and Gordon H Guyatt

BMJ 2000;321;73-77
doi:10.1136/bmj.321.7253.73

Table 1 Baseline characteristics and criteria for inclusion in randomised controlled trials of percutaneous transluminal coronary angioplasty (PCTA) compared with medical treatment in non-acute coronary heart disease

Study	Inclusion criteria		No of vessels (% successful dilatation)	Complications related to PTCA in intervention groups	Follow up (months)	Pre-existing condition (%)		Mean ejection fraction (%)	Trial quality score*
	Clinical	Angiographic				MI	Non-Q MI		
Parisi 1992[17]	Stable angina, history of angina, MI within 3 months, exercise test with ST depression >3 mm, no previous PTCA	Single or serial stenosis within same artery 70% to 99% proximal two thirds	1 (82)	CABG (2.0%); MI (1.0%); non-Q wave MI (3.0%)	6	0	28.8	65	4
Sievers 1993[16]	Previous non-Q wave MI, no angina in daily life, no previous Q wave MI	Mean (SD) degree of stenosis: 86% (11)	1 (100)	None	24	0	54.5	NA	2
MASS 1995[18]	Stable angina, no Q wave MI, no left ventricular dysfunction	Stenosis ⩾80% before first diagonal branch, length <12 mm, no total occluded lesion	1 (96)	CABG (2.8%); MI (2.8%)	30	0	0	76	3
Folland 1997[13]	Stable angina, history of angina, MI within 3 months, exercise test with ST depression >3 mm, no previous PTCA	Stenosis ⩾70% proximal two thirds, no main artery stenosis >50%, no 3 vessel disease	2 (69)	CABG (2%); MI (0.01%); non-Q wave MI (3.0%)	57	59	NA	66	2
RITA-2 1997[14]	Angina leading to admission within 90 days, previous Q wave MI, no previous PTCA, no left main stem disease	Stenosis ⩾50% stenosis in two projections or 70% stenosis in one projection or occluded arteries	1-3 (93)	CABG (1.4%); MI (1.4%); death (0.2%)	32	47	NA	Normal function in 54% of patients	4
AVERT 1999[15]	Angina or asymptomatic, MI or unstable angina but not within 14 days, no triple vessel disease	Stenosis ⩾50% in one or two vessels, no main artery stenosis	2 (99)	MI (0.5%)	18	43†		61	4

*See methods section for details of scoring.
†Figure for MI and non-Q wave MI.
MI: myocardial infarction, CABG: coronary artery bypass graft; NA: not available.

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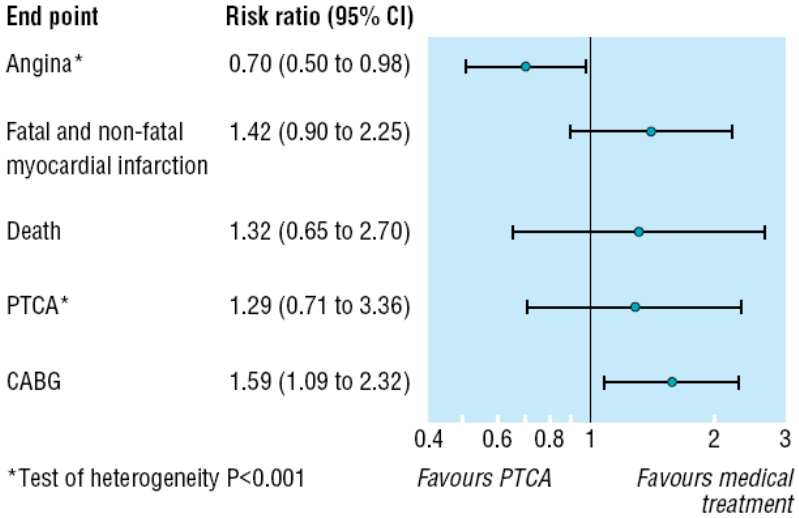

Pooled risk ratios for various end points from six randomised controlled trials comparing percutaneous transluminal coronary angioplasty (PCTA) with medical treatment in patients with non-acute coronary heart disease; (CABG: coronary artery bypass grafting; n=953 for PTCA and 951 for medical treatment)

What is already known on this topic

Percutaneous transluminal coronary angioplasty is increasingly used in the management of non-acute coronary disease

What this study adds

In non-acute coronary disease percutaneous transluminal coronary angioplasty may result in greater relief from angina than medical treatment, though the magnitude of effect varies considerably

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The procedure may lead to an increase in coronary bypass grafting compared with medical treatment and is unlikely to reduce non-fatal myocardial infarction, death, or repeated angioplasty

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The procedure should be use only in patients with non-acute coronary in whom angina cannot be controlled by medical treatment, though coronary artery bypass grafting is an alternative

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2000

Coronary Heart Disease

Percutaneous Coronary Intervention Versus Conservative Therapy in Nonacute Coronary Artery Disease

A Meta-Analysis

Demosthenes G. Katritsis, MD, PhD; John P.A. Ioannidis, MD

Background—Percutaneous coronary intervention (PCI) has been shown to improve symptoms compared with conservative medical treatment in patients with stable coronary artery disease (CAD); however, there is limited evidence on the effect of PCI on the risk of death, myocardial infarction, and subsequent revascularization. Therefore, we performed a meta-analysis of 11 randomized trials comparing PCI to conservative treatment in patients with stable CAD.

Methods and Results—A total of 2950 patients were included in the meta-analysis (1476 received PCI, and 1474 received conservative treatment). There was no significant difference between the 2 treatment strategies with regard to mortality, cardiac death or myocardial infarction, nonfatal myocardial infarction, CABG, or PCI during follow-up. By random effects, the risk ratios (95% CIs) for the PCI versus conservative treatment arms were 0.94 (0.72 to 1.24), 1.17 (0.88 to 1.57), 1.28 (0.94 to 1.75), 1.03 (0.80 to 1.33), and 1.23 (0.80 to 1.90) for these 5 outcomes, respectively. A possible survival benefit was seen for PCI only in trials of patients who had a relatively recent myocardial infarction (risk ratio 0.40, 95% CI 0.17 to 0.95). Except for PCI during follow-up, there was no significant between-study heterogeneity for any outcome.

Conclusions—In patients with chronic stable CAD, in the absence of a recent myocardial infarction, PCI does not offer any benefit in terms of death, myocardial infarction, or the need for subsequent revascularization compared with conservative medical treatment. (***Circulation*. 2005;111:2906-2912.**)

Key Words: meta-analysis ■ angioplasty ■ myocardial infarction ■ mortality

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PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2005

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TABLE 4. Random Effects Risk Ratios (95% CIs Intervals) for PCI vs Conservative Medical Management in Subgroup Analyses

Subgroups	Death	Cardiac Death or MI	Nonfatal MI	CABG	PCI
Stent availability					
Yes	0.89 (0.33–2.36)	1.28 (0.66–2.48)‡	1.32 (0.81–2.15)	0.99 (0.35–2.77)	1.42 (0.67–3.00)‡
No	0.99 (0.71–1.39)	1.18 (0.85–1.63)	1.26 (0.84–1.89)	1.06 (0.80–1.40)	1.11 (0.64–1.94)‡
Mean follow-up >2 years					
Yes	0.88 (0.64–1.22)	0.99 (0.68–1.46)	1.15 (0.80–1.65)	1.06 (0.80–1.40)	1.22 (0.64–2.31)‡
No	1.39 (0.60–3.22)	1.82 (1.10–2.99)	1.72 (0.95–3.13)	0.97 (0.42–2.25)	1.27 (0.66–2.42)‡
All patients with recent MI*					
Yes	0.40 (0.17–0.95)§	1.01 (0.18–5.60)	1.26 (0.27–5.83)	0.24 (0.04–1.42)	0.42 (0.20–0.91)§
No	1.04 (0.78–1.39)§	1.31 (1.00–1.73)	1.35 (0.96–1.90)	1.06 (0.82–1.38)	1.41 (0.88–2.24)‡§
Ischemia documented in >80%†					
Yes	0.98 (0.63–1.55)	1.50 (0.88–2.56)	1.13 (0.60–2.14)	1.11 (0.64–1.90)	1.85 (0.87–3.91)‡
No	0.86 (0.42–1.74)‡	1.10 (0.71–1.72)	1.33 (0.93–1.91)	1.00 (0.58–1.72)	0.96 (0.56–1.65)‡

*Eight days to 3 months before entry into the trial.
†Based on exercise test with or without scintigraphy.
‡Statistically significant between-study heterogeneity ($P<0.10$ for heterogeneity in studies of this subgroup).
§Statistically significant heterogeneity between the 2 subgroups of studies ($P<0.05$ for comparison of subgroups).

TABLE 2. Number of Patients With Major Clinical Outcomes per Arm

	Death		Cardiac Death or MI		Nonfatal MI		CABG		PCI	
Study	MT	PCI	MT	PCI	MT	PCI	MT	PCI	MT	PCI
RITA-2	43	43	42	44	23	32	63	64	139	86
ACME-1	15	16	8	14	7	6	12	13	34	31
ACME-2	10	9	6	6	6	6	1	3	8	11
AVERT	1	1	5	6	4	5	2	9	18	21
Dakik et al	1	1	1	3	0	2	2	0	0	0
MASS	6	6	5	7	3	4	8	8	4	21
MASS II	3	11	13	25	10	16	12	7	4	18
ALKK	17	6	26	14	12	10	4	1	20	8
Sievers et al	1	0	1	2	0	2	2	2	7	5
Hambrecht et al	0	0	0	1	0	1	0	1	3	9
Bech et al	4	2	2	4	0	3	0	1	6	9

MT indicates medical (conservative) treatment.
In ACME-1, for data on nonfatal MI, CABG, and PCI, there was information on 107 patients treated conservatively and 105 treated with PCI. For ALKK, separate data for CABG and PCI pertain to 6 months of follow-up. Otherwise, patient denominators and follow-up for all trial outcomes are as shown in Table 1.

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association.
Learn and Live.

Percutaneous Coronary Intervention Versus Conservative Therapy in Nonacute Coronary Artery Disease: A Meta-Analysis
Demosthenes G. Katritsis and John P.A. Ioannidis
Circulation 2005;111;2906-2912; originally published online May 31, 2005;

1. availability of stents did not make a substantial difference for any of the 5 end points considered.
2. trials with follow-up exceeding 2 years showed no differences between PCI and conservative treatments
3. trials that exclusively enrolled patients with relatively recent MIs showed a statistically significant reduction in the risk of death (P 0.037) and risk for subsequent PCI (P0.029) and possibly also CABG (P 0.12) in the PCI arms.
4. there was no evidence that trials with definitive documentation of ischemia by exercise test or scintigraphy had different risk ratios than trials in which functional ischemia was not documented as thoroughly

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2005

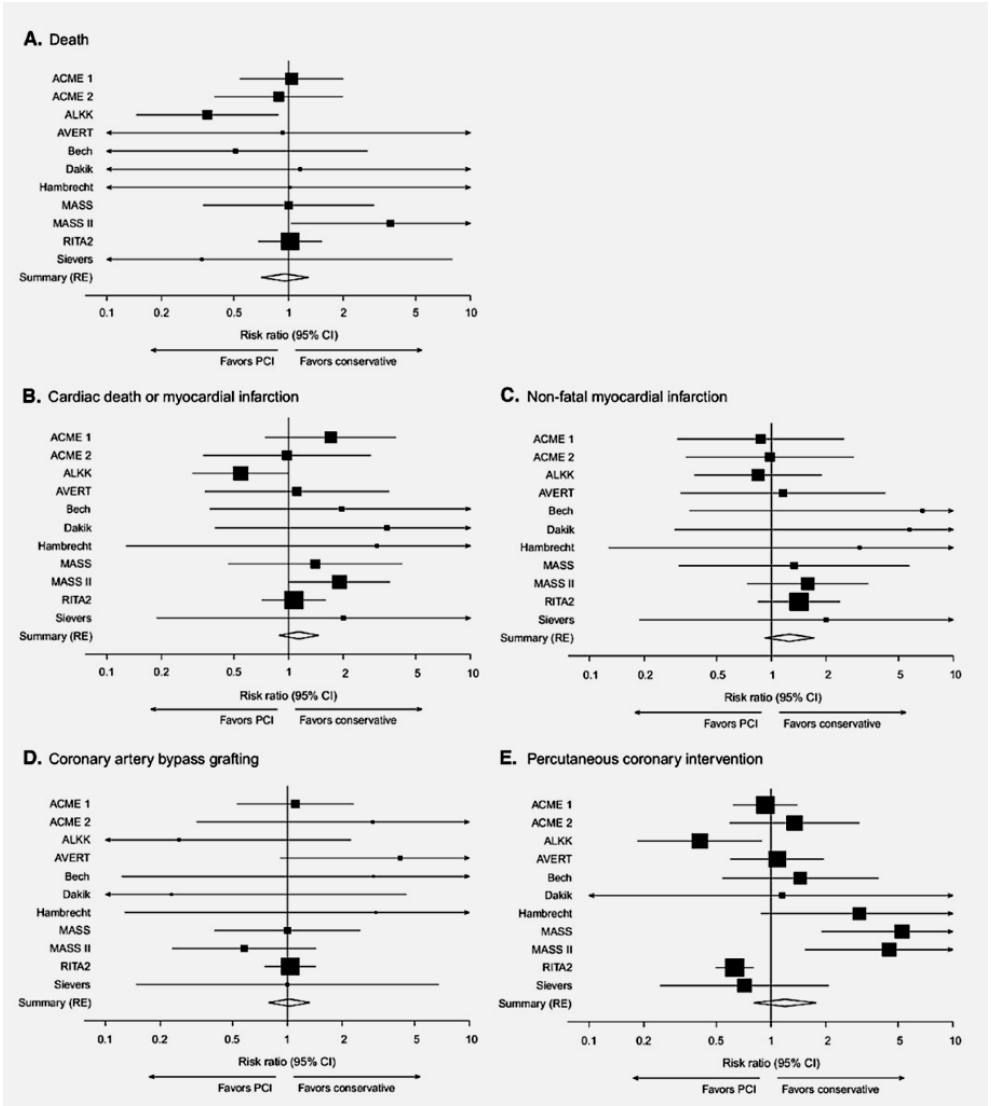

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TABLE 3. Summary Risk Ratios for Major Outcomes with PCI vs Conservative Medical Treatment

Outcome	RE Risk Ratio (95% CI)	*P*	Q (I^2)	FE Risk Ratio (95% CI)	*P*
Death	0.94 (0.72–1.24)	0.68	10.05 (0%)	0.95 (0.72–1.23)	0.68
Cardiac death or MI	1.17 (0.88–1.57)	0.28	11.3 (13%)	1.16 (0.91–1.48)	0.24
Nonfatal MI	1.28 (0.94–1.75)	0.12	4.93 (0%)	1.32 (0.97–1.79)	0.077
CABG	1.03 (0.80–1.33)	0.82	9.16 (0%)	1.04 (0.81–1.34)	0.76
PCI	1.23 (0.80–1.90)	0.34	38.4 (74%)	0.91 (0.77–1.07)	0.25

RE indicates random effects; FE, fixed effects.

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American Heart Association. Learn and Live.

Percutaneous Coronary Intervention Versus Conservative Therapy in Nonacute Coronary Artery Disease: A Meta-Analysis
Demosthenes G. Katritsis and John P.A. Ioannidis
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we conclude that for patients with chronic CAD and good left ventricular function, PCI does not confer any clear benefit in terms of long-term hard clinical outcomes compared with conservative medical treatment.

PCI may be indicated in special circumstances, eg, relatively early after MI.

By comparing the benefits, if any, against cost considerations, we believe that many percutaneous interventions that currently are performed in patients with nonacute CAD probably are not justified

COURAGE TRIAL

2007

Patients with stable CAD and those in whom initial CCS class IV angina subsequently stabilized medically were included in the study.

- **Entry criteria included stenosis of at least 70% in at least one proximal epicardial coronary artery and objective evidence of myocardial ischemia (substantial changes in ST-segment depression or T-wave inversion on the resting electrocardiogram or inducible ischemia with either exercise or pharmacologic vasodilator stress) or at least one coronary stenosis of at least 80% and classic angina without provocative testing.**
- **Exclusion criteria included persistent CCS class IV angina, a markedly positive stress test (substantial ST-segment depression or hypotensive response during stage 1 of the Bruce protocol), refractory heart failure or cardiogenic shock, an ejection fraction of less than 30%, revascularization within the previous 6 months, and coronary anatomy not suitable for PCI.**

COURAGE TRIAL

2007

- All patients received antiplatelet therapy with ASA or clopidogrel. Patients undergoing PCI received ASA and clopidogrel, in accordance with accepted treatment guidelines. Medical antiischemic therapy in both groups included long-acting metoprolol, amlodipine, and isosorbide mononitrate, alone or in combination, along with either lisinopril or losartan as standard secondary prevention. All patients received aggressive therapy to ↓ LDL (simvastatin alone or in combination with ezetimibe) with a target level of 60 to 85 mg % After the LDL cholesterol target was achieved, an attempt was made to ↑ HDL to a level above 40 mg % and ↓ triglyceride to a level below 150 mg %, with exercise, extended-release niacin, or fibrates, alone or in combination
- At the 5-year follow-up visit, 70% of subjects had an LDL level < 85 mg % (median, 71±1.3 mg %), 65% and 94% had systolic and diastolic BP targets of < 130 mm Hg and 85 mm Hg, respectively; and 45% of patients with diabetes had a glycated hemoglobin level ≤ 7.0%. Patients had high rates of adherence to the regimen of diet, regular exercise, and smoking cessation, although the mean body-mass index did not decrease.

COURAGE TRIAL

2007

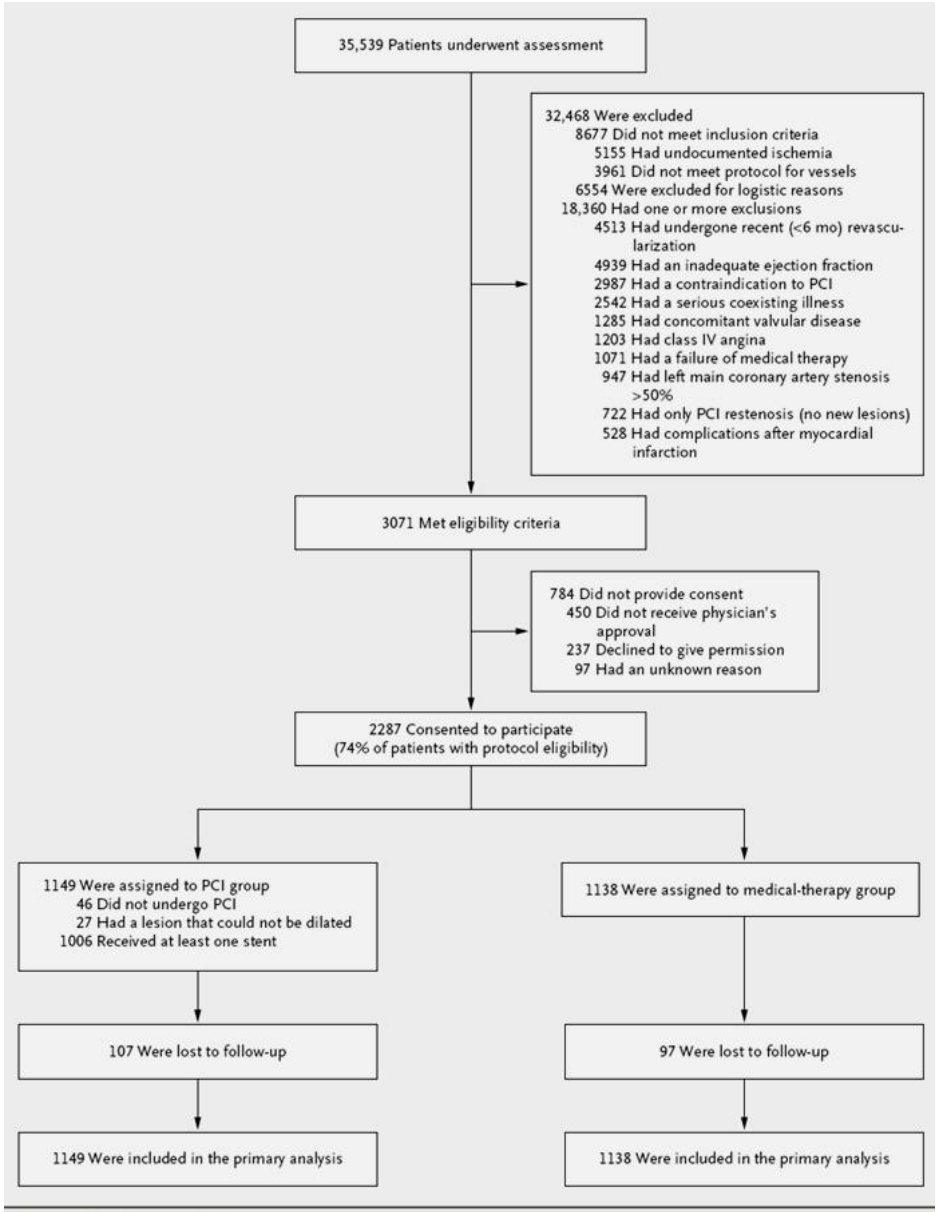

Figure 1. Enrollment and Outcomes.

Of 35,539 patients who were assessed for eligibility in the trial, 32,468 were excluded for a variety of reasons (patients could have more than one reason for exclusion). A total of 3071 patients met all inclusion criteria. Of these, 2287 (74%) consented to participate in the study (932 in Canada, 968 in U.S. Veterans Affairs facilities, and 387 in U.S. facilities other than Veterans Affairs hospitals). Of these patients, 1149 were randomly assigned to the PCI group and 1138 to the medical-therapy group. The median follow-up was 4.6 years for both study groups.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 12, 2007 VOL. 356 NO. 15

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*

The median follow-up period was 4.6 years. There were no significant differences between the PCI group and the medical-therapy group

1. **in the composite of death, myocardial infarction, and stroke (20.0% vs. 19.5%; hazard ratio, 1.05;95% CI, 0.87 to 1.27; P = 0.62);**
2. **hospitalization for acute coronary syndrome (12.4% vs. 11.8%; hazard ratio, 1.07; 95% CI, 0.84 to 1.37; P = 0.56);**
3. **myocardial infarction (13.2% vs. 12.3%; hazard ratio, 1.13; 95% CI, 0.89 to 1.43; P = 0.33);**

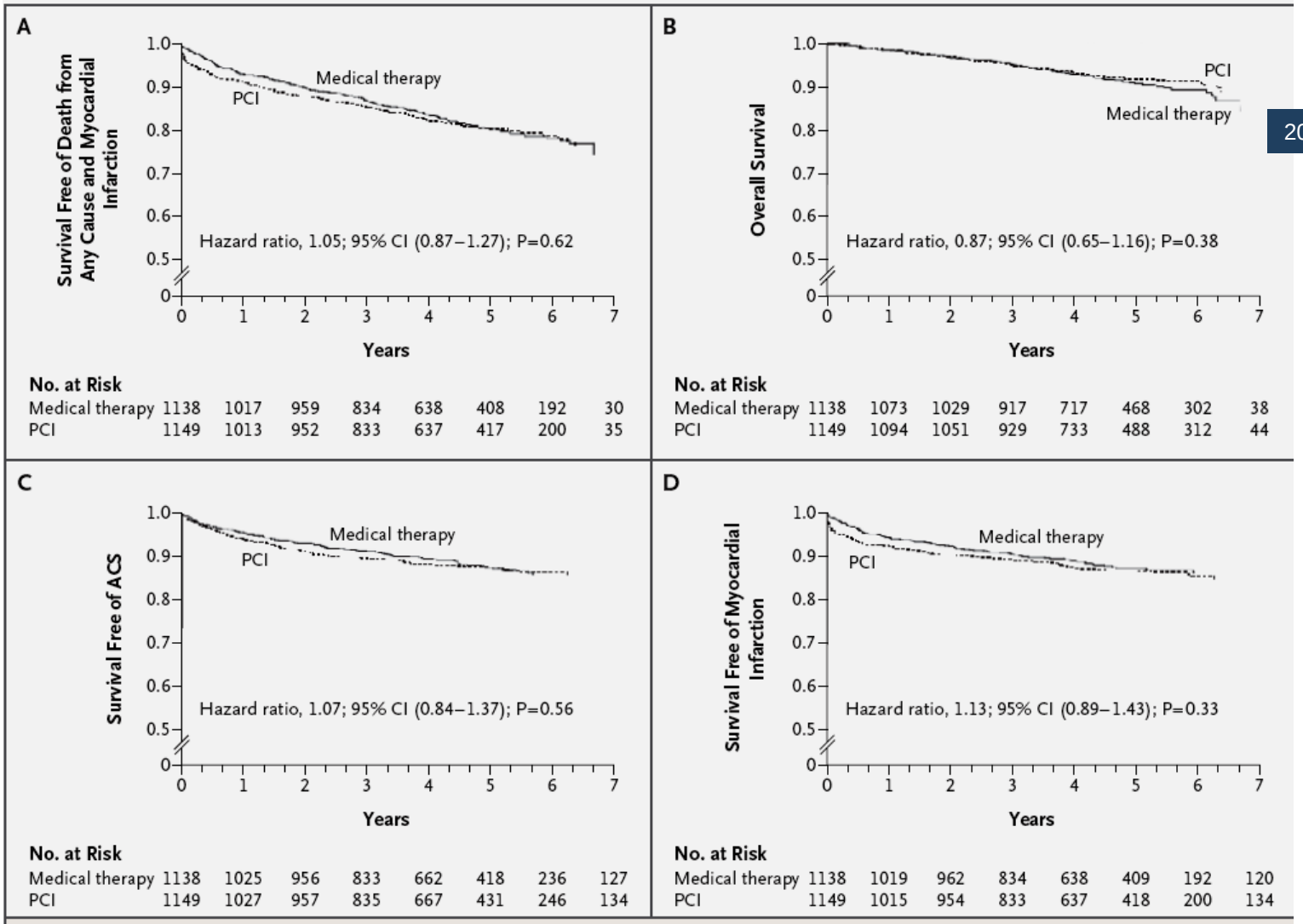

Figure 2. **Kaplan–Meier Survival Curves.**

In Panel A, the estimated 4.6-year rate of the composite primary outcome of death from any cause and nonfatal myocardial infarction was 19.0% in the PCI group and 18.5% in the medical-therapy group. In Panel B, the estimated 4.6-year rate of death from any cause was 7.6% in the PCI group and 8.3% in the medical-therapy group. In Panel C, the estimated 4.6-year rate of hospitalization for acute coronary syndrome (ACS) was 12.4% in the PCI group and 11.8% in the medical-therapy group. In Panel D, the estimated 4.6-year rate of acute myocardial infarction was 13.2% in the PCI group and 12.3% in the medical-therapy group.

2007

COURAGE TRIAL

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Baseline Characteristics	No. of Patients	Hazard Ratio (95% CI)	Event Rate for the Primary Outcome		P Value
			PCI	Medical Therapy	
Overa					
Sex					
Ma					
Fer					
Myoc					
Yes					
No					
Exten					
Mu					
Sin					
Smok					
Cu					
No					
Diabe					
Yes					
No					
CCS a					
0 o					
II o					
Ejecti					
≤5(					
>5(					
Age					
>6!					
≤6!					
Previ					
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	

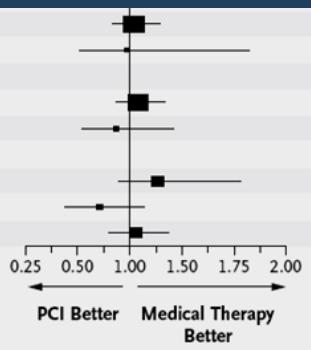

Figure 3. Subgroup Analyses.

The chart shows hazard ratios (black squares, sized in proportion to the number of subjects in a group), 95% CIs (horizontal lines), cumulative 4.6-year event rates for the composite primary outcome (death from any cause and nonfatal myocardial infarction) for the PCI group versus the medical-therapy group for the specified subgroups, and P values for the interaction between the treatment effects and subgroup variables. P values were calculated with the use of the Wald statistic. There was no significant interaction between treatment and subgroup variables as defined according to the prespecified value for interaction (P<0.01), although there was a trend for interaction with respect to sex (P=0.03). PCI denotes percutaneous coronary intervention, CAD coronary artery disease, CCS Canadian Cardiovascular Society, CABG coronary-artery bypass grafting, and VA Veterans Affairs.

Pts with greater than 10% residual ischaemia on stress myocardial perfusion scintigraphy had a higher rate of death or myocardial infarction than did those without ischaemia (39% vs 0%, p<0 · 0001), suggesting a potentially important role of cardiac imaging in the risk stratification of pts with a higher ischaemic burden and who are more likely to benefit from revascularisation than are those with no or only mild ischaemia.

Lancet 2010 375:763-772

2007

At a median FU of 4.6 yrs, 21.1% of pts in the PCI gr. had additional revasc, vs 32.6% of those in the MT gr. (HR, 0.60; 95% CI, 0.51 to 0.71; P<0.001).

There was a substantial ↓ in the prevalence of angina in both gr. There was a statistically sign. difference in the rates of freedom from angina throughout most of the FU period, in favor of the PCI gr. At 5 yrs, 74% of pts in the PCI gr and 72% of MT gr were free of angina (P = 0.35).

Of note, among pts with multivessel CAD, previous MI, and diabetes, the rate of the primary end point was similar for both groups.

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2008

CLINICAL RESEARCH — Interventional Cardiology

A Meta-Analysis of 17 Randomized Trials of a Percutaneous Coronary Intervention-Based Strategy in Patients With Stable Coronary Artery Disease

Albert Schömig, MD, Julinda Mehilli, MD, Antoinette de Waha, MD, Melchior Seyfarth, MD, Jürgen Pache, MD, Adnan Kastrati, MD

Munich, Germany

Objectives This study assessed the impact on long-term mortality of percutaneous coronary intervention (PCI) versus medical treatment in patients with symptoms or signs of myocardial ischemia but no acute coronary syndrome.

Background The impact of PCI on the long-term prognosis of patients with stable coronary artery disease has not been established.

Methods We identified 17 randomized trials comparing a PCI-based invasive treatment strategy with medical treatment in 7,513 patients with symptoms or signs of myocardial ischemia but no acute coronary syndrome. Of these patients, 3,675 were assigned to the PCI group and 3,838 to the medical treatment group. The primary end point was all-cause death. The length of follow-up was in the range between 12 and 122 months, 51 months on average.

Results In the PCI group, 271 patients died compared with 335 patients in the medical treatment group, which corresponds to a 20% reduction in the odds ratio (OR) of all-cause death (OR: 0.80; 95% confidence interval [CI]: 0.64 to 0.99, p = 0.263 for heterogeneity across the trials). Allocation to the PCI group was associated with a nonsignificant 26% reduction in the OR of cardiac death (OR: 0.74, 95% CI: 0.51 to 1.06). In the PCI group, 319 patients had a nonfatal myocardial infarction after randomization compared with 357 patients in the medical treatment group (OR: 0.90, 95% CI: 0.66 to 1.23).

Conclusions These findings suggest that a PCI-based invasive strategy may improve long-term survival compared with a medical treatment-only strategy in patients with stable coronary artery disease. (J Am Coll Cardiol 2008;52:894–904) © 2008 by the American College of Cardiology Foundation

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Major limitations of this analysis were that it included not only patients with chronic stable angina but also other patient groups, and that the trials analysed were completed in the 1980s, indicating that both pharmacological treatment and PCI techniques were outdated by contemporary standards.

Lancet 2010 375:763-772

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2009

CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

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The Impact of Revascularization on Mortality in Patients with Nonacute Coronary Artery Disease

Allen Jeremias, MD, MSc,[a] Sanjay Kaul, MD,[c] Todd K. Rosengart, MD,[b] Luis Gruberg, MD,[a] David L. Brown, MD[a]

Departments of [a]Medicine (Cardiovascular Medicine) and [b]Surgery (Cardiothoracic Surgery), Stony Brook University Medical Center, Stony Brook, NY; [c]Division of Cardiology, Cedars-Sinai Medical Center and David Geffen School of Medicine, University of California, Los Angeles, Calif.

ABSTRACT

BACKGROUND: Although early revascularization improves outcomes for patients with acute coronary syndromes, the role of revascularization for patients with nonacute coronary artery disease is controversial. The objective of this meta-analysis was to compare surgical or percutaneous revascularization with medical therapy alone to determine the impact of revascularization on death and nonfatal myocardial infarction in patients with coronary artery disease.

METHODS: The Medline and Cochrane Central Register of Controlled Trials databases were searched to identify randomized trials of coronary revascularization (either surgical or percutaneous) versus medical therapy alone in patients with nonacute coronary disease reporting the individual outcomes of death or nonfatal myocardial infarction reported at a minimum follow-up of 1 year. A random effects model was used to calculate odds ratios (OR) for the 2 prespecified outcomes.

RESULTS: Twenty-eight studies published from 1977 to 2007 were identified for inclusion in the analysis; the revascularization modality was percutaneous coronary intervention in 17 studies, coronary bypass grafting in 6 studies, and either strategy in 5 studies. Follow-up ranged from 1 to 10 years with a median of 3 years. The 28 trials enrolled 13,121 patients, of whom 6476 were randomized to revascularization and 6645 were randomized to medical therapy alone. The OR for revascularization versus medical therapy for mortality was 0.74 (95% confidence interval [CI], 0.63-0.88). A stratified analysis according to revascularization mode revealed both bypass grafting (OR 0.62; 95% CI, 0.50-0.77) and percutaneous intervention (OR 0.82; 95% CI, 0.68-0.99) to be superior to medical therapy with respect to mortality. Revascularization was not associated with a significant reduction in nonfatal myocardial infarction compared with medical therapy (OR 0.91; 95% CI, 0.72-1.15).

CONCLUSION: Revascularization by coronary bypass surgery or percutaneous intervention in conjunction with medical therapy in patients with nonacute coronary artery disease is associated with significantly improved survival compared with medical therapy alone.

 • *The American Journal of Medicine (2009) 122, 152-161*

KEYWORDS: Angioplasty; Bypass surgery; Coronary artery disease; Stents

CLINICAL SIGNIFICANCE

- In patients with nonacute coronary artery disease, the odds ratio for revascularization versus medical therapy for mortality was 0.74 (95% CI, 0.63-0.88, $P<.001$), indicating a significant mortality reduction with coronary revascularization.
- A stratified analysis according to revascularization mode revealed both coronary artery bypass grafting and percutaneous coronary intervention to be superior to medical therapy with respect to mortality.
- Revascularization was not associated with a significant reduction in nonfatal myocardial infraction compared with medical therapy.

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2009

Percutaneous coronary interventions for non-acute coronary artery disease: a quantitative 20-year synopsis and a network meta-analysis

Thomas A Trikalinos, Alawi A Alsheikh-Ali, Athina Tatsioni, Brahmajee K Nallamothu, David M Kent

Summary

Background Over the past 20 years, percutaneous transluminal balloon coronary angioplasty (PTCA), bare-metal stents (BMS), and drug-eluting stents (DES) succeeded each other as catheter-based treatments for coronary artery disease. We undertook a systematic overview of randomised trials comparing these interventions with each other and with medical therapy in patients with non-acute coronary artery disease.

Methods We searched Medline for trials contrasting at least two of the four interventions (PTCA, BMS, DES, and medical therapy). Eligible outcomes were death, myocardial infarction, coronary artery bypass grafting, target lesion or vessel revascularisation, and any revascularisation. Random effects meta-analyses summarised head-to-head (direct) comparisons, and network meta-analyses integrated direct and indirect evidence.

Findings 61 eligible trials (25 388 patients) investigated four of six possible comparisons between the four interventions; no trials directly compared DES with medical therapy or PTCA. In all direct or indirect comparisons, succeeding advancements in percutaneous coronary intervention did not produce detectable improvements in deaths or myocardial infarction. The risk ratio (RR) for indirect comparisons between DES and medical therapy was 0·96 (95% CI 0·60–1·52) for death and 1·15 (0·73–1·82) for myocardial infarction. By contrast, we recorded sequential significant reductions in target lesion or vessel revascularisation with BMS compared with PTCA (RR 0·68 [0–60·0·77]) and with DES compared with BMS (0·44 [0·35–0·56]). The RR for the indirect comparison between DES and PTCA for target lesion or vessel revascularisation was 0·30 (0·17–0·51).

Interpretation Sequential innovations in the catheter-based treatment of non-acute coronary artery disease showed no evidence of an effect on death or myocardial infarction when compared with medical therapy. These results lend support to present recommendations to optimise medical therapy as an initial management strategy in patients with this disease.

Funding US National Institutes of Health.

Lancet 2009; 373: 911–18

See Comment page 870

Institute for Clinical Research and Health Policy Studies (T A Trikalinos MD, A A Alsheikh-Ali MD, A Tatsioni MD, D M Kent MD) **and Division of Cardiology, Department of Medicine** (A A Alsheikh-Ali), **Tufts Medical Center, Boston, MA, USA; and VA Health Services Research and Development Center of Excellence, Ann Arbor VA Medical Center, Ann Arbor, MI, USA** (B K Nallamothu MD)

Correspondence to: Thomas A Trikalinos, Center for Clinical Evidence Synthesis, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Box #63, 800 Washington St, Boston, MA 02111, USA
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- ✓ **Despite the sequential testing of PTCA versus MT, BMS versus PTCA, and DES versus BMS, the cumulative benefits of technological innovations after 20 years of clinical trials in this area have not been systematically assessed.**
- ✓ **We undertook a systematic overview of all RCT comparing MT, PTCA, BMS, and DES in the treatment of pts with non-acute CAD.**
- ✓ **We explored the succession of these interventions over time with traditional meta-analysis and network meta-analysis**

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2009

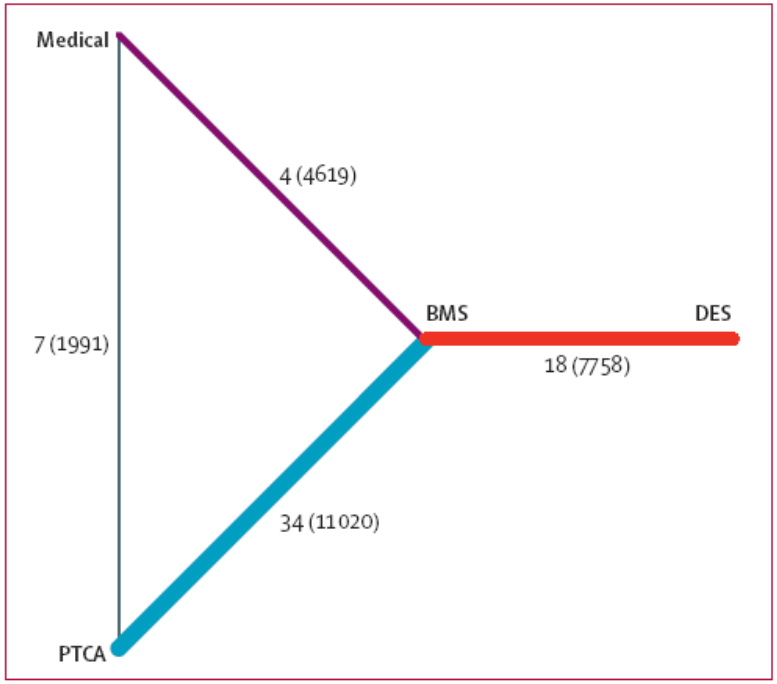

Figure 1: **Graphical representation of the network of eligible trials**
Lines connect the interventions that have been studied in head-to-head (direct) comparisons in the eligible randomised trials. The width of the lines represents the relative amount of information for each comparison in terms of the cumulative number of randomised patients. The numbers correspond to the number of trials entries, and in parentheses the cumulative number of randomised patients per comparison. BMS=bare-metal stents. DES=drug-eluting stents. PTCA=percutaneous transluminal coronary angioplasty.

- ✓ **Eligible RCT were those of pts with symptomatic or asymptomatic non-acute CAD. This criterion included RCT with pts with stable and unstable angina but excluded those with pts with an AMI within the previous 72 h at the time of first enrolment**
- ✓ **We excluded RCT that enrolled only pts with diabetes mellitus and those that enrolled any pts with AMI within the previous 72 h. We also excluded those focusing only on venous bypass grafts, in-stent restenosis, or left main disease. We excluded trials comparing two different types of non-stenting techniques (eg, cutting balloon angioplasty or directional coronary atherectomy vs PCI), and those assessing two different BMS or two different DES classes.**
- ✓ **Eligible outcomes were death, fatal and non-fatal MI, target vessel or lesion revascularisation, any subsequent PCI (revascularisation), and CABG.**

THE LANCET
www.thelancet.com Vol 373 March 14, 2009

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2009

	PTCA *vs* medical	BMS *vs* PTCA	BMS *vs* medical*	DES *vs* BMS
Number of trials	7	34	4	18
Number of patients	201 (101–227)	249 (116–407)	1134 (66–2286)	268 (175–500)
Follow-up (months)	60 (36–84)	9 (6–12)	30 (12–60)	9 (9–12)
Year of publication	1998 (1997–2003)	2000 (1999–2002)	2005 (2002–2007)	2004 (2003–2005)
Year of enrolment	1990 (1988–1992)	1996 (1994–1997)	1997 (1997–2000)	2001 (2001–2002)
Demographics				
Unstable angina (%)	0% (0–0)	34% (18–48)	0% (0–0)	34% (31–50)
Mean age (years)	56 (56–58)	60 (58–61)	60 (59–62)	62 (61–65)
Men (%)	85% (71–94)	78% (72–82)	83% (78–100)	76% (70–79)
Diabetic (%)	11% (9–18)	16% (11–21)	22% (14–34)	20% (17–25)
Multivessel disease (%)	0% (0–40)	38% (33–57)	60% (49–70)	42% (40–44)
Number including only lesions in small arteries†	0	9	0	0
Number including only complex lesions‡	0	0	0	3

Data are median (IQR), unless otherwise indicated. BMS=bare-metal stents. DES=drug-eluting stents. PTCA=percutaneous transluminal coronary angioplasty. *Data for this column are median (range). †Small arteries are arteries with a diameter of 3·0 mm or less. ‡Complex lesions are lesions near bifurcations or in tortuous vessels.

Table 1: **Characteristics of trials across different comparisons**

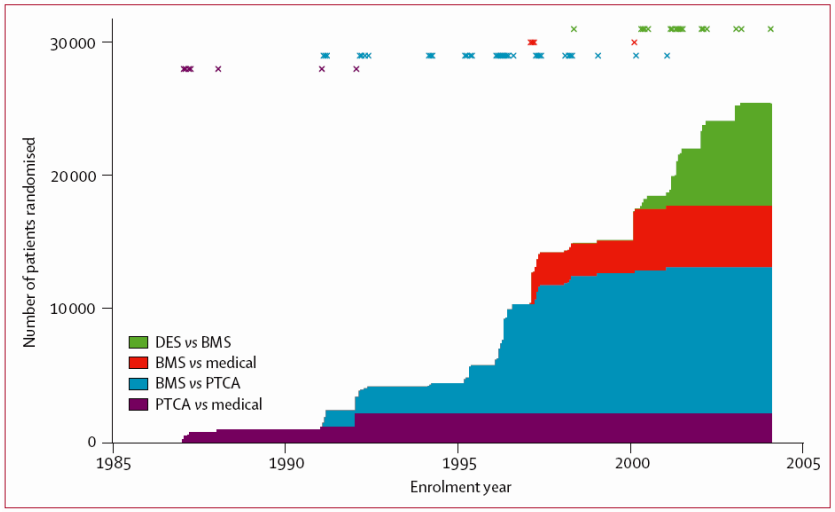

Figure 2: **Accumulation of randomised evidence per comparison type over time**
The graph shows the cumulative number of patients randomly assigned in each comparison against the year of patient enrolment in each trial. The year of first patient enrolment in each trial is marked with a cross in the upper part of the graph, with colours corresponding to comparison type. BMS=bare-metal stents. DES=drug-eluting stents. PTCA=percutaneous transluminal coronary angioplasty.

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2009

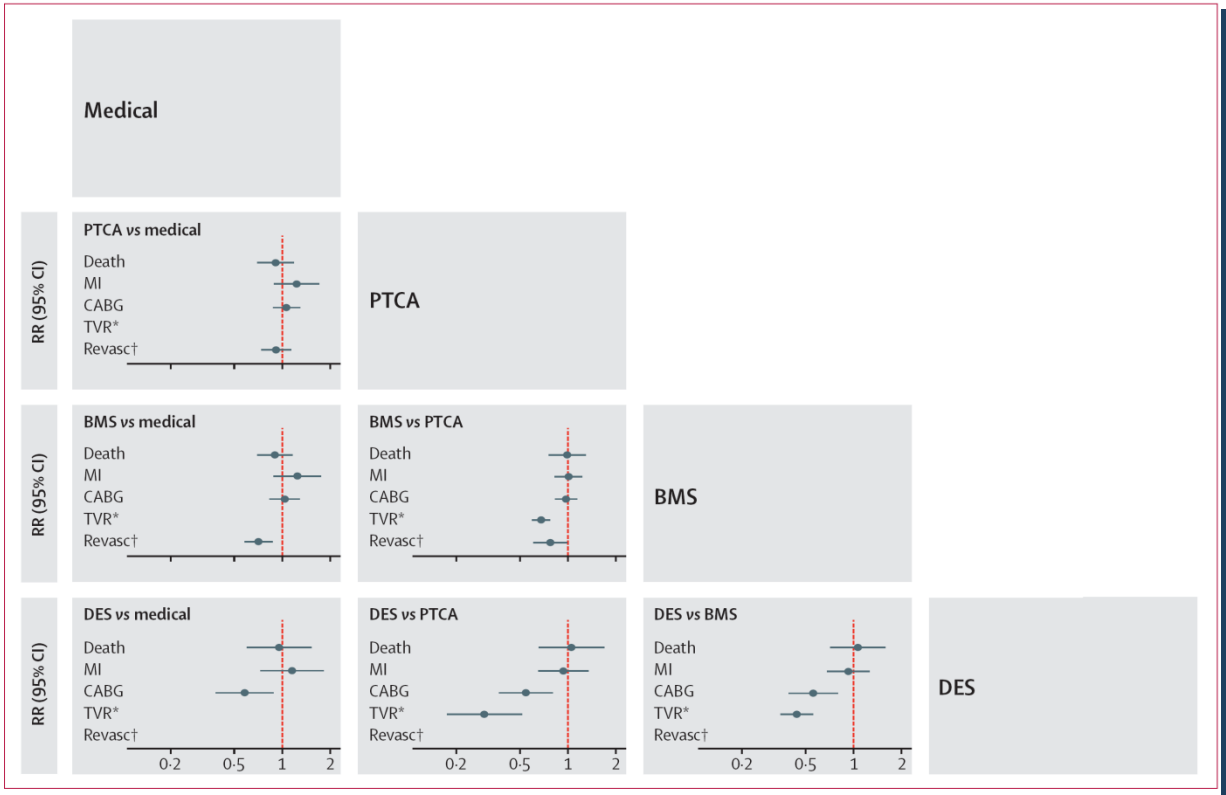

Figure 3: **Results from network meta-analyses incorporating direct and indirect comparisons between the eligible interventions**
Matrix of summary risk ratio (RR) plots from the comparisons between the four interventions, with respect to five outcomes. Note that cells of the matrix for DES versus PTCA and DES versus medical therapy are based on indirect data only. Each summary risk ratio is depicted by a filled circle, and the corresponding 95% CIs are shown as horizontal lines. Red vertical lines correspond to the line of no effect. The webappendix (p 2) shows the corresponding figure for direct effects only. BMS=bare-metal stents. DES=drug-eluting stents. MI=myocardial infarction. PTCA=percutaneous transluminal balloon angioplasty. Revasc=total number of revascularisations. TVR=target vessel (or lesion) revascularisation. *TVR could not be assessed in medical therapy trials. †The total number of revascularisations (not only those of the target vessel/lesion) was not extractable from DES versus BMS trials, and was only extractable from three of 34 BMS versus PTCA trials.

- ✓ **Interpretation: sequential innovations in the catheter-based treatment of non-acute coronary artery disease showed no evidence of an effect on death or myocardial infarction when compared with medical therapy.**
- ✓ **These results lend support to present recommendations to optimise medical therapy as an initial management strategy in patients with this disease.**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 14, 2008 VOL. 359 NO. 7

Effect of PCI on Quality of Life in Patients with Stable Coronary Disease

William S. Weintraub, M.D., John A. Spertus, M.D., M.P.H., Paul Kolm, Ph.D., David J. Maron, M.D., Zefeng Zhang, M.D., Ph.D., Claudine Jurkovitz, M.D., M.P.H., Wei Zhang, M.S., Pamela M. Hartigan, Ph.D., Cheryl Lewis, R.N., Emir Veledar, Ph.D., Jim Bowen, B.S., Sandra B. Dunbar, D.S.N., Christi Deaton, Ph.D., Stanley Kaufman, M.D., Robert A. O'Rourke, M.D., Ron Goeree, M.S., Paul G. Barnett, Ph.D., Koon K. Teo, M.D., and William E. Boden, M.D., for the COURAGE Trial Research Group*

ABSTRACT

BACKGROUND

It has not been clearly established whether percutaneous coronary intervention (PCI) can provide an incremental benefit in quality of life over that provided by optimal medical therapy among patients with chronic coronary artery disease.

METHODS

We randomly assigned 2287 patients with stable coronary disease to PCI plus optimal medical therapy or to optimal medical therapy alone. We assessed angina-specific health status (with the use of the Seattle Angina Questionnaire) and overall physical and mental function (with the use of the RAND 36-item health survey [RAND-36]).

RESULTS

At baseline, 22% of the patients were free of angina. At 3 months, 53% of the patients in the PCI group and 42% in the medical-therapy group were angina-free (P<0.001). Baseline mean (±SD) Seattle Angina Questionnaire scores (which range from 0 to 100, with higher scores indicating better health status) were 66±25 for physical limitations, 54±32 for angina stability, 69±26 for angina frequency, 87±16 for treatment satisfaction, and 51±25 for quality of life. By 3 months, these scores had increased in the PCI group, as compared with the medical-therapy group, to 76±24 versus 72±23 for physical limitation (P=0.004), 77±28 versus 73±27 for angina stability (P=0.002), 85±22 versus 80±23 for angina frequency (P<0.001), 92±12 versus 90±14 for treatment satisfaction (P<0.001), and 73±22 versus 68±23 for quality of life (P<0.001). In general, patients had an incremental benefit from PCI for 6 to 24 months; patients with more severe angina had a greater benefit from PCI. Similar incremental benefits from PCI were seen in some but not all RAND-36 domains. By 36 months, there was no significant difference in health status between the treatment groups.

CONCLUSIONS

Among patients with stable angina, both those treated with PCI and those treated with optimal medical therapy alone had marked improvements in health status during follow-up. The PCI group had small, but significant, incremental benefits that disappeared by 36 months. (ClinicalTrials.gov number, NCT00007657.)

From the Christiana Care Health System, Newark, DE (W.S.W., P.K., C.J., W.Z., J.B.); Mid America Heart Institute/University of Missouri–Kansas City, Kansas City (J.A.S.); Vanderbilt University Medical Center, Nashville (D.J.M.); Emory University, Atlanta (Z.Z., C.L., E.V., S.B.D.); Cooperative Studies Program Coordinating Center, Veterans Affairs Connecticut Healthcare System, West Haven, CT (P.M.H.); Manchester University, Manchester, United Kingdom (C.D.); the Epimetrics Group, San Francisco (S.K.); McMaster University, Hamilton, ON, Canada (R.A.O.); San Antonio Veterans Affairs Medical Center, San Antonio, TX (R.G., K.K.T.); Veterans Affairs Health Economics Resource Center, Palo Alto, CA (P.G.B.); and Western New York Veterans Affairs Healthcare Network and Kaleida Health System, Buffalo (W.E.B.). Address reprint requests to Dr. Weintraub at the Cardiology Section, Christiana Care Health System, 4755 Ogletown-Stanton Rd., Newark, DE 19718, or at wweintraub@christianacare.org.

*Members of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial are listed in the Supplementary Appendix, available with the full text of this article at www.nejm.org.

N Engl J Med 2008;359:677-87.

COURAGE QOL

2008

Among patients with stable angina, both those treated with PCI and those treated with OMT alone had marked improvements in health status during follow-up. The PCI group had small, but significant, incremental benefits that disappeared by 36 months.

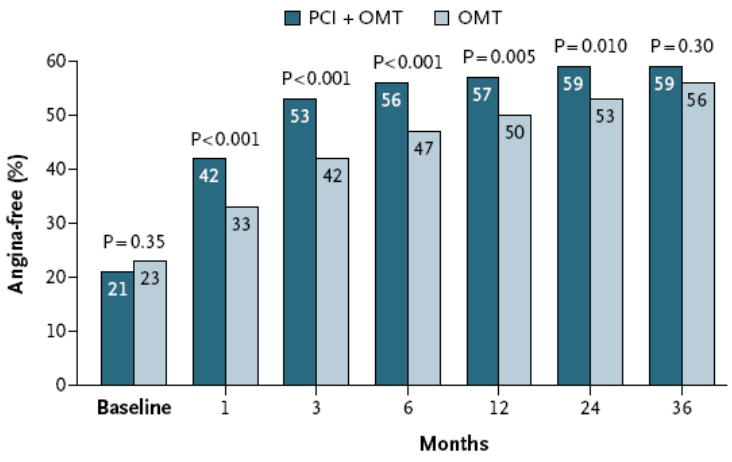

Figure 1. Freedom from Angina over Time as Assessed with the Angina-Frequency Scale of the Seattle Angina Questionnaire, According to Treatment Group.

OMT denotes optimal medical therapy, and PCI percutaneous coronary intervention.

COURAGE QOL

2008

Original Articles

Cost-Effectiveness of Percutaneous Coronary Intervention in Optimally Treated Stable Coronary Patients

William S. Weintraub, MD; William E. Boden, MD; Zugui Zhang, PhD; Paul Kolm, PhD; Zefeng Zhang, MD, PhD; John A. Spertus, MD, MPH; Pamela Hartigan, PhD; Emir Veledar, PhD; Claudine Jurkovitz, MD, MPH; Jim Bowen; David J. Maron, MD; Robert O'Rourke, MD; Marcin Dada, MD; Koon K. Teo, MD; Ron Goeree, MS; Paul G. Barnett, PhD; on Behalf of the Department of Veterans Affairs Cooperative Studies Program No. 424 (COURAGE Trial) Investigators and Study Coordinators*

Background—The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive druG Evaluations) trial compared the effect of percutaneous coronary intervention (PCI) plus optimal medical therapy with optimal medical therapy alone on cardiovascular events in 2287 patients with stable coronary disease. After 4.6 years, there was no difference in the primary end point of death or myocardial infarction, although PCI improved quality of life. The present study evaluated the relative cost and cost-effectiveness of PCI in the COURAGE trial.

Methods and Results—Resource use was assessed by diagnosis-related group for hospitalizations and by current procedural terminology code for outpatient visits and tests and then converted to costs by use of 2004 Medicare payments. Medication costs were assessed with the *Red Book* average wholesale price. Life expectancy beyond the trial was estimated from Framingham survival data. Utilities were assessed by the standard gamble method. The incremental cost-effectiveness ratio was expressed as cost per life-year and cost per quality-adjusted life-year gained. The added cost of PCI was approximately $10 000, without significant gain in life-years or quality-adjusted life-years. The incremental cost-effectiveness ratio varied from just over $168 000 to just under $300 000 per life-year or quality-adjusted life-year gained with PCI. A large minority of the distributions found that medical therapy alone offered better outcome at lower cost. The costs per patient for a significant improvement in angina frequency, physical limitation, and quality of life were $154 580, $112 876, and $124 233, respectively.

Conclusions—The COURAGE trial did not find the addition of PCI to optimal medical therapy to be a cost-effective initial management strategy for symptomatic, chronic coronary artery disease. (***Circ Cardiovasc Qual Outcomes*. 2008;1:12-20.**)

Key Words: coronary disease ■ angina ■ epidemiology ■ cost-benefit analysis ■ stents

Conclusions

The COURAGE trial did not find the addition of PCI to optimal medical therapy to be a cost-effective initial management strategy for symptomatic, chronic coronary artery disease.

Circ Cardiovasc Qual Outcomes. 2008;1:12-20.

Circulation
Cardiovascular Quality and Outcomes
Journal of the American Heart Association

DIABETE II° E CAD

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2009

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 11, 2009 VOL. 360 NO. 24

A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease

The BARI 2D Study Group*

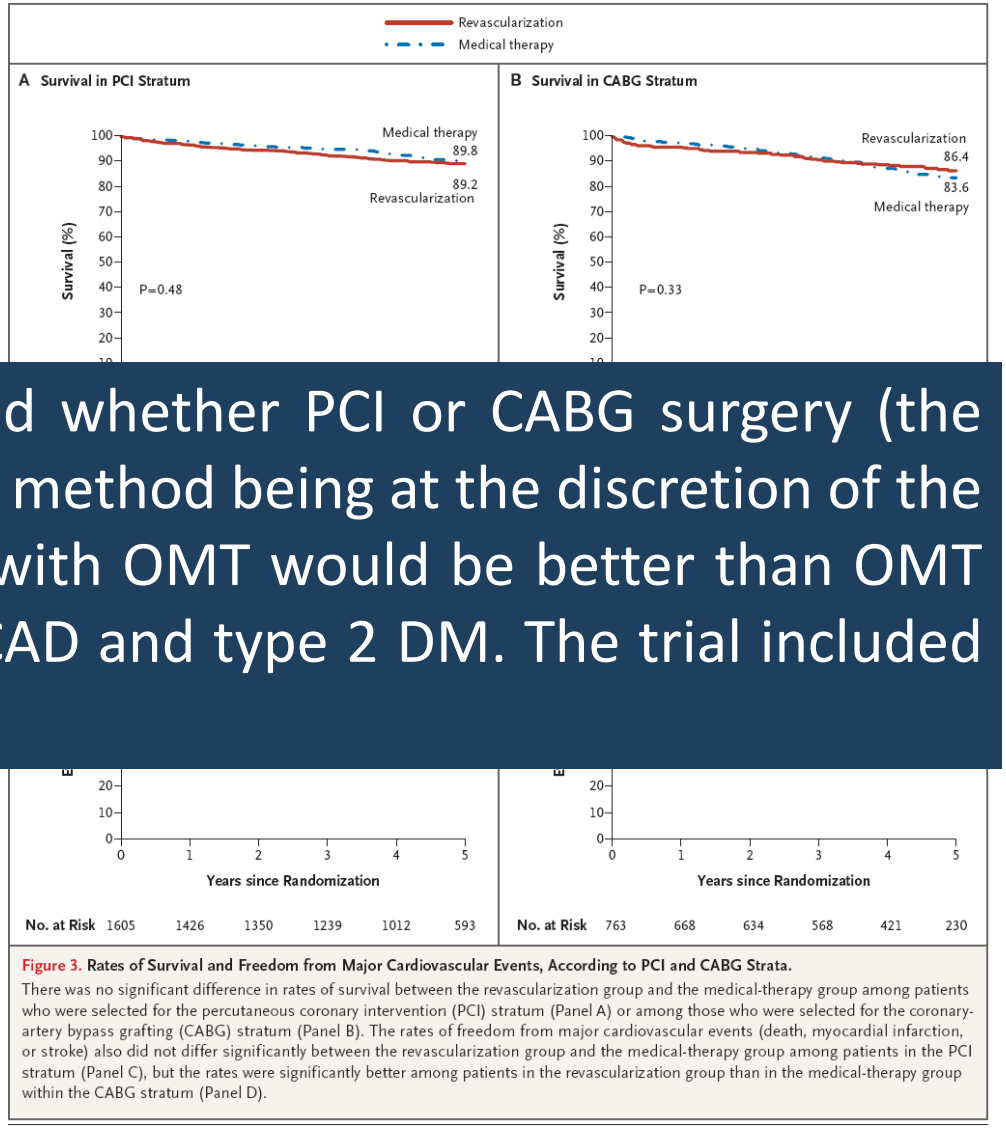

Figure 3. Rates of Survival and Freedom from Major Cardiovascular Events, According to PCI and CABG Strata.
There was no significant difference in rates of survival between the revascularization group and the medical-therapy group among patients who were selected for the percutaneous coronary intervention (PCI) stratum (Panel A) or among those who were selected for the coronary-artery bypass grafting (CABG) stratum (Panel B). The rates of freedom from major cardiovascular events (death, myocardial infarction, or stroke) also did not differ significantly between the revascularization group and the medical-therapy group among patients in the PCI stratum (Panel C), but the rates were significantly better among patients in the revascularization group than in the medical-therapy group within the CABG stratum (Panel D).

The BARI-2D trial2 investigated whether PCI or CABG surgery (the choice of the revascularisation method being at the discretion of the treating physician) combined with OMT would be better than OMT alone in patients with stable CAD and type 2 DM. The trial included 2368 pts.

Odds between prompt revascularization and those undergoing medical therapy or between strategies of insulin sensitization and insulin provision.

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2012

REVIEW ARTICLE

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Meta-analysis of Randomized Controlled Trials

Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

Background: Prior meta-analyses have yielded conflicting results regarding the outcomes of treatment of stable coronary artery disease (CAD) with initial percutaneous coronary intervention (PCI) vs medical therapy. However, most of the studies in prior systematic reviews used balloon angioplasty as well as medical therapies that do not reflect current interventional or medical practices. We therefore performed a meta-analysis of all randomized clinical trials comparing initial coronary stent implantation with medical therapy to determine the effect on death, nonfatal myocardial infarction (MI), unplanned revascularization, and persistent angina.

Methods: Prospective randomized trials were identified by searches of the MEDLINE database from 1970 to September 2011. Trials in which stents were used in less than 50% of PCI procedures were excluded. Data were extracted from each study, and summary odds ratios (ORs) were obtained using a random effects model.

Results: Eight trials enrolling 7229 patients were identified. Three trials enrolled stable patients after MI, whereas 5 studies enrolled patients with stable angina and/or ischemia on stress testing. Mean weighted follow-up was 4.3 years. The respective event rates for death with stent implantation and medical therapy were 8.9% and 9.1% (OR, 0.98; 95% CI, 0.84-1.16); for nonfatal MI, 8.9% and 8.1% (OR, 1.12; 95% CI, 0.93-1.34); for unplanned revascularization, 21.4% and 30.7% (OR, 0.78; 95% CI, 0.57-1.06); and for persistent angina, 29% and 33% (OR, 0.80; 95% CI, 0.60-1.05).

Conclusion: Initial stent implantation for stable CAD shows no evidence of benefit compared with initial medical therapy for prevention of death, nonfatal MI, unplanned revascularization, or angina.

Arch Intern Med. 2012;172(4):312-319

The significant finding of this analysis is that compared with a strategy of initial medical therapy alone, coronary stent implantation in combination with medical therapy for stable CAD is not associated with a significant reduction in mortality, nonfatal MI, unplanned revascularization, or angina after a mean follow-up of 4.3 years.

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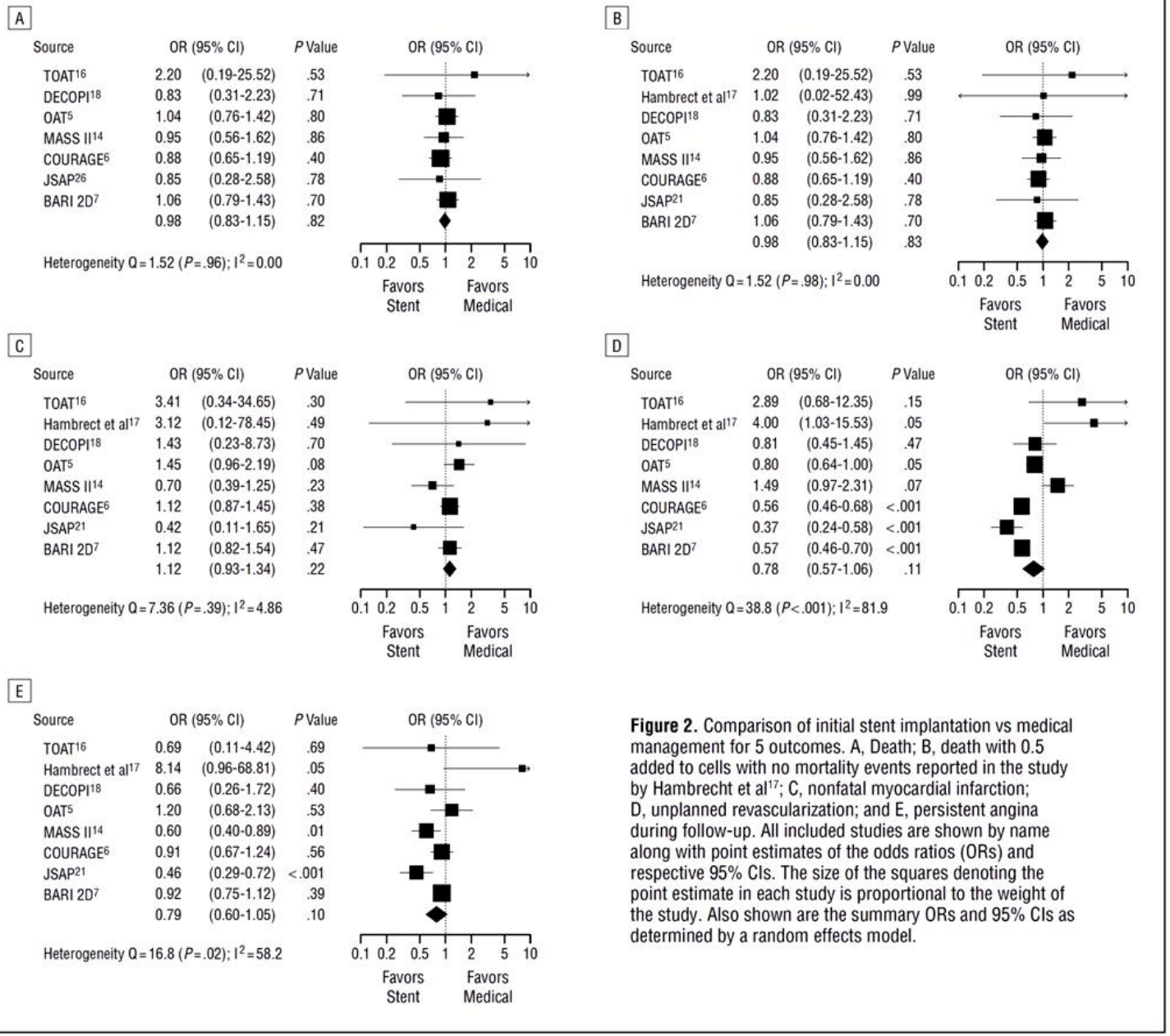


Figure 2. Comparison of initial stent implantation vs medical management for 5 outcomes. A, Death; B, death with 0.5 added to cells with no mortality events reported in the study by Hambrecht et al[17]; C, nonfatal myocardial infarction; D, unplanned revascularization; and E, persistent angina during follow-up. All included studies are shown by name along with point estimates of the odds ratios (ORs) and respective 95% CIs. The size of the squares denoting the point estimate in each study is proportional to the weight of the study. Also shown are the summary ORs and 95% CIs as determined by a random effects model.

REVIEW ARTICLE

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Meta-analysis of Randomized Controlled Trials

Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

PTCA VS TERAPIA MEDICA IN NONACUTE CAD

2012

- Over 400.000 PCI procedures are performed for the treatment of stable CAD in the USA each year.
- Despite publication of clinical trials and guidelines supporting the initial use of optimal medical therapy prior to PCI, only 44% of patients are treated with optimal medical therapy prior to PCI, and approximately 50% of patients with an occluded infarct-related artery after an MI undergo PCI of that artery.


REVIEW ARTICLE

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Meta-analysis of Randomized Controlled Trials

Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

RESISTANCE TO ADHERENCE TO RECOMMENDATIONS

2012

- The existing data do not demonstrate the clear superiority of medical therapy for any clinical outcome.
- Financial rewards for physicians and hospitals to perform PCI in the fee-for-service health care environment of the United States may contribute to the persistent use of PCI in settings where it has been shown to offer no clinical benefit.


REVIEW ARTICLE

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Meta-analysis of Randomized Controlled Trials

Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

RESISTANCE TO ADHERENCE TO RECOMMENDATIONS

2012

While physicians outwardly worship at the altar of evidence-based medicine, in reality, we more often tend to practice selective evidence-based medicine by adopting and embracing those trials and studies with results that reinforce our existing clinical practice preferences or biases, while we ignore or disdain the results of studies with results that are unpopular, conflict with our existing clinical practice beliefs, or collide with the conventional wisdom.

Boden WE
Mounting Evidence for Lack of PCI Benefit in Stable Ischemic Heart Disease
What More Will It Take to Turn the Tide of Treatment?
***Arch Int Med* 2012;172:320-21**

POSSIBILI SPIEGAZIONI

- **Una spiegazione possibile del fallimento della PCI nel ↓ morte /IMA: è una procedura locale (mirata a lesioni focali) su una patologia diffusa (> probabilità di successo di una terapia sistemica, ovvero medica).**
- **Nel trial BARI (1800 pz multivasali randomizzati BPAC vs PCI) al FU angiografico (5 aa) la ricorrenza di angina è > secondaria a progressione di malattia che a restenosi/occlusione graft**

The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. *N Engl J Med* 1996; **335:** 217–25.

POSSIBILI SPIEGAZIONI

- La placca ha morfologie ≠ in ACS vs CAD stabile.
- La placca vulnerabile ha un fibrous cap sottile, un core lipidico grande > macrofagi < collagene. Sono meno stenosanti.
- La placca stabile hanno un fibrous cap spesso, core lipidico piccolo, < macrofagi > collagene. Restringono il lume.
- Le lesioni instabili che portano a IMA/SCA non sono necessariamente severamente stenotiche e le lesioni severamente stenotiche non sono necessariamente instabili.

CAD STABILE

The Medscape Journal of Medicine

Based on COURAGE, it is difficult to defend a routine strategy of up-front PCI in patients with stable angina. Optimal medical therapy should be routine first-line therapy, with PCI reserved for patients with severe baseline angina or symptoms unresponsive to medical therapy. This makes it incumbent upon those of us who treat patients with stable angina to provide comprehensive and intensive medical therapy, and tailor subsequent therapy based on the patients' response. This is challenging in a healthcare system that provides strong financial reward for PCI and little incentive to provide optimal medical therapy, but this is what evidence-based medicine is supposed to be.

David Maron, Associate Professor of Medicine and Emergency Medicine at Vanderbilt University, Nashville, Tennessee.

CAD STABILE: NON TUTTI I PAZIENTI SONO UGUALI.

- if the ischaemic burden is moderate to severe - ie, greater than 10%, with or without angina - a case an be made for revascularisation.
- if significant ischaemia can be excluded by an adequate stress test, even in presence of chest discomfort or known previous coronary artery disease, the prognosis is good and an invasive approach is not indicated
- An important message from the randomised trials is that an initial strategy of pharmacological therapy with the option of revascularisation if that fails is not associated with any increase in mortality or myocardial infarction.

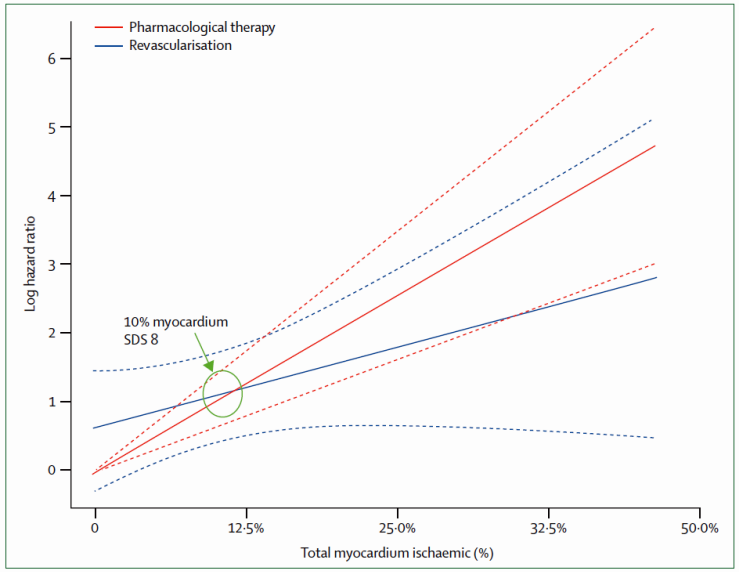


***Figure 3*: Relation between extent of ischaemia and outcome by pharmacological versus revascularisation therapy in 10 627 patients referred for nuclear stress testing before 2000**
Log hazard ratio for revascularisation versus medical therapy as a function of percentage of ischaemic myocardium based on the final Cox proportional hazards model. Adjusted risk of cardiac death versus ischaemia by myocardial perfusion scintigraphy; adjusted for clinical, history, stress single-photon emission CT, and referral data. p<0·001 for medical therapy versus revascularisation. SDS=summed difference score (a measure of the extent of ischaemia). Dotted lines indicate 95% CI. Adapted from reference 40.

Management of stable coronary artery disease
Lancet 2010 375:763-772

Hachamovitch R et al Comparison of the short-term survival benefi t associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography.
Circulation 2003; ***107: 2900–07***

DIAGNOSI DI CAD

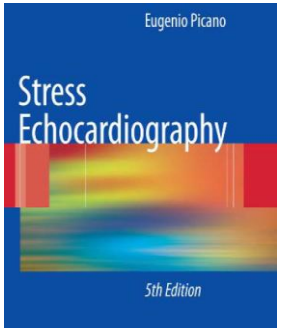
Table 11.3 Sensitivity and specificity of exercise echocardiography (*echo*) according to meta-analysis of 55 studies with 3,714 patients (adapted from [37])

Test	No. of studies	Sensitivity % (95% CI)	Specificity % (95% CI)	lnDOR (95% CI)
Exercise echo	55	82.7 (80.2–85.2)	84.0 (80.4–87.6)[a]	3.0 (2.7–3.3)
Adenosine echo	11	79.2 (72.1–86.3)	91.5 (87.3–95.7)	3.0 (2.5–3.5)
Dipyridamole echo	58	71.9 (68.6–75.2)	94.6 (92.9–96.3)[a]	3.0 (2.8–3.2)
State of the art dipyridamole echo	5	81 (79–83)	91 (88–94)	3.1 (1.9–3.3)
Dobutamine echo	102	81.0 (79.1–82.9)	84.1 (82.0–86.1)[a]	2.9 (2.7–3.0)
Combined echo	226	79.1 (77.6–80.5)	87.1 (85.7–88.5)[a]	2.9 (2.8–3.0)
Combined SPECT	103	88.1 (86.6–89.6)[b]	73.0 (69.1–76.9)	2.8 (2.6–3.0)

CI confidence interval, *lnDOR* natural logarithmic of the diagnostic odds ratio

[a] Nonoverlapping confidence intervals indicating a statistically higher specificity than the corresponding SPECT test

[b] Nonoverlapping confidence intervals indicating a statistically higher sensitivity than all other tests, except for adenosine and dipyridamole SPECT and a statistically lower specificity than all other tests except for exercise SPECT



DIAGNOSI DI CAD

Frequency of Stress Testing to Document Ischemia Prior to Elective Percutaneous Coronary Intervention

Grace A. Lin, MD, MAS
R. Adams Dudley, MD, MBA
F. L. Lucas, PhD
David J. Malenka, MD
Eric Vittinghoff, PhD
Rita F. Redberg, MD, MSc

Context Guidelines call for documenting ischemia in patients with stable coronary artery disease prior to elective percutaneous coronary intervention (PCI).

Objective To determine the frequency and predictors of stress testing prior to elective PCI in a Medicare population.

Design, Setting, and Patients Retrospective, observational cohort study using claims data from a 20% random sample of 2004 Medicare fee-for-service beneficiaries aged 65 years or older who had an elective PCI (N=23 887).

Main Outcome Measures Percentage of patients who underwent stress testing within 90 days prior to elective PCI; variation in stress testing prior to PCI across 306 hospital referral regions; patient, physician, and hospital characteristics that predicted the appropriate use of stress testing prior to elective PCI.

Results In the United States, 44.5% (n=10 629) of patients underwent stress testing within the 90 days prior to elective PCI. There was wide regional variation among the hospital referral regions with stress test rates ranging from 22.1% to 70.6% (national mean, 44.5%; interquartile range, 39.0%-50.9%). Female sex (adjusted odds ratio [AOR], 0.91; 95% confidence interval [CI], 0.86-0.97), age of 85 years or older (AOR, 0.83; 95% CI, 0.72-0.95), a history of congestive heart failure (AOR, 0.85; 95% CI, 0.79-0.92), and prior cardiac catheterization (AOR, 0.45; 95% CI, 0.38-0.54) were associated with a decreased likelihood of prior stress testing. A history of chest pain (AOR, 1.28; 95% CI, 1.09-1.54) and black race (AOR, 1.26; 95% CI, 1.09-1.46) increased the likelihood of stress testing prior to PCI. Patients treated by physicians performing 150 or more PCIs per year were less likely to have stress testing prior to PCI (AOR, 0.84; 95% CI, 0.77-0.93). No hospital characteristics were associated with receipt of stress testing.

Conclusion The majority of Medicare patients with stable coronary artery disease do not have documentation of ischemia by noninvasive testing prior to elective PCI.

JAMA. 2008;300(15):1765-1773 www.jama.com

In the United States, percutaneous coronary intervention (PCI) has become a common treatment strategy for patients with stable coronary artery disease (CAD) and such patients now account for the majority of PCIs performed.[1,2] However, multiple studies have established that some important outcomes for patients with stable CAD (death and risk of future myocardial infarction) do not differ between patients treated with PCI plus optimal medical therapy and patients treated with optimal medical therapy alone.[3-10] The addition of PCI does offer quicker relief of angina than medical therapy alone but also carries an increased risk of repeat revascularization, late-stent thrombosis, and a decreased

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evidence of ischemia (not just visualization of anatomy) is crucial in determining if the use of PCI is appropriate.

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CAD STABILE: UNA GESTIONE CONGIUNTA EVIDENCE-BASED

Table 8 Indications for revascularization in stable angina or silent ischaemia

	Subset of CAD by anatomy	Class[a]	Level[b]	Ref.[c]
For prognosis	Left main >50%[d]	I	A	30, 31, 54
	Any proximal LAD >50%[d]	I	A	30–37
	2VD or 3VD with impaired LV function[d]	I	B	30–37
	Proven large area of ischaemia (>10% LV)	I	B	13, 14, 38
	Single remaining patent vessel >50% stenosis[d]	I	C	—
	1VD without proximal LAD and without >10% ischaemia	III	A	39, 40, 53
For symptoms	Any stenosis >50% with limiting angina or angina equivalent, unresponsive to OMT	I	A	30, 31, 39–43
	Dyspnoea/CHF and >10% LV ischaemia/viability supplied by >50% stenotic artery	IIa	B	14, 38
	No limiting symptoms with OMT	III	C	—

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
[d]With documented ischaemia or FFR <0.80 for angiographic diameter stenoses 50–90%.
CAD = coronary artery disease; CHF = chronic heart failure; FFR = fractional flow reserve; LAD = left anterior descending; LV = left ventricle; OMT = optimal medical therapy; VD = vessel disease.

Table 6 Recommendations for decision making and patient information

	Class[a]	Level[b]
It is recommended that patients be adequately informed about the potential benefits and short- and long-term risks of a revascularization procedure. Enough time should be spared for informed decision making.	I	C
The appropriate revascularization strategy in patients with MVD should be discussed by the Heart Team.	I	C

[a]Class of recommendation.
[b]Level of evidence.
MVD = multivessel disease.

European Heart Journal (2010) **31**, 2501–2555
doi:10.1093/eurheartj/ehq277

ESC/EACTS GUIDELINES

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

CAD STABILE: UNA GESTIONE CONGIUNTA EVIDENCE-BASED

The findings from individual studies and systematic reviews of PCI versus medical therapy can be summarized as follows:

- PCI reduces the incidence of angina.[366,407,1016,1020,1033,1045]
- PCI has not been demonstrated to improve survival in stable patients.[138,1041,1042]
- PCI may increase the short-term risk of MI.[366,397,1041,1045]
- PCI does not lower the long-term risk of MI.[138,366,397,408,1041,1042]

Class III: Harm

1. **CABG or PCI should not be performed with the primary or sole intent to improve survival in patients with SIHD with 1 or more coronary stenoses that are not anatomically or functionally significant (eg, <70% diameter non–left main coronary artery stenosis, FFR >0.80, no or only mild ischemia on noninvasive testing), involve only the left circumflex or right coronary artery, or subtend only a small area of viable myocardium.[306,327,412,985,990,995–998] (*Level of Evidence: B*)**

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease : A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

Stephan D. Fihn, Julius M. Gardin, Jonathan Abrams, Kathleen Berra, James C. Blankenship, Apostolos P. Dallas, Pamela S. Douglas, JoAnne M. Foody, Thomas C. Gerber, Alan L. Hinderliter, Spencer B. King III, Paul D. Kligfield, Harlan M. Krumholz, Raymond Y.K. Kwong, Michael J. Lim, Jane A. Linderbaum, Michael J. Mack, Mark A. Munger, Richard L. Prager, Joseph F. Sabik, Leslee J. Shaw, Joanna D. Sikkema, Craig R. Smith, Jr, Sidney C. Smith, Jr, John A. Spertus and Sankey V. Williams

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PCI VS ESERCIZIO IN NONACUTE CAD

2004

Percutaneous Coronary Angioplasty Compared With Exercise Training in Patients With Stable Coronary Artery Disease

A Randomized Trial

Rainer Hambrecht, MD; Claudia Walther, MD; Sven Möbius-Winkler, MD; Stephan Gielen, MD; Axel Linke, MD; Katrin Conradi, MD; Sandra Erbs, MD; Regine Kluge, MD; Kai Kendziorra, MD; Osama Sabri, MD; Peter Sick, MD; Gerhard Schuler, MD

Background—Regular exercise in patients with stable coronary artery disease has been shown to improve myocardial perfusion and to retard disease progression. We therefore conducted a randomized study to compare the effects of exercise training versus standard percutaneous coronary intervention (PCI) with stenting on clinical symptoms, angina-free exercise capacity, myocardial perfusion, cost-effectiveness, and frequency of a combined clinical end point (death of cardiac cause, stroke, CABG, angioplasty, acute myocardial infarction, and worsening angina with objective evidence resulting in hospitalization).

Methods and Results—A total of 101 male patients aged ≤70 years were recruited after routine coronary angiography and randomized to 12 months of exercise training (20 minutes of bicycle ergometry per day) or to PCI. Cost efficiency was calculated as the average expense (in US dollars) needed to improve the Canadian Cardiovascular Society class by 1 class. Exercise training was associated with a higher event-free survival (88% versus 70% in the PCI group, $P=0.023$) and increased maximal oxygen uptake (+16%, from 22.7±0.7 to 26.2±0.8 mL O_2/kg, $P<0.001$ versus baseline, $P<0.001$ versus PCI group after 12 months). To gain 1 Canadian Cardiovascular Society class, $6956 was spent in the PCI group versus $3429 in the training group ($P<0.001$).

Conclusions—Compared with PCI, a 12-month program of regular physical exercise in selected patients with stable coronary artery disease resulted in superior event-free survival and exercise capacity at lower costs, notably owing to reduced rehospitalizations and repeat revascularizations. **(*Circulation*. 2004;109:1371-1378.)**

Key Words: coronary disease ■ exercise ■ angina ■ angioplasty ■ cost-benefit analysis

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Learn and Live.

Percutaneous Coronary Angioplasty Compared With Exercise Training in Patients With Stable Coronary Artery Disease: A Randomized Trial
Rainer Hambrecht, Claudia Walther, Sven Möbius-Winkler, Stephan Gielen, Axel Linke, Katrin Conradi, Sandra Erbs, Regine Kluge, Kai Kendziorra, Osama Sabri, Peter Sick and Gerhard Schuler
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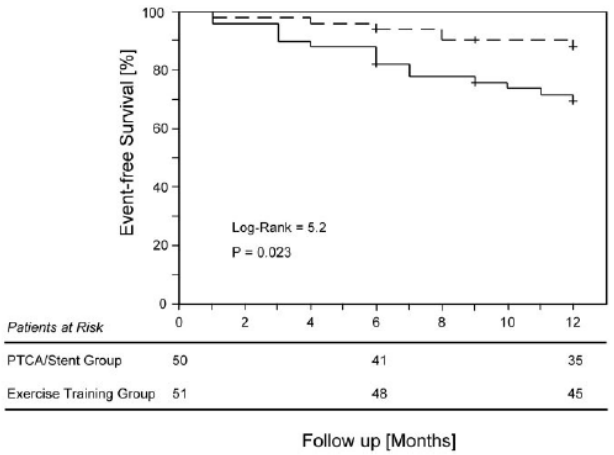

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Lancet 2009; 373: 929–40

See Editorial page 867

See Comment page 873

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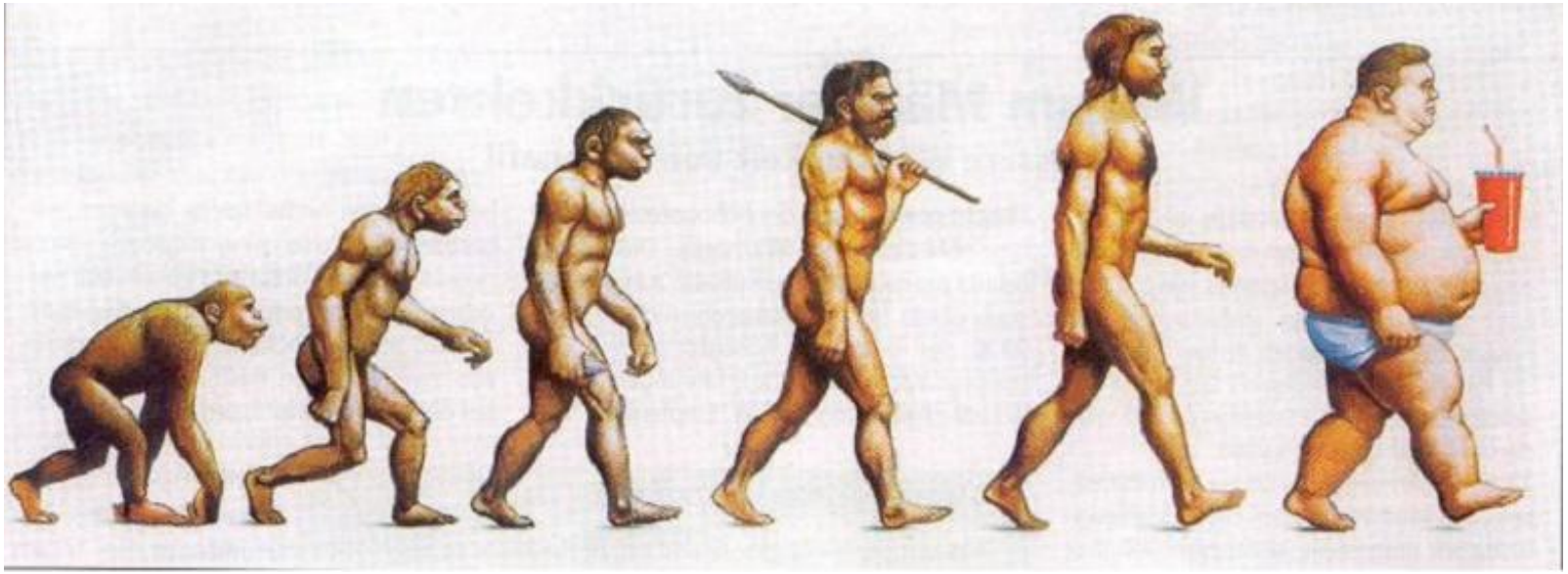

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BMI

ADERENZA A LUNGO TERMINE

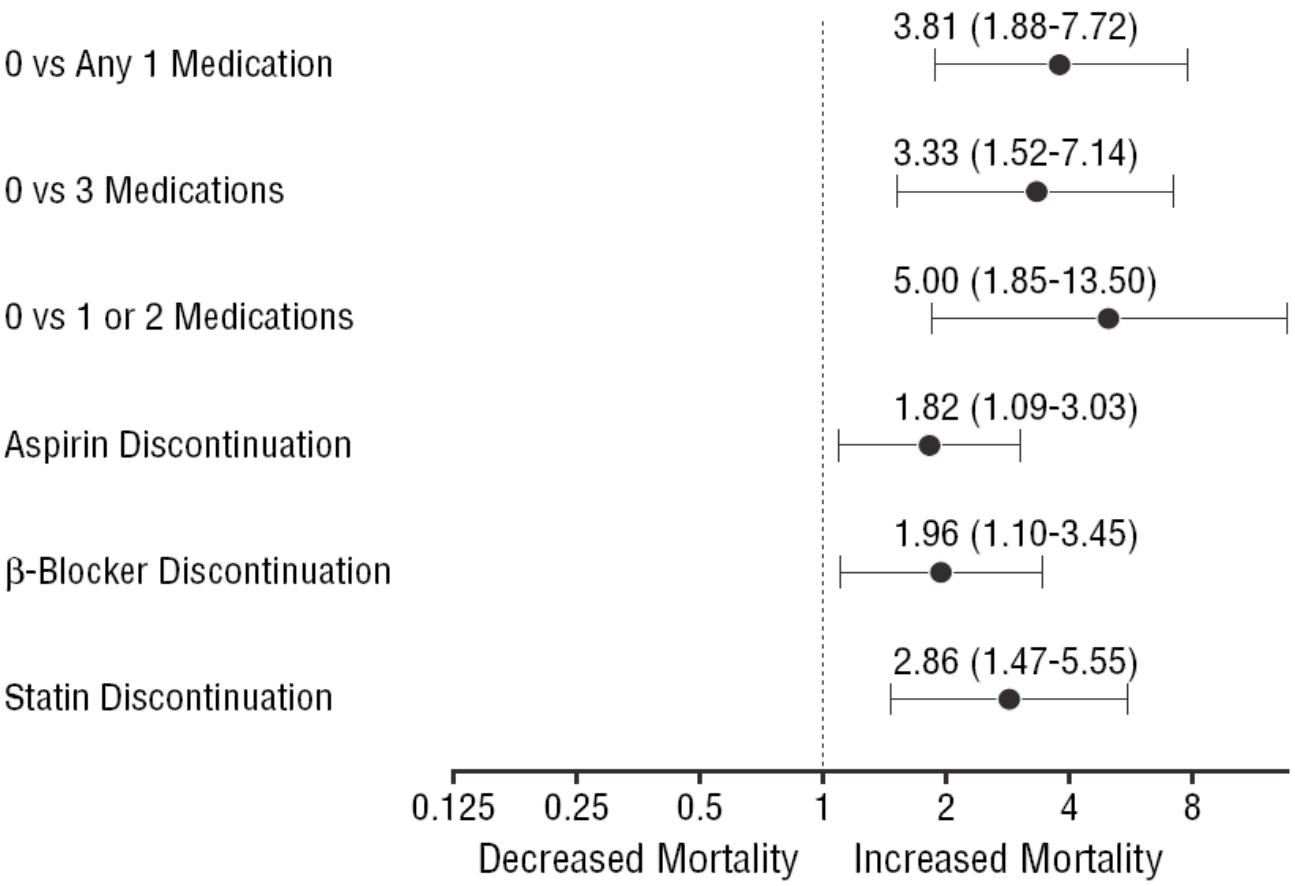
Long-term adherence to EB secondary prevention therapies after ACS (Duke Databank n=31750 pts)

Adherence to pharmacological therapy after 6 months

Aspirin	76.6%
B-blockers	50.9%
Statins	40.5%
ACE-i/ATII	31.0%
CC blockers	29.4%

Newby et al, Circulation 2006; 113: 203-12

DISCONTINUATION OF EB THERAPIES AFTER ACS AND CLINICAL OUTCOME



Ho PM, et al Arch. Int. Med. 2006; 166:1842-1846

ADHERENCE TO MEDICATION

Drugs don't work in patients

who don't take them

The NEW ENGLAND JOURNAL of MEDICINE

Orsterberg L and Blaschke T, *N Engl J Med* 2005;353:487-97

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CAD STABILE:
PTCA O TERAPIA MEDICA ?

Revascularization versus medical therapy

- Initial pharmacological approach to symptom control may be taken in patients not at high risk
- Revascularization may be recommended for patients with suitable anatomy who do not respond adequately to medical therapy, or for the patient who wishes to remain physically active
- Optimal secondary preventative medical therapy (e.g., antiplatelet therapy, statins) should be continued in patients after revascularization irrespective of the need for anti-anginal therapy

European Heart Journal

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Bassand JP, Priori S, Tendera M. Evidence-based vs “impressionist” medicine: how best to implement guidelines. *Eur Heart J* 2005; 26: 1155-8.

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