

Summit TCT Asia Pacific 2009

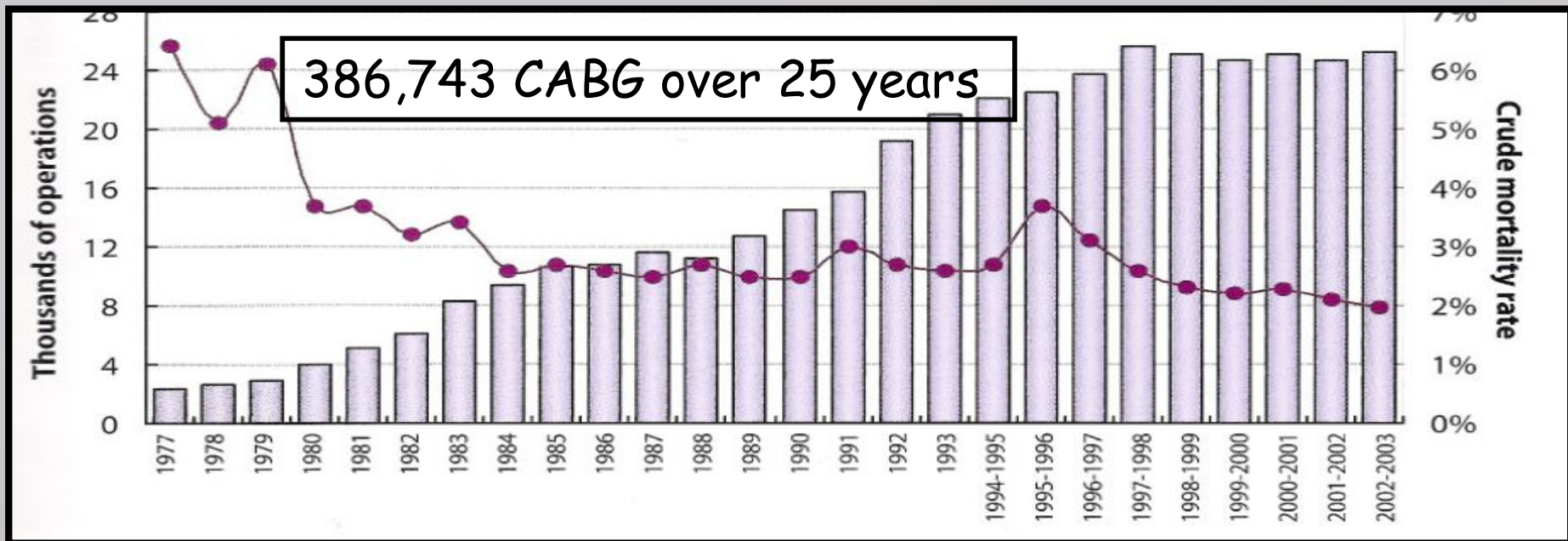
Treatment of Multivessel Disease:
Surgical Perspective:
CABG is The Standard for Complete Revascularization

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Conflict of Interest: Cardiac Surgeon



CABG: a very safe, effective procedure (with >40 yr follow-up data)
 • Most intensively studied surgical procedure ever undertaken



○ Current UK results for **ALL** 114,000 FIRST TIME CABG (2004-2008)

- Overall 30 day mortality 1.8%
- Includes >30% who are high risk (urgent, elderly, poor LV)
- In elective patients (70%) 30 day mortality for all of UK 1.1%

○ BUT CABG RESULTS CAN BE EVEN BETTER

- 1 yr mortality for 504 CABG patients in SoS RCT: 0.8%
- MRC/BHF ART trial of 2 vs 1 IMA: 30 day mortality in 3102 pts 1.2%
- SYNTAX 1 yr mortality: 1974 CABG (2.9%) vs 903 PCI (4.3%); (p=0.056)

EVIDENCE BASIS FOR CABG: STRONG SCIENTIFIC RATIONALE

Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration* LANCET 1994

Salim Yusuf, David Zucker, Peter Peduzzi, Lloyd D Fisher, Timothy Takaro, J Ward Kennedy, Kathryn Davis, Thomas Killip, Eugene Passamani, Robin Norris, Cynthia Morris, Virendra Mathur, Ed Varnauskas, Thomas C Chalmers

- 7 RCT of CABG vs medical therapy (2650 patients followed for 10 years)
- CABG improved SURVIVAL and symptom relief
- L main stem, TRIPLE vessel disease (esp proximal LAD disease)
- Benefits greater if severe symptoms, +ve exercise ECG, impaired LV

All current studies show that these conclusions remain valid


- 1 ○ "benefits of CABG in more extensive disease are underestimated"
 - (i) relatively low-risk patients
 - (ii) results analysed on ITT basis (40% of medical group had CABG)
 - (iii) only 10% of CABG patients received an IMA graft (now >90%)
- 2 ○ BUT: "no survival benefit for CABG if 1 or 2 VD and normal LV function"
- 3 ○ Recommendations for future trials of PCI vs CABG
"should include a high proportion of patients for whom CABG is known to be superior to medical therapy"

15 RCT of PCI vs CABG in 'Multivessel' Disease [Taggart ATS 2006]

TRIAL	nos	stent	% pop	% 1 or 2VD	EF >5 0%	%Left Main	Proximal LAD (%)	%DM	% IMA
RITA	1011	-	4%	88	-	0	-	6	74
ERACI	127	-	9%	55	100	0	-	11	75
LAUSANNE	134	-	3%	100	-	0	100	12	100
GABI	359	-	4%	82	-	0	-	10	37
EAST	392	-	4%	60	100	0	70	25	-
CABRI	1054	-	3%	60	100	0	-	12	75
MASS	142	-	69%	-	100	0	100	21	100
BARI	1829	-	12%	59	100	0	36	24	80
TOULOUSE	152	-	3%	71	-	0	-	14	58
SIMA	121	-	-	-	100	0	100	11	100
ERACI II	450	+	2%	44	-	0	-	17	88
AWESOME	454	+	-	55	-	0	-	-	70
MASS II	408	+	2%	59		0			
ARTS	1205	+	?5%	68	100	0	-	19	93
SOS	988	+	?5%	62	100	0	45	14	81
SUMMARY	8826		5%	65%	100%	0%	41%	16%	79%
CABG (UK)				<10%	70%	>20%	>90%	25%	>90%

RCT were biased against survival benefit of CABG by exclusion of patients who are known to benefit from CABG in favour of those who do not !!!

Lancet 2009; 373;1190-97

➔  Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials

Mark A Hlatky, Derek B Boothroyd, Dena M Bravata, Eric Boersma, Jean Booth, Maria M Brooks, Didier Carrié, Tim C Clayton, Nicolas Danchin, Marcus Flather, Christian W Hamm, Whady A Hueb, Jan Kähler, Sheryl F Kelsey, Spencer B King, Andrzej S Kosinski, Neuza Lopes, Kathryn M McDonald, Alfredo Rodriguez, Patrick Serruys, Ulrich Sigwart, Rodney H Stables, Douglas K Owens, Stuart J Pocock

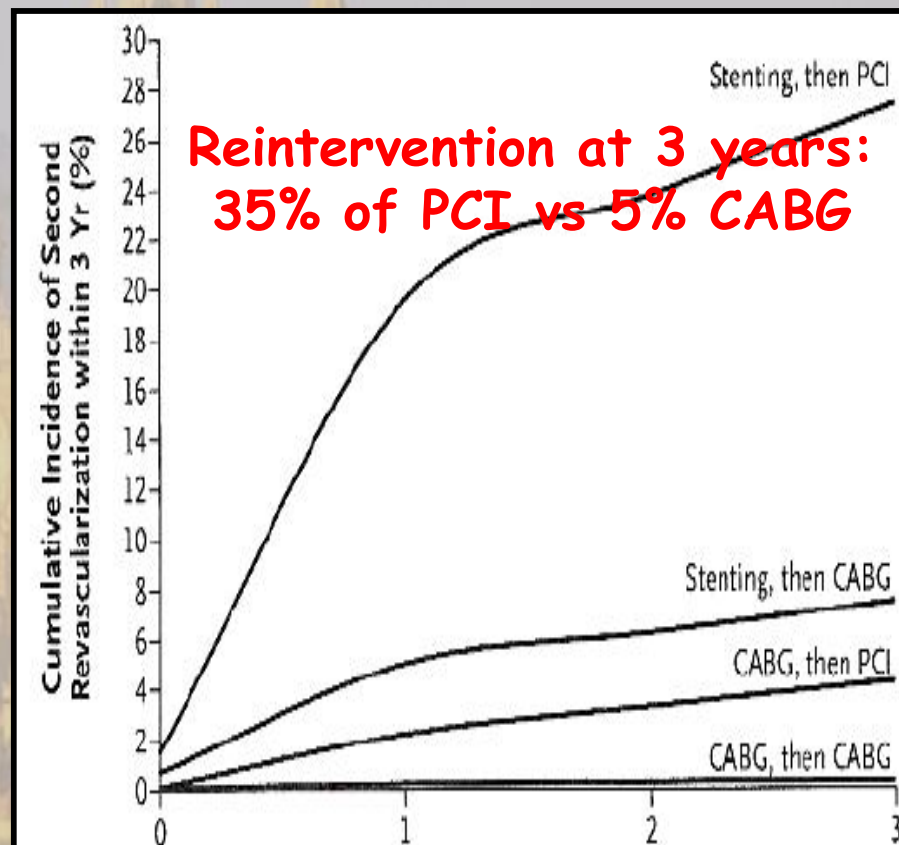
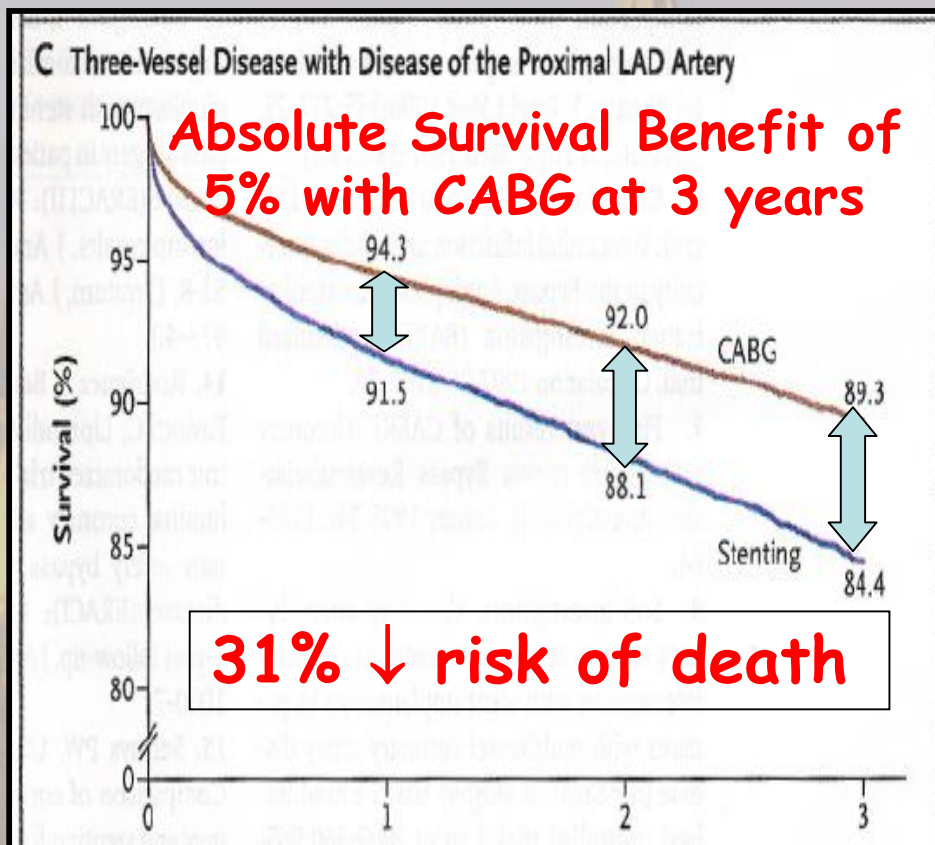
- 24 authors...not a single surgeon !!!
- Almost 8000 patients with median follow up of 6 years
- Overall CABG mortality was lower but not statistically significant
 - [CABG:PCI HR = 0.91 (95% CI 0.82 - 1.02; p=0.12)]
- Significantly lower mortality with CABG than PCI
 - in diabetes (HR 0.70; 95% CI 0.56-0.87; p=0.014)
 - patients >65 years (HR 0.82; 95% CI 0.70-0.97; p=0.002)
- HR for death/repeat intervention
 - CABG 9.9% vs 24.5% PCI (p< 0.0001)

NEJM 2005

Long-Term Outcomes of Coronary-Artery Bypass Grafting versus Stent Implantation

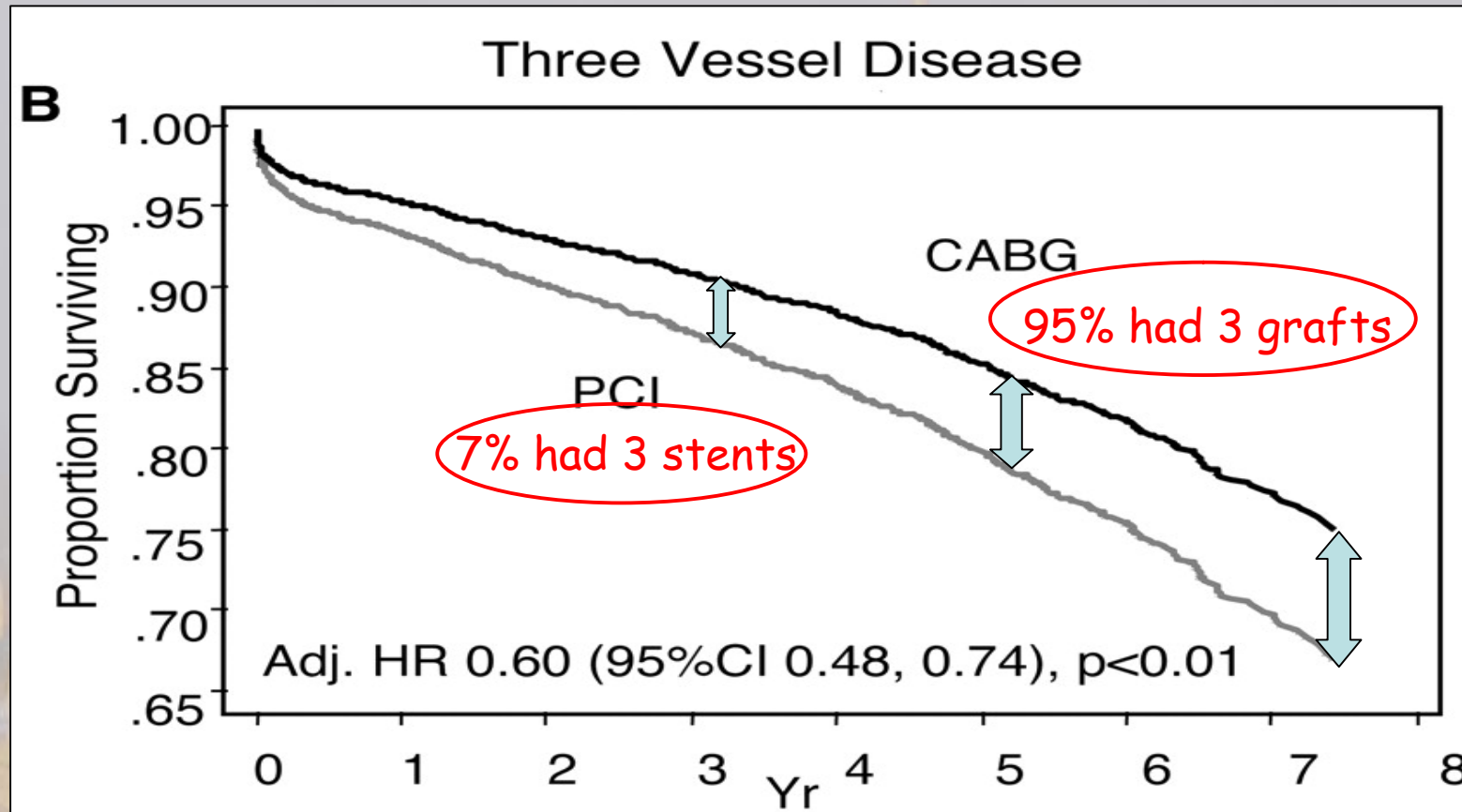
Edward L. Hannan, Ph.D., Michael J. Racz, Ph.D., Gary Walford, M.D., Robert H. Jones, M.D., Thomas J. Ryan, M.D., Edward Bennett, M.D., Alfred T. Culliford, M.D., O. Wayne Isom, M.D., Jeffrey P. Gold, M.D., and Eric A. Rose, M.D.

- New York Registry: 37,212 CABG and 22,102 PCI (BMS) patients with > 2VD
- Propensity matched for cardiac and non-cardiac co-morbidity risk



PCI is not as effective as CABG in the 'real' world

Long Term Survival in patients with multivessel disease after CABG or PCI
Malenka, D. J. et al. Circulation 2005



○ Effect true for all groups (elderly, gender, diabetics, stents, EF $< / >$ 40%)

Conclusion: 'In contemporary practice survival for patients with 3-vessel coronary artery disease is better after CABG than PCI, an observation that patients and physicians should carefully consider when deciding on revascularization strategy'

CABG Has Consistent Survival Benefit Over Initial Strategy of PCI

Author	Year	Patients	DM	Stents	Follow-Up	CABG vs PCI
Hannan	NEJM 2008	17,400p	-	DES	1.5 yrs	HR 0.8 (p=0.03)
Bair	CIRC 2007	6,369	-	DES	5 yrs	HR 0.85 (p<0.001)
Javaid	CIRC 2007	1,680	-	DES	1 yr	97% vs 89%
Hannan	NEJM 2005	59,314p	-	BMS	3 yrs	↓ mortality 5%
Malenka	CIRC 2005	14,493	-	BMS	7 yrs	HR 0.6 (p <0.01)
BARI	JACC 2007	353	+	-	10 yrs	58% vs 46%
Javaid	CIRC 2007	601	+	DES	1 yr	3% vs 12-18%
Niles	JACC 2001	2,766	+	-	5 yrs	HR 0.25-0.5
SUMMARY		102,976			1-10 yrs	↓ mortality

In >100,000 propensity matched patients PCI with stents decreases survival by around 5% at 3 years vs CABG

SYNTAX BEWARE !!!!

THE SYNTAX TRIAL

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

MARCH 5, 2009

VOL. 360 NO. 10

Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease

Patrick W. Serruys, M.D., Ph.D., Marie-Claude Morice, M.D., A. Pieter Kappetein, M.D., Ph.D.,
Antonio Colombo, M.D., David R. Holmes, M.D., Michael J. Mack, M.D., Elisabeth Stähle, M.D.,
Ted E. Feldman, M.D., Marcel van den Brand, M.D., Eric J. Bass, B.A., Nic Van Dyck, R.N., Katrin Leadley, M.D.,
Keith D. Dawkins, M.D., and Friedrich W. Mohr, M.D., Ph.D., for the SYNTAX Investigators*

Landmark trial (most important trial ever of PCI vs CABG)

- Designed to look at 5 year outcomes death and MACCE
- 'All comer' trial (rather than highly select patients)
- Parallel Registry (patients ineligible for randomization)

SYNTAX (1 year results)	RCT		Registry	
	CABG: 897	PCI:903	CABG: 1077	PCI: 198
age	65 (10)	65 (10)	66 (9)	71 (10)
male (%)	79	76	81	70
DM (%)	29	28	30	35
Unstable (%)	28	29	22	38
Euroscore (Surgical Risk)	3.8 (2.7)	3.8 (2.6)	3.9 (2.7)	5.8 (3.1)
Syntax score (severity CAD)	29(11)	28 (11)	38 (13)	32 (12)
EF	-	-	-	-
LMS (any) (%)	34	35		
3 vd (%)	66	65		
Anastomoses/lesions	3.2 (0.9)	3.6 (1.6)		
% Off Pump; % BIMA	15%; 28%	-	19%; 16%	
Nos stents	-	4.6 (2.3)		3.1 (1.8)
Stent length	-	86 (48)		59 (41)
MACCE	12.1	17.8	8.8	20.4
All deaths	3.5	4.3	2.5	7.3
CVA	2.2	0.6	2.2	0
MI	3.2	4.8	2.5	4.2
Repeat Revasc	5.9	13.7	3	12

SYNTAX at 1 year (interim analyses of 5 year outcome)

- 1/3 of patients are suitable only for CABG (1077 CABG registry pts)
- PCI failed to reach criteria for non-inferiority on MACCE
 - At 1 year MACCE still increasing sharply for PCI but NOT for CABG
- **MORTALITY in 1974 CABG patients=2.9% (vs 4.3% in 903 PCI): p=0.056**
 - ie 33% decrease in deaths at 1 year with CABG
 - Mortality in RCT: 3.5% for 897 CABG vs 4.3% for 903 PCI
 - Mortality in Registry: 2.5% for 1077 CABG
- **As the survival advantage for CABG usually appears at 2-3 yrs, 1 yr outcome of SYNTAX underestimates the long-term benefit of CABG**
- Reintervention 3%-6% CABG vs 14% PCI (p<0.001)
- Risk of stroke 2.2% CABG vs 0.6% PCI (p<0.05)
 - 1% perioperative and 1% over following year
 - but substantially lower use of secondary prevention in CABG vs PCI with lower Dual Antiplatelets, Statins, ACE inhibitors, Beta Blockers
 - **Unacceptable and unethical not to ensure OMT**

CONCLUSION (NEJM 2009) 'CABG remains the standard of care for patients with three-vessel or left main coronary artery disease'

Fundamental Question

WHY DOES CABG HAVE SUCH A SURVIVAL BENEFIT OVER PCI ?

Anatomically, atheroma is mainly located in the proximal coronary vessels

1. By placing grafts to the mid coronary vessel CABG has **two** effects
 - (i) treats the '**CULPRIT**' lesion (regardless of complexity)
 - (ii) over the longer term, CABG offers prophylaxis against **FUTURE** 'culprit' lesions by protecting whole zones of vulnerable proximal myocardium in diffusely unstable coronary endothelium
 - In contrast, PCI only deals with '**suitable**' localised proximal culprit lesions but has no prophylactic benefit against new disease (proximal to, within or distal to the stent)

2. PCI means incomplete revascularization ([Hannan Circ 2006](#))
 - Of 22,000 PCI 69% had incomplete revascularization
 - >2 vessels (+/- CTO) HR for mortality 1.4 (95% CI = 1.1-1.7)

**PCI will never match the results of CABG for LM/MVD
(For POBA; BMS; DES)**

Taggart DP. *Lancet* 2009; 373:1150-2

PCI or CABG in coronary artery disease?

Published Online
March 20, 2009
DOI:10.1016/S0140-
6736(09)60574-2
See [Articles](#) page 1190

In *The Lancet* today, Mark Hlatky and colleagues¹ report a pooled analysis of individual data from almost 8000 patients enrolled in ten randomised trials of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) over the past two decades. They conclude that while at a median

already well established that there was no prognostic benefit with CABG.⁴ By largely excluding patients with a known survival benefit from CABG (left-main or triple-vessel coronary artery disease, or both, and especially with impaired ventricular function⁴), the trials ignored the prognostic benefit of surgery in

Finally, in view of the prognostic benefit of surgery, a multi disciplinary team approach should be the standard of care when recommending interventions in more complex coronary artery disease, to ensure transparency, real patient choice and genuine informed consent in the decision making process. For elective patients this will necessitate separation of angiography from the intervention to allow appropriate time to make a truly informed decision.

Taggart DP. *Lancet* 2009; 373:1150-2

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' however, it is necessary to consider two potentially important limitations of the current analyses. Most significantly, the randomized trials only enrolled around 5%-10% of the eligible population, the majority of whom had single or double vessel disease and normal left ventricular function [2], a group in whom it was already well established that there was no prognostic benefit of CABG [3]. By largely excluding patients with a known survival benefit from CABG (left main+/- triple vessel coronary artery disease and especially with impaired ventricular function [3]), the trials ignored the prognostic benefit of surgery in more complex coronary artery disease. Nevertheless, the inappropriate generalization of the trial results from their highly select populations to most patients with multivessel disease has been ubiquitous in the literature and has, at least in part, justified the explosive growth in PCI in developed countries.'

STATE-OF-THE-ART PAPER AND COMMENTARY

Revascularization for Unprotected Left Main Stem Coronary Artery Stenosis

Stenting or Surgery

David P. Taggart, MD (HONS), PhD, FRCS,* Sanjay Kaul, MD, FACC,†
William E. Boden, MD, FACC,‡ T. Bruce Ferguson, JR, MD, FACC,§
Robert A. Guyton, MD, FACC,¶ Michael J. Mack, MD,# Paul T. Sergeant, MD, PhD,††
Richard J. Shemin, MD, FACC,** Peter K. Smith, MD, FACC,||
Salim Yusuf, DPHIL, FRCPC, FRSC, FACC‡‡

Oxford, United Kingdom; Los Angeles, California; Buffalo, New York; Greenville and Durham.

- <90% of LMS are distal/bifurcation (very high risk of restenosis)
- <90% have multivessel CAD (CABG already offers survival benefit)

(CABG) is traditionally regarded as the “standard of care” because of its well-documented and durable survival advantage. There is now an increasing trend to use drug-eluting stents for LMS stenosis rather than CABG despite very little high-quality data to inform clinical practice. We herein: 1) evaluate the current evidence in support of the use of percutaneous revascularization for unprotected LMS; 2) assess the underlying justification for randomized controlled trials of stenting versus surgery for unprotected LMS; and 3) examine the optimum approach to informed consent. We conclude that CABG should indeed remain the preferred revascularization treatment in good surgical candidates with unprotected LMS stenosis. (J Am Coll Cardiol 2008;51:885-92) © 2008 by the American College of Cardiology Foundation

Health Economists: Drug Eluting Stents (DES) vs CABG

Coronary artery stents: a rapid systematic review and economic evaluation

R Hill,¹ A Bagust,¹ A Bakhai,² R Dickson,^{1*}
Y Dündar,¹ A Haycox,¹ R Mujica Mota,¹
A Reaney,³ D Roberts,⁴ P Williamson⁵ and
T Walley¹

NICE 2003/
HTA 2004

'in the absence of substantive clinical evidence of the superiority of stenting with DES over CABG (for 2 and 3 vessel disease), to encourage the widespread use of DES will drive up the cost of stenting and if allowed to displace CABG, reduce the gain in quality and possibly duration of life arising from CABG in the long term

Cost-effectiveness of Stents and CABG (Griffin et al; *BMJ* 2007)

Appropriateness of Coronary Revascularization (ACRE) *NEJM* 2001

2552 patients (1353 CABG; 908 PCI; 521 either) therapy by panel of 9 experts

CONCLUSION: Both CABG and medical therapy (BUT NOT Stents) are cost effective at a conventional QALY of £30K (\$60K)

...'additional benefit of Stents over medical therapy is 'too small to justify its additional costs'

NICE (Recommendation TA 152) July 2008

DES are recommended as a possible treatment only if:

- the artery to be treated is less than 3 mm in diameter or the affected section of the artery is longer than 15 mm, and
- the additional cost of the DES over bare-metal stents is £300 or less.

Are Recommendations for PCI in MVD Appropriate ?

Society	Recommendations for PCI	Written by
ACC/AHA Circ 2006	'Patients with 2 or 3 vessel disease who are otherwise eligible for CABG including diabetes' NO SURGICAL OPINION RECOMMENDED	23 cardiologists 1 surgeon
ESC Eur HJ 2005	'all patients except diabetics with multivessel disease, unprotected left main, chronic total occlusions' NO SURGICAL OPINION RECOMMENDED	46 cardiologists 0 surgeon
BCS Heart 2005	'patients to be fully informed in decisions, treatment options' (GMC Good Medical Practice) NO SURGICAL OPINION RECOMMENDED	8 cardiologists 1 surgeon
Summary	almost all patients can be treated by PCI NONE RECOMMEND SURGICAL OPINION	77 cardiologists 2 surgeons

Based on 15 'manufactured' RCT of PCI vs CABG !!



1st PCI: Zurich 1977

AR Gruentzig 1939-1985

(NEJM 1979) "We estimate that only about 10 to 15 per cent of candidates for bypass surgery have lesions suitable for PCI. A prospective randomized trial will be necessary to evaluate its usefulness in comparison with surgical and medical management."

Opie LH, Commerford PJ, Gersh BJ
Lancet 2006; 367:69-78

07 Jan 2005
367
9504

CURRENT ISSUE - NOT to be taken away

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THE LANCET

Volume 367 Number 9504 Pages 1-84 January 7-13, 2006 www.thelancet.com

"In view of the survival benefit shown for coronary-artery bypass grafting, the real controversy is why patients with symptoms and anatomy known to benefit from the procedure are still submitted to percutaneous coronary intervention."

See Series page 69

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- 9 JAN 2006
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Articles	Articles	Articles	Articles	Seminar
Etanercept in psoriasis See page 29	Maternal vitamin D and bone mass in children at age 9 years See page 36	Mortality in Democratic Republic of Congo See page 44	Deaths from liver cirrhosis in UK See page 52	Urinary incontinence in women See page 57

The Controversy and the Solution

○ Patients are denied access to the 'gold standard' treatment by the interventional cardiologist ('the gatekeeper')

Califf RM. Stenting or Surgery JACC 2005; 46: 589-91 :

“It is likely that most people undergoing coronary angiography are not told the entire story when a decision is made about undergoing PCI ... self-referral.. financial incentives ..without surgical opinion the patient is in no position to have rational input into the decision”

○ The solution is the Multidisciplinary Team (MDT) [BMJ 2005,2007]

- As for lung cancer
- No doctor with the real interests of the patient would object to an MDT
- MDT should include non-interventional and interventional cardiologist, surgeon and payer (economic implications)

○ In elective patients ALL interventions should be agreed by an MDT

- Ensure real patient choice and genuine informed consent
- Being given a few minutes to consent to a procedure in a cath lab with a catheter in the groin is not informed consent

○ If MDT is not agreed voluntarily then should be enforced by external regulatory/statutory bodies to protect the best interests of patients

Background PCI vs CABG in STABLE CAD

OPCI: GENERAL PERSPECTIVE

- Used appropriately PCI can be a very effective treatment
 - especially in unstable haemodynamics/ acute MI
 - in **some** patients with multivessel/left main stem disease
- "Patients want less invasive treatment"
 - (assumes that therapies are otherwise equally effective)

○ BUT THREE IMPORTANT QUESTIONS REGARDING PCI

1. Is the routine use of PCI in multivessel/LM disease appropriate?
 - is it evidence based?
2. Is consent for PCI obtained appropriately ?
 - are patients told that CABG is more effective + better survival?
 - are the real **risks** and **limitations** of PCI explained?
 - ❖ (essential for consent in UK: GMC 'Good Medical Practice')
3. Is PCI a cost effective treatment?
 - do numerous/ repeat PCI make economic/medical sense?