13th Summit TCT Asia Pacific

Choice of Left Main Revascularization Therapy: CABG

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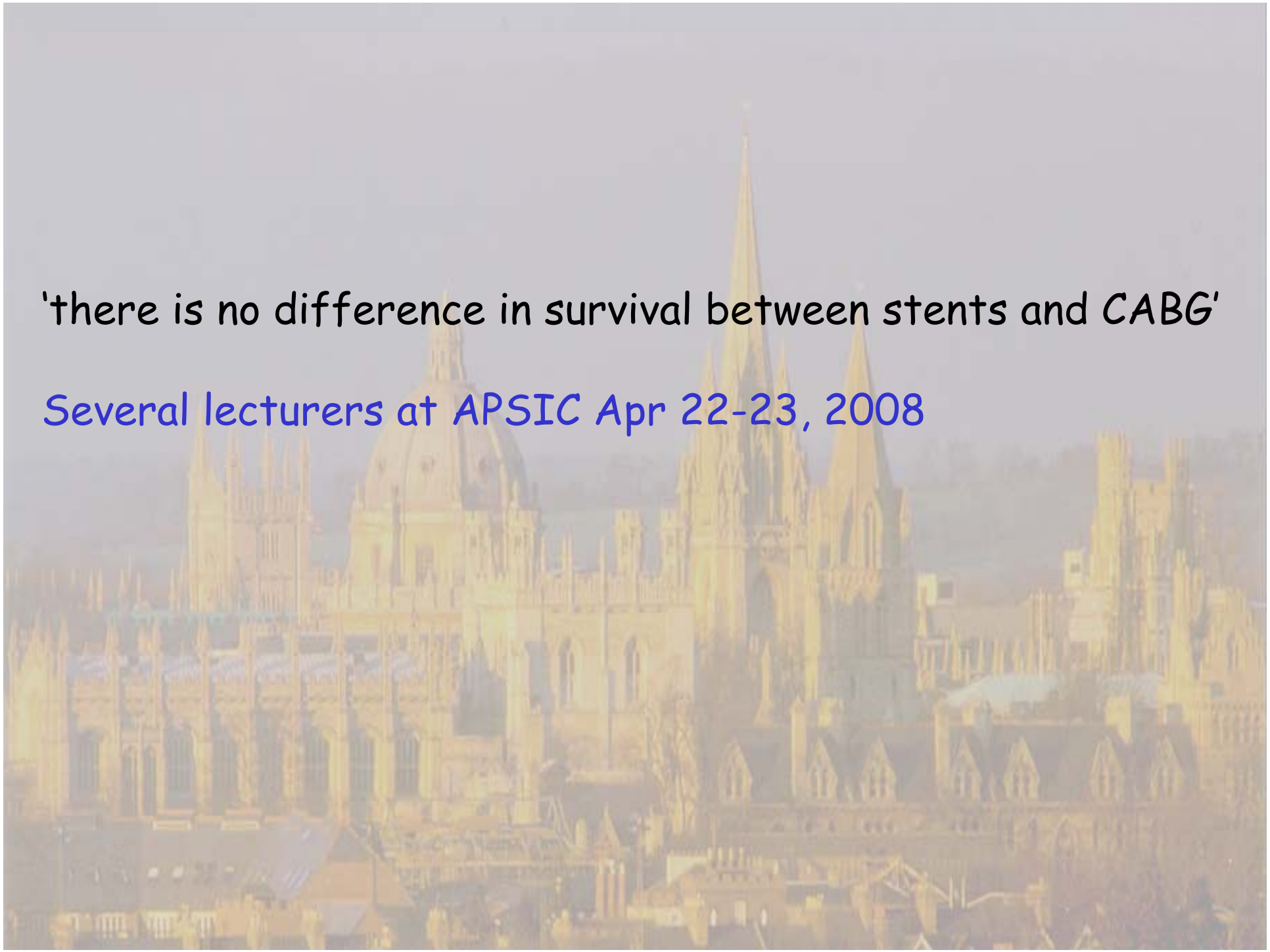
Conflict of Interest: Cardiac surgeon
No other disclosures



'there is no difference in survival between stents and CABG'

Several lecturers at APSIC Apr 22-23, 2008

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

TRIAL	nos	stent	% pop	% 1 or 2VD	EF >50%	%Left Main	Proximal LAD (%)	%DM	% IMA
BARI	1829	-	12%	59	100	0	36	24	80
TOULOSE	152	-	3%	71	-	0	-	14	58
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%

'Apparent' equivalence of survival reported for PCI and CABG in the individual 15 RCT was 'MANUFACTURED'

1. by mainly including patients known to have NO prognostic benefit from CABG (ie 1 or 2 VD and normal LV function)
2. by actively excluding those who benefit from CABG (L main, severe 3VD, occluded vessels, poor LV)

Subsequent meta-analyses showed CABG better (Hoffman 2005)

- significant survival benefit ($p<0.05$) for CABG (NNT=53)
- four fold decrease in need for reintervention

6 Propensity Matched studies of PCI and CABG in 3v CAD

- >105,000 patients
- all published after 2005

	Stents	Patients	HR for death with CABG (1-5 years)	p
Hannan NEJM 2005	BMS	59324	0.69	<0.01
Malenka Circ 2005	BMS	14493	0.60	<0.01
Brener Circ 2005	BMS	6033	0.40	<0.01
Bair Circ 2007	BMS	6369	0.85	<0.01
Javaid Circ 2007	DES	1680	0.33	<0.01
Hannan NEJM 2008	DES	17400	0.75	<0.01

- Reintervention with CABG decreased 3-8 fold

"There is no survival difference between CABG and PCI"

- The most widely perpetuated myth in cardiovascular medicine
  - ubiquitous in the literature,
  - repeated in cardiology lectures,
  - frequently - but erroneously- told to patients
- *"The great enemy of the truth is very often not the lie – deliberate, contrived and dishonest – but the myth – persistent, persuasive and unrealistic."* (JF Kennedy; S Yusuf)
- Securing the myth
  - Based on 15 RCT where results were stacked against CABG
  - Ignoring evidence from numerous large databases which consistently demonstrates a survival benefit of CABG

Is PCI in stable coronary artery disease Evidence Based?

1. Is PCI more more effective than medical therapy ?

NO: Meta-analysis of 11 RCT PCI vs Medical Therapy (Katritsis Circ 2005)

- **2950 patients with 1-7 yr follow up**

CONCLUSION 'In patients with chronic stable coronary artery disease PCI **does not offer any benefit in terms of death, myocardial infarction or subsequent revascularization**'

COURAGE: 2287 pts OMT vs OMT+PCI: 5 yr Survival and MI same

2. Is PCI with stents more effective than PCI without stents ?

NO: Meta-analysis of 29 RCT of PCI +/- Stenting (Brophy Ann Int Med 2003)

- **9918 patients with 16 month follow up**

CONCLUSION 'Stenting is safe **but not associated with important reductions in mortality, myocardial infarction or CABG**

3. Are DES more effective than BMS ?

NO: Five meta-analysis (Lancet/EHJ 2004;AJC 2005;EHJ 2006)

- **5103, 5747, 5066, 8221 patients followed for 2 years**
- **4958 pts in 14 RCT up to 5 yrs (Kastrati NEJM 2007)**
- **18000 pts in 38 trials up to 4 yrs (Stettler Lancet 2007)**

CONCLUSION: "DES decrease risk of restenosis in **low risk** coronary lesions **but not the risk of mortality or MI at 2-5 years"**

- **1% decrease in risk of MI over 4 years (Stettler Lancet 2007)**

Surgery as 'gold standard' in LMS stenosis

- CABG: a safe, durable, effective procedure with > 40 yrs follow-up data
- 10 year survival benefit of CABG in LMS [Cohen and Gorlin Circ 1975]
- 3 RCT and numerous prospective studies confirm this over next 20 yrs

Comparison of Surgical and Medical Group Survival in Patients With Left Main Coronary Artery Disease.Long-term CASS Experience. **Caracciolo E.A. *Circ* 1995; 91:2325-34**

- 1484 LMS (>50% stenosis) [ACC/AHA 2004 Guideline Update for CABG]

'The benefit of surgery over medical treatment … is little argued. The median survival for surgically treated patients is 13.3 years versus 6.6 years in medically treated patients'

Current Results of CABG in LM stenosis [Taggart et al JACC 2008]

All published within last 10 years and with at least 300 patients

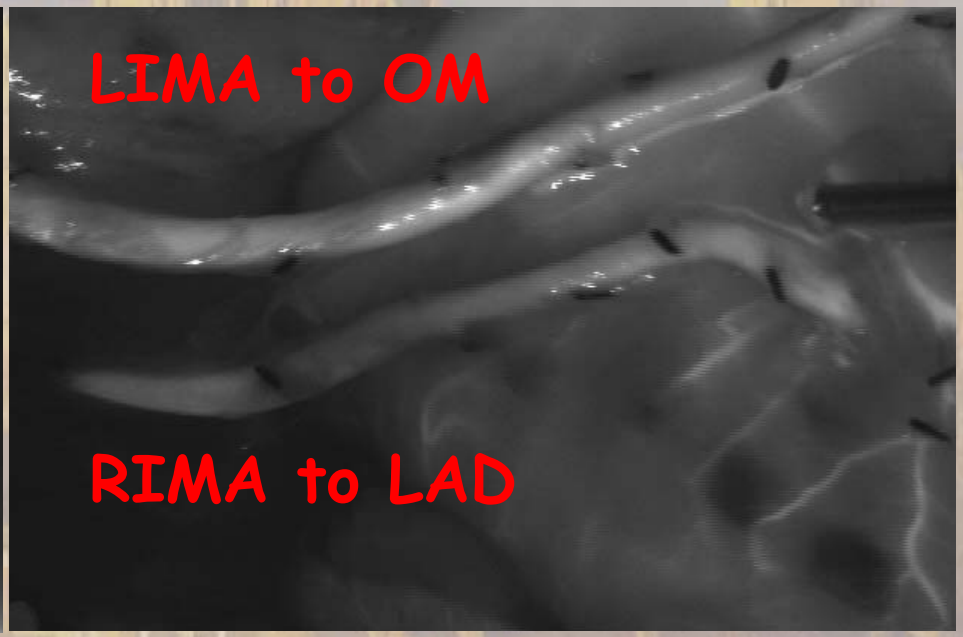
Author	Year	Nos	% urgent	30 day mortality
Jonsson (2006)	1970-1999	1888	26%	2.7%
Lu (2005)	1997-2003	1197	5%	2.6%
UK SCTS (2003)	2003	5003	-	3%
Dewey (2001)	1998-1999	728	46%	4.2%
Yeatman (2001)	1996-2000	387	57%	2.6%
Ellis (1998)	1990-1995	1585	47%	2.3%
SUMMARY		10788	32%	2.8%

But Results of CABG Can Be Even Better !!!

- ART trial of 2 vs 1 IMA
- 28 centres in 7 countries
- 30 day mortality in 3100 patients: 1%

- Best Treatment for LMS Stenosis is IMA x 2 (OPCABG)

Intraoperative Graft Images

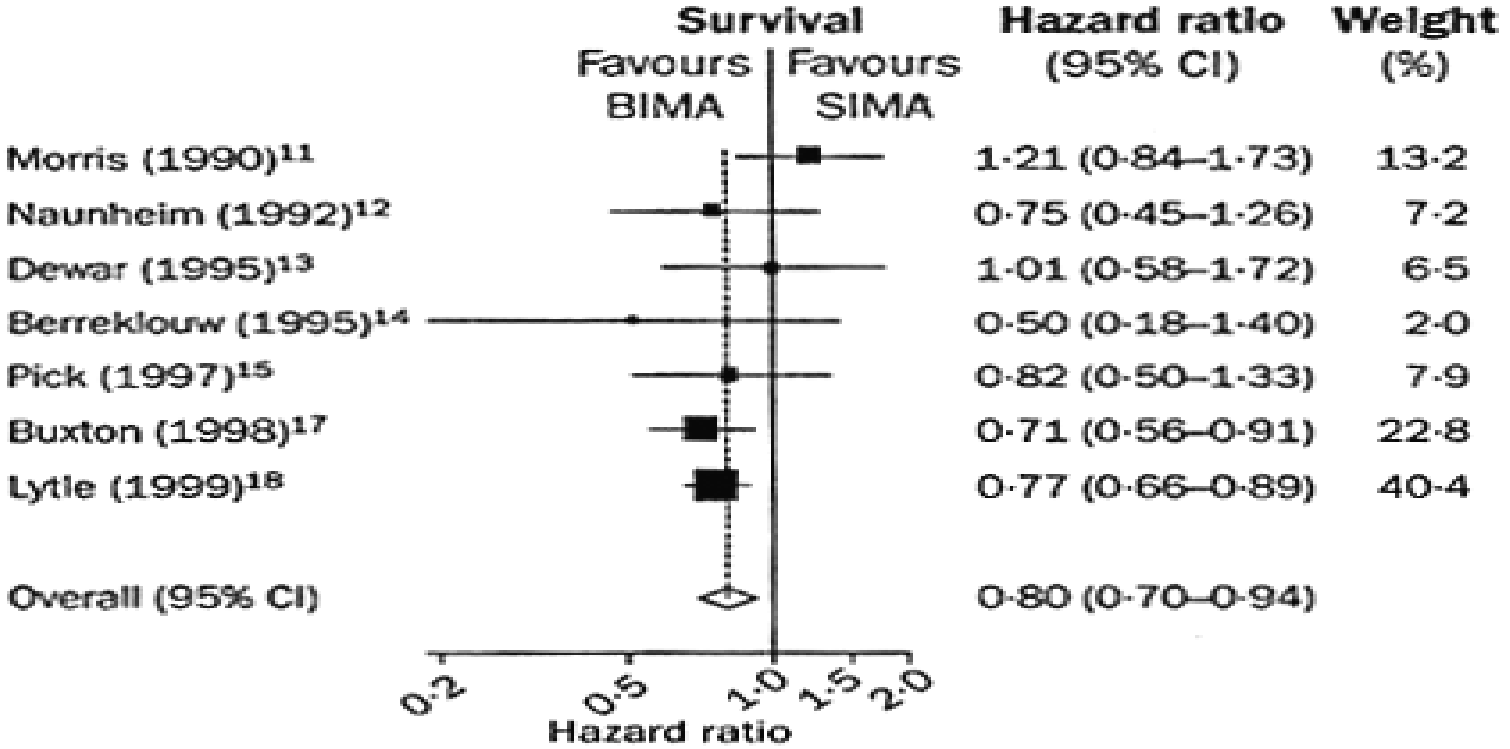


SURVIVAL BENEFIT WITH TWO IMA GRAFTS ?

- >95% of right (RIMA) and Left (LIMA) patent at 7 years [Dion 2001]

Effect of arterial revascularisation on survival: a systematic review of studies comparing bilateral and single internal mammary arteries

David P Taggart, Roberto D'Amico, Douglas G Altman — **Lancet;2001:870-5**



- 4693 BIMA vs 11269 SIMA (from 7 databases)
- Matched for age, gender, LV function, DM (PREDICTS LONGEVITY)
- HR for death with BIMA: 0.80 [95% CI=0.74 to 0.94]
- NNT of 13-16 (to prevent one death)

PCI in LMS Stenosis [Taggart et al JACC 2008]

- Why is PCI unlikely to give long-term success in LMS stenosis?
  - Up to 90% are distal/bifurcation and at high risk of restenosis [Serruys 2005]
  - Up to 90% have 3 vessel CAD: CABG better [Taggart Curr Op Cardiol 2007]
- POBA: 127 patients 3 yr mortality of 64% [O'Keefe Am J Cardiol 1989]

BARE METAL STENTS		% all	Hospital		1-2 year	
	Nos	%	Death	Revasc	Die	Revas
Keeley (Am J Cardiol 1999)	54	?	5%	20%	31%	15%
Silvestri (JACC 2000): High Risk	47	?	9%	?	11%	15%
Silvestri (JACC 2000): LOW RISK	93	?	0%	?	3%	28%
Tan (Circ 2001): ALL	279	?	14%	?	24%	34%
Tan (Circ 2001): LOW RISK	89	?	3.4%	?	3.4%	31%
Black (JACC 2001)	92	?	4%	?	6.5%	16%
Takagi (Circ 2002)	63	?	0%	10%	16%	31%
Park (Am J Cardiol 2003)	270	?	0%	4%	7%	29%
Brueren (Heart 2003)	71	?	1%	4%	10%	25%
Kelley (Eur H J 2003)	43	?	9%	?	28%	20%
Weighted Average (8 studies)	1155	?	6%	3%	17%	29%

- All 8 PCI (BMS) studies concluded that CABG is still best therapy for LM
- PCI studies must have a minimum follow-up of two years (1 yr inadequate)

Guidelines for PCI in LMS Stenosis (based on BMS)

ACC/AHA guidelines for percutaneous coronary interventions [JACC 2005]

- PCI is CLASS III indication in virtually all patients (2001)
- PCI is CLASS III indication in candidate for CABG (2005)

(Class III: conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective, and may be harmful)

Guidelines for percutaneous coronary interventions. Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. [Eur Heart J 2005;26:804-47]

- 'Stenting for unprotected LM disease should only be considered in the absence of other revascularization options'

BUT !!!!!!!!!

Current percutaneous coronary intervention and coronary artery bypass grafting practices for three-vessel and left main coronary artery disease. Insights from the SYNTAX run-in phase. [Eur J Cardiothorac Surg 2006]

- 29% of LMS in Europe and 18% in USA now treated with DES

Drug Eluting Stents in LMS Stenosis pre 2008 [Taggart et al JACC 2008]

		% all	Distal	3 VD	30 Day (%)		6-18 mth (%)	
	Nos	%	%	%	Death	Revas	Death	Resten
De Lezo (2004)	52	?	42	37	0	0	0	6
Valgimigli (2005)	130	?	72	85	10	0	14	9
Price (2005)	50	?	94	?	0	6	10	42*
Chieffo (2006)	107	?	82	?	0	0	3	-
Lee (2006)	50	?	60	66	2	0	4	-
Kim (2006)	116	?	100	76	0	0	0	11
Palmerini (2006)	94	?	80	100	3	1	13	20*
WEIGHTED	599	?	40-100	37-100	2.4	2	7	21

*Asymptomatic

OBaim (JACC 2005) 'with 2% stent thrombosis and 20%-44% angiographic restenosis.. necessary to perform routine angiography perhaps at both 3 and 9 months. Without that safety net, one would expect an up-tick in late mortality from unrecognized restenosis in this critical location.'

'Because the merit of surgery for LM lesions is based mostly on mortality reduction .. equivalent mortality reduction should be demonstrated by PCI. This may be difficult (despite CABG surgery's higher initial mortality) because over the longer term it protects against events related to entire zones of proximal vulnerability, thereby reducing the incidence or lethality of subsequent myocardial infarctions'.

Stents versus Coronary-Artery Bypass Grafting for Left Main Coronary Artery Disease

NEJM 2008

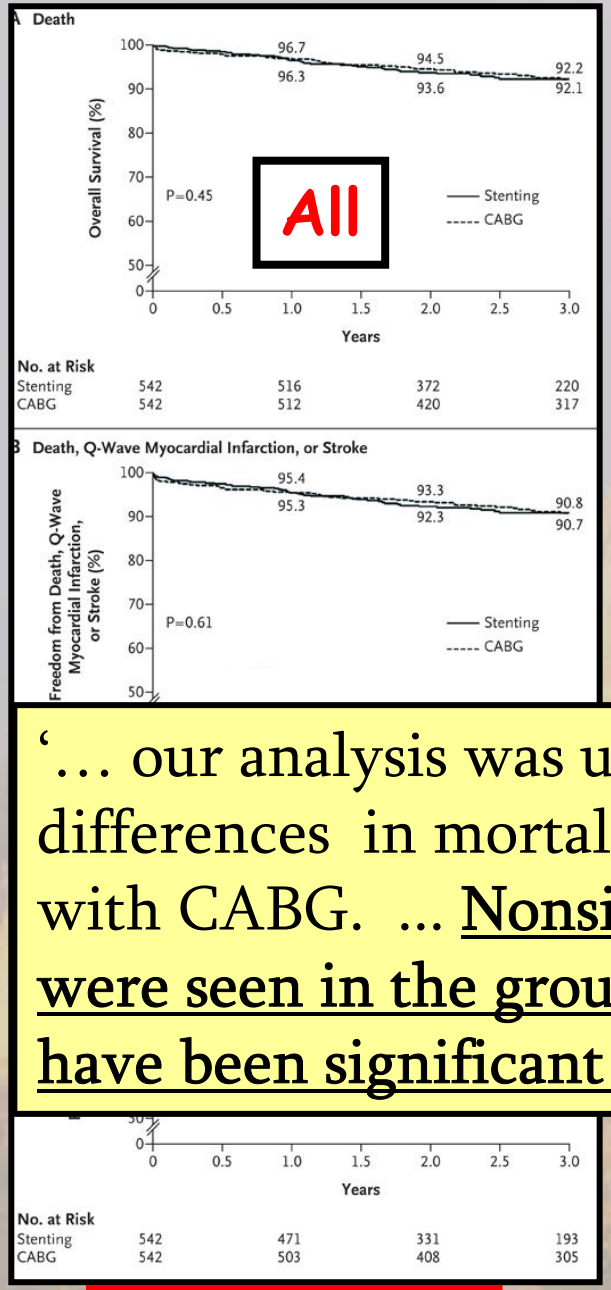
Ki Bae Seung, M.D., Duk-Woo Park, M.D., Young-Hak Kim, M.D., Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Myeong-Ki Hong, M.D., Seong-Wook Park, M.D., Sung-Cheol Yun, Ph.D., Hyeon-Cheol Gwon, M.D., Myung-Ho Jeong, M.D., Yangsoo Jang, M.D., Hyo-Soo Kim, M.D., Pum Joon Kim, M.D., In-Whan Seong, M.D., Hun Sik Park, M.D., Taehoon Ahn, M.D., In-Ho Chae, M.D., Seung-Jea Tahk, M.D., Wook-Sung Chung, M.D., and Seung-Jung Park, M.D.

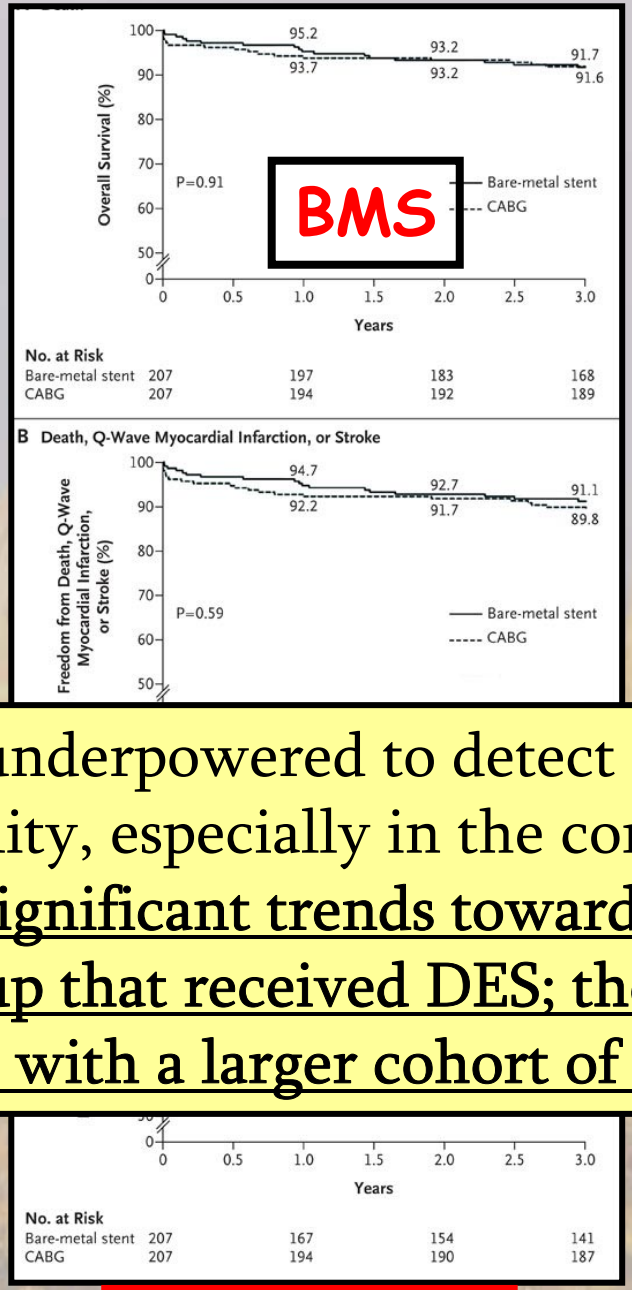
Conclusions In a cohort of patients with unprotected left main coronary artery disease, we found no significant difference in rates of death or of the composite end point of death, Q-wave myocardial infarction, or stroke between patients receiving stents and CABG. **However, stenting, even with drug-eluting stents, was associated with higher rates of target-vessel revascularization than was CABG.**

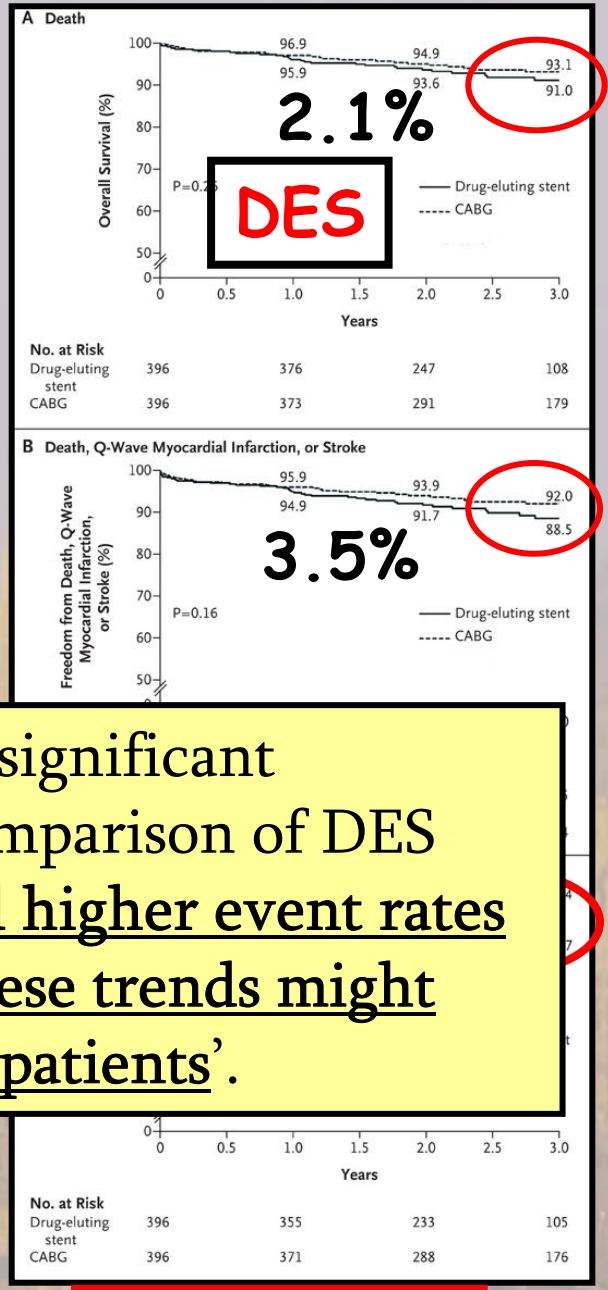
		PCI (1102)	CABG (1138)	
Peripheral Vascular Disease		1.5%	5.4%	<0.001
Unstable angina		55%	68%	<0.001
Distal LMS		49%	54%	0.04
LMS	alone	25	6	<0.001
	1VD	24	11	
	2VD	26	26	
	3VD	25%	57%	
	RCA	36%	71%	

- CONGRATULATE- superb registry data .but no routine surgical opinion
- Overall relatively low rate of distal left main stem stenosis
- Overall relatively low rate of 3 vessel CAD
- ?applicable in Europe/USA ???

Outcome in PCI and CABG propensity matched patients:All;BMS; DES







'… our analysis was underpowered to detect significant differences in mortality, especially in the comparison of DES with CABG. … <u>Nonsignificant trends toward higher event rates were seen in the group that received DES; these trends might have been significant with a larger cohort of patients</u>'.

ALL TVR: HR x5

BMS TVR: HR x11

DES TVR: HR x6

A collaborative systematic review and meta-analysis on 1278 patients undergoing percutaneous drug-eluting stenting for unprotected left main coronary artery disease

Am H J 2008

Giuseppe G.L. Biondi-Zoccai, MD,[a,o] Marzia Iotrionte, MD,[b,o] Claudio Moretti, MD,[a] Emanuele Meliga, MD,[a] Pierfrancesco Agostoni, MD,[c] Marco Valgimigli, MD, PhD,[d,e] Angela Migliorini, MD,[f] David Antoniucci, MD,[f] Didier Carrié, MD,[g] Giuseppe Sangiorgi, MD,[h,i] Alaide Chieffo, MD,[h,i] Antonio Colombo, MD,[h,i] Matthew J. Price, MD,[j] Paul S. Teirstein, MD,[j] Evald H. Christiansen, MD,[k] Antonio Abbate, MD,[l] Luca Testa, MD,[b] Julian P.G. Gunn, MD,[m] Francesco Burzotta, MD,[b] Antonio Laudito, MD,[n] Gian Paolo Trevi, MD,[a] and Imad Sheiban, MD[a] *Turin, Rome, Ferrara, Gussago, Florence, and Milan, Italy; Antwerp, Belgium; Toulouse, France; La Jolla, CA; Aarhus, Denmark; Richmond, VA; and Sheffield, United Kingdom*

CATEGORY		In-hospital (%)		6-10 month follow up		
	n	death	MI	death	TVR	MACE
All DES	1278	2.3	2.5	5.5	6.5	16.5
Nonbifurcation (25%)	285	0.9	3.2	4.1	6.7	14.7
Low –risk: ES<6	260	3	3	4.8	8.5	15.7
High-risk: ES>6	312	6.6	1.3	12	6.4	20.6

OBaim [JACC 2005] '<u>one would expect an up-tick in late mortality from unrecognized restenosis in this critical location</u>.'

Are stents ever indicated for LMS in good surgical candidates ?

Favorable Long-Term Outcome After Drug-Eluting Stent Implantation in Nonbifurcation Lesions That Involve Unprotected Left Main Coronary Artery

A Multicenter Registry [*Circulation.* 2007;116:158-162]

Alaide Chieffo, MD; Seung J. Park, MD, PhD; Marco Valgimigli, MD; Young H. Kim, MD, PhD; Joost Daemen, MD; Imad Sheiban, MD; Alessandra Truffa, MD; Matteo Montorfano, MD; Flavio Airoldi, MD; Giuseppe Sangiorgi, MD; Mauro Carlino, MD; Iassen Michev, MD; Cheol W. Lee, MD, PhD; Myeong K. Hong, MD, PhD; Seong W. Park, MD, PhD; Claudio Moretti, MD; Erminio Bonizzoni, PhD; Renata Rogacka, MD; Patrick W. Serruys, MD, PhD; Antonio Colombo, MD

- 147 NonBifurcation Lesions (19% of 790 LMS)
  - ostial (52%) or mid shaft (28%) or both (+35% RCA disease)
  - mean age 62 yrs; Mean EF 55%; 20% DM
- Results
  - 1 hospital death (unrelated)
  - 73% repeat angio at 6 months with 1 restenosis
  - at 2.5 years 5 deaths (3.4%) and 8 revascularization (5.4%)

'Stent thrombosis could not be excluded in the 4 patients (2.7%) who died of unknown causes'

Non Randomized Comparisons of Stents and CABG in LMS Stenosis

Study		nos	1 yr mortality	1 year repeat revasc
Bologna Registry [Palmerini 2006]	CABG	154	12%*	3%
	Stents	157	13%*	26%
*1 yr mortality in low risk patients 3%				

Study		nos	1 yr mortality	1 year repeat revasc
Italian Registry [Chieffo 2006]	CABG*	142	8.4%	4%
	Stents	107	2.8%	20%
CABG patients significantly older (68 vs 64 yrs) with increased renal failure (8% vs 2%)				

Study		nos	1 yr mortality	1 year repeat revasc
Lee [JACC 2006]	CABG*	123	25%*	5%
	Stents	50	17%	15%
*Of 7 additional CABG deaths at 6 months 5 were NOT cardiac related				

- CABG very high mortality (high risk patients or poor surgery ?)
- **PCI: 3 to 8 fold increase in repeat revascularization by 1 yr**

- RCT of DES vs CABG for LMS stenosis
  - LeMans RCT: no difference in MACE at 1 yr in 103 patients (Poor RCT!!!)
  - SYNTAX trial of 1800 patients with LMS +/- CAD (nb 12 months outcome)
  - PRECombat trial (Korea)

Fundamental Question

WHY DOES CABG HAVE SURVIVAL BENEFIT OVER PCI in LMS ?

1. By placing grafts to mid coronary vessels CABG has two effects
(i) treats the 'CULPRIT' lesion (regardless of complexity)
(ii) 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

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)

- Up to 90% are distal/bifurcation and at high risk of restenosis [Serruys 2005]
- Up to 90% of patients have multivessel coronary artery disease (CABG better)

Health Economists: Drug Eluting Stents (DES) vs CABG

Coronary artery stents: a rapid systematic review and economic evaluation

NICE 2003/
HTA 2004

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 Williamson[5] and T Walley[1]

Eleven health economists: 'In the absence of substantive clinical evidence of the superiority of stenting with DES over CABG (for 2 and3 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 QUALY of £30K ($60K)

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

Summary of Stents and Surgery in LMS Stenosis

- Effectiveness of CABG has been demonstrated over 40 years
- Evidence basis for PCI, BMS, DES is not apparent
- Early mortality for both CABG and PCI patients is around 1%-3%
- However for most LMS stenosis there is continuing risk of death because of restenosis (20% at one year) and up to an 8 fold increase in repeat revascularization within one year even with DES
- Up to 90% of patients with LMS stenosis have multivessel coronary artery disease where CABG already has proven survival advantage
- As restenosis is often asymptomatic how frequently and for how long should repeat angiography be performed ?
- RCT of PCI vs CABG with 1 year outcome are stacked against CABG because they will underestimate both MACE for PCI and survival benefit of CABG which both increase with time (and should be DES vs IMA x2)
- Health economists report that stents are not cost effective vs CABG

- All patients with LMS who are candidates for CABG should be treated by an MDT <u>including a surgeon</u> and advised about the survival benefit of CABG…without this there is no real informed consent for PCI …

- In the absence of true clinical equipoise the ethics of randomized trials of PCI and CABG in most patients with LMS (90% distal; 90% 3VD) are questionable

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STATE-OF-THE-ART PAPER AND COMMENTARY

Revascularization for Unprotected Left Main Stem Coronary Artery Stenosis

Stenting or Surgery

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For coronary artery disease with unprotected left main stem (LMS) stenosis, coronary artery bypass grafting (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

O<90% of LMS are distal/bifurcation and <90% have multivessel CAD

"There is no survival difference between CABG and PCI"

- The most widely perpetuated myth in cardiovascular medicine
  - ubiquitous in the literature,
  - repeated in cardiology lectures,
  - frequently - but erroneously- told to patients
- *"The great enemy of the truth is very often not the lie – deliberate, contrived and dishonest – but the myth – persistent, persuasive and unrealistic."* (JF Kennedy; S Yusuf)
- Securing the myth
  - Based on 15 RCT where results were stacked against CABG
  - Ignoring evidence from numerous large databases which consistently demonstrates a survival benefit of CABG

Three reasons to predict that DES will not be superior to BMS

1. Two key features of LMS predict that PCI will NOT be successful
   - I. < 90% of lesions are distal/bifurcation (high risk of restenosis)
   - II. <90% of patients have multivessel CAD (CABG better)

2. **DES do not improve clinical outcome vs BMS**

OFive meta-analysis (Lancet/EHJ 2004;AJC 2005;EHJ 2006)

- **5103, 5747, 5066, 8221 patients followed for 2 years**
- **4958 pts in 14 RCT up to 5 yrs (Kastrati NEJM 2007)**

CONCLUSION: "DES decrease risk of restenosis in **low risk** coronary lesions **but not the risk of mortality or MI at 2-5 years**"

3. Six **'IGNORED'** facts about DES

- do not improve clinical outcome vs BMS (NEJM 2007)
- risk of stent THROMBOSIS of 1%-5% per yr (NEJM 2007)
- real RESTENOSIS rate 10%-30% per yr (Research, Delivery)
- 10% have MRI defined MI of >5g (Selvanaygam Circ 2005)
- PCI Increases subsequent CABG mortality x 3 (Thielman Circ 2006)
- Risk of cognitive dysfunction same as CABG (SoS, BARI Trials)

Are RCT of Stents and Surgery Justifiable in LMS stenosis ?

- There is NOT Clinical equipoise between Surgery and Stents

- Serruys (Circ 2005): **'CABG should remain the preferred revascularization treatment in good surgical candidates with LMCA disease'**

- Stone, Moses, Leon (JACC 2007) **'Thus the principles of evidence based medicine would dictate that CABG remain the gold standard for most patients with unprotected LMCA disease who are good surgical candidates'**

- **With strong evidence that CABG is superior to stents for LMS stenosis (ie lack of equipoise) RCT of DES vs CABG are not justifiable or ethical** (Taggart NEJM 2006)

Table 3. Hazard Ratios for Clinical Outcomes after Stenting as Compared with after CABG among Propensity-Matched Patients.*

Outcome	Overall Cohort (N=542 pairs)		Wave 1 (N=207 pairs)		Wave 2 (N=396 pairs)	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Death	1.18 (0.77–1.80)	0.45	1.04 (0.59–1.83)	0.90	1.36 (0.80–2.30)	0.26
Composite outcome of death, Q-wave myocardial infarction, or stroke	1.10 (0.75–1.62)	0.61	0.86 (0.50–1.49)	0.59	1.40 (0.88–2.22)	0.15
Target-vessel revascularization	4.76 (2.80–8.11)	<0.001	10.70 (3.80–29.90)	<0.001	5.96 (2.51–14.10)	<0.001

* CABG denotes coronary-artery bypass grafting. Wave 1 shows comparisons between bare-metal stents and CABG, and Wave 2 shows comparisons between drug-eluting stents and CABG. Hazard ratios are for the stenting group as compared with the CABG group.

PCI is less invasive than CABG but is it safer ?

FACT 1: DES do NOT improve clinical outcome vs BMS

- Four Meta-analysis of 11 RCT of DES vs (BMS) of >5000 patients
- (Lancet 2004; Eur Heart J 2004; Am J Cardiol 2005; Eur H J 2006)

FACT 2: DES predispose to THROMBOSIS

Risk of 1-5% per annum and 40% mortality (NEJM 2007)
Especially if antiplatelets stopped (Lancet 2004,JAMA2005)
Particular lesions and patient groups

FACT 3: REAL rate of restenosis with DES is 10%-28% at 1 year

- 10% RESEARCH Registry (Lemos Circ 2004).
- 20% DELIVER trial (Lansky Circ 2004)
- 28% Bifurcating Lesions (Tanabe Am J Cardiol 2004)

FACT 4: 10% of PCI cause SIGNIFICANT Myocardial Infarct

- 37% of patients have raised troponin (Selvanygam 2005, Thomas 2005)
- of whom 28% have MRI defined mean loss of 6g of LV muscle (ie 5% LV mass)

FACT 5: Multiple previous PCI strongly associated with in-hospital CABG mortality (OR: 3.01; p<0.0017) and MACES (OR: 2.31; p<0004) (Thielman Circ 2006)

FACT 6: Risk of cognitive dysfunction SAME for PCI and CABG

- SoS trial: no difference at 6 months and 1yr (Wahrborg P Circ 2004)
- BARI trial: no difference at 5 years (Hlatky MA et al Circ 1997)

Summary of Stents and Surgery in LMS Stenosis

- Effectiveness of CABG has been demonstrated over 40 years
- Early mortality for both CABG and PCI patients is around 1%-3%
- However for most LMS stenosis there is continuing risk of death because of restenosis (20% at one year) even with DES and up to an 8 fold increase in repeat revascularization within one year
- As restenosis is often asymptomatic how frequently and for how long should repeat angiography be performed ?
- Up to 90% of patients with LMS stenosis have multivessel coronary artery where CABG already has proven survival advantage
- Real risks and limitations of DES rarely discussed with patients
- Health economists report that stents are not cost effective vs CABG

- It is inappropriate that intervention should be decided by cardiologist
- An MDT should be the 'minimum standard of care' **(BMJ 2007)**
  - Cardiologists (including non-interventional) and Surgeons
  - Health care providers
  - Patients (with MVD or LMS should be told that an initial strategy of PCI reduces life expectancy vs CABG)
  - MDT should be enshrined by external Regulatory/Legislative bodies

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STATE-OF-THE-ART PAPER AND COMMENTARY

Revascularization for Unprotected Left Main Stem Coronary Artery Stenosis

Stenting or Surgery

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For coronary artery disease with unprotected left main stem (LMS) stenosis, coronary artery bypass grafting (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

O<90% of LMS are distal/bifurcation and <90% have multivessel CAD

- LMS stenosis in up to 10% of angiograms and 30% of CABG
- When symptomatic annual mortality of around 20%

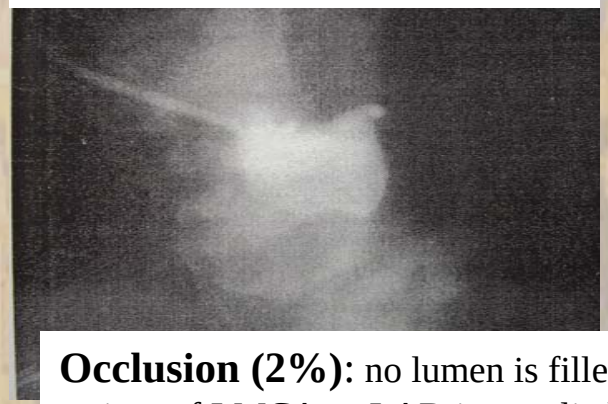
LMS stenosis: angiographic lesion in 384 patients (Jonsson A 2003)

Mid-shaft (24%): apparently normal proximal/ distal segments

Ostial (9%): exclusive narrowing at the aortic ostium of LMCA

Bifurcation (40%-90%): distal stenosis +/- LAD and Cx

Circular (25%): involves entire lenght of LM with > two narrowings



Occlusion (2%): no lumen is filled with the contrast injected into the ostium of LMCA;or LAD is supplied only via collaterals from the RCA.

- Up to 90% are distal/bifurcation and at high risk of restenosis (Serruys 2005)
- Up to 90% of patients also have multivessel coronary artery disease

- CABG treats EVERY type of LM and associated multivessel CAD
- PCI needs 'SUITABLE' LM and offers incomplete revascularization

Surgery in LMS stenosis

- Cohen and Gorlin report 10 year survival advantage for CABG (Circ 1975)
- CABG improves life expectancy (3 RCT: VA, ECSS, CASS: 1972-1979)

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*

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

- "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 patients received an IMA graft (now >90%)

Comparison of Surgical and Medical Group Survival in Patients With Left Main Coronary Artery Disease.Long-term CASS Experience. Caracciolo E.A. *Circ* 1995; 91:2325-34

- 1484 LM (>50% stenosis) (ACC/AHA 2004 Guideline Update for CABG)

'The benefit of surgery over medical treatment for patients with significant left main stenosis (>50%) is little argued. The median survival for surgically treated patients is 13.3 years versus 6.6 years in medically treated patients'

Table 1. Baseline Characteristics of the Patients.*

Variable	Stent Group (N = 1102)	CABG Group (N = 1138)	P Value
Demographic characteristics			
Age (yr)			<0.001
Median	62	64	
Interquartile range	52–70	57–70	
Male sex (%)	70.7	72.9	0.24
Cardiac or coexisting conditions			
Diabetes mellitus (% of patients)			
Any diabetes	29.7	34.7	0.01
Insulin-dependent	6.8	8.2	0.22
Hypertension (% of patients)	49.5	49.4	0.94
Hyperlipidemia (% of patients)	28.5	32.6	0.04
Current smoker (% of patients)	25.6	29.8	0.03
Previous coronary angioplasty (% of patients)	18.1	11.0	<0.001
Previous myocardial infarction (% of patients)	8.1	11.6	0.005
Previous congestive heart failure (% of patients)	2.5	3.3	0.21
Chronic obstructive pulmonary disease (% of patients)	2.0	2.0	0.97
Cerebrovascular disease (% of patients)	7.1	7.3	0.84
Peripheral vascular disease (% of patients)	1.5	5.4	<0.001
Renal failure (% of patients)	2.7	3.0	0.71
Ejection fraction (%)			<0.001
Median	62	60	
Interquartile range	57–67	52–66	
Electrocardiographic findings (% of patients)			0.53
Sinus rhythm	97.8	97.1	
Atrial fibrillation	2.0	2.7	
Other	0.2	0.2	

Table 2. Baseline Characteristics of the Propensity-Matched Patients.*

Variable	Overall Cohort			Wave 1†			Wave 2‡		
	Stents (N=542)	CABG (N=542)	P Value§	Bare-Metal Stents (N=207)	CABG (N=207)	P Value§	Drug-Eluting Stents (N=396)	CABG (N=396)	P Value§
Age (yr)			0.41			0.57			0.23
Median	64	64		61	61		66	66	
Interquartile range	56–71	56–70		51–69	53–67		57-72	58-70	
Male sex (% of patients)	71.6	71.2	0.95	72.0	71.0	0.91	71.5	71.7	0.99
Diabetes mellitus (% of patients)									
Any diabetes	32.7	33.0	0.95	26.1	26.6	0.99	36.1	36.9	0.86
Insulin-dependent	7.6	7.9	0.91	4.8	5.3	0.99	10.1	10.9	0.77
Hypertension (% of patients)	49.4	50.0	0.90	44.9	45.4	0.99	52.3	53.0	0.81
Hyperlipidemia (% of patients)	29.3	30.1	0.84	27.1	27.1	0.99	32.6	33.6	0.81
Current smoker (% of patients)	27.7	27.1	0.89	28.5	28.0	0.99	26.3	25.5	0.87
Previous coronary angioplasty (% of patients)	14.8	15.1	0.93	14.0	14.5	0.99	15.4	15.4	0.99
Previous myocardial infarction (% of patients)	9.0	10.0	0.68	9.7	10.6	0.87	8.8	9.3	0.90
Previous congestive heart failure (% of patients)	2.8	3.0	0.99	2.4	2.9	0.99	3.0	3.3	0.99
Chronic obstructive pulmonary disease (% of patients)	2.6	2.2	0.85	2.4	1.9	0.99	2.8	2.5	0.99
Cerebrovascular disease (% of patients)	7.4	6.6	0.72	6.8	6.3	0.99	8.1	7.3	0.76
Peripheral vascular disease (% of patients)	2.0	2.0	0.99	1.0	1.0	0.99	2.5	3.3	0.79
Renal failure (% of patients)	3.7	3.9	0.99	1.9	2.4	0.99	5.3	4.8	0.83
Ejection fraction (%)			0.62			0.67			0.53
Median	61	61		61	61		60	60	
Interquartile range	54–66	55–66		57–67	56–66		55-66	56-66	
Electrocardiographic findings (% of patients)			0.80			0.99			0.62
Sinus rhythm	97.6	96.7		97.6	97.1		97.7	96.5	
Atrial fibrillation	2.4	3.1		2.4	2.9		2.3	3.0	
Other	0.0	0.2		0	0		0	0.5	
Clinical indication (% of patients)			0.97			0.78			0.41
Silent ischemia	2.8	2.6		2.9	3.4		2.3	2.8	
Chronic stable angina	29.2	28.4		16.4	16.4		30.1	28.8	
Unstable angina	57.4	57.9		69.6	69.6		57.8	57.8	
Non–ST-elevation myocardial infarction	10.7	11.1		11.1	10.6		9.8	10.6	
Involved location (% of patients)			0.90			0.99			0.93
Ostium, midshaft, or both	48.3	47.8		61.8	61.4		39.4	38.9	
Distal bifurcation	51.7	52.2		38.2	38.6		60.6	61.1	
Extent of diseased vessel (% of patients)			0.81			0.99			0.63
Left main only	11.8	11.1		21.3	21.3		5.8	5.8	
Left main plus single-vessel disease	17.0	16.2		29.0	29.0		12.4	11.6	
Left main plus double-vessel disease	31.7	33.9		33.8	33.8		29.0	29.5	
Left main plus triple-vessel disease	39.5	38.7		15.9	15.9	0.99	52.8	53.0	
Right coronary artery disease (% of patients)	53.7	53.7	0.99	29.5	29.5	0.99	65.9	66.9	0.64
Restenotic lesion (% of patients)	1.8	1.8	0.99	1.9	2.4	0.99	1.8	1.3	0.77

* CABG denotes coronary-artery bypass grafting. Percentages may not total 100 because of rounding.

Table 1. Three-Year Mortality Rates in 2240 Patients with Left Main Coronary-Artery Stenosis in the MAIN-COMPARE Registry.*

Cohort and Enrollment Era	PCI Group	CABG Group	Total
	no. of deaths/total no. of patients (%)		
Propensity-score matched			
Early	17/207 (8.2)	17/207 (8.2)	34/414 (8.2)
Late	31/396 (7.8)	25/396 (6.3)	56/792 (7.1)
Total cohort	48/603 (8.0)	42/603 (7.0)	90/1206 (7.5)
Unmatched			
Early	4/111 (3.6)	20/241 (8.3)	24/352 (6.8)
Late	15/388 (3.9)	32/294 (10.9)	47/682 (6.9)
Total cohort	19/499 (3.8)	52/535 (9.7)	71/1034 (6.9)
Total population			
Early	21/318 (6.6)	37/448 (8.3)	58/766 (7.6)
Late	46/784 (5.9)	57/690 (8.3)	103/1474 (7.0)
Total cohort	67/1102 (6.1)	94/1138 (8.3)	161/2240 (7.2)

* CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

- LMS stenosis in up to 10% of angiograms and 30% of CABG
- When symptomatic annual mortality of around 20%

Fundamental Question

WHY DOES CABG HAVE SUCH A SURVIVAL BENEFIT OVER PCI ?

- , 90% are distal/bifurcation and at high risk of restenosis [Serruys 2005]
- Up to 90% of patients also have multivessel coronary artery disease

1. By placing grafts to mid coronary vessels CABG has two effects
(i) treats the 'CULPRIT' lesion (regardless of complexity)
(ii) 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

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)