

**Summit
TCT Asia Pacific 2009**

**DEBATE: Treatment Decision:
Stenting vs CABG for Unprotected Left Main Disease:
CABG Remains an Excellent Selection for All Patients**

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**Conflict of Interest: Cardiac surgeon
No other disclosures**



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

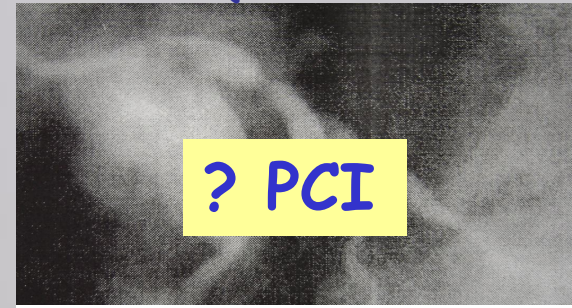
LMS stenosis: angiographic lesion in 384 patients (Jonsson A 2003)



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

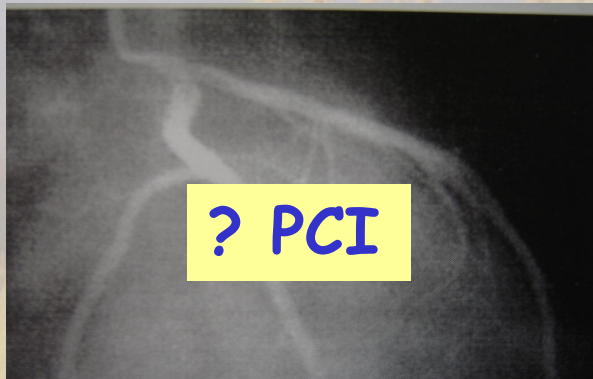


Circular (25%): involves entire length of LM with > two narrowings



? PCI

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



? PCI

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



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.



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

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

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,†

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

- 8 studies of BMS (>1150 patients): in hospital MORTALITY of 6%
 - Mortality increased to 17% by 2 years
 - 29% required repeat revascularization at 2 years

- 7 studies of DES (599 patients): in hospital MORTALITY of 2.4%
 - Mortality increased to 7% by 1 year
 - 21% required repeat revascularization at 1 year
 - **Restenosis was asymptomatic in 20-40%**
 - (5 meta-analyses of 18000 pts: no clinical benefit of DES vs BMS)

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 30 yrs

Comparison of Surgical and Medical Group Survival in Patients With Left Main Coronary Artery Disease. Long-term CASS Experience. [Caracciolo Circ 1995]

- 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'

UK: all 114,300 CABG patients 2004-08: [Blue Book June 2009]

	NO LMS	LMS	
	69,775	30,128	
In hospital mortality	1.5% *	2.5 *	<0.001
1 year survival	97%	95%	<0.001
5 year survival	90%	87%	<0.001

(i) *= all comers: 1/3 high risk (urgent, elderly, comorbidity)

(ii) UK MORTALITY for ALL 70,000 Elective CABG 1.1%

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

NEJM 2008

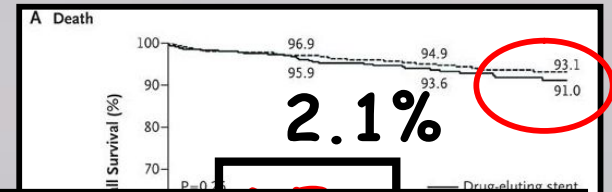
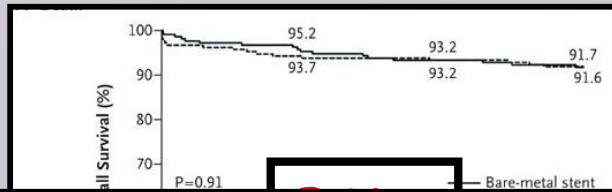
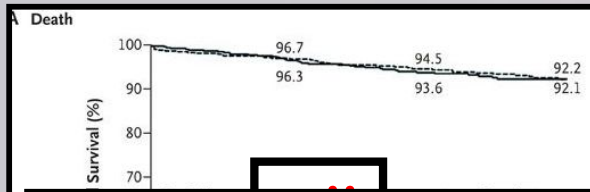
Ki Bae Seung, M.D., Duk-Woo Park, M.D., Young-Hak Kim, M.D., Seung-Whan Lee, M.D., Cheol Whan Lee, M.D., Myeong-Ki Hong, M.D., Seong-Wook Park, M.D., Sung-Cheol Yun, Ph.D., Hyeon-Cheol Gwon, M.D., Myung-Ho Jeong, M.D., Yangsoo Jang, M.D., Hyo-Soo Kim, M.D., Pum Joon Kim, M.D., In-Whan Seong, M.D., Hun 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%	

- Superb registry data
- Overall relatively low rate of distal LMS and 3 vessel CAD
- ?applicable in Europe/USA ???
- **NO ROUTINE SURGICAL OPINION**

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

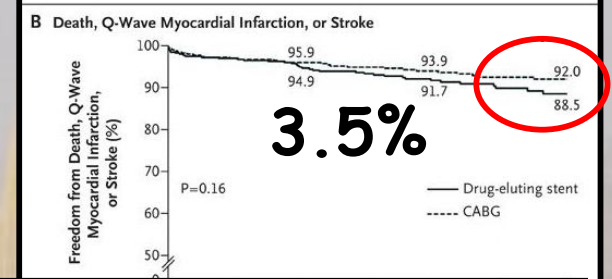
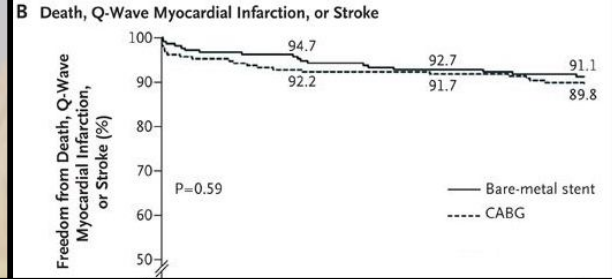
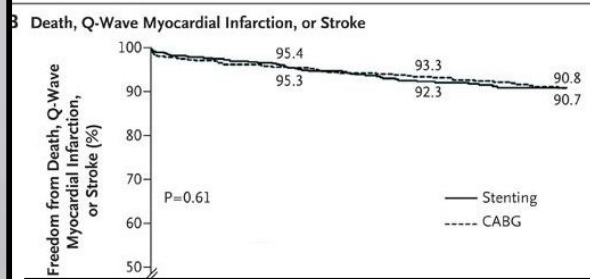


○ Propensity matching is towards lower risk PCI patients
 ● Biases results against benefits of CABG in higher risk patients

No. at Risk				
Stenting	542	516	372	220
CABG	542	512	420	317

No. at Risk				
Bare-metal stent	207	197	183	168
CABG	207	194	192	189

No. at Risk				
Drug-eluting stent	396	376	247	108
CABG	396	373	291	179



‘... our analysis was underpowered to detect significant differences in mortality, especially in the comparison of DES with CABG. ... 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’.

No. at Risk				
Stenting	542	471	331	193
CABG	542	503	408	305

No. at Risk				
Bare-metal stent	207	167	154	141
CABG	207	194	190	187

No. at Risk				
Drug-eluting stent	396	355	233	105
CABG	396	371	288	176

ALL TVR: HR x5

BMS TVR: HR x11

DES TVR: HR x6

Are stents ever indicated for LMS ?

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'

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

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Pierfrancesco Agostoni, MD,^c Marco Valgimigli, MD, PhD,^{d,e} Angela Migliorini, MD,^f David Antoniucci, MD,^f
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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	n	In-hospital (%)		6-10 month follow up		
		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] '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.'**

THE SYNTAX TRIAL

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

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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)**

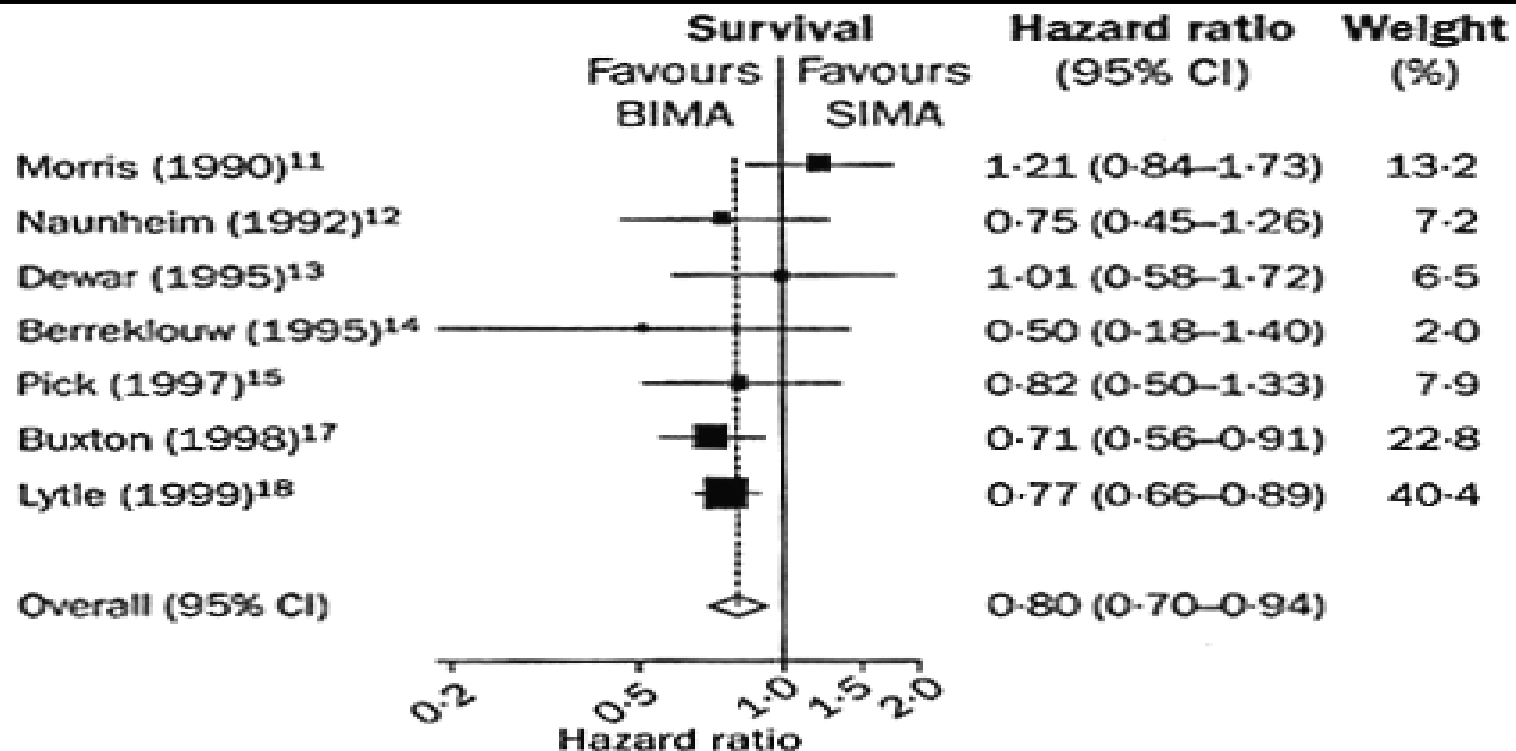
SURVIVAL BENEFIT WITH TWO IMA GRAFTS ?

>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



04693 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]

NNNT of 13-16 (to prevent one death)

Cardiology Conclusions about Treatment of Left Main Stenosis

○ 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'

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

■ Comment

Taggart DP. Lancet 2009; 373:1150-2

Ⓜ PCI or CABG in coronary artery disease?

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.

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

- In recommending interventions an MDT should be the 'minimum standard of care' (**BMJ 2007, Lancet 2009**)
 - 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

Comment

Taggart DP. Lancet 2009; 373:1150-2

Ⓜ PCI or CABG in coronary artery disease?

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.

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)

'CABG remains the standard of care for patients with three-vessel or left main coronary artery disease'

Longest Available Clinical Outcomes After Drug-Eluting Stent Implantation for Unprotected Left Main Coronary Artery Disease

The DELFT (Drug Eluting stent for LeFT main) Registry

Emanuele Meliga, MD,*† Hector Manuel Garcia-Garcia, MD, MSc,* Marco Valgimigli, MD, PhD,‡
 Alaide Chieffo, MD, PhD,§ Giuseppe Biondi-Zoccai, MD,† Andrew O. Maree, MD,||
 Stephen Cook, MD,¶ Lindsay Reardon, MD,|| Claudio Moretti, MD,† Stefano De Servi, MD,#
 Igor F. Palacios, MD, FACC,|| Stephen Windecker, MD,¶ Antonio Colombo, MD, FACC, FESC,§
 Ron van Domburg, PhD,* Imad Sheiban, MD,† Patrick W. Serruys, MD, PhD, FACC, FESC*
Rotterdam, the Netherlands; Turin, Ferrara, and Milan, Italy; Boston, Massachusetts; and Bern, Switzerland

		30 day	1yr	3yr
ARC defined CARDIAC DEATH (%)	All (358)	3.3	6.7	9.2
	Elective (288)	0.7	3.8	6.2
	Urgent (70)	14.3	18.6	21.4
TVR (%)	All (358)	0.8	10	14.2
	Elective (288)	0.7	11.1	16
	Urgent (70)	1.4	5.7	7.1

- Incomplete Reporting: How many 'non-cardiac' deaths occurred?
- 680 patients underwent CABG..how was intervention decided?

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 !!!!!!!!!

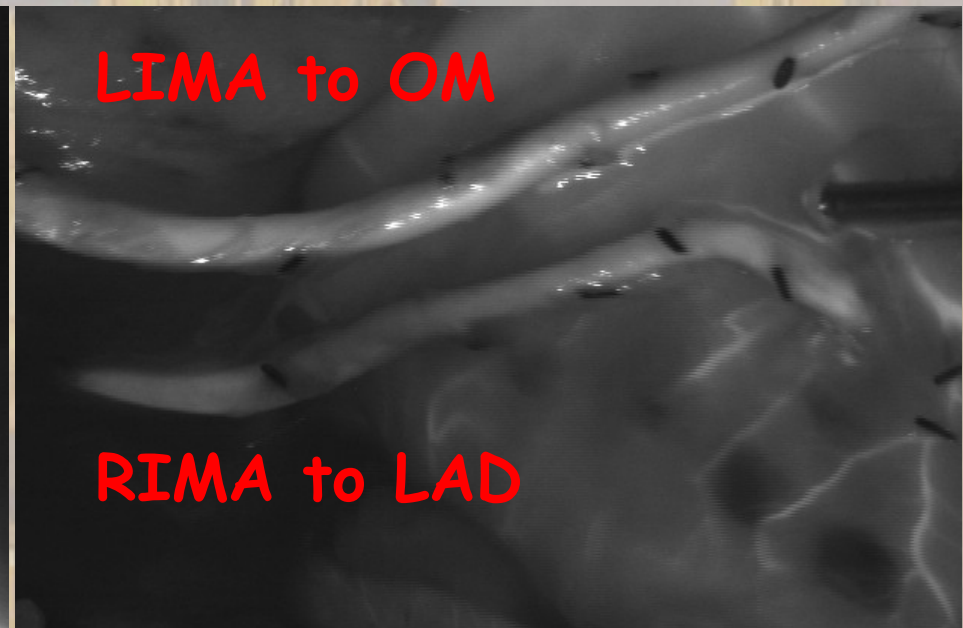
Current percutaneous coronary intervention and coronary artery bypass grafting practices for three-vessel and left main coronary artery disease. Insights from the SYNTAX run-in phase. [[Eur J Cardiothorac Surg 2006](#)]

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

But Results of CABG Can Be Even Better !!!

- ART trial of 2 vs 1 IMA (funded by MRC)
 - 28 centres in 7 countries
 - 30 day mortality in 3100 patients: 1%
- Best Treatment for LMS Stenosis is IMA x 2 (OPCABG) ?
 - No age limit (young=survival benefit; elderly=avoid aorta)

Intraoperative Graft Images



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

○ Six 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"

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)

PCI in LMS Stenosis [Taggart et al JACC 2008]

OPOBA: 127 patients 3 yr mortality of 64% [O'Keefe Am J Cardiol 1989]

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

O All 8 PCI (BMS) studies concluded that CABG is still best therapy for LM
O PCI LMS had early mortality = to CABG but with 30% reintervention
O PCI studies must have a minimum follow-up of two years (1 yr inadequate)
 • RCT of PCI vs CABG with 1 yr outcome are stacked against benefit of CABG

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

	Nos	% all	Distal	3 VD	30 Day (%)		6-18 mth (%)	
		%	%	%	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.'

Health Economists: Drug Eluting Stents (DES) vs CABG

Coronary artery stents: a rapid systematic review and economic evaluation

NICE 2003/
HTA 2004

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Eleven health economists: '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'

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				

O CABG very high mortality (high risk patients or poor surgery ?)

O PCI: 3 to 8 fold increase in repeat revascularization by 1 yr

O RCT of DES vs CABG for LMS stenosis

- LeMans RCT: MACE = at 1 yr in 103 patients
- (Poor RCT!!!; early CABG mortality 4% and IMA use only 72%)
- SYNTAX trial of 1800 patients with LMS +/- CAD (nb 12 months outcome)
- PRECombat trial (Korea)

Summary of Stents and Surgery in LMS Stenosis

- Effectiveness of CABG has been demonstrated over 40 years
 - Best evidence shows DES are not clinically or economically cost effective
- Pathophysiology of LMS (90% bifurcation and 90% simultaneous 3vCAD) predict that results of DES will not be durable over the longer term
- Hospital mortality for both CABG and PCI patients is around 1%-3%
 - with PCI there is continuing risk of death because of restenosis /thrombosis 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 ?
- DES have a role in patients unfit for CABG or who refuse CABG
- DES may have a role in isolated ostial/mid shaft LMS with careful follow-up
- RCT with 1 year outcome are stacked against CABG
 - underestimate increase MACE for PCI and better survival of CABG over time
 - Compared best PCI techniques but not best CABG (OPCABG IMAx2)

○ All patients with LMS who are candidates for CABG should be advised by an MDT including a surgeon and informed about the survival benefit of CABG...without this there is no real patient choice and consent for PCI is not informed or legitimate

○ 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

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)

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

	Nos	% all %	Distal %	3 VD %	30 Day (%)		6-18 mth (%)	
					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'.

Table 2 Baseline Clinical Characteristics

Age (yrs)	66.1 ± 11.2
Men	264 (73.7)
BMI (kg/m ²)	26.7 ± 4.7
Arterial hypertension	238 (66.5)
Hypercholesterolemia	230 (64.2)
Current smoking	120 (33.5)
Diabetic patients	108 (30.2)
IDDM	58 (16.2)
NIDDM	50 (14)
Familial risk factor	93 (26)
Previous AMI	162 (45.3)
Previous PCI	108 (30.2)
Previous CABG	68 (18.9)
Diagnosis at admission	
Stable angina	158 (44.1)
Unstable angina	150 (41.9)
AMI	30 (8.4)
AMI + shock	10 (2.8)
Silent ischemia	10 (2.8)
LVEF	48.6 ± 12.8
EuroScore	6.4 ± 4.1
>6	73 (20.1)
>9	111 (31)
Average elective	5.7 ± 3.8
Average emergent	9.9 ± 3.5

Values given as n (%).

AMI = acute myocardial infarction; BMI = body mass index; IDDM = insulin-dependent diabetes mellitus; NIDDM = noninsulin-dependent diabetes mellitus; PCI = percutaneous coronary intervention; other abbreviations as in Table 1.

"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 (Katristsis 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)



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, JAMA 2005)

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<0.0004) (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)

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'

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 30 yrs

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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%