Asian Pacific TCT

Perspective of LM stenting with Current registry and Randomized Clinical Data

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Contemporary Reviews in Interventional Cardiology

Percutaneous Coronary Intervention With Stent Implantation Versus Coronary Artery Bypass Surgery for Treatment of Left Main Coronary Artery Disease

Is It Time to Change Guidelines?

Seung-Jung Park, MD, PhD; Duk-Woo Park, MD, PhD

Our perspectives are very close, and they are very well expressed in this article.

Circ Cardiovasc Intervent. 2009;2:59-68

Overview of this presentation

1. LMCA Medical treatment versus Bypass surgery
2. LMCA PCI with stent implantation
    a. BMS and DES
    b. Ostial and mid-shaft lesions
    c. bifurcation lesions
    d. Role of IVUS guidance
    e. Risk stratification after PCI for LMCA disease
    f. Stent thrombosis and Long-term clinical outcomes with DES
3. Stents vs. Surgery for LMCA
    a. Patient selection & possible indication / contraindication for PCI or CABG
    b. Clinical evidence supporting PCI or CABG for LMCA disease
        1. Registry data
        2. Meta-analysis and review
        3. Randomized trials
4. Conclusions

2. PCI with Stent Implantation

Bare-metal and drug-eluting stents

Table 2. Drug-Eluting Stents vs Bare-Metal Stents for Unprotected Left Main Coronary Artery Disease

	Park et al[22] (2005)		Valgimigli et al[23] (2005)		Chieffo et al[24] (2005)	
No. of patients	102	121	95	86	85	64
Stent type	SES	BMS	SES or PES	BMS	SES or PES	BMS
Age (mean, years)	60	58	64	66	63	66
Ejection fraction, %	60	62	41	42	51	57
Acute myocardial infarction, %	10	7	17	20	…	…
Bifurcation involvement, %	71	43	65	66	81	58
Bifurcation 2-stent technique, %	41	18	40	15	74	…
Early outcomes, %	In-hospital		1 month		In-hospital	
Death	0	0	11	7	0	0
Myocardial infarction	7	8	4	9	6	8
Target-vessel revascularization	0	0	0	2	0	2
MACE	7	8	15	19	…	…
Midterm outcomes, %	12 months		12 months		6 months	
Death	0	0	14	16	4	14
Myocardial infarction	7	8	4	12	…	…
Target-vessel revascularization	2	17	6	12	19	31
MACE	8	26	24	45	…	…

MACE indicates major adverse cardiac events.

"Most initial reports documented that DES afforded higher procedural success rates and lower rates of angiographic restenosis and target-vessel revascularization with similar or lower rates of death and MI compared with BMS."

2. PCI with Stent Implantation

Bare-metal and drug-eluting stents

Table 2. Drug-Eluting Stents vs Bare-Metal Stents for Unprotected Left Main Coronary Artery Disease

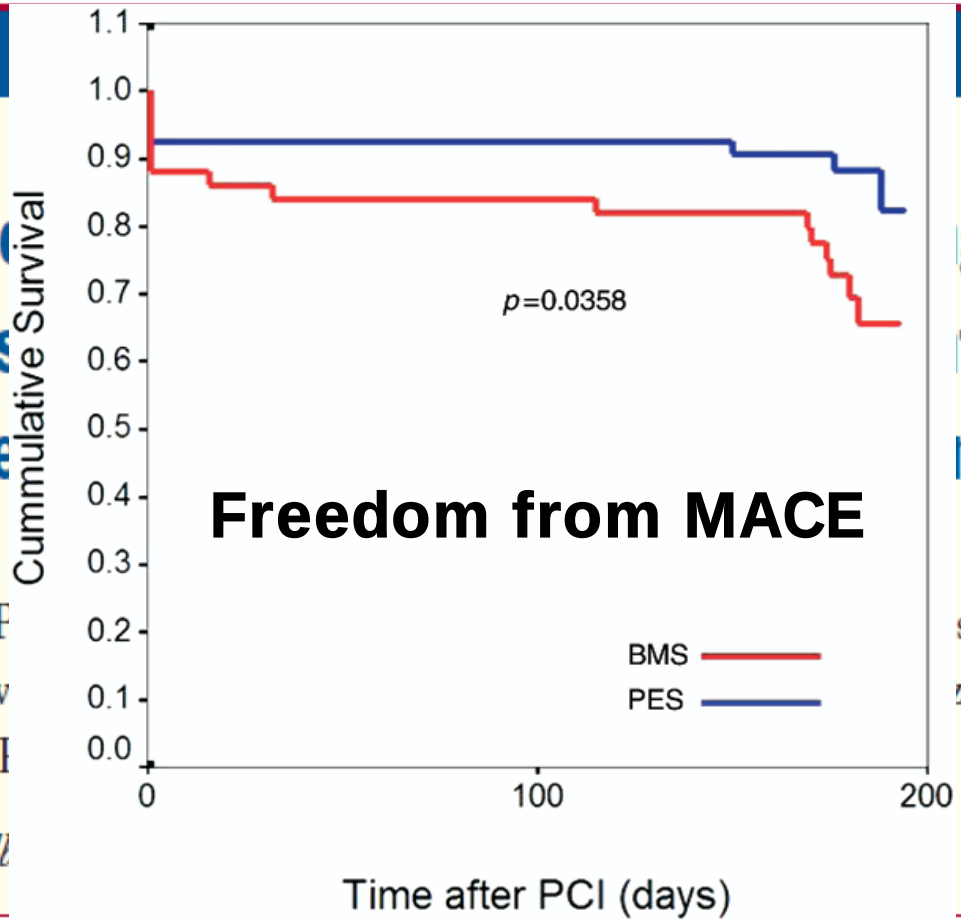
CLINICAL RESEARCH

Clinical Trials

A Randomize g
Stents Versus t
of Unprotecte nosis

Andrejs Erglis, MD, F sars, MD,*
Sanda Jegere, MD,* Iv dins, MD,*
Andris Saltups, MD, I

Riga, Latvia; and Mell



"In a direct comparison 103 patients with ULMCA were randomly assigned to receive BMS(n=50) or PES(n=53) implantation, and confirmed the previous observations."

2. PCI with Stent Implantation
Ostial and Midshaft Lesions

- **Park et al reported a lower restenosis rate after LMCA nonbifurcation intervention compared with bifurcation intervention (1.7 vs. 10.9%). Similarly, the risk of TVR was significantly lower in nonbifurcation than in bifurcation (3% vs. 13%).**

- **A multicenter observational study of 147 patients with unprotected nonbifurcation LMCA lesions demonstrated favorable long-term outcome with DES. In the 106 patients who underwent angiographic follow-up at 4 to 6 months, mean late lumen loss was 0.01 mm and restenosis occurred in only one patient (0.9%). At a mean follow-up of 886 days, there were 5 deaths (3.4%), 7 TVR (4.7%), and, of these, only 1 patient had a TLR.**

Park SJ et al. JACC 2005; 45: 351-356
Chieffo et al. Circ 2007; 116: 158-162

2. PCI with Stent Implantation
Bifurcation Lesions

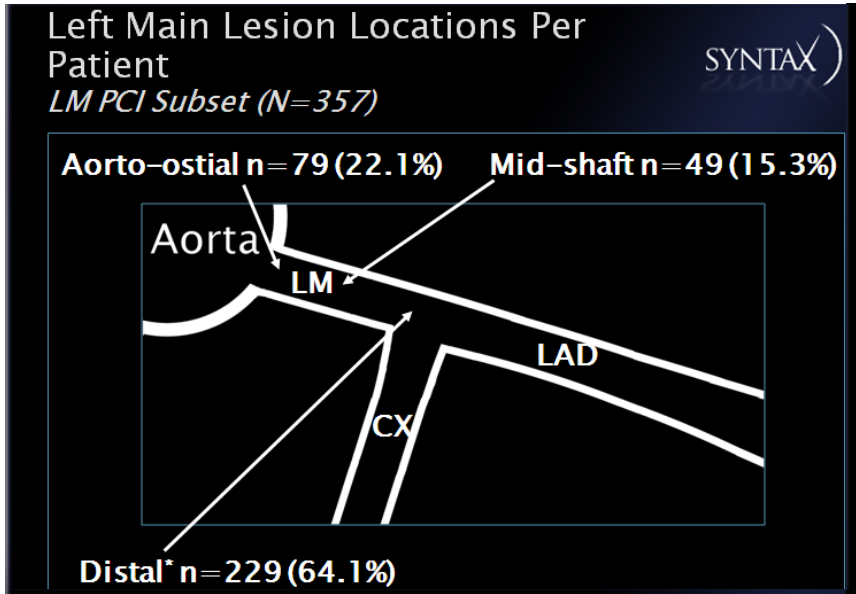
- **"Currently available evidence suggest that results are less favorable when distal LMCA lesions are treated by a 2-stent approach compared with single-stent approach."**

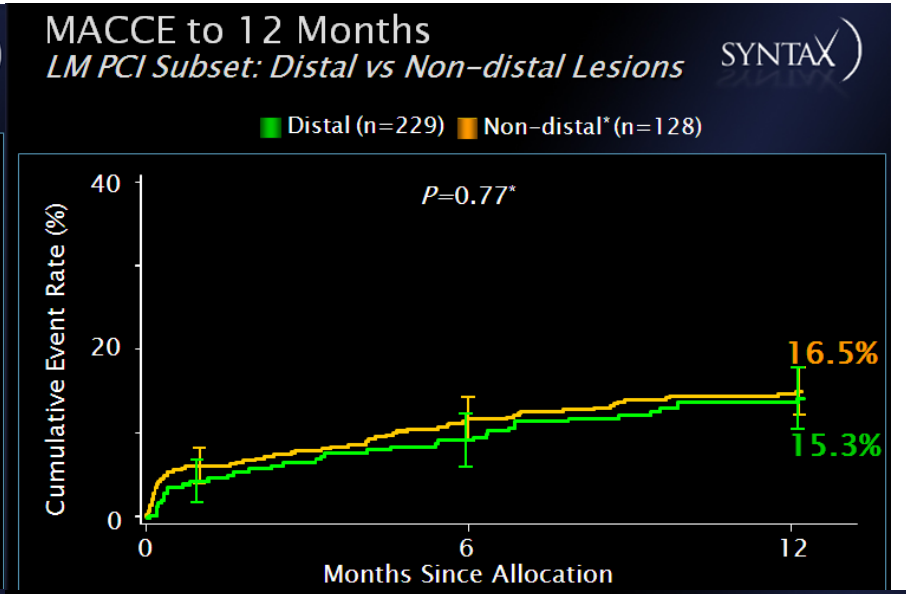
- **"The TLR late is relatively low (<5%) with single stent approaches, even for distal LMCA lesions, and is nearly equivalent to results obtained with DES for ostial or mid-left main lesions."**

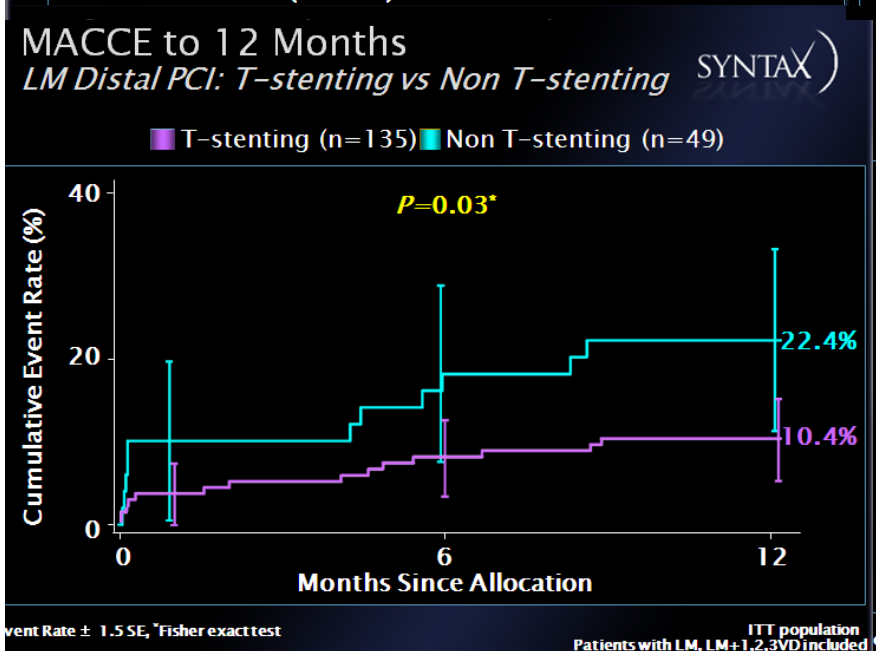
- **"However, patients with distal LMCA lesions treated with 2-stent techniques showed a TLR rate as high as 25% with restenosis confined mainly to the left circumflex ostium."**

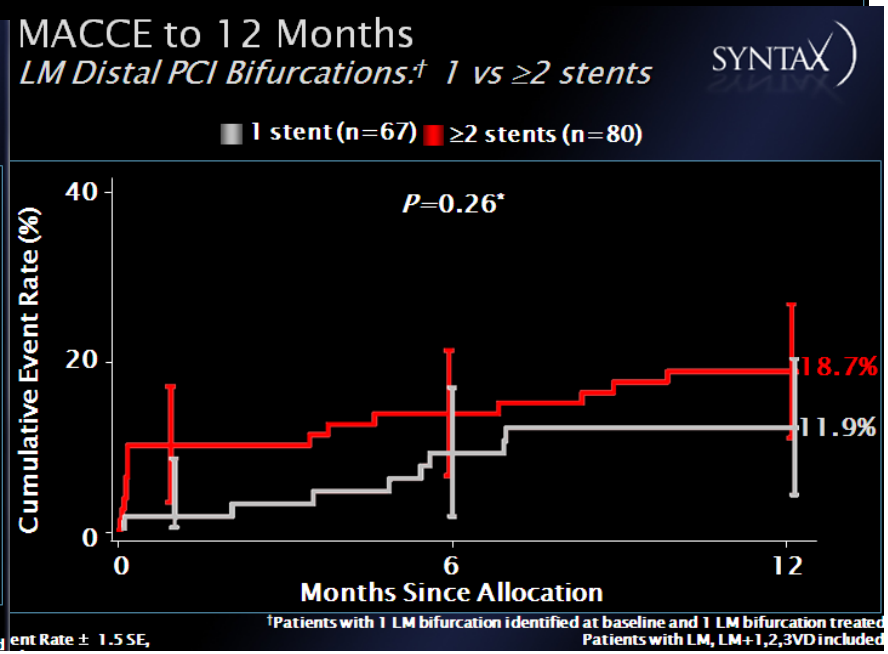
Kim et al. AJC 2006; 97: 1597-1601
Valgimigli et al. AHJ 2006; 152: 896-902

2. PCI with Stent Implantation
Bifurcation Lesions







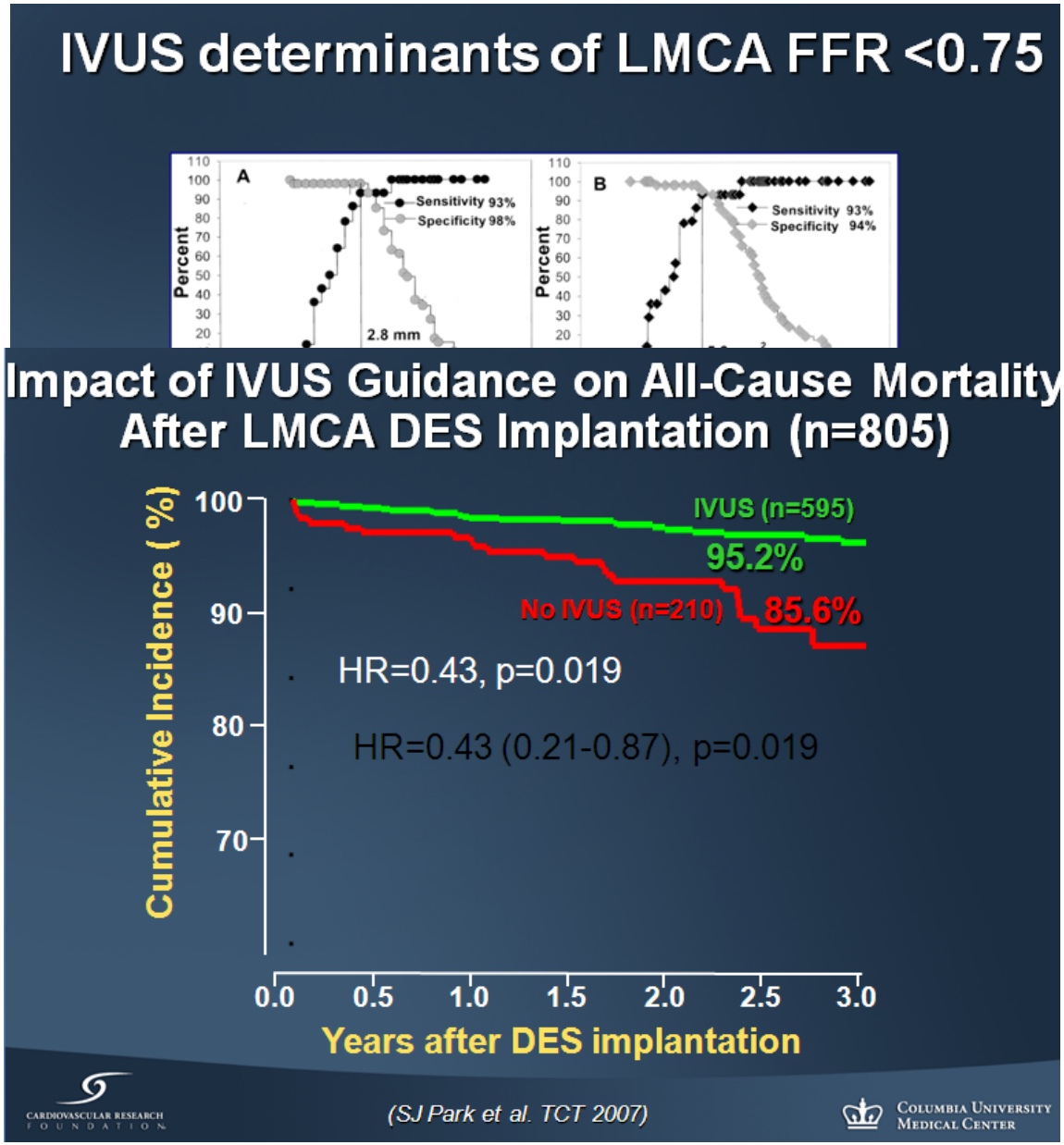


2. PCI with Stent Implantation

Role of IVUS guidance

"IVUS evaluation before the stenting procedure cannot only measure the degree of stenosis, plaque involvement, and anatomic configuration but can also select the appropriate diameter and length of the stent and the optimal stent strategy."

"Postprocedure IVUS interrogation is very helpful in detection of stent underexpansion, incomplete lesion coverage, large residual plaque and stent inapposition."



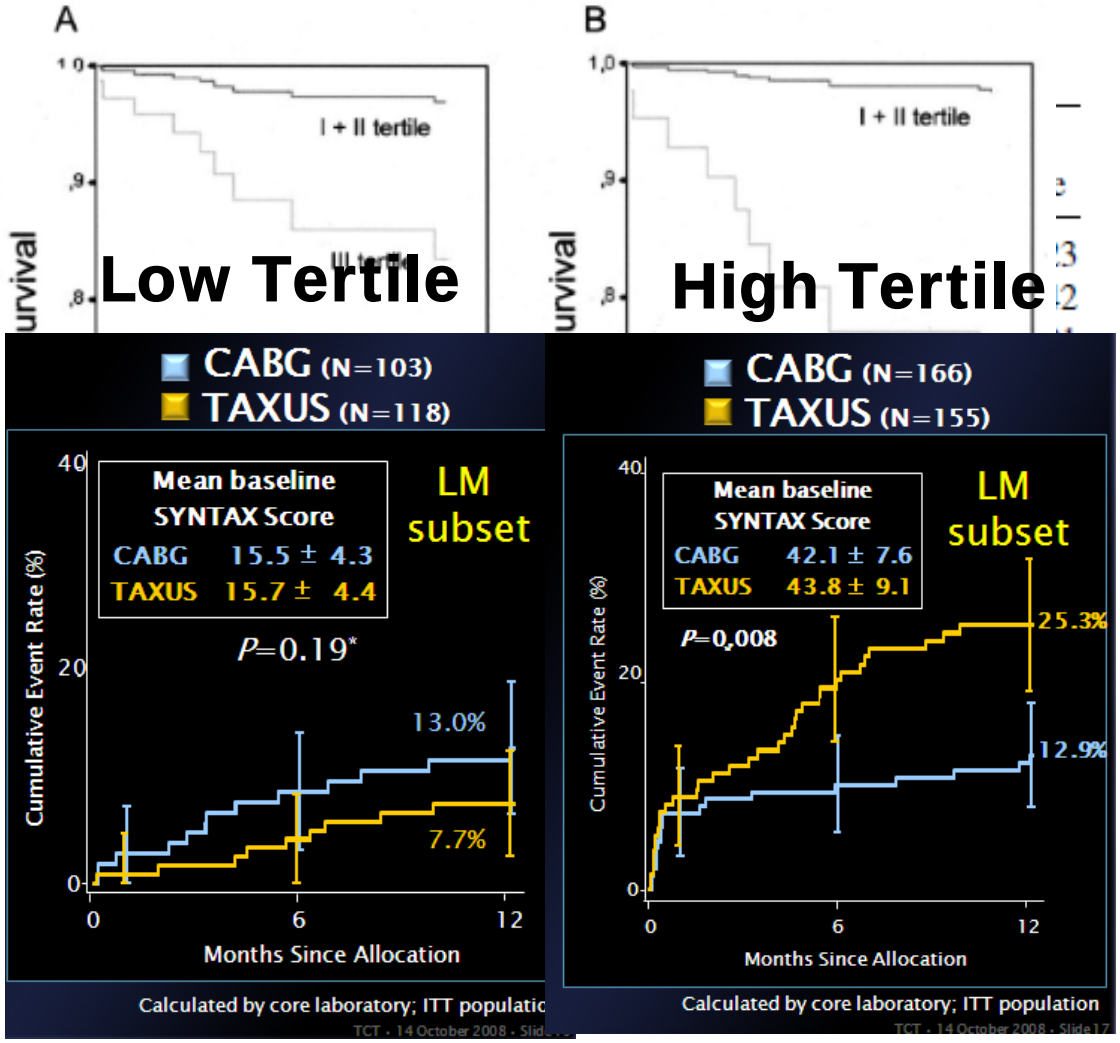
2. PCI with Stent Implantation

Risk stratification after PCI for LMCA Disease

"A previous study found that patients with a high EuroSCORE (≥6) were at greater risk of death or MI than those with a low EuroSCORE."

"Higher levels of C-reactive protein are associated with increased risk of death (19% and 0%) and death/MI (31% vs. 0%)."

"The Syntax score is related to coronary lesion complexity and may be useful in guiding optimal revascularization strategies and in prediction of future cardiovascular events."



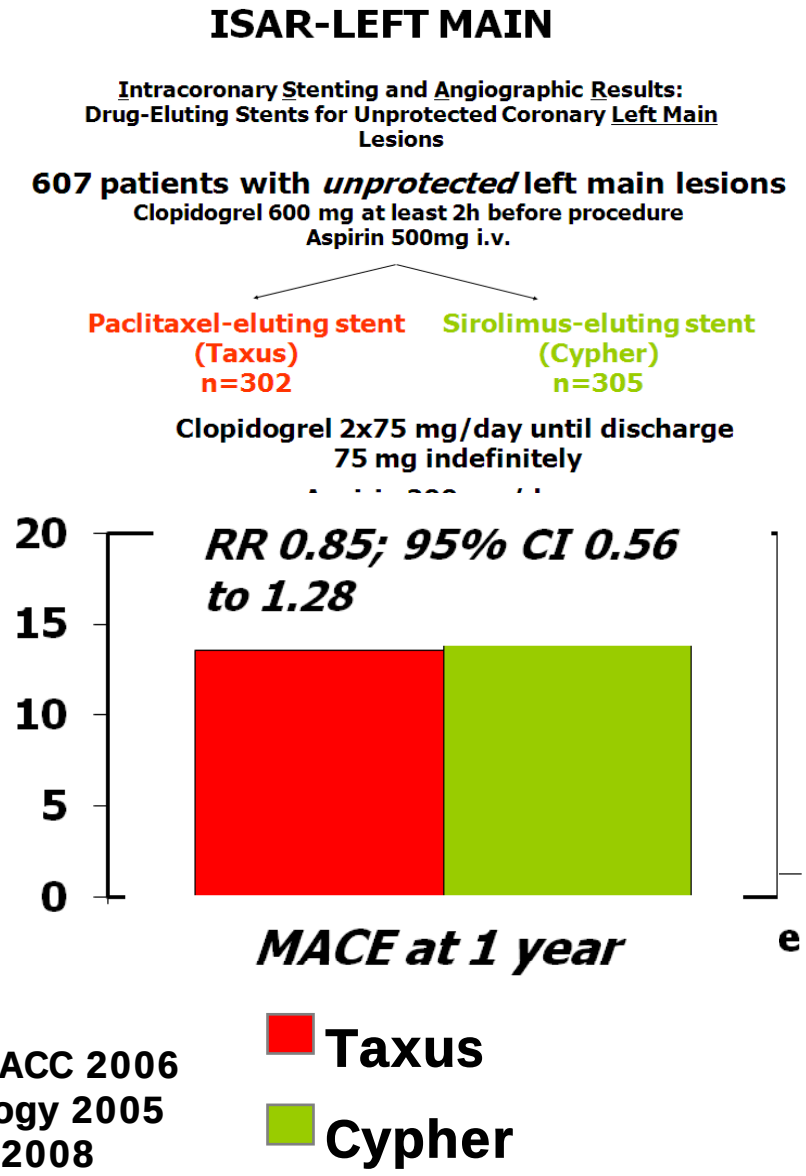
Palmerini et al. Circ 2005

Serruys et al. NEJM 2009

2. PCI with Stent Implantation
Which DES is better? SES vs. PES

"In a single center, nonrandomized study comparing SES and PES in 110 patients, angiographic results and side branch and long-term clinical outcomes were comparable. (death/MI [16% vs 18%] and TVR [9% vs 11%])"

"The recent large randomized trial (the ISAR-LEFT MAIN trial) found that SES and PES were equally effective and safe in patients undergoing unprotected LMCA stenting."



Valgimigli et al. JACC 2006
Lee et al. Cardiology 2005
Mehilli et al. TCT 2008

2. PCI with Stent Implantation

Stent Thrombosis and Long-Term Clinical Outcomes with DES

"In a recent multicenter registry by Chieffo et al. (n=731), at 30 months a combined incidence of definite or probable thrombosis was 0.95%."

"In DELFT registry (n=358) at ≥ 3-year follow-up, the incidence of definite, probable, and possible stent thrombosis were 0.6%, 1.1% and 4.4%."

"In ISAR-LEFT MAIN trial (n=607), the 2-year rate of definite or probable stent thrombosis was about 0.5 to 1.0%."

"How long should dual antiplatelet therapy be continued after LMCA stenting with DES?"

"The long-term benefits of LMCA revascularization 6 to 12 months are, however, unclear in such patients."

"Additional studies with large population and longer-term follow-up are warranted to evaluate the antithrombotic benefit versus bleeding risk of prolonged dual clopidogrel (Prasugrel) use and to determine the optimal duration of clopidogrel therapy after DES placement in patients with LMCA disease."

These results indicated that DES implantation in patients with unprotected LMCA disease results in relatively lower, or at worst, similar rates of stent thrombosis and long-term mortality than seen when DES is used in subset of patient with other coronary lesion.

Chieffo et al. EHJ 2008, Meliga et al. JACC 2008, Seung KB et al. NEJM 2008

3. Stent vs. Surgery

Patient Selection: Possible Indication or Contraindication for PCI or CABG

Table 3. Clinical or Angiographic Characteristics Influencing the Choice Between Stenting and Surgery for Patients With Unprotected Left Main Coronary Artery Disease

Favor stenting

- Ostium or midshaft lesions.
- Distal left main disease anatomically suitable for stenting with intact left ventricular function.
- Isolated left main disease.
- Unstable hemodynamic conditions requiring urgent revascularization: bail-out procedure, acute myocardial infarction, or cardiogenic shock due to left main stenosis.
- Serious comorbidity (high surgical risk): chronic lung disease, poor general performance status, advanced age such that major surgery cannot be tolerated, limited life expectancy, prior bypass surgery, unsuitable coronary anatomy for bypass grafting.
- Patient refusal of surgery.

Favor bypass surgery

- Complex coronary anatomy unsuitable for stenting: severe calcification, severe tortuosity, total occlusions at other major epicardial coronary arteries (≥2), multiple and diffuse long coronary lesions, complex in-stent restenosis unsuitable for repeat stenting procedure.
- Severely compromised left ventricular function.
- Extensive peripheral vascular disease unsuitable for placement of a guiding catheter or intraaortic balloon pump.
- Contraindication to antiplatelet therapy including aspirin, heparin, or thienopyridine.
- Patient refusal of stenting.

APPROPRIATENESS CRITERIA

ACCF/SCAI/STS/AATS/AHA/ASNC 2009 Appropriateness Criteria for Coronary Revascularization

A Report of the American College of Cardiology Foundation Appropriateness Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, and the American Society of Nuclear Cardiology

Endorsed by the American Society of Echocardiography, the Heart Failure Society of America, and the Society of Cardiovascular Computed Tomography

	CABG			PCI		
	No diabetes and normal LVEF	Diabetes	Depressed LVEF	No diabetes and normal LVEF	Diabetes	Depressed LVEF
Two vessel coronary artery disease with proximal LAD stenosis	A	A	A	A	A	A
Three vessel coronary artery disease	A	A	A	U	U	U
Isolated left main stenosis	A	A	A	I	I	I
Left main stenosis and additional coronary artery disease	A	A	A	I	I	I

A: Appropriate, U: Uncertain, I: Inappropriate

PCI is still considered to be "INAPPROPRIATE" for Left Main disease.

3. Stent vs. Surgery

Current Evidence supporting PCI or CABG for LMCA Disease

Registry Data

Table 4. Summary of Left Main Coronary Revascularization With Stenting vs Bypass Surgery

	Chieffo et al[53]		Lee et al[54]		Palmerini et al[55]		Sanmartin et al[56]	
No. of patient	107	142	50	123	157	154	96	245
Group	DES	CABG	DES	CABG	DES/BMS	CABG	DES	CABG
Age (mean, years)	64	68	72	70	73	69	66	66
Diabetes, %	19	23	36	31	26	25	19	32
Ejection fraction, %	52	52	51	52	52	55	…	…
High surgical risk score, %*	32	29	64	46	64	61	27	25
Bifurcation involvement, %	81	…	60	…	80	83	62	…
Early outcomes, %	In-hospital		1 month		1 month		In-hospital	
Death	0	2	2	5	3	5	2	6
Myocardial infarction	9	26	2	2	5	2	0	1
Target-vessel revascularization†	0	2	0	1	1	1	0	1
Mid-term outcomes, %	12 months		12 months		14 months		12 months	
Death	3	6	4	15	14	12	5	8
Myocardial infarction	1	1	…	…	8	5	0	1
Target-vessel revascularization†	20	4	13	5	26	3	5	1

*Stratified as high-risk by a EuroSCORE ≥6 or Parsonnet score ≥15.
†If the rate of TVR was not available, the rate of TLR was used as an approximate measure.

"The early clinical events of approximately 1 year was similar in the PCI and the CABG groups. However the risk of TVR was consistently higher with PCI than with CABG."

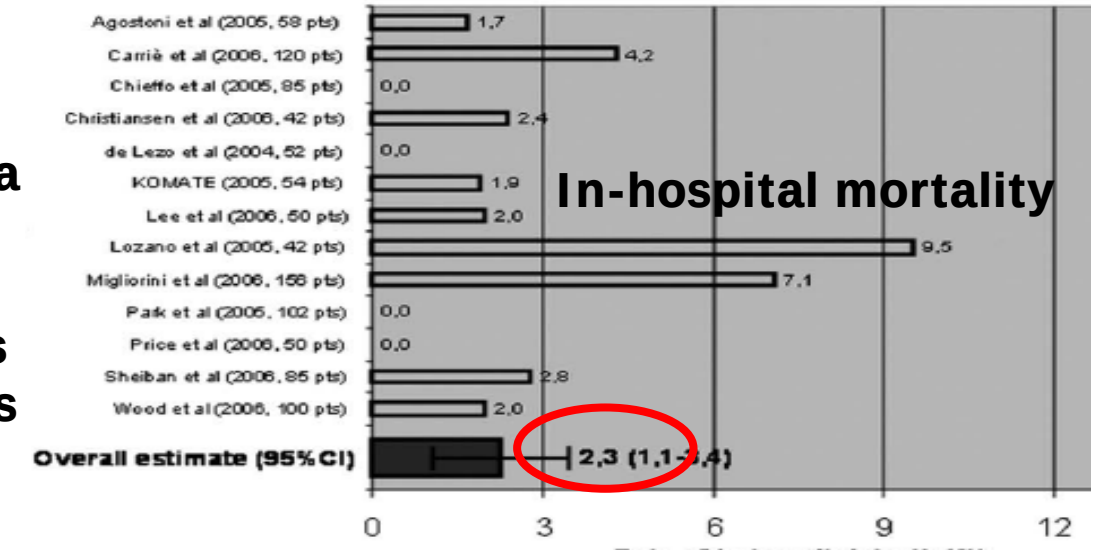
~~The long-term mortality up to approximately 1 year was similar or superior to those of bypass surgery because of significant increase in peri-procedural MI or cerebrovascular events in the CABG patients."~~

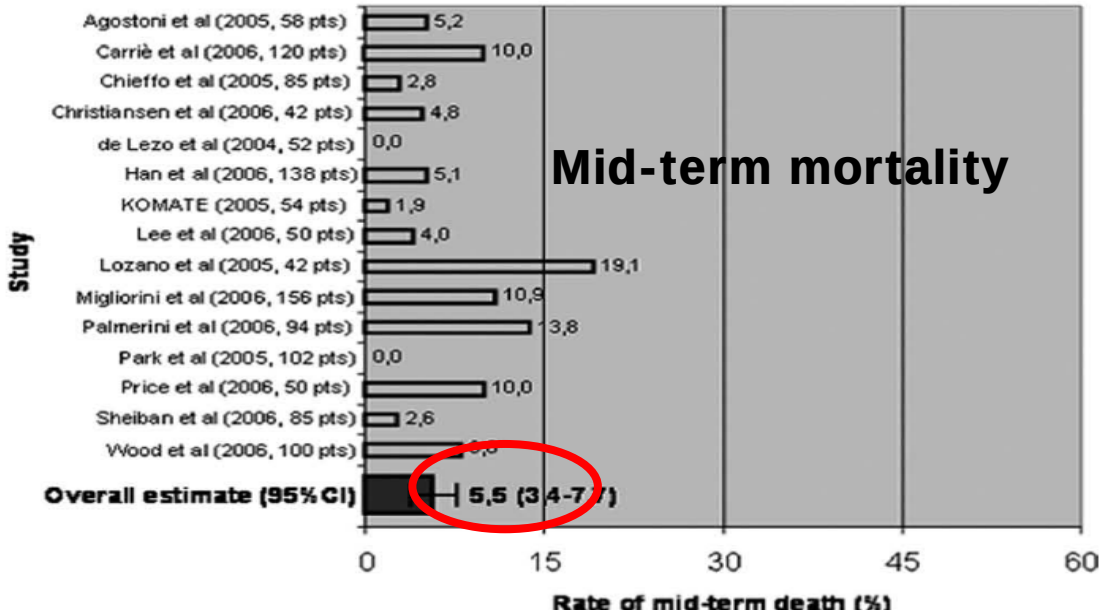
3. Stent vs. Surgery

Current Evidence supporting PCI or CABG for LMCA Disease

3) Meta-analysis and Systematic Review

"A recent meta-analysis of 1278 patients from 16 observational studies showed a low in-hospital mortality (2.3%) and a low mid-term mortality (5.5%) at 10 months follow-up. Adjusted odds ratios for MACCE (death, MI, TVR, or stroke) of 0.46, favoring PCI with DES over CABG."





Biondi-Zoccai et al. AHJ 2008

3. Stent vs. Surgery

Current Evidence supporting PCI or CABG for LMCA Disease

3) Meta-analysis and Systematic Review

"Another systematic review suggested that early and longer-term mortality rates were better after CABG (early 2-4% [Average 3%], late 5-6% [Average 5%]) than PCI with BMS (early 0-14% [Average 6%], late 3-31% [Average 17%]) or DES (early 0-10% [Average 2%], late 0-14% [Average 7%])."

"However, these results should be interpreted with caution and regarded as only exploratory findings, given the limited number of patients, selection or publication bias in the literature reviewed, and caveats on internal validity of the included clinical studies."

Taggart et al. JACC 2008

Table 1 Current Results of CABG for LMS Stenosis

CABG

Author (Ref. #) (Year)	Year of Surgery	n	Mortality (%) Hospital	30-Day	1-Year	2-Year
Jonsson et al. (31) (2006)	1970 to 1999	1,888	2.7	–	–	–
Lu et al. (30) (2006) (2005)	1997 to 2003	1,197	2.8	3	5	6
Keogh and Kinsman (16) (2003)	2003	5,003	3	–	–	–
Dewey et al. (29) (2006) (2001)	1998 to 1999	728	–	4.2	–	–
Yeatman et al. (28) (2006) (2001)	1996 to 2000	387	2.4	–	–	5
Ellis et al. (27) (2006) (1998)	1990 to 1995	1,585	2.3	–	11	–
Weighted average	–	10,788	2.8	–	–	–

Table 3 DES in LMS

PCI with DES

Author (Ref. #)	n	30-Day Death (%)	30-Day MI (%)	30-Day TLR (%)	Follow-Up, Months	Death (%)	MI (%)	TLR/TVR (%)
De Lezo et al. (17)	52	0	4	0	12	0	0	2
Valgimigli et al. (19)*	130	10	4	0	18	14	4	6
Price et al. (20)	50	0	8	6	9	10	2	38
Chieffo et al. (21)	107	0	9	0	12	3	1	20
Lee et al. (23)	50	2	0	0	6	4		7
Kim et al. (22)*	116	0	6	0	18	0	0	5
Palmerini et al. (24)	94	3.2	4.5	1	14	13.4	8.3	20
Weighted average	599	2.4	6	2.1%	11	7	1.6	13%

3. Stent vs. Surgery

Current Evidence supporting PCI or CABG for LMCA Disease
MAIN-COMPARE registry with Propensity analysis

"The MAIN-COMPARE registry is the first long-term study comparing PCI with stenting with bypass surgery for LMCA disease. This study evaluated 2240 patients with unprotected LMCA disease who underwent stenting or CABG at 12 major centers in Korea."

"The risks of death and the composite of death, Q-wave MI or stroke were similar in the PCI and CABG groups and these results were consistent when either BMS or DES was compared with concurrent CABG. However, the rate of TVR was significantly lower in the CABG group than in the PCI group with hazard ratio varying by the stent type"

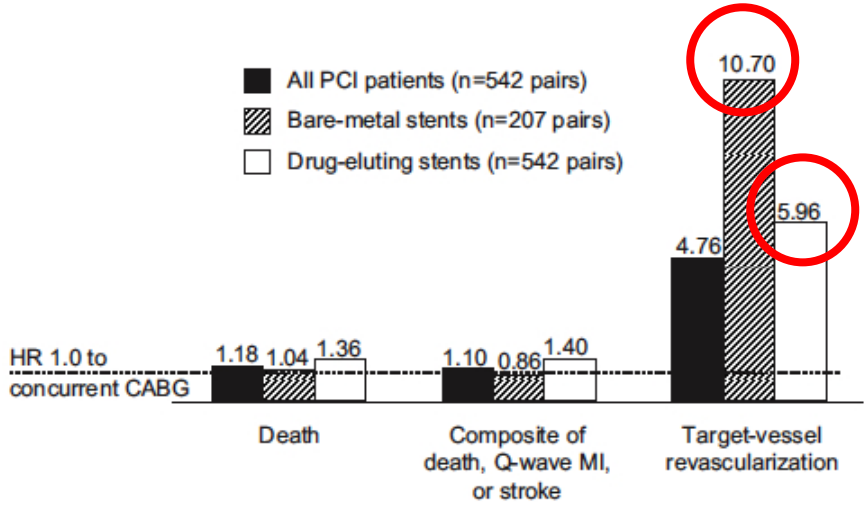


Figure. Hazard ratios for clinical outcomes of stenting, compared with bypass surgery, among propensity-matched cohorts in the MAIN-COMPARE study. Note that the risks of death or the composite of death, Q-wave MI, or stroke were similar, but the risk of revascularization was significantly higher, in PCI patients.

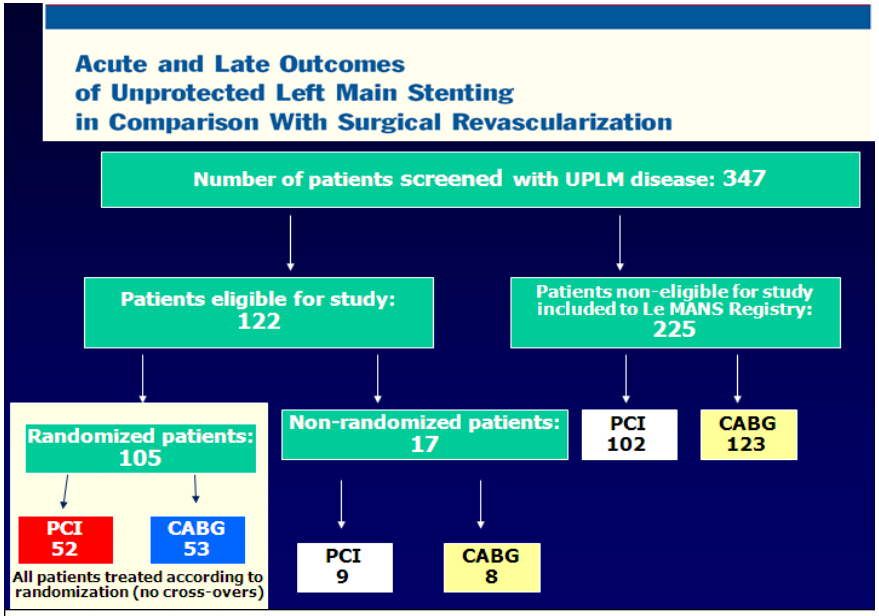
3. Stent vs. Surgery

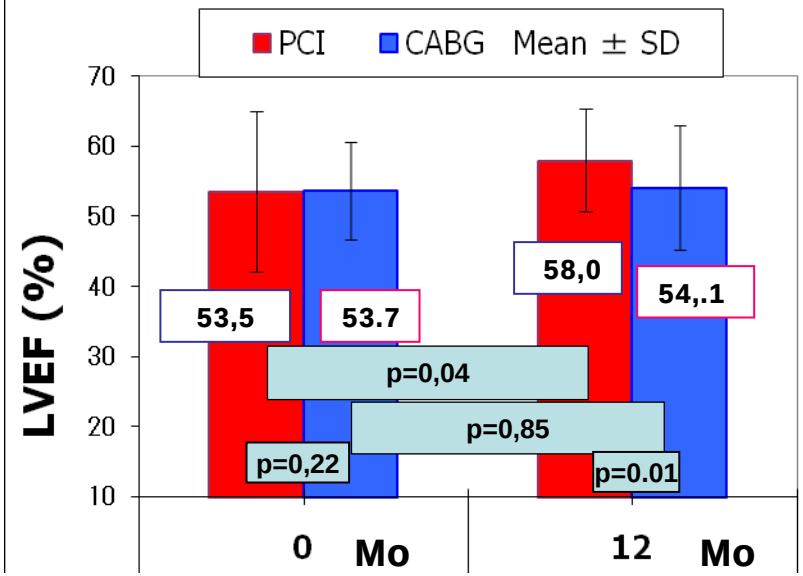
Current Evidence supporting PCI or CABG for LMCA Disease

Randomized trial: 1) LeMANS trial

"At one year, the primary end point of absolute change in left ventricular ejection fraction was significantly greater in the PCI than in the CABG (p=0.047), whereas the secondary endpoints, survival and MACCE, were comparable in the 2 groups."

"Although this was a prospective RCT, the results were limited by the small number of patients, and limited by the nonspecific and inconclusive primary endpoint chosen to evaluate treatment effects."





3. Stent vs. Surgery

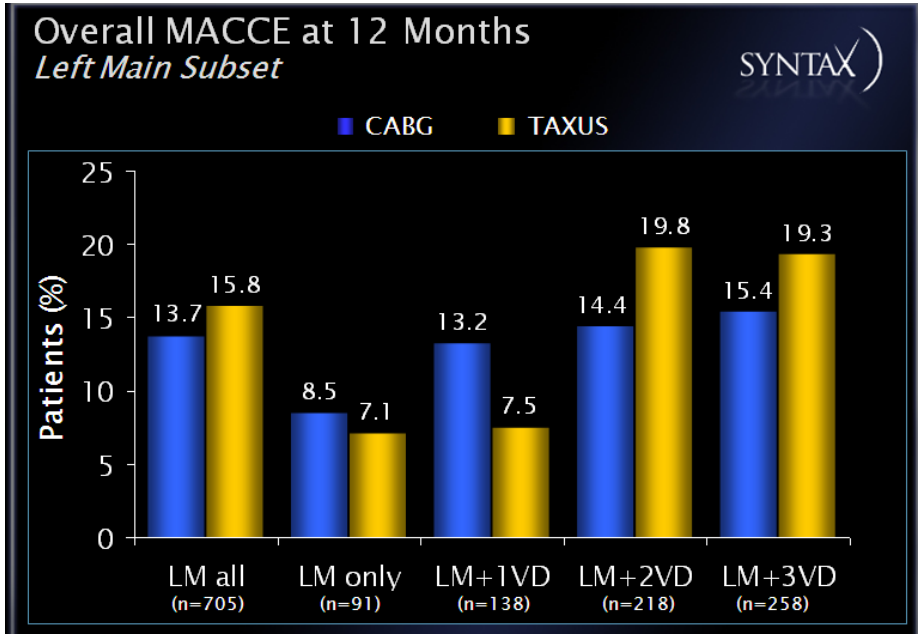
Current Evidence supporting PCI or CABG for LMCA Disease

Randomized trial: 2) Syntax Trial

"In the left main subsets from the Syntax trial, PCI demonstrated one-year clinical outcomes equivalent to those seen after standard bypass surgery."

"In particular, PCI-treated patients showed a trend toward lower MACCE rates in cases with anatomically simple LMCA (LMCA only and LMCA plus single-vessel disease)."

"However, because of the exploratory hypothesis-generating nature of subgroup analysis, results from more specific LMCA-targeted trial are needed."



MACCE			
Overall LMCA disease (n=705)	13.6	15.8	0.44
Isolated LMCA disease (n=91)	8.5	7.1	1.00
LMCA plus 1-vessel disease (n=138)	13.2	7.5	0.27
LMCA plus 2-vessel disease (n=218)	14.4	19.8	0.29
LMCA plus 3-vessel disease (n=258)	15.4	19.3	0.42

MACCE indicates major adverse cardiac and cerebrovascular events, including death, stroke, myocardial infarction, and repeat revascularization, as a primary study-end point.

3. Stent vs. Surgery

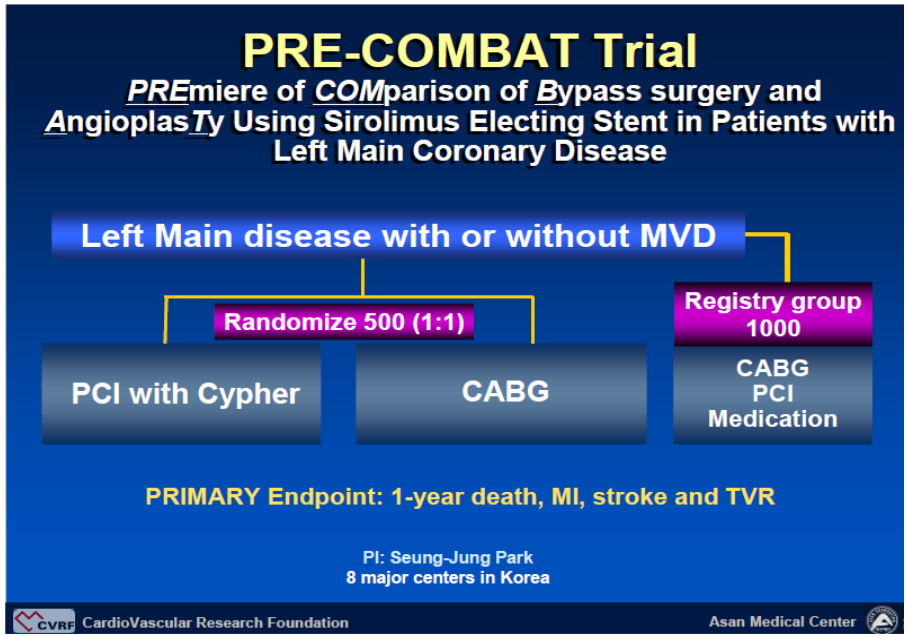
Current Evidence supporting PCI or CABG for LMCA Disease

Randomized trial: 3) PRE-COMBAT Trial

"Since current results from randomized trial are relatively short term in nature (up to 1 year), longer-term data may also be needed to assess the long-term value of LMCA stenting compared with bypass surgery."

"If these studies provide long-term follow-up data supporting the clinical equivalence of PCI and CABG, PCI with stenting could become a viable strategy for treatment of LMCA disease. However, the choice of revascularization modality should still be made after thorough consideration of clinical and lesion characteristics."

"The ongoing PRECOMBAT trial, which is a prospective, multicenter, randomized study to compare the safety and efficacy of SES and CABG for treatment of unprotected LMCA disease with a primary study end-pont of 1-year MACCE is expected to provide a more definitive evaluation of the 2 primary interventions."



4. Conclusions

“Current evidence indicates that in specific subset of patients, stenting yields mortality and morbidity rates that compare favorably with CABG, suggesting that the current guidelines (class III recommendation of PCI for unprotected LMCA disease) may no longer be justified.”

“The most recent results may impact on the future guidelines and support the need for well-designed, adequately powered, prospective randomized trials comparing the 2 revascularization strategies in patients with unprotected LMCA disease.”