Left Main Intervention Comes of Age: A 40-Year Odyssey from Balloon **Angioplasty to Drug-Eluting Stents** Gregg W. Stone, MD Columbia University Medical Center NewYork-Presbyterian Hospital Cardiovascular Research Foundation





Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.







VA Randomized Trial (n=113) LM Stenosis



A Printer for Innovation

- NewYork-Presbyterian

Gruntzig's 3rd PTCA



"Third PCI patient ever treated. Forty-three year old man with severe angina pectoris since September, 1977. First angiogram (November 11) revealed severe stenosis of the main L.C.A..." Note: The patient expired suddenly about 4 months after this procedure.



Gruntzig A. Lancet 1978;1:263.



The Rocky Road to PCI of LM Ds. - Balloon angioplasty -

127 pts at MAHI: elective protected (n=84), elective unprotected (n=33;
18 surgical contraindications; 15 surgical candidates), AMI (n=10)

	Elective protected (n=84)	Elective unprotected (n=33)	AMI unprotected (n=10)
Procedural success	94%		90%
Mortality			
- In-hospital	2.4%	9.1%	50%
- Mean 2-year	10.7%	60.6%	70%
Post d/c MI	5.9%	8.0%	20%
Post d/c revasc	37.3%	42.3%	60%



O'Keefe JH, Hartzler GO, et al. Am J Cardiol. 1998;64:144-7

COLUMBIA UNIVERSITY MEDICAL CENTER The Rocky Road to PCI of LM Ds. - Atherectomy and bare metal stents -107 pts from 25 centers (all unprotected): elective (n=91; 47 absolute or

relative surgical contraindications; 44 surgical candidates), AMI (n=16). BMS in 50% (remainder atherectomy or PTCA)

	Elective (n=91)	AMI (n=16)
Procedural success	96.2	2%
Mortality, in-hospital	12.1%	68.8%
Mortality, 9-months	34.0%	75.0%
- Stent	29.5%	
- CABG candidate	15.7%	
- Not CABG cand.	70.5%	
Restenosis >4 mos	22.0%	



Ellis SG et al. Circulation 1997;96:3867–72



NewYork-Presbyterian

PCI vs. CABG for Left Main Disease Meta-analysis of 4 RCTs, 1,611 Patients

Trial	LEMANS	SYNTAX LM	Boudriot et al.	PRECOMBAT
Year	2008	2009	2010	2011
N total	105	705	201	600
Age, mean years	61	65	68	62
Male	67%	74%	75%	77%
Diabetes	18%	25%	36%	32%
Distal LM involved	58%	61%	71%	65%
+0/1/2/3 VD, %	0/9/23/68	13/20/31/36	29/31/27/14	10/17/32/41
Syntax Score, mean	25	30	24	25
Log Euroscore, mean	3.4	3.9	2.5	2.7
LIMA-LAD	81%	97%	99%	94%



Capodanno et al, JACC 2011;58:1426-32



PCI (1st gen DES) vs. CABG for Left Main Ds. Meta-analysis of 4 RCTs, 1,611 Patients 1-Year Outcomes

	PCI	CABG	OR (95%CI)	OR (95%CI)	<i>p</i> -Value
Death	<mark>3.0%</mark> (24/807)	4.1% (32/790)		0.74 (0.43-1.28)	0.29
MI	<mark>2.8%</mark> (23/807)	<mark>2.9%</mark> (23/790)		0.98 (0.54-1.78)	0.95
Stroke	0.1% (1/707)	1.7% (12/689)		0.15 (0.03-0.67)	0.01
Death, MI, or stroke	<mark>5.3%</mark> (35/655)	<mark>6.8%</mark> (43/636)		0.77 (0.48-1.22)	0.26
Repeat Revasc	11.4% (92/807)	<mark>5.4%</mark> (43/790)		2.25 (1.54-3.28)	<0.001
MACCE	14.5% (117/807)	11.8% (93/790)		1.28 (0.95-1.72)	0.11
			0.01 0.1 1 10 10 Favors PCI Favors CA	BG	



Capodanno D et al. JACC 2011;58:1426-32



SYNTAX: MACCE to 5 Years Left Main Subset



CABG (N=348)

TAXUS (N=357)







Morice MC et al. Circulation. 2014;129:2388-94

SYNTAX 3VD 5-year Outcomes • TCT 2012 • Serruys • 23 October 2012 • Slic



SYNTAX 3VD 5-year Outcomes • TCT 2012 • Serruys • 23 October 2012 • Slide

SYNTAX Score I vs II: The SYNTAX Trial LM pts: Risk Predictions



CABG favored Overall 50.1% >95%CI 11.5%

PCI favored Overall 49.9% >95%CI 8.8%

79.7% lie within 95%CI

Faroog V et al. Lancet 2013;381:639-50

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Follow-up: 1 month, 6 months, 1 year, annually through 5 years Primary endpoint: D/MI/CVA at median 3-yr FU, minimum 2-yr FU



EXCEL



EXCEL Primary Endpoint Death, Stroke or MI at 3 Years



Stone GW et al. N Engl J Med 2016;375:2223-35

Adjudicated Outcomes at 30 Days

EXCEL

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI	4.9%	7.9%	0.61 [0.42, 0.88]	0.008
- Death	1.0%	1.1%	0.90 [0.37, 2.22]	0.82
- Stroke	0.6%	1.3%	0.50 [0.19, 1.33]	0.15
- MI	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Peri-procedural	3.6%	5.9%	0.61 [0.40, 0.93]	0.02
- Spontaneous	0.3%	0.3%	1.00 [0.20, 4.95]	1.00
- STEMI	0.7%	2.3%	0.32 [0.14, 0.74]	0.005
- Non-STEMI	3.2%	3.9%	0.82 [0.50, 1.32]	0.41
Death, stroke, MI or IDR	4.9%	8.4%	0.57 [0.40, 0.82]	0.002
- Ischemia-driven revasc (IDR)	0.6%	1.4%	0.46 [0.18, 1.21]	0.11
Stent thrombosis, def/prob	0.6%	0.0%	-	0.01
Graft occlusion, symptomatic	0.0%	1.2%	-	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.3%	1.2%	0.27 [0.08, 0.97]	0.03

Major Adverse Events Within 30 Days

EXCEL

	PCI (n=948)	CABG (n=957)	RR [95%CI]	P-value
Peri-procedural MAE, any	8.1%	23.0%	0.35 [0.28, 0.45]	<0.001
- Death*	0.9%	1.0%	0.91 [0.39, 2.23]	0.83
- Stroke*	0.6%	1.3%	0.50 [0.19, 1.34]	0.16
- Myocardial infarction*	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Ischemia-driven revascularization*	0.6%	1.4%	0.47 [0.18, 1.22]	0.11
- TIMI major/minor bleeding	3.7%	8.9%	0.42 [0.28, 0.61]	<0.001
- Transfusion ≥2 units	4.0%	17.0%	0.24 [0.17, 0.33]	<0.001
- Major arrhythmia**	2.1%	16.1%	0.13 [0.08, 0.21]	<0.001
- Surgery/radiologic procedure	1.3%	4.1%	0.31 [0.16, 0.59]	<0.001
- Renal failure [†]	0.6%	2.5%	0.25 [0.10, 0.61]	<0.001
- Sternal wound dehiscence	0.0%	2.0%	0.03 [0.00, 0.43]	<0.001
- Infection requiring antibiotics	2.5%	13.6%	0.18 [0.12, 0.28]	<0.001
- Prolonged intubation (>48 hours)	0.4%	2.9%	0.14 [0.05, 0.41]	<0.001
- Post-pericardiotomy syndrome	0.0%	0.4%	0.11 [0.01, 2.08]	0.12

*Adjudicated events; others are site-reported. **SVT requiring cardioversion, VT or VF requiring treatment, or bradyarrhythmia requiring temporary or permanent pacemaker. †Serum creatinine increased by ≥0.5 mg/dL from baseline or need for dialysis.

Adjudicated Outcomes at 3 Years (i)

EXCEL

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke or MI (1° endpoint)	15.4%	14.7%	1.00 [0.79, 1.26]	0.98
- Death	8.2%	5.9%	1.34 [0.94, 1.91]	0.11
- Definite cardiovascular	3.7%	3.4%	1.10 [0.67, 1.80]	0.71
- Definite non-cardiovascular	3.9%	2.3%	1.60 [0.91, 2.80]	0.10
- Undetermined cause	0.8%	0.3%	2.00 [0.50, 7.98]	0.32
- Stroke	2.3%	2.9%	0.77 [0.43, 1.37]	0.37
- MI	8.0%	8.3%	0.93 [0.67, 1.28]	0.64
- Peri-procedural	3.8%	6.0%	0.63 [0.42, 0.96]	0.03
- Spontaneous	4.3%	2.7%	1.60 [0.95, 2.70]	0.07
- STEMI	1.3%	2.8%	0.46 [0.23, 0.91]	0.02
- Non-STEMI	7.0%	5.9%	1.15 [0.80, 1.65]	0.46

Adjudicated Outcomes at 3 Years (ii)

EXCEL

	PCI (n=948)	CABG (n=957)	HR [95%CI]	P-value
Death, stroke, MI or IDR	23.1%	19.1%	1.18 [0.97, 1.45]	0.10
- Ischemia-driven revasc (IDR)	12.6%	7.5%	1.72 [1.27, 2.33]	<0.001
- PCI	10.3%	6.8%	1.57 [1.13, 2.18]	0.006
- CABG	3.5%	0.8%	4.29 [1.88, 9.77]	<0.001
All revascularization	12.9%	7.6%	1.72 [1.27, 2.33]	<0.001
Stent thrombosis, def/prob	1.3%	0.0%	-	<0.001
- Definite	0.7%	0.0%	-	0.01
- Probable	0.7%	0.0%	-	0.01
- Early (0 - 30 days)	0.7%	0.0%	-	0.008
- Late (30 days – 1 year)	0.1%	0.0%	-	0.32
- Very late (1 year - 3 years)	0.5%	0.0%	-	0.05
Graft occlusion, symptomatic	0.0%	5.4%	-	<0.001
Definite stent thrombosis or symptomatic graft occlusion	0.7%	5.4%	0.12 [0.05, 0.28]	<0.001

NOBLE Trial

LM disease + ≤3 additional non-complex lesions Clinical equipoise for PCI vs. CABG Excluded: CTO, 2-stent bif, severe calc/tortuous N=1201

22.5±7.5 **SYNTAX score** 22.4±8.0

CABG (n=603)

PCI (Biomatrix; n=598)

Primary endpoint

MACCE: death, non-procedural MI, repeat revasc, stroke at median 3 years (with FU up to 5 years)





NOBLE

Primary Endpoint: MACCE (w/o proc MI)



PCI did not show non-inferiority and CABG was superior to PCI





NOBLE All-cause Mortality







NOBLE

Non-procedural Myocardial Infarction







NOBLE Stroke







NOBLE

Total Repeat Revascularization







NOBLE Secondary Endpoints

	PCI	CABG	P value
Definite ST or symptomatic graft occlusion*	3% (9)	4% (15)	0.22
Procedural myocardial infarction (post hoc)	5% (16/296)	7% (16/238)	0.52

* Kaplan-Meier 5-year estimates by intention-to-treat





EXCEL Was Peri-procedural MI as Defined in EXCEL a Valid Component of the Primary Endpoint?

Peri-procedural MI was defined as the occurrence within 72° after either PCI or CABG of:

- CK-MB >10x upper reference limit (URL)*, OR
- CK-MB >5x URL*, PLUS
 - new pathological Q waves in at least 2 contiguous leads or new persistent non-rate related LBBB, or
 - angiographically documented graft or native coronary artery occlusion or new severe stenosis with thrombosis and/or diminished epicardial flow, or
 - imaging evidence of new loss of viable myocardium or new regional wall motion abnormality

	Frequency	HR [95%CI] of 3-year mortality
PCI	3.6%	3.04 [1.39, 6.63]
CABG	5.9%	2.44 [1.10, 5.40]



EXCEL vs NOBLE

	EXCEL	NOBLE
Number of patients	1905	1201
Number of centers	126	36
Number of countries	17 (US, EU, SA, Asia Pacific, Middle East)	7 (UK, Scandinavia)
SYNTAX score inclusion	≤32	No restriction
Primary endpoint	D, MI or stroke	D, MI, stroke or revasc
- Included peri-procedural MI	Yes	No
Stent	Xience	Biomatrix
- 3-year definite ST rate	0.7%	3%
 Def ST < symptomatic graft occlusion 	Yes	No
Stroke: PCI vs CABG	Less with PCI	More with PCI!
Worse PCI prognosis with higher SYNTAX score	Yes	No!

LM Revascularization with Low/Int SS CABG vs. PCI with Contemporary DES

- Mortality: Similar with PCI and CABG
- MI: Lower with PCI in the peri-procedural period; higher with PCI during long-term FU similar through 5 years
- Stroke: Not a major reason to prefer PCI over CABG
- Short-term morbidity: Substantially less with PCI
- Revascularization: Less with CABG than PCI (~5%)

PCI with contemporary DES (especially Xience, as proven in EXCEL) may be considered an <u>acceptable or even preferred</u> revascularization modality for <u>selected pts</u> with LMCAD, a decision which should be made after heart team discussion, taking into account each patient's individual circumstances and preferences – and yes, I do think PCI should be class I

The End (Result)





