New Meta-analysis of RCTs in LM Revascularization

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Disclosure

- Speaker fee from Abbott
- Research grant from Eli Lilly

Percutaneous Coronary Intervention Versus Coronary Artery Bypass Graft Surgery in Left Main Coronary Artery Disease

A Meta-Analysis of Randomized Clinical Data

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1-year clinical outcomes

Death

l.	Study name	Sta	tistics fo	or each	study	Events		1	
		Odds ratio	Lower limit	Upper limit	p-Value	PCI	CABG		
	LEMANS	0.240	0.026	2.225	0.209	1/52	4/53	- Ĩ 4	
	SYNTAX left main	0.944	0.454	1.963	0.878	15/355	15/336		
	Boudriot et al.	0.392	0.074	2.069	0.270	2/100	5/101		
	PRECOMBAT	0.745	0.255	2 173	0.590	6/300	8/300		
d	Pooled estimate	0.741	0.427	1.284	0.285				
n	Pooled estimate	0.741	0.427	1.284	0.285				
	1 ² = 0%							0.01	1



Myocardial infarction

Myocardial Infarction

Model	tel Study name	Statistics for each study			Events / Total			Odds ratio and 95% Cl				
		Odds ratio	Lower limit	Upper limit	p-Value	PCI	CABG					
	LEMANS	0.327	0.033	3.248	0.340	1/52	3/53					
	SYNTAX left main	1.015	0.482	2 136	0.969	15/355	14/336					
	Boudriot et al.	1.010	0.199	5.129	0.990	3/100	3/101		57		5,6	
	PRECOMBAT	1.338	0.297	6.029	0.705	4/300	3/300		2		-	
Fixed	Pooled estimate	0.981	0.541	1.781	0.950					•		
Random	Pooled estimate	0.981	0.541	1.781	0.950					•		
	F = 0%							0.01	0.1	1	10	100

Favors PCI Favors CABG

Stroke

	Study name	St	atistics fo	or each s	study	Events	/ Total	
		Odds ratio	Lower limit	Upper limit	p-Value	PCI	CABG	
	LEMANS	0.196	0.009	4.187	0.297	0/52	2/53	
	SYNTAX left main	0.116	0.014	0.931	0.043	1/355	8/336	
	FRECOMBAT	0.199	0.009	4.156	0.298	0/300	2/300	
d	Pooled estimate	0.150	0.033	0.671	0.013			
n	Pooled estimate	0.150	0.033	0.671	0.013			
	I ² = 0%							0

TVR



Favors PCI **Favors CABG**

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Clinical outcomes in relation to CAD



Capodanno et al; JACC 2011

Limits

- Relatively small RCTs
- Clinical endpoints determined at 1 year
- Composite endpoint of death, MI, TVR
- Underpowered for clinically relevant endpoint such as death, MI or stroke
- First generation DES

Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease

G.W. Stone, J.F. Sabik, P.W. Serruys, C.A. Simonton, P. Généreux, J. Puskas, D.E. Kandzari, M.-C. Morice, N. Lembo, W.M. Brown III, D.P. Taggart, A. Banning, B. Merkely, F. Horkay, P.W. Boonstra, A.J. van Boven, I. Ungi, G. Bogáts, S. Mansour, N. Noiseux, M. Sabaté, J. Pomar, M. Hickey, A. Gershlick, P. Buszman, A. Bochenek, E. Schampaert, P. Pagé, O. Dressler, I. Kosmidou, R. Mehran, S.J. Pocock, and A.P. Kappetein, for the EXCEL Trial Investigators*

VS

Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial

Timo Mäkikallio, Niels R Holm, Mitchell Lindsay, Mark S Spence, Andrejs Erglis, Ian B A Menown, Thor Trovik, Markku Eskola, Hannu Romppanen, Thomas Kellerth, Jan Ravkilde, Lisette O Jensen, Gintaras Kalinauskas, Rikard B A Linder, Markku Pentikainen, Anders Hervold, Adrian Banning, Azfar Zaman, Jamen Cotton, Erlend Eriksen, Sulev Margus, Henrik T Sørensen, Per H Nielsen, Matti Niemelä, Kari Kervinen, Jens F Lassen, Michael Maeng, Keith Oldroyd, Geoff Berg, Simon J Walsh, Colm G Hanratty, Indulis Kumsars, Peteris Stradins, Terje K Steigen, Ole Fröbert, Alastair N J Graham, Petter C Endresen, Matthias Corbascio, Olli Kajander, Uday Trivedi, Juha Hartikainen, Vesa Anttila, David Hildick-Smith, Leif Thuesen, Evald H Christiansen, for the NOBLE study investigators^{*}

EXCEL vs NOBLE



Capodanno et al; Circ Cv Int 2016

Definite or probable stent thrombosis



Long-Term Safety of Drug-Eluting and Bare-Metal Stents



Evidence From a Comprehensive Network Meta-Analysis

Tullio Palmerini, MD,* Umberto Benedetto, MD,† Giuseppe Biondi-Zoccai, MD,‡ Diego Della Riva, MD,* Letizia Bacchi-Reggiani, MSTAT,* Pieter C. Smits, MD, PHD,§ Georgios J. Vlachojannis, MD, PHD,§ Lisette Okkels Jensen, MD, || Evald H. Christiansen, MD, PHD,¶ Klára Berencsi, MSTAT, || Marco Valgimigli, MD,# Carlotta Orlandi, MD,* Mario Petrou, MD,† Claudio Rapezzi, MD,* Gregg W. Stone, MD**



RCT with at least 3-year fup 51 RCTs with 52,158 patients Mean follow up 4 years

Palmerini et al; JACC 2015



Palmerini et al; JACC 2015

What do we expect from a new metaanalysis?

More power to address difference in mortality

 More power to address time related differences in clinical outcomes

 More power to address differences in clinical outcomes related to the SYNTAX score

Clinical outcomes stratified by SYNTAX score in NOBLE



Data collected from principal investigators

Study	30 days	I stort follow up svsilsble
Study	Studys Studies	
	Stroke Dooth/MI/stroke	Stroke Deeth/MU/stroke
BUDRIOT et al	Death/MI/stroke	Death/MI/stroke
	Death/MI/Stioke/OK	Deaul/MI/Sti oke/OK
		All cause death/741
	All cause death	All cause death stratified by Syntax score
	Cardiac death	Cardiac death stratified by Syntax score
	MI	MI stratified by Syntax score
	Stroke	Stroke stratified by Syntax score
PRECOMBAT		UR stratified by Syntax score
	All cause death/WI	All cause death/MI strat fied by Syntax score
	All cause death/MI/stroke	All cause death/MI/stroke stratified by Syntax score
	All cause death/M1/stroke/UK	All cause death/MI/stroke/UR stratified by Syntax score
	All cause death Cardiac death MI	
SYNTAX LEFT	Stroke	All cause death/MI
MAIN	All cause death/MI	
	All cause death/MI/stroke	
	All cause death/MI/stroke/UR	
	All cause death/MI All cause death/MI/stroke	All cause death/MI
NOBLE	All cause death/MI/stroke/UK	All cause death/MI/stroke
		All cause death/MI All cause death/M//UR All cause death stratified by Syntax score Cardiac death stratified by Syntax score
		MI stratified by syntax score

Stroke stratified by Syntax score

UR stratified by Syntax score All cause death/MI strat fied by Syntax score All cause death/MI/stroke stratified by Syntax score All cause death/MI/stroke/UR stratified by Syntax score

EXCEL

All cause death/MI

Clinical Outcomes with Percutaneous Coronary Revascularization versus Coronary Artery Bypass Grafting Surgery in Patients with Unprotected Left Main Coronary Artery Disease: A Meta-Analysis of Six Randomized Trials and 4,686 Patients

Tullio Palmerini, Patrick Serruys, Arie Pieter Kappetein, Philippe Genereux, Diego Della Riva, MD; Letizia Bacchi Reggiani, Evald Christiansen, Niels R Holm, Leif Thuesen, Timo Makikallio, Marie Claude Morice, Jung-Min Ahn, Seung-Jung Park, Holger Thiele, Enno Boudriot, Mario Sabatino, Mattia Romanello, Giuseppe Biondi-Zoccai, Raphael Cavalcante, Joseph F. Sabik, Gregg W. Stone

Flow diagram



Palmerini et al; submitted

Angiographic and procedural characteristics

Study	PCI vs CABG	Isolated LM	LM + 1 vessel	LM + 2 vessels	LM + 3 vessels	Distal LM	Mean Syntax score	CR	Type of stent/LIMA to LAD
BOUDRIOT et	PCI	28%	35%	26%	11%	74%	24.0	98%	SES 98%
al	CABG	29%	27%	28%	17%	69%	23.0	97%	99%
EXCEL	PCI	17%	31%	35%	17%	82%	20.6	NA	EES 100%
	CABG	18%	31%	32%	19%	79%	20.5	NA	98.8%
I F MANS	PCI	0	13%	27%	60%	56%	25.2	79%	DES 35%
	CABG	0	6%	19%	75%	60%	24.7	89%	81%
NORI F	PCI	NA	NA	NA	NA	81%	22.5	NA	DES 100%
NODLE	CABG	NA	NA	NA	NA	81%	22.4	NA	93%
DDECOMDAT	PCI	9%	8%	16%	25%	67%	24.4	68%	DES 100%
PKECONIDAI	CABG	11%	8%	19%	13%	62%	25.8	70%	94%
					\frown		\frown		
SYNTAX	PCI	12%	19%	31%	38%	56%	29.6	64%	PES 100%
LEFT MAIN	CABG	14%	20%	30%	35%	52%	30.2	72%	97%

30-day outcomes









All cause mortality



Myocardial infarction



Stroke



Repeat revascularization



Effect of removing individual trials on the estimate of mortality at long-term follow up

Study omitted

OR (95% CI)

Boudriot et al.

EXCEL

LE MANS

NOBLE

PRECOMBAT

SYNTAX

1.01 (0.76-1.36) 0.87 (0.65-1.15) 1.01 (0.77-1.35) 0.91 (0.61-1.36) 1.03 (0.75-1.44)

0.99 (0.67-1.47)

All cause death, MI, stroke



Palmerini et al; submitted





Stroke HR (95% CI) Events Events Study PCI CABG Within 30 days BOUDRIOT 0.20(0.01-4.18) 0/100 2101 EXCEL 0.51 (0.20-1.29) 6/948 12/967 LE MANS 0.20(0.01-4.18) 0/52 253 0.12(0.02-2.05) 0/582 NOBLE . 4/592 SYNTAX. 0.19(0.01-3.14) 0.055 2/336 FV Subtotal (p=0.01, (2=0.0%) 0.36(0.17-0.78) 6/2647 22/2039 D+L Overall (p=0.01) 0.36(0.17-0.78) 31 days to latest follow up EXCEL 1.00(0.48-2.10) 14/942 14/945 NOBLE 3.93(1.60-9.66) 16/592 3588 PRECOMBAT 1.00/0.14-7.101 2/300 2/300 SYNTAX 0.44 (0.17-1.14) 5/355 12/334 I-V Subtotal (p=0.47, (2=73.0%, p=0.01) 1.19/0.74-1.92) 37/2189 35/2187 D+L Overall (p=0.76) 1.17 (0.43.3.15) leterogeneity between groups: p = 0.01 I-V Subtotal (p=0.47.12=59.5%, p=0.01) 0.85(0.57-1.29) D+L Overall (p=0.30) 0.67 (0.32-1.42) 0.1 10 1 PCI better CABG better

Periprocedural vs spontaneous MI



Cardiac mortality and the SYNTAX score

Study	HR (95% CI)	Events PCI	Events CABG
SYNTAX score ≤ 22 EXCEL PRECOMBAT SYNTAX I-V Subtotal (p=0.23, 12=0.0%) D+L Overall (p=0.23)	0.57 (0.26-1.25) 0.67 (0.19-2.32) 1.25 (0.34-4.61) 0.70 (0.38-1.26) 0.70 (0.38-1.26)	9/317 4/131 5/118 18/566	16/326 6/110 4/104 26/540
SYNTAX score 23 to 32 EXCEL PRECOMBAT SYNTAX I-V Subtotal (p=0.33, I2=41.4%, p=0.18) D+L Overall (p=0.48)	1.59 (0.53-4.71) 0.67 (0.19-2.32) 0.39 (0.14-1.08) 0.73 (0.39-1.38) 0.74 (0.32-1.70)	8/292 9/102 4/103 21/497	11/312 6/97 6/92 23/501
SYNTAX score > 32 EXCEL PRECOMBAT SYNTAX I-V Subtotal (p=0.04, 12=70.0%, p=0.04) D+L Overall (p=0.48)	1.80 (0.92-3.53) 0.40 (0.12-1.31) 2.45 (1.18-5.08) 1.63 (1.03-2.57) 1.37 (0.57-3.29)	22/337 3/58 21/135 46/530	12/317 8/68 8/149 28/534
Heterogeneity between groups: p = 0.03 I-V Subtotal (p=0.75, I2=55.0%, p=0.02) D+L Overall (p=0.83)	1.05 (0.77-1.44) 0.95 (0.58-1.54)	85/1593	77/1575
0.1	1 10		
PCI better	CABG better		

Palmerini et al; submitted



 Outcomes were analyzed from aggregate data and thus we cannot exclude effects from small differences in baseline characteristics.

 Definition of clinical endpoints differed slightly across trials, likely explaining the moderate inter-study heterogeneity which was present for the MI outcome measure.

 Median follow-up was only 39 months, and longer-term outcomes are required to determine whether additional differences between PCI and CABG emerge over time.

Conclusions

- Across 6 randomized trials and almost 5000 patients no significant difference in the risk of death, overall MI and stroke is apparent between PCI vs CABG in pts with ULMCA stenosis.
- PCI is associated with higher rates of repeat revascularization compared to CABG.
- A significant interaction was be present between treatment effect and the SYMTAX score for the risk of cardiac mortality.

Conclusions II

- Although longer-term follow up is needed, PCI can be considered an acceptable strategy of revascularization in selected patients with ULMCA stenosis as an alternative to CABG.
- Heart team discussion remains a fundamental step for the decision making of the otpimal sartegy of revasculatization in this subset of patients.