Updated meta-analysis for PCI vs CABG for Left Main Disease

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Randomzied trials of CABG vs PCI in ULMCA disease

Study	Period of enrollment	No. of patients in each treatment arm	Design and time point measurement of the primary end point	Primary end point	Median follow-up duration after randomization (y)	Results of the primary end point
LE MANS	2001-2004	PCI (n = 52) CABG (n = 53)	Multicenter, noninferiority	Change in LVEF	1	PCI was superior to
BUDRIOT et al	July 2003 to February 2009	PCI (n = 100) CABG (n = 100)	Multicenter, noninferiority at 1 y	Cardiac death, MI, or repeat revascularization	1	Noninferiority of PCI was not demonstrated.
PRECOMBAT	April 2004 to August 2009	PCI (n = 300) CABG (n = 300)	Multicenter, noninferiority at 1 y	Death, MI, stroke, or TVR	5	PCI was noninferior to CABG.
SYNTAX LEFT MAIN	March 2005 to April 2007	PCI (n = 357) CABG (n = 348)	Multicenter, noninferiority at 1 y	Death, MI, stroke, or UR	5	PCI was noninferior to CABG for the subgroup of patients with ULMCAD.
NOBLE	December 2008 to January 2015	PCI (n = 592) CABG (n = 592)	Multicenter, noninferiority at 3 y	Death, nonprocedural MI, stroke, or UR	3.1	Noninferiority of PCI was not demonstrated.
EXCEL	September 2010 to March 2014	PCI (n = 948) CABG (n = 957)	Multicenter, noninferiority at 3 y	Death, stroke, or MI	3	PCI was noninferior to CABG.

Palmerini et al; AHJ 2017

Eighteen meta-analyses after Excel and Noble



Six meta-analyses in the same journal



Percutaneous Coronary Intervention Using Drug-Eluting Stents Versus Coronary Artery Bypass Grafting for Unprotected Left Main Coronary Artery Stenosis

A Meta-Analysis of Randomized Trials



Nerlekar et al; Circ CV Int 2016



Nerlekar et al; Circ CV Int 2016

Clinical outcomes with percutaneous coronary revascularization vs coronary artery bypass grafting surgery in patients with unprotected left main coronary artery disease: A meta-analysis of 6 randomized trials and 4,686 patients



	Excluded	n=797
Review of titles	Not related	n=559
and abstract	Observational studies	n=109
	Comments and reviews	n=125
Articles requiring full review	Meta-analysis of RCT	n=4
iled text review	Excluded	n=2
	Duplicate RCT with different fup	n=2

Data collected from principal investigators

Study	30 days	Latest follow up available
	Stroke	Stroke
PUDDIOT of al	Death/MI/stroke	Death/MI/stroke
DUDRIOT et al	Death/MI/stroke/UR	Death/MI/stroke/UR
PRECOMBAT	All cause death Cardiac death MI Stroke TVR All cause death/MI All cause death/MI/stroke All cause death/MI/stroke/UR	All cause deatl/MI All cause death stratifie 4 by Syntax score Cardiac death stratified by Syntax score MI stratified by Syntax score Stroke stratified 1 y Syntax score UR stratified by Syntax score All cause death/MI strath ied by Syntax score All cause death/MI/stroke stratified by Syntax score All cause death/MI/stroke stratified by Syntax score
	All cause death Cardiac death	
SYNTAX LEFT MAIN	MI Stroke All cause death/MI All cause death/MI/stroke All cause death/MI/stroke/UR	All cause death/MI
NOBLE	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/M All cause death/M/UR All cause death stratified by Syntax score Cardiac death stratified by Syntax score MI stratified by Syntax score
EXCEL	All cause death/MI	Stroke stratified by Syntax score

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

All cause death/MI strath ied by Syntax score

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%
LE 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%
	CABG	NA	NA	NA	NA	81%	22.4	NA	93%
PRECOMBAT	PCI	9%	8%	16%	25%	67%	24.4	68%	DES 100%
	CABG	11%	8%	19%	13%	62%	25.8	70%	94%
SYNTAX	PCI	12%	19%	31%	38%	56%_	29.6	64%	PES 100%
LEFT MAIN	CABG	14%	20%	30%	35%	52%	30.2	72%	97%

Death, MI, stroke



Myocardial infarction

Stroke



Periprocedural versus non periprocedural MI



All cause death



Cardiac death and the Syntax Score



Network meta-analysis comparing



Shah et al; AM J Cardiol 2017

Network meta-analysis

		OR (95% CI)
A: 1 Year Mortality		
DES versus Medical therapy alone		0.26 (0.08 - 0.69)
CABG versus Medical therapy alone		0.38 (0.13 - 0.96)
DES versus CABG	⊢< <u>−</u> 1	0.66 (0.40 - 1.13)
Heterogeneity (Inform.) = 0.126		
B: 2-3 Year Mortality		
CABG versus Medical therapy alone		0.23 (0.08 - 0.61)
DES versus Medical therapy alone		0.25 (0.08 - 0.71)
CABG versus DES		0.92 (0.61 - 1.38)
Heterogeneity (Inform.) = 0.1512		
C: 5 year Mortality		
DES versus Medical therapy alone		0.20 (0.08 - 0.46)
CABG versus Medical therapy alone		0.21 (0.09 - 0.47)
DES versus CABG	HQ-1	0.94 (0.68 – 1.32)
Heterogeneity (Inform.) = 0.1179		
0.0	01 0.1 1 1	0
	Favours Treatment 1 Favours Treatment 2	

Meta-analysis study comparing percutaneous coronary intervention/drug eluting stent versus coronary artery bypass surgery of unprotected left main coronary artery disease

Clinical outcomes during short-term versus long-term (> 1 year) follow-up

Waleed E. Ali, MD^{a,b,*}, Satyanarayana R. Vaidya, MD^{a,b}, Sylvester U. Ejeh, MD, FACC, FSCAl^{a,b}, Kingsley U. Okoroafor, MD^b

Ahn et al (PRECOMBAT) 2015	۲	۲		۲	•
Boudriot et al 2011	۲	۲		•	۲
Cavalcante et al 2015	•	۲	•	•	•
Chang et al 2012	•			۲	•
Cheng et al 2009		•	•	۲	۲
Chieffo et al 2012					۲
Ghenim et al 2009				۲	۲
Kang et al 2010			۲	۲	۲
Kaweccki et al 2012				•	۲
Lu et al 2016		۲		•	۲
Makikallio et al 2008				۲	۲
Makkallio et al (NOBLE) 2016	۲	۲		۲	۲
Morice et al (SYNTAX) 2014	۲	۲		۲	۲
Naganuma et al 2014				•	۲
Palmerini et al 2006				•	•
Park et al 2010	•		•	•	۲
Oin et al 2013					

29 studies with 4 RCT and 25 observational studies

М	A		Ε

	Experim	ental	Cont	nol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Ahn et al (PRECOMBAT) 2015	52	300	42	300	10.4%	1 29 [0.83, 2.00]	++
Cavalcante et al 2015	186	657	149	648	13.3%	1 32 [1 03, 1 70]	-
Chang et al 2012	63	556	51	309	11.0%	0.65 [0.43, 0.96]	
Lu et al 2016	91	208	114	270	11.6%	1.06 [0.74, 1.53]	+
Makkallio et al (NOBLE) 2016	121	592	81	592	12.5%	1.62 [1.19, 2.21]	-
Morice et al (SYNTAO 2014	130	357	103	348	12.3%	1.36 (0.99, 1.87)	+-
Park et al 2010	17	176	41	219	8.1%	0.46 [0.25, 0.85]	
Yi Gijong et al 2012	39	128	17	128	7.7%	2.86 [1.52, 5.39]	
Yu et al 2016	232	465	178	457	13.2%	1.56 [1.20, 2.03]	-
fotal (95% CI)		3439		3271	100.0%	1.22 [0.95, 1.56]	•
Total events	931		776				
Heterogeneity Tau* = 0.10; Chi*	= 33.93, df	= 8 (P +	0.0001)	P= 76	56		
Test for overall effect Z = 1.56 (P	= 0.12)						Favours PCI Favours CABG

Potential problem

Individual Small Trial

Meta-analysis of several such trials

If all the trials have the same systemic bias, all we have done is to tighten the confidence intervals!



Conclusions I

- Across all meta-analyses comparing CABG vs PCI for the treatment of ULMCA stenosis no significant difference in mortality, cardiac mortality, MI or stroke is apparent between the two strategies of revascularization.
- PCI, however, is associated with higher rates of repeat revascularization compared with CABG
- Heterogeneity was apparent for MI (different definitions) and stroke (due to the Noble trial acting as an outlier)

Conclusions II

- A significant interatction was apparent between treatment effect and time of follow up, such that the composite of death, MI, or stroke rates were lower within the first 30 days, and higher from day 31 to the end of follow up with PCI compared with CABG.
- A significant interaction was also apparent between treatment effect and the SS, such that cardiac mortality tended to be lower in patients with low SS and higher in patients with high SS with PCI compared with CABG.