

## Review

# Coronary artery bypass graft surgery versus percutaneous coronary intervention in unprotected left main coronary artery disease: A systematic review

Liviu Macovei<sup>1,2</sup>, Robert Magopet<sup>1,\*</sup>, Ana Tanasa<sup>1,2</sup>, Cezara Raileanu<sup>1</sup>, Cristina Prisacariu<sup>1,2</sup>, Mihai Razvan Presura<sup>3</sup> and Mircea Ovanez Balasanian<sup>1,2</sup>

<sup>1</sup>*Institute of Cardiovascular Diseases "Prof. dr. George I.M. Georgescu", Iasi 700503, Romania*

<sup>2</sup>*University of Medicine and Pharmacy "Grigore T. Popa", Iasi 700115, Romania*

<sup>3</sup>*Cardiology Clinic of Piatra Neamt General Hospital, Neamt 610136, Romania*

\*Correspondence: [robert.magopet@gmail.com](mailto:robert.magopet@gmail.com) (Magopet Robert)

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Critical lesion of the unprotected left main coronary disease carries a tremendous mortality burden, often associated with a diabetes status or multivessel disease, with coronary artery bypass grafting being the standard treatment for over 40 years. Percutaneous coronary intervention with drug eluting stents should be taken into consideration and could be a better option for patients with low SYNTAX score as validated by the recently published studies. This review summarizes the major randomized clinical trials and meta-analyses concerning the debate regarding percutaneous coronary intervention with drug eluting stents versus coronary artery bypass grafting for unprotected left main coronary disease, along with the latest European and American revascularization guidelines and tries to shed light on this matter. The most results advocate that there is no convincing difference in survival rate for both therapies, especially in patients with isolated left main disease but with fewer major ischemic events for coronary artery bypass grafting when compared with percutaneous coronary intervention in multivessel coronary artery disease, at the rate of a higher stroke incidence. The gaps in evidence are also highlighted, especially the lack of randomized clinical trials with new generation drug eluting stents versus coronary artery bypass grafting or those regarding the best revascularization strategy for an acute coronary syndrome when unprotected left main coronary disease is involved.

## Keywords

Left main disease; revascularization strategies; debate

## 1. Introduction

Myocardial revascularization with coronary bypass graft surgery (CABG) or percutaneous coronary intervention (PCI) is the standard therapy for coronary artery disease for decades. A gradual refinement of technique for both treatments has substantially improved clinical outcomes, but the clarification on which of

the two is more adequate in certain clinical scenarios still requires well designated randomized clinical trials (RCT). A convincing comparison of CABG versus angioplasty in RCTs may be affected by patient and procedure selection bias, the extent of follow-up, and the variety of events considered for study (Brener et al., 2004).

## 2. Purpose

This review aims to analyze and summarize the most important clinical trials, along with systematic reviews, meta-analyses and current practice guidelines regarding the optimal choice of myocardial revascularization type when we are dealing with a patient with unprotected left main coronary disease (ULMCAD), while also presenting the areas of uncertainty, which deserve further investigation. Moreover, new studies, including observational ones, emerged after the publication of the European and American guidelines, are underlined, which may change clinical practice and decision making in the future, this aspect representing the novelty that this review is trying to emphasize.

## 3. Material and Methods

We searched the electronic database of PubMed for studies published in the last 12 years that evaluated the best revascularization strategy for the unprotected left main coronary artery disease. The terms used for searching were "unprotected", "left main coronary artery", "PCI", "CABG", "angioplasty", "revascularization", "coronary artery bypass graft", "percutaneous coronary intervention", "stent", "versus". The reference sections of relevant articles were also searched manually for additional publications. Observational studies including prospective or retrospective cohort studies, RCTs, meta-analyses, and guidelines were included if referring to this particular issue. Case reports were excluded. Studies were selected by two independent reviewers by screening the title and abstract. In a second phase, the full articles which conformed to the selection criteria were obtained, the essential data (general characteristics of the studies, sample size, outcome in terms of safety and efficacy) was extracted independently, and the results compared. Discrepancies were resolved by discussion and consensus.

71 studies were found on PubMed. Duplicates or similar studies were excluded manually. Of these, only 31 met the inclusion criteria. For the selected ones, we reviewed the full text article and additional relevant publications were added after screening the reference section.

## 4. Short History

For almost half a century, CABG has been the conventional treatment for unprotected (not protected by a patent bypass graft) left main coronary artery disease (ULMCAD). The diagnosis and management of significant left main coronary artery disease (LMCAD) continues to be a source of unpredictability and disquiet, taking into consideration that LMCAD is commonly found also in patients with chronic coronary syndromes who go through a coronary angiography and is generally identified with complementary multivessel disease (MVD). Moreover, medical therapy alone for significant ULMCAD has been proved to be inferior to CABG in terms of mortality for over 25 years. (Knuuti et al., 2019; Yusuf et al., 1994).

The first outcomes of PCI with balloon angioplasty for the treatment of ULMCAD were unremarkable and did not initially modify American or European guidelines, which recommended CABG for almost all patients with ULMCAD, but the launch of coronary stents, followed by upgraded procedures have shown progressively better results (Boudriot et al., 2011; O'Keefe et al., 1989).

Stent thrombosis or restenosis was a major impediment with bare-metal stents (BMS) but this issue was partially resolved with the advancement of drug-eluting stents (DES1), and in the latest years, a second generation drug eluting stents (DES2) emerged with undoubtedly better results. DES 2 have thinner struts of 80-90  $\mu\text{m}$ , mostly composed of platinum or cobalt alloy, compared to DES1, which are thicker, with stainless steel struts, and a higher likelihood of intimal hyperplasia, as revealed by histopathological data (Jonar et al., 2008).

## 5. Current practice guidelines overview

The latest European guidelines, focused on myocardial revascularization, issued in 2018 and the current clinical practice American guidelines, published in 2011 and revised in 2017, suggest the need of revascularization for patients with more than 50% stenosis of the left main coronary artery (LMCA), irrespective of symptoms or correlated ischemic load. Moreover, both guidelines have similarities for this topic, when suggesting that PCI for left main disease "is indicated" when we face a patient with a SYNTAX score between 0-22 as IA recommendation and "should be considered" for a SYNTAX score between 23-32, as a IIa recommendation. Maybe of a bigger importance in American guidelines, the need of a heart team discussion before choosing the best revascularization therapy is a class I recommendation (Levine et al., 2011; Neumann et al., 2018; Patel et al., 2017).

## 6. Randomized clinical trials published up to 2016 (BMS and DES1)

In our opinion, there are 4 major randomized clinical trials, prior to 2016 (published between 2008-2011), which debated over PCI versus CABG for ULMCAD-a study by Boudriot et

al. (2011), PRECOMBAT (2011), SYNTAX-LM (2010) and LEMANS (2008). Their most important data is outlined in Table 1 (Ahn et al., 2015; Boudriot et al., 2011; Buszman et al., 2008, 2016; Morice et al., 2010, 2014).

One of the first prospective randomized study to debate over this issue was the LEMANS trial, published in 2008, which included 105 patients, with a 10-year follow-up published in 2016. It is worth-mentioning that the PCI group consisted of 52 patients with 65% of them receiving BMS, while the rest of them DES1. No difference was seen at 10 years for myocardial infarction, stroke, mortality or repeat revascularization regarding PCI vs. CABG in patients with low and even moderate complexity disease and even a probability of long-term survival was comparable between the two arms at 14 years (Buszman et al., 2008, 2016).

The SYNTAX trial that initiated the SYNTAX score (well-known between cardiologists or cardiac surgeons) was published in 2010, with a 5-year follow-up published in 2014, and consisted of a large cohort of 1800 patients, with a pre-defined, well-powered subgroup of 705 randomized patients who only had left main disease (SYNTAX-LM subgroup/trial). At 5 years, there were no differences between the two groups in major cardiac and cerebrovascular events (MACCE) or cardiac death, but only if the SYNTAX score was less than 33. Albeit using paclitaxel-eluting stent (DES1), repeat revascularization was significantly higher in the PCI arm but with less stroke when compared with CABG (Morice et al., 2010, 2014).

A study by Boudriot et al. (2011) (201 patients) and the PRECOMBAT trial (600 patients) were both published in 2011, with a 5-year follow-up for PRECOMBAT reported in 2015 and had similar results in terms of MACCE-free survival, proving non-inferiority for PCI (with sirolimus-eluting stents-DES1 in both studies) when compared to CABG at 1 year or 5 years. Maybe as could be expected, and already seen with the shortly discussed SYNTAX-LM trial, these 2 studies had comparable but significant need for ischemia-driven revascularization with PCI (Table 1) (Ahn et al., 2015).

Up to 2016, we consider the PRECOMBAT and SYNTAX trials as landmarks in terms of usefulness in real life, with mid and long term follow-up prospects. Very recently, the 10-year results of the SYNTAX trial, concerning all-cause death were reported and investigators found no significant difference between PCI using DES1 (paclitaxel-eluting stents) and CABG in all-cause death, with commensurate surviving benefit in both arms, but only in patients with ULMCAD and not in those with multivessel disease (Thuijs et al., 2019).

## 7. "The era to EXCEL in NOBLE trials" (DES2 trials)

Recent large trials, published in 2016 like EXCEL (Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease), with a recently published 5-year follow-up, and NOBLE (Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis) have shown similarities in survival and cardiovascular outcomes when comparing PCI versus CABG in patients with a low SYNTAX score (0-22), even though there

Table 1. Summary of randomized clinical trials on PCI vs. CABG for ULMCAD up to 2016

Trial	SYNTAX score (mean)	Primary endpoint				Secondary endpoint			
		Outcomes	PCI	CABG	P	Outcomes	PCI	CABG	P
LEMANS	unknown	Change at 1 year in left ventricular ejection fraction	3.3 ± 6.7%	0.5 ± 0.8%	0.047	Repeat revascularization	26.10%	31.30%	0.39
Results at 1 and 10 years						Death (10 years)	8.70%	30.20%	0.41
						MI (10 years)	8.70%	10.40%	0.68
						Stroke (10 years)	4.30%	6.30%	0.58
						Composite	52.20%	62.50%	0.42
Boudriot et al. (2011)	23	Death, repeat revascularization or MI, at 1 year.	19%	13.90%	Non-inf. = 0.19	MI	3%	3%	Non-inf. = 0.002
Results at 1 year						Death	2%	5%	Non-inf. < 0.001
						Repeat revascularization	14%	5.90%	Non-inf. = 0.019
SYNTAX-LM	30	Death, MI, stroke or repeat revascu- larization (1 year)	15.80%	13.60%	Non-inf. = 0.19	Stroke (5 years)	1.50%	4.30%	0.03
Results at 1 and 5 years						Death (5 years)	12.80%	14.60%	0.53
						MI (5 years)	8.20%	4.80%	0.1
						Repeat revascularization (5 years)	26.70%	15.50%	< 0.001
						Death, stroke, MI or repeat revascu- larization (5 y)	36.90%	31%	0.12
PRECOMBAT	25	Death, stroke, MI or ischemia- driven target lesion revasculariza- tion (only at 1 year)	8.70%	6.70%	Non-inf. = 0.01	Stroke (5 years)	0.70%	0.70%	0.99
Results at 1 and 5 years						Repeat revascularization (5 years)	13%	7.30%	0.02
						MI (5 years)	2%	1.70%	0.76
						Death (5 years)	5.70%	7.90%	0.32
						Death, stroke or MI (5 y)	8.40%	9.60%	0.66
						Death, stroke, MI, or ischemia- driven target lesion revasculariza- tion (5 y)	17.50%	14.30%	0.26

were some dissonant issues. These trials led to the conclusion that both therapies remain important for the treatment of left main/multivessel disease, but with bearing in mind that a heart team discussion is of outmost importance when managing these difficult cases. Their most important data is marked in [Table 2](#) ([Mäkikallio et al., 2016](#); [Stone et al., 2016, 2019](#)).

The EXCEL trial, the largest published to date on this matter, admitted 1905 patients with important left main stenosis ( $\geq 70\%$ ) or which is hemodynamically significant, defined by invasive or non-invasive assessment, with low to moderate SYNTAX score. The NOBLE trial included 1201 patients with 50% or more left main stenosis or fractional flow reserve (FFR) below 0.80 with maximum 3 further low complexity lesions. A rate of composite event of all-cause death, myocardial infarction and stroke was the primary endpoint at 3 years in EXCEL study, also tested for non-inferiority, with a margin of 4.2 percent points, while any new revascularization had been additional counted at 5 years in composite primary outcomes in NOBLE trial ([Table 2](#)) ([Mäkikallio et al., 2016](#); [Stone et al., 2016](#)).

The primary endpoint at 3 years in EXCEL trial revealed that PCI was non-inferior to CABG, with similar percentages of composite end points of myocardial infarction, stroke, or even death, but with higher amount of events (consisting of stroke, early death or myocardial infarction), at 30 days in the surgery arm, when compared to angioplasty. When taking into consideration the rates of ischemia driven repeat revascularization at 3 years, the rates were higher in the PCI group, with a difference of 5.1%, but with fewer rates of stent thrombosis when compared to acute graft occlusion. Less common recorded were also major and minor bleeding events after angioplasty than after surgery ([Table 2](#)) ([Stone et al., 2016](#)).

On 28 September 2019 was published the 5-year follow-up for EXCEL trial, with essentially the same results: the frequency of cardiovascular death and myocardial infarction were not statistically different, with a similar incidence of stroke in both groups and with less numerous cerebrovascular events following angioplasty than after CABG (a total difference of 1.9%); moreover, there was no compelling disparity between PCI and CABG at 5 years when taking into consideration the rate of the composite outcome (stroke, myocardial infarction and death). At the end of the trial, death from any cause was more often identified in the angioplasty group than in the CABG arm, with a crucial difference of 3.1% ([Table 2](#)) ([Stone et al., 2019](#)).

On the contrary, the outcomes of the NOBLE trial (with results similar to the SYNTAX-LM trial already reviewed) significantly favored CABG at 5 years, with less all-cause mortality (but  $P = 0.84$ ) and with 46% excess hazard for PCI over CABG at 5 years. Higher nonprocedural MI, repeat revascularization, and notably, a greater tendency for stroke were more often seen in the PCI arm. We consider interesting the fact that at 1 year MACCE proportions were similar between the two arms ([Table 2](#)) ([Mäkikallio et al., 2016](#)).

## 8. Small different characteristics led to divergent results ?

Although there were some discrepancies, and in the end, different conclusions, we must consider the important diversity between the two trials: distinction in end-points, study designs and types

of stents used.

EXCEL was larger in number and a quarter of patients were found to have a greater SYNTAX score than at inclusion, detected when reviewing the angiographic images in laboratory; less often Intravascular Ultrasound (IVUS) or mammary grafts were used in NOBLE trial (74%), compared to the EXCEL trial (77%). The first 10% patients enrolled in the PCI group in the NOBLE trial received DES1 before biolimus-eluting biodegradable stent (Biomatrix Flex, Biosensors, Morges, Switzerland) was recommended as a primary stent. Although this is a second generation stent, it has thicker-struts than the fluoropolymer-based everolimus-eluting stent (XIENCE, Abbott Vascular) used by EXCEL investigators. The primary endpoint estimation was lowered (from 5 to 3 years) in the NOBLE trial by reason of low event rates, and Kaplan-Meier estimates were proposed to report 5-year outcomes. We consider that these measurements could have been afflicted by an adjustment in risk for patients introduces in the study at different moments. Moreover, revascularization rates, which we know that are definitely lower in patients treated with CABG, in comparison to PCI, were comprised in the primary composite endpoint in NOBLE trial, but not in EXCEL.

A longer follow-up of these two major trials is of pivotal importance to grasp the relative strengths and weaknesses of PCI and CABG for ULMCAD ([Mäkikallio et al., 2016](#); [Stone et al., 2016](#)).

## 9. Meta-analysis (published after 2016)

In 2017, [Giacoppo et al. \(2017\)](#) released a meta-analysis regarding PCI versus CABG as standard therapies of ULMCAD, which included almost 4400 patients from trials like EXCEL, NOBLE, PRECOMBAT and SYNTAX. Angioplasty with drug eluting stents (DES) and CABG were correlated with commensurate rates of myocardial infarction, stroke or death from any cause (18.3% with PCI vs. 16.9% with CABG), in the end producing no decisive differences concerning sizable detrimental cardiovascular events. A greater tendency of stroke was associated with surgery and more repeat revascularization with angioplasty, but interestingly, no difference was seen in revascularization rate risk reduction between DES2 and DES1 (hazard ratio 1.70,  $P < 0.001$ ).

With similar outcomes as the above-mentioned study, [Verdoia et al. \(2018\)](#) presented a noteworthy meta-analysis, which included 8 randomized trials (SYNTAX, FREEDOM, PRECOMBAT, VA-CARDS, BEST, [Boudriot et al. \(2011\)](#), NOBLE, EXCEL) with 8694 patients and a mean follow-up of 39.7 month, comparing PCI (with DES) versus CABG and having the primary end point the overall mortality, in ULMCAD and multivessel CAD. This meta-analysis revealed that in patients with isolated left main disease there was no difference in survival rate in both groups, but when there is also multivessel CAD associated, there is a presumed superiority for surgery compared with angioplasty with DES, regarding especially considerable ischemic accidents, at the cost of a higher stroke extent. We must take into consideration that an extensive volume of the data comes from patients with diabetes, enrolled in Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease trial (FREEDOM) and VA-CARD study (Coronary Artery Revascularization in Diabetes), most of whom had MVD and a mortality benefit from CABG already confirmed by SYNTAX trial ([Farkouh](#)



et al., 2012; Kamalesh et al., 2013; Mohr et al., 2013; Verdoia et al., 2018).

On September 2018, a large, collaborative individual patient merged analysis of randomized clinical trials tried to clarify this topic even more, without bringing forward more questions. Head et al. (2018) reviewed the accessible data from 11 randomized trials which evaluated angioplasty versus CABG for left main or multivessel disease and did a systematic review up to mid of 2017, which included 11,518 patients, having a primary outcome the difference in mortality of any cause between these two revascularization strategies. Overall, CABG had a compelling survival benefit during the follow-up (all-cause mortality at 5 years: 9.2% for surgery vs. 11.2% for PCI,  $P = 0.0038$ ) but regarding interference in patients with ULMCAD, related mortality was noted between the two arms, irrespective of SYNTAX score or even the diabetes status (10.5% for surgery vs. 10.7% after PCI, but  $P = 0.52$ ) (Head et al., 2018).

A systematic review with meta-analysis and subgroup evaluation, conducted by Negreiros et al. (2019) was published in 2019 and regarded the same objective. With title "Stent versus Coronary Artery Bypass Surgery in Multi-Vessel and Left Main Coronary Artery Disease", this study encompassed 15 trials (compelling 12,781 patients) and their results were pooled, with similar outcomes as what was already reviewed, but with definitely more statistical significance due to the larger number of patients: at 30 days, with angioplasty there were fewer events regarding mortality and stroke (1.7% for CABG vs. 1% for PCI, with  $P = 0.01$  and 1.7% vs. 0.6%,  $P < 0.0001$ ), with no distinction in one and two year mortality in both arms; long term mortality favored surgery, particularly in trials of drug eluting stents (8.5% for CABG versus 10.1% for PCI,  $P = 0.01$ ), with most benefit seen in diabetics (13.7% versus 10.3%;  $P < 0.0001$ ). Regarding only LMCAD (6 trials-4700 patients), at 30 days there was no difference in mortality (0.5% total difference), or even 1-year mortality (0.7% total difference, with  $P = 0.18$ ), with no distinction for long term mortality (both groups: 8.1%) between angioplasty with DES and CABG, but, maybe as expected and seen before, a lower rate of stroke with PCI (total difference of 1.2% with  $P < 0.001$ ) (Negreiros et al., 2019).

## 10. Areas of uncertainty-acute coronary syndromes

When taking into consideration an acute coronary syndrome (ACS), the debate between PCI vs. CABG concerning ULMCAD is weaker due to the lack of trials published on this matter. Notably, there are NO major randomized clinical trials at this moment to compare the differences between these two revascularization therapies when an acute coronary syndrome is unfolding. Moreover, the best trials already published such as SYNTAX, PRECOMBAT, EXCEL or NOBLE have an acute myocardial infarction or elevated cardiac enzymes as major exclusion criteria and included only unstable angina in different proportions ranging from 17% to 45% (Table 3), even supposing this particular very high-risk subgroup of patients, at first glance, did not change primary or secondary endpoints (Ahn et al., 2015; Mäkilä et al., 2016; Morice et al., 2010; Stone et al., 2016).

We believe that the most important conclusions on this matter

can be extracted from data which comes from Drug Eluting Stents for Left Main Coronary Artery Disease (DELTA) multicentre registry, which compared the long-term clinical outcomes after PCI with DES1 or CABG in patients with ACS (STEMI or NSTEMI). Although this is an observational study, with no randomization whatsoever and maybe some selection biases, we consider their results reassuring and similar to the larger randomized clinical trials already reviewed: there is no difference between CABG versus PCI with DES1 for the composite of MI, cerebrovascular accidents or death at long-term follow-up (1120 days) with (as expected), more frequent need of vessel revascularization in the PCI arm, only when propensity score matching was performed. Analogous results were reported in 2018 by another large observational study-MAIN COMPARE, at 3, 5 and 10 years, albeit patients with STEMI or cardiogenic shock were excluded from this investigation (Park et al., 2018; Pyxaras et al., 2016).

Some might even wonder if do we really need a randomized clinical trial between PCI vs. CABG in an acute setting when time really matters and PCI is within our reach? But we must not forget nor minimize the high mortality which comes with critical lesion of the LMCA, often correlated with multivessel disease or a diabetes status and the uncertainty that arises when we have to make a life-saving decision. In consequence, a well-powered randomized trial of PCI versus CABG in the ACS population is justified because these patients have been predominantly ruled out from prior trials.

## 11. Novelty-future directions

Interventional cardiology and cardiac surgery are areas where constant progress predominates and in recent years this has become even more evident with new technologies such as IVUS-assisted PCI of the LMCAD with drug eluting stents or Robot-assisted CABG.

Intravascular ultrasound (IVUS) grants a unique method to examine the regression or progression of atherosclerotic lesions, along with a more detailed and extensive assessment of the structure of the coronary arteries. IVUS-guided PCI significantly lowers MACCE when compared to conventional PCI, irrespective of drug eluting stent generation, as proved by a meta-analysis published in 2016 and is correlated to positive results even in patients with chronic total occlusion lesions (Nerlekar et al., 2016; Shin et al., 2016).

Current European practice guidelines suggest that IVUS should be used to determine the severity and the optimal treatment of ULMCAD. A convincing meta-analysis which compared IVUS-guided PCI versus standard, angiography-guided PCI in order to highlight the best choice in patients with ULMCAD and their effects on mortality (all-cause death and cardiac death), was reported in 2017. The study included 6480 patients (10 studies) and revealed that at 3 years follow-up, IVUS-guided PCI was associated with lower risk of all-cause death (40% risk reduction) when compared with conventional angiography-guided PCI. Moreover, important risk reduction was seen on cardiac death, target lesion revascularization or stent thrombosis along with its favorable outcome consistent on all subgroups studied (Neumann et al., 2018; Ye et al., 2017).

Table 2. Summary of endpoints concerning EXCEL and NOBLE trials

Trial	SYNTAX score (mean)	Primary endpoint				Secondary endpoint			
		Outcomes	PCI	CABG	<i>P</i>	Outcomes	PCI	CABG	<i>P</i>
EXCEL	21	Composite: stroke, MI, death	15.40%	14.70%	Non-inf. = 0.02	Ischemia-driven revascularization	12.60%	7.50%	0.001
Results at 3 years					Super. = 0.98	Death	8.20%	5.90%	0.11
						MI	8%	8.30%	0.64
						Stroke	2.30%	2.90%	0.37
						Composite	23.10%	19.10%	Non-inf. 0.01
EXCEL	21	Composite: stroke, MI, death	22%	19.20%	0.13	Ischemia-driven revascularization	16.90%	10%	
Results at 5 years						Death	13%	9.90%	
						MI	10.60%	9.10%	
						Stroke	2.90%	3.70%	
						Composite	31.10%	24.90%	0.002
NOBLE	22	Composite-repeat revascularization, death, MI (non-procedural) and stroke	29%	19%	0.007	MI (non-procedural)	7%	2%	0.004
Results at 5 years						Death	12%	9%	0.77
						Repeat revascularization	16%	10%	0.032
						Stroke	5%	2%	0.073

Table 3. Summary of trials which included patients with ACS

Trial	No. of patients	ACS%	Exclusion criteria (only ACS-related)
PRECOMBAT	600	45%	Acute MI within 7 days, cardiogenic shock
SYNTAX-LM	705	30	Acute MI (with creatinine kinase > 2x normal)
EXCEL	1905	24%	CK-MB > upper limit of normal, or recent MI with CK-MB levels still elevated
NOBLE	1201	17%	
			ST-elevation infarction within 24 hours

Hybrid coronary revascularization and Robot-assisted CABG (R-CABG) surgery have emerged in the last years as cornerstone treatments for frail patients who demand a less traumatic approach. One of the first retrospective studies to debate over the clinical outcomes of patients with ULMCAD who undergo three different revascularization therapies (PCI vs. CABG vs. R-CABG) was published in 2018 and reported very interesting results which need further investigation in the future but certainly will change the whole perspective in less than a decade. The study included 472 ULMCAD patients and 186 received PCI, 139-R-CABG and the rest of them-conventional CABG. The investigators concluded that PCI remains a fair choice in older patients with low to moderate SYNTAX score and R-CABG is a competent surrogate to standard CABG, with significantly lower duration of intensive care unit and total hospital stay. A similar, retrospective study compared the clinical outcomes of patients with MVD treated either by R-CABG or PCI with DES and reported similar in-hospital and long term-survival rates (follow-up for  $5.7 \pm 3.0$  years,  $P < 0.001$ ) for both arms, along with commensurate rates of stroke, MI and as expected, significant higher rates of revascularization with PCI (Su et al., 2018, 2019).

Hybrid coronary revascularization combines a minimally-invasive direct coronary bypass technique of grafting the left internal mammary artery to left descending coronary artery, followed by PCI for the remaining vessel in a subsequent time. At the moment there is limited evidence supporting this revascularization approach but a large randomized trial, still in process, such as Hybrid Coronary Revascularization (HYBRID) should decipher the advantages on this novel strategy (Gasior et al., 2014).

## 12. Sex-specific prognosis

Patients with obstructive left main coronary artery disease are at very high risk for cardiovascular events. Albeit the prevalence of this disease is higher amongst men, there are studies that outlined worse events and higher mortality among women, even after the completion of a revascularization strategy whatsoever (Min et al., 2011).

Furthermore, a recently published long term registry-CONFIRM (Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter registry) detected adverse effects among women with non-obstructive LMCAD (1%-49% stenosis), for a follow-up of 5 years, with an almost 80% higher risk than in men with non-obstructive LMCAD (hazard ratio, 1.78,  $P = 0.017$ ), with a definite synergy between the left main plaque and female sex, powerfully increasing the composite outcome (all-cause mortality, nonfatal MI) only in women. At the moment there is no ideal tool to stratify risk for sex-specific prognosis significance and efforts should be made in this direction (hazard ratio 1.48,  $P = 0.005$ ) but not in men (Xie et al., 2017).

## 13. Discussions and conclusions

Advances in CABG and PCI techniques evaluated in contemporary trials and meta-analysis display that angioplasty with DES for ULMCAD is a cherished preference, having commensurate long-term survival rates, compared to surgery, notably in those with low and intermediate SYNTAX score and maybe not in an

acute setting. Even so, a greater need for repeat revascularization may be seen in the future in patients treated with angioplasty and DES implantation, thus requiring close clinical follow-up.

New additional large randomized trials are surely desired, with new generation drug eluting stents and improved techniques or therapies. CABG remains a better option for patients with increased anatomical complexity, diabetes and multivessel disease. This ongoing debate between CABG and PCI will probably remain firm in the next decade and will be influenced by constant progress within the stent commerce. Clinical practice will be determined by our analysis of current evidence and guidelines, along with the claim of the patients to have the least invasive procedures, along with a definite necessity of a debate between the heart team and the patient when weighing the pros and cons of this different revascularization techniques.

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## Conflict of Interest

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