

CARDIOVASCULAR SURGERY UPDATE

Left Main Coronary Artery Disease: CABG is superior to PCI

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KEY WORDS: *Left main coronary
artery disease, CABG, PCI*

ABBREVIATIONS

ACC = American College of Cardiology
AHA = American Heart Association
BMS = bare metal stents
CABG = coronary artery bypass grafting
CAD = coronary artery disease
DES = drug-eluting stents
ESC = European Society of Cardiology
LM = left main
MACCE = major adverse cardiac and
cerebral events
MI = myocardial infarction
PCI = percutaneous coronary intervention
3VD = three-vessel (coronary) disease

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ABSTRACT

Left main coronary artery disease (LMCAD) is a special part of coronary pathology and its gold standard treatment is coronary artery bypass surgery (CABG). Over the last two decades, the evolution in technology and materials and the growing experience of interventional cardiologist treating acute coronary syndrome improved the results of percutaneous coronary interventions even in patients with LM disease. Recent prospective randomized studies though (SYNTAX) as well as large registries comparing the two methods showed comparable results concerning safety and inferiority of PCI regarding restenosis and need for reintervention. Up to now CABG remains the treatment of choice for LM disease with PCI being a reliable alternative solution in cases of patients of high surgical risk. The above is strongly recommended by the new guidelines.

INTRODUCTION

Cardiovascular disease is by far the first cause of death in the western world. The prevention and the reduction of cardiac risk factors have beneficial results in the general population, moving the main problem to more elder group of people.

Coronary-artery bypass grafting (CABG) was introduced in 1968 and rapidly became the standard of care for symptomatic patients with coronary artery disease.¹ Advances in coronary surgery (e.g., off-pump CABG, smaller incisions, enhanced myocardial preservation, use of arterial conduits, improved postoperative care as well as widely published surgical outcomes) have reduced morbidity, mortality, and rates of graft occlusion.²⁻⁴ The rate of mortality at a global level is less than 2% and in most recent studies it is less than 1.3%, including emergency and complex cases.

The incidence of left main (LM) coronary artery disease (LMCAD) among patients undergoing coronary angiography ranges from 4% to 6%.⁵ The same percentage for those undergoing surgery is as much as 30%. Although uncommon, LMCAD is a constant topic of discussion between cardiac surgeons and interventional cardiologists. This discussion began in 1975, when Gorlin and Cohen⁶ first compared a surgical approach for LM stenosis to any other treatment option and reported that CABG showed significant benefits.

Since then and for over 45 years researchers are trying to find alternative and less

Conflict of Interest: none declared

interventional methods to treat LMCAD. Thus, almost one decade following the first CABG (1977), the percutaneous coronary intervention (PCI) with the use of plain balloon angioplasty was first introduced and then there followed the introduction of bare metal stents (BMS), which significantly reduced the restenosis rate of plain angioplasty.⁷ This particular method, coupled with improved technology, has made it possible to treat increasingly complex lesions and patients with a history of clinically significant cardiac disease, risk factors for coronary artery disease (CAD), coexisting conditions, or anatomical risk factors.^{8,9} Still, however, the high rates of mortality and restenosis with the use of BMS in the case of LM disease led the American Heart Association – AHA, the American College of Cardiology – ACC and the European Society of Cardiology – ESC to announce strict guidelines confirming CABG as the treatment of choice for LMCAD.¹⁰⁻¹³ The percutaneous method with use of BMS was given a class III designation for this particular subgroup and was made available only to patients disqualified from all other possible methods of treatment.

Nevertheless, over the last several years, with improved PCI methods, use of adjunctive medical therapy and the development of new stent design with the drug-eluting stents (DES), which have significantly curtailed the restenosis rate, PCI has emerged as a possible alternative in patients with complex coronary disease.^{9,14} Recent revisions to revascularization guidelines have reflected these improvements in PCI outcomes for patients with complex coronary disease.^{15,16} In general, during the first year after the index procedure, PCI has been found to be as safe as CABG in patients with severe coronary artery disease; however, the rates of recurrences are significantly higher and PCI has again failed to show non-inferiority compared with CABG due to increased need for repeat revascularization.^{17,18}

New randomized trials with large series of patients, like the SYNTAX trial (SYNergy Between PCI with TAXUS and Cardiac Surgery), try to clarify the advantages and disadvantages of the two methods. The results of these studies will possibly answer the question whether modern PCI with DES can compete with CABG in the treatment of LMCAD concerning safety and long-term results.

GENERAL STATEMENT

Before proceeding to the analysis of the recent data about PCI and CABG, it would be proper to make the following statements:

1. Patients prefer less interventional therapies
2. The proper and well documented use of PCI can be a useful tool in the management of coronary artery disease. For example, the advantages of PCI in the treatment of acute coronary syndrome are undoubtful.

LEFT MAIN CORONARY ARTERY DISEASE (LMCAD) – CURRENT PERSPECTIVES

Left main CAD is part of the pathology in 4-6%¹⁹ of the patients undergoing PCI and in almost 30%²⁰ of the patients undergoing CABG. Although CABG is the gold standard treatment for LMCAD, according to all major cardiology societies,¹⁰⁻¹³ 29% of the patients with LMCAD in Europe and 18% in North America are still being treated with PCI.²¹

The large size of the left main coronary artery renders it an “attractive” site for the use of endovascular stents when compared with the other coronary arteries. Nevertheless there are two anatomical elements because of which PCI cannot guarantee long term results: 1) Almost 90% of the lesion of the LM involves its bifurcation or its distal segment,²²⁻²⁴ sites which present high rates of restenosis,²⁵ 2) 80% of the patients with LMCAD have additional multiple lesions in other coronary arteries.²²⁻²⁴ In these cases the treatment is obviously surgical.

Serruys *et al* give emphasis to the significance of distal lesions in the LM coronary artery and their role in the appearance of major adverse cardiovascular or cerebrovascular events (MACCE) shortly after PCI is performed. Their study revealed a 30% rate of MACCE in patients with distal stenosis, whereas only 11% of the patients without distal stenosis suffered from MACCE. It must be pointed out that the procedures in this study were performed by one of the most experienced team of interventional cardiologists.²⁵

The outcome of the use of BMS was not satisfactory in the treatment of LMCAD. The analysis of the results of 8 studies performed in the period between 1999 and 2003 concerning 1100 patients showed in-hospital mortality of 6%, need for repeat revascularization 0-20% and 2-year mortality 17%.²⁶ The results were better in young patients with good ventricular function and lesion in the middle segment of LM coronary artery. The 3-year mortality in this group was 7.4%.²⁷⁻²⁹ On the other hand the results of CABG in low risk patients are excellent. For example in the SOS study the mortality rate after 1 year follow-up was 0.8%.

Drug eluting stents (DESs) were expected to be the solution to the problem of restenosis of BMS and therefore their use, even in cases with LM disease, started to expand.²²⁻²⁴ Studies with DES showed impressive results reaching 2% in-hospital mortality rate and 2% need for urgent repeat revascularization. Nevertheless all these studies were badly designed and included a small sample of patients (50-130) and also had a small period of follow-up (in most studies less than one year). Price *et al.* conducted the only study with angiographic examination for restenosis at 3 and 9 months after PCI and found rates of restenosis 34% and 44% respectively.²⁴

The need for a large scale randomized study comparing PCI and CABG led to the design of the SYNTAX trial. The

purpose of this trial was to determine whether or not the PCI method using DES (Taxus Express 2, Boston Scientific) has comparable safety rates and success with CABG in patients with three vessel disease (3VD) or LM disease.

The results of the SYNTAX trial after 1 year of follow-up revealed that the major cardiovascular and cerebrovascular events (MACCE) were more frequent in the PCI group than in the CABG group but with no significant difference (15.8% vs. 13.7% respectively, $p=0.44$). The major difference among the two groups concerning MACCE was detected in the rate of repeat revascularization, where the PCI group had almost double percentage in comparison with the CABG group (6.5% vs. 11.8% respectively, $p=0.02$). Angioplasty was found to be as safe as the surgical treatment and with comparable rates of mortality. On the other hand, the CABG group had significantly greater incidence of stroke comparing to the PCI group

(2.7% vs. 0.3% respectively, $p=0.01$)¹⁸ (Figure 1).

The above results were confirmed and further emphasized by the analysis of the data after a 3-year follow-up period and even more recently in the 4-year follow-up report. More specifically in the LM cohort, the rates of MACCE and death/stroke/myocardial infarction (MI) were not significantly different in PCI- and CABG-treated patients. The 3-year rate of repeat revascularization was increased in PCI-treated LM patients (20% vs. 11.7% respectively, $p=0.004$). There was no difference in all-cause or cardiac death rates in CABG- or PCI-treated patients with LM disease (all-cause: CABG 8.4% vs. PCI 7.3%, $p=0.64$; cardiac death 4.6 vs. 5.7%, $p=0.48$)³⁰ (Figure 2).

It must be pointed out that the results described here are only a part of the SYNTAX trial and have to do only with the subgroup of patients suffering from LM disease. The rates

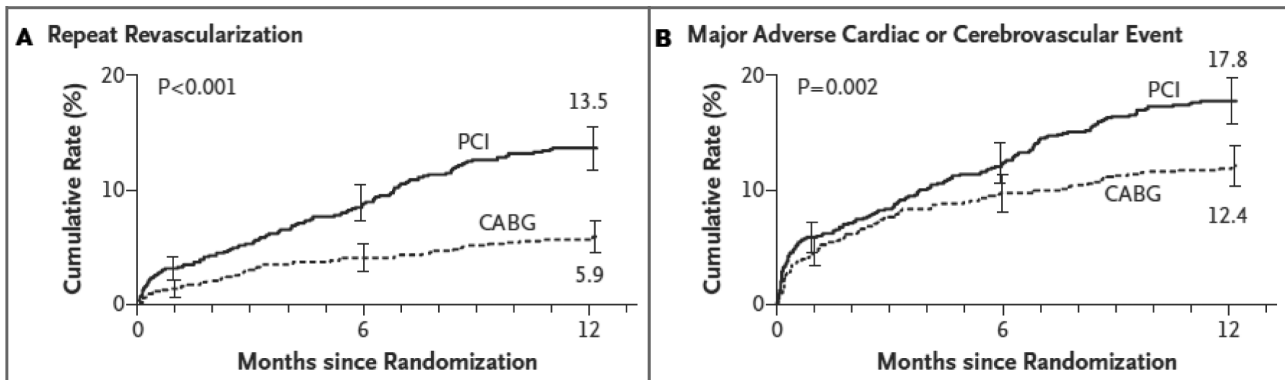


FIGURE 1. Rates of outcomes among the patients (3VD and LM subgroups), according to treatment – 1 year follow-up of “SYNTAX trial”. Kaplan–Meier curves are shown for the percutaneous coronary intervention (PCI) group and the coronary-artery bypass grafting (CABG) group for repeat revascularization (Panel A); and the composite primary end point of major adverse cardiac or cerebrovascular events (Panel B). The rate of repeat revascularization was significantly increased with PCI (relative risk, 2.29; 95% CI, 1.67 to 3.14), as was the overall rate of major adverse cardiac or cerebrovascular events (relative risk, 1.44; 95% CI, 1.15 to 1.81). P values were calculated with the use of the chi-square test. (N Engl J Med, 2009.360, 10: 961-972, Modified).

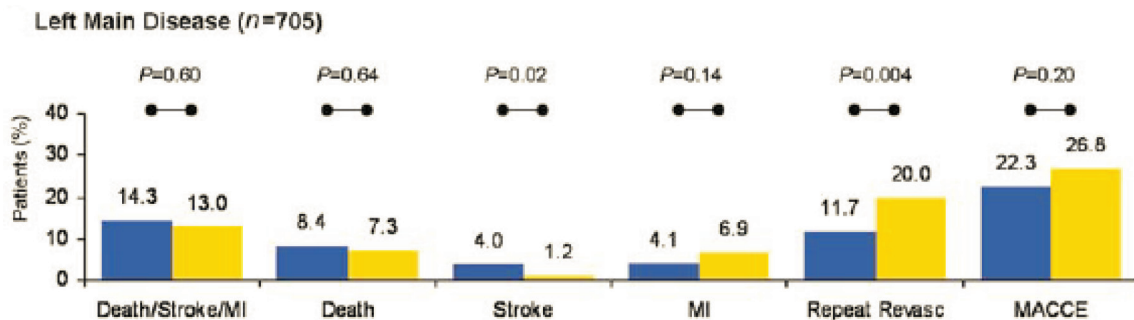


FIGURE 2. Three-year clinical outcomes according to the treatment group in patients with left main disease – 3 year follow-up of “SYNTAX trial”. Death/stroke/myocardial infarction, all-cause death, stroke, myocardial infarction, repeat revascularization (repeat revasc), and major adverse cardiac and cerebrovascular event rates at 3 years in coronary artery bypass grafting (blue bars) or percutaneous coronary intervention-treated (yellow bars). P-value from log-rank test. (Eur Heart J, 2011. 32: 2125-2134, Modified).

of three-year clinical outcomes in the overall randomized cohort (LM and 3 vessel subgroups together) were even more favorable for those who underwent surgery concerning cardiac death, stroke, MI, revascularization and MACCE³⁰ (Figure 3).

Furthermore the SYNTAX trial introduced a helpful “tool”, the “*SYNTAX score*”, which was designed to predict outcomes related to anatomical characteristics and, to a lesser extent, the functional risk of occlusion for any segment of the coronary-artery bed (as reflected by the Leaman score³¹). The Syntax score is calculated with the use of a complicated algorithm which takes into account the vascular dominance, the number, the length and the topography of the lesions, the presence of total occlusion, the existence and the type of bi- or trifurcations, the presence or not of endovascular thrombus, the morphology of the coronary vessels and the severity of the calcifications. When the population of the study was divided into three subgroups according to the SYNTAX score (low – 0-22, intermediate – 23-32 or high – ≥33), the LM patients with the most complex anatomy who were treated with PCI were found to have significantly increased incidence of MACCE (CABG 21.2% vs. PCI 37.3%, $p=0.003$) and need for repeat revascularization (CABG 9.2% vs. PCI 27.7%, $p<0.001$) (Figure 4).

Taking all the above data under consideration, the current US and European revascularization guidelines assign CABG a IA indication in most patients with 1, 2, or 3VD with low, intermediate, or high SYNTAX scores.^{15,32} However, due to positive outcomes from other recent studies of LM patients,

these guidelines have upgraded the indication for PCI in the LM artery from a Class III to a Class IIb (ACC/AHA)^{15,32} and a Class IIb C to IIa B (ESC-EACTS)³³ indication in patients with isolated LM (ostial or trunk) and with associated 1 vessel disease. Additionally, the ESC-EACTS guidelines have also included the treatment of patients with 3VD and low SYNTAX scores as a Class IIa B indication³³ (Figure 5).

Moreover the use of the SYNTAX score revealed that surgical revascularization remains the standard treatment for patients with more complex coronary anatomy, whereas PCI demonstrates similar outcomes when compared to CABG in patients with less complex disease and lower SYNTAX score for 3VD and lower and intermediate scores for LM disease. Retrospective application of the SYNTAX score to other patient groups has shown value in predicting or correlating high anatomical complexity with increased adverse cardiac events making it an effective risk assessment tool.³⁴⁻³⁷

DEBATE BETWEEN CARDIAC SURGEON AND INTERVENTIONAL CARDIOLOGIST

The modern surgeons, after studying all the results from the latest trials and combining them with their experience, reached the conclusion that CABG is the treatment of choice for patients with LM disease and especially for those with complicated stenosis (high SYNTAX score). In this group of people, PCI failed to present similar results

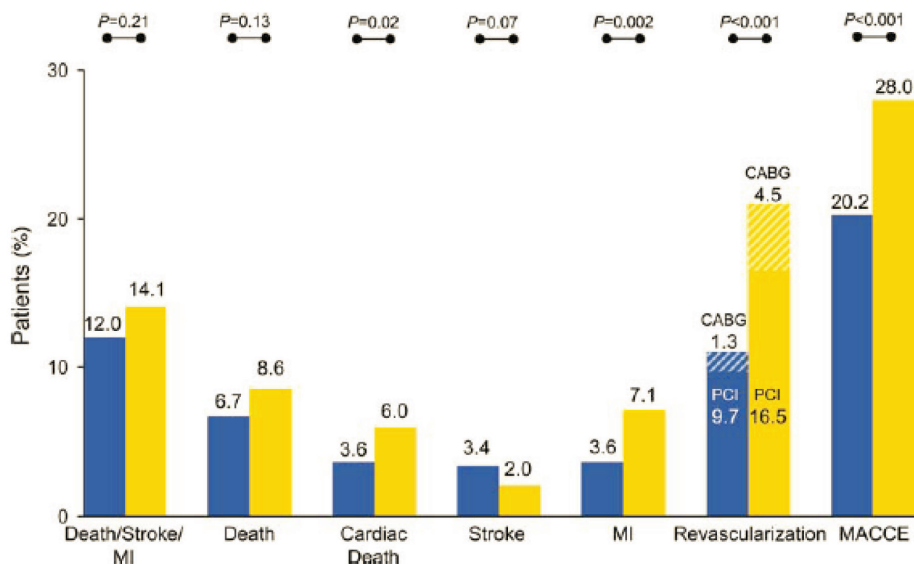


FIGURE 3. Rates of clinical outcomes among randomized treatment groups – 3 year follow-up of “SYNTAX trial”. Three-year clinical outcomes in coronary artery bypass grafting (blue bars) or percutaneous coronary intervention (yellow bars). Repeat revascularization is broken down into repeat percutaneous coronary intervention (yellow or blue bars) and repeat coronary artery bypass grafting (striped yellow or blue bars). The Kaplan–Meier event rates, P-value from log-rank test. (Eur Heart J, 2011. 32: 2125-2134, Modified).

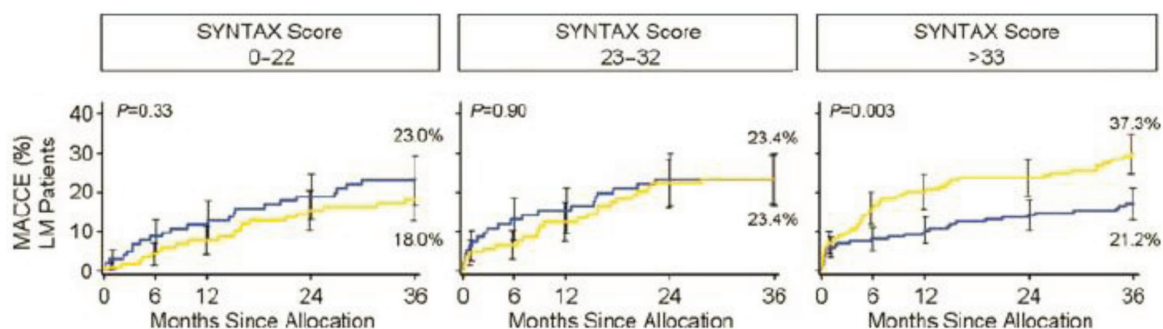


FIGURE 4. Major adverse cardiac and cerebrovascular event rates according to the subset, treatment group, and SYNTAX score category – 3 year follow-up of “SYNTAX trial”. Time-to-event curves in the coronary artery bypass grafting (blue line) or percutaneous coronary intervention (yellow line) overall cohorts to 3 years according to the low (0–22), intermediate (23–32), or high (≥ 33) SYNTAX scores. Major adverse cardiac and cerebrovascular events in patients with left main disease with low, intermediate, or high SYNTAX scores. P-value from log-rank test. (*Eur Heart J*, 2011. 32: 2125-2134, Modified).

Classes of Recommendations	Definition
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
<i>Class IIa</i>	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>
<i>Class IIb</i>	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.
Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

	Favours CABG	Favours PCI
Left main (isolated or 1VD, ostium/shaft)	I A	IIa B
Left main (isolated or 1VD, distal bifurcation)	I A	IIb B
Left main + 2VD or 3VD, SYNTAX score ≤ 32	I A	IIb B
Left main + 2VD or 3VD, SYNTAX score ≥ 33	I A	III B

FIGURE 5. ESC-EACTS guidelines. Indications for coronary bypass grafting vs. PCI in patients with lesions suitable for both procedures and low predicted surgical mortality.

concerning MACCE incidence. Additionally, more than 1/3 of the patients with LM disease seeking medical help are characterized unsuitable for PCI treatment from the beginning. This fact on its own indicates that CABG remains the best way to deal with complex coronary and LM disease. It is associated with a relatively low mortality and clearly lesser need for re-intervention. Should this rare necessity occur, reintervention is almost absolutely a safe PCI as opposed to surgical reintervention following PCI which is of a higher risk procedure.

On the other hand, interventional cardiologists still believe that PCI is a reliable solution for managing coronary disease even in some cases of LM disease. This opinion is based on the fact that PCI is not an inferior method compared to CABG when taking under consideration the overall mortality rates and MACCE incidences apart from repeat revascularization. Moreover the convenience of the method for the patient, the fewer days the patient has to stay in the hospital, the faster recovery and the ability to be performed on emergency basis are some arguments in favor of PCI with the use of DES, especially for elderly people (octogenarians) and patients with other co-morbidities and a high surgical risk (high EUROscore).

In addition, it should be emphasized that more complete information about the patient's clinical and angiographic profile and comorbidities is warranted, while the patient and family should also be fully informed about the available options and the associated procedural risks and benefits; finally, publication of procedure outcomes should be mandated for either team, as it is already done by the surgeons in several US states.

CONCLUSION

After taking all the above under consideration we can reach the conclusion that CABG remains the treatment of choice for patients with complex coronary disease (3VD patients with intermediate/high SYNTAX scores and LM patients with high scores) because they seem to have an increased risk of a MACCE event when treated with the PCI method. Patients with less complex coronary anatomy (low SYNTAX scores in 3VD patients or low/intermediate SYNTAX scores in LM patients) can be alternatively treated with PCI, but CABG remains the preferred treatment option in this last cohort of patients.

In closing we must say that the decision for the appropriate treatment for the patient should be the outcome of the close and impartial cooperation of interventional cardiologist and cardiac surgeon. The goal of this cooperation should be only the best interest of the patient and in cases of disagreement the patient himself should take the decision after being fully informed by the medical team.

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