

CABG, stents, or hybrid procedures for left main disease?

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- hybrid revascularisation
- left main disease
- stents

Abstract

Coronary artery bypass graft (CABG) surgery, including grafting of the left internal mammary artery (LIMA) to the left anterior descending artery (LAD) with additional vein or IMA grafts to other vessels, remains the standard technique for treatment of three-vessel coronary artery disease in patients with an intermediate or high SYNTAX score. Unprotected left main coronary disease is most often found in association with multivessel disease. In these patients, CABG has long been considered the gold standard for revascularisation. However, the evidence is being challenged by technological and procedural advances in percutaneous coronary intervention. Especially in patients with low to intermediate anatomic complexity of left main disease, PCI can be an effective and durable treatment option. Left main bifurcation lesions, however, remain a challenging subset for PCI due to possible plaque shift and occlusion of a major side branch. While there is general agreement that coronary bypass revascularisation using the LIMA to the LAD provides the best long-term prognostic benefit, a combination of CABG to the LAD and PCI of the remaining lesions, a hybrid approach, takes advantage of the survival benefit of the LIMA to LAD bypass, while minimising invasiveness and lowering morbidity by avoiding median sternotomy, rib retraction, aortic manipulation, and cardiopulmonary bypass. In particular, elderly patients with severe concomitant diseases may benefit from this approach by avoiding CPB.

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Introduction

The left main (LM) stem of the coronary tree is of vital importance to supply blood to the myocardium. The CASS trial¹ was the first study to show that LM disease is best treated with coronary artery bypass grafting (CABG) compared to medical treatment. Percutaneous coronary intervention (PCI) was introduced almost 15 years later than CABG. A complication of PCI for LM disease would lead to a major myocardial infarction and high death rate, as the left main coronary artery supplies 75% of the blood to the myocardium of the left ventricle and 100% in the case of left dominant type. The LIMA to LAD bypass shows excellent long-term patency in angiographic follow-up, reaching as high as 95% to 98% at 10 years².

The availability of drug-eluting stents (DES) led to a significant reduction in restenosis and target lesion revascularisation rate when compared to bare metal, and therefore PCI is increasingly considered as an alternative to CABG for patients with LM disease³.

For the first time in a randomised controlled trial, the SYNTAX trial randomised 705 patients with LM disease and followed these up to five years. SYNTAX is currently the largest randomised, controlled trial comparing PCI with CABG for LM disease. The overall results of SYNTAX showed that PCI with DES in a cohort of patients with three-vessel disease and LM disease was inferior to CABG. However, in the LM group major adverse cardiac or cerebrovascular events (MACCE) were not statistically significantly different, i.e., 36.9% in PCI and 31.0% in CABG patients (hazard ratio 1.23 [95% confidence interval, 0.95-1.59]; $p=0.12$)⁴. From the 705 LM patients, however, there were only 91 (13%) with isolated LM disease. The other patients had associated one- ($n=138$, 20%), two- ($n=218$, 31%) or three-vessel disease ($n=258$, 37%).

The SYNTAX study restricted further analysis beyond the primary endpoint, as many patients with left main stenosis also had three-vessel disease and the protocol stated that no subgroup analysis would be performed on groups of patients with LM and three-vessel disease if the null hypothesis could not be rejected. The performed analyses can only be considered observational and hypothesis-generating⁵. To be able to correct for the complexity of coronary lesions the SYNTAX score has been developed⁶.

The results of the SYNTAX study and a recent meta-analysis of 24 studies comparing DES versus CABG³ suggest that PCI can be an effective and durable treatment option in patients with low to intermediate anatomic complexity and that it is associated with a lower risk of stroke than CABG. In the most recent 2012 American College of Cardiology/American Heart Association guidelines, CABG is the only Class I recommendation for revascularisation to improve survival in LM disease, irrespective of coronary complexity. On the other hand, PCI has been upgraded to a Class IIa indication for patients with favourable anatomy (SYNTAX score <22 , ostial or trunk lesion) and who are at increased risk with CABG surgery due to comorbidities⁷. The 2014 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines on myocardial revascularisation consider the presence of an LM coronary lesion and a SYNTAX score ≤ 22 a class I indication

for PCI and CABG. For an LM lesion and a SYNTAX score 23-32, CABG has a class I and PCI has a IIa recommendation. In case of LM disease with a SYNTAX score >32 , PCI is not recommended (class III), while CABG has a class I recommendation⁸.

Left main bifurcation

Up to 80% of LM disease involves the bifurcation. PCI for unprotected distal left main bifurcation or trifurcation is a challenging percutaneous procedure and has worse long-term clinical outcome than the favourable results obtained with ostial or shaft left main lesions⁹. These lesions carry an increased risk for procedural complications (plaque shift, dissection, and side branch trapping), late in-stent restenosis, and thrombosis. In studies with more distal LM disease, higher rates of target vessel revascularisation have been reported³, and the optimal strategy for every anatomical subset has not yet been established⁸. Moreover, while there is no strong evidence to suggest that LM disease may safely be treated with PCI, there is even less proof concerning PCI for LM bifurcation lesions.

Another specific subset of patients which poses special challenges to PCI includes patients with heavily calcified LM disease, reduced left ventricular function, and LM bifurcation with an occluded right coronary artery⁸. Numerous clinical studies have also shown that diabetic patients with LM disease have accelerated restenosis, a need for repeat revascularisation, and an increased mortality at long-term follow-up when treated with PCI in comparison with CABG. The higher risk of restenosis in these patients is primarily due to an exaggerated intimal hyperplasia.

Hybrid coronary revascularisation

The feasibility of hybrid CABG followed by PCI has been re-established in several reports¹⁰⁻¹². This hybrid revascularisation strategy combines surgical and catheter-based procedures for the treatment of multivessel disease and aims to combine the advantages of the superior patency rates of the LIMA to LAD graft with those of PCI to non-LAD vessels. Both CABG and PCI have their specific advantages, which hybrid coronary revascularisation aims to combine in an attempt to provide a technique that is less invasive than conventional surgery without diminishing efficacy¹³.

The minimally invasive approach to coronary revascularisation seeks to eliminate cardiopulmonary bypass (CPB), sternotomy, or both. The techniques and incisions which are used range from LIMA bypass grafting via full sternotomy, and small anterior or lateral thoracotomy to completely endoscopic robotic double-vessel CABG. The avoidance of aortic manipulation and CPB reduces the incidence of adverse neurologic events, bleeding, infection, and pulmonary complications compared with conventional CABG¹⁴. This minimally invasive surgery is limited mostly to revascularisation of the LAD territory, as the circumflex and right coronary arteries (RCAs) are less accessible. These vessels can therefore be treated by PCI in single or multiple vessels. Fractional flow reserve-guided PCI may be used in hybrid revascularisation to avoid unnecessary stenting of lesions that are haemodynamically non-significant¹⁵.

Minimally invasive direct coronary artery bypass grafting (MIDCAB)

Hybrid revascularisation fostered a renewed interest in performing the LIMA to LAD graft through a small anterior or lateral thoracotomy incision through the fourth or fifth intercostal space. With this technique a special retractor is used to harvest the LIMA. MIDCAB has the advantage of not requiring any special endoscopic or robotic skills to harvest the LIMA. The LIMA to LAD graft is performed via a hand-sewn anastomosis on the beating heart. With the introduction of stabiliser technology, suturing to the beating heart became easier and more reproducible. MIDCAB is an attractive operation in experienced hands but single surgeon learning curves in the range of 100 cases are necessary to get this procedure to a reproducible and high-quality stage¹⁶.

A thoracoscopic endoscopic atraumatic CABG technique allows excellent visualisation and complete mobilisation of the LIMA. This technique requires one lung ventilation and chest cavity insufflation with carbon dioxide to allow exploration of the anterior mediastinum in which the LIMA lies. A hand-sewn anastomosis is performed through a non-rib-spreading thoracotomy using a soft-tissue retractor.

Robotic technology allows a shorter learning curve and quicker take-down of the LIMA. Single lung ventilation and chest cavity insufflation are also critical. After harvesting of the LIMA, a small anterior thoracotomy is used to perform a hand-sewn anastomosis on a beating heart. The LAD is stabilised with an endoscopic stabiliser delivered into the wound through the left arm port of the robot. A downside is that robotic technology is extremely expensive, being more expensive than classic CABG. Furthermore, the learning curve is long and only a few centres around the world use this technique.

Timing of the procedure

The best timing of the interventions of hybrid procedures remains a matter of debate. There are three strategies: 1) performing PCI first, followed later by minimally invasive LIMA to LAD bypass grafting, or 2) performing CABG first followed later by PCI (a benefit of using this sequence is that patency of the LIMA bypass can be verified with angiography at the time of PCI), or 3) combining LIMA to LAD bypass grafting and PCI in the same setting in a hybrid operating room. Again the additional benefit is that an intraoperative angiography is theoretically able to detect suboptimal anastomosis and bypasses to non-diseased vessels. In addition, it reduces discomfort for the patient, hospital stay, and costs. The major concern with this strategy is that dual antiplatelet therapy may increase postoperative bleeding. The antiplatelet strategy varies substantially among institutions performing hybrid revascularisation, and standardised guidelines have not been determined¹³. In some situations, it is preferable to perform the procedure in one stage, whereas in others a two-stage approach might be more appropriate. Staged procedures are always associated with time between both procedures, leaving patients incompletely revascularised and in theory at risk for cardiovascular events.

Discussion and future prospects

Results from recent studies suggest that PCI for unprotected LM disease is a reasonable treatment option, especially in patients with a low SYNTAX score and when comorbidities are present. However, in more complex disease, the best outcome is achieved with CABG. Second-generation stents with new stent platforms and superior polymer and drug coating have been shown to have increased benefits and may also result in better outcomes in more complex disease¹⁷. The results of the EXCEL and NOBLE trials, comparing the safety and efficacy of drug-eluting stents with CABG for patients with LM disease and a low or intermediate SYNTAX score, are therefore eagerly awaited^{3,18,19}.

There is general agreement that revascularisation using the LIMA to LAD provides a long-term prognostic benefit. Through its resistance to thrombosis and atherosclerosis, the LIMA has demonstrated excellent patency rates. The LIMA to LAD graft continues to have unrivalled safety and efficacy, even in the DES era. LIMA to LAD bypass grafting is more effective in preventing angina pectoris and further myocardial events in comparison with PCI. On the other hand, PCI of the right and circumflex coronary is reported to be less frequent in comparison with the LAD stenosis. These considerations suggest that a group of selected patients might benefit from a hybrid approach. Another advantage of hybrid revascularisation and performing CABG first followed later by PCI is that verification of patency of the LIMA bypass is enabled and PCI of the remaining lesions - especially left main stem/bifurcation stenosis - can be performed more safely under "protection" of the independently and adequately perfused anteroseptal wall. Recommendations on the optimal choice of hybrid revascularisation are based on expert opinion and supported by very few data that actually support one strategy over another.

Data regarding hybrid coronary revascularisation are limited¹². However, angiography in most studies does demonstrate that patency of minimally invasive LIMA-LAD compares favourably with conventional CABG¹⁴. No prospective randomised trials on hybrid coronary revascularisation have been published but case series suggest a faster recovery, with lower transfusion requirements and less in-hospital MACCE, than in patients treated by on-pump or off-pump CABG.

Further research with larger, multicentre, prospective, randomised trials with long-term clinical and angiographic follow-up and cost analysis comparing hybrid coronary revascularisation with both conventional on-pump and off-pump CABG or multivessel PCI will be necessary to evaluate further whether this hybrid approach is associated with similar promising long-term results. There are concerns that hybrid revascularisation will increase the cost of the procedure, as the incremental cost of two procedures, CABG and DES, will increase the financial burden. There are also unresolved logistical concerns relating to the order and staging of the two procedures, the dosage and timing of antiplatelet therapy¹³, and the physical location of the two procedures.

Patients of an advanced age or with comorbidities such as diabetes, major obesity, depressed pulmonary function, or a combination

of these conditions are the most likely to benefit from a hybrid approach. The more widespread availability of drug-eluting stents will increase the number of patients in whom a hybrid strategy can be proposed.

A hybrid strategy could be a reasonable alternative that offers the best of both the surgical and the interventional worlds. The evidence from a randomised trial, that hybrid revascularisation is safe and effective, is however lacking. The costs of hybrid revascularisation might be higher than off-pump CABG. Additional resources are needed for the construction of a cardiac hybrid operating room as well as training of personnel. An operational cardiac hybrid room requires a radiolucent operating table suitable for CABG and PCI, X-ray source and imaging camera equipment, surgical and interventional equipment, echocardiography

machine, equipment for continuous arterial monitoring and digital imaging, cardiac anaesthesia monitoring equipment, and a cardiopulmonary bypass pump. Construction of these rooms usually requires the conversion of at least two standard operating rooms²⁰. Until more evidence becomes available, the appropriate revascularisation strategy should be discussed within the Heart Team and the decision based on the comorbidities as well as the complexity of the coronary lesions²¹.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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The references can be found in the online version of the paper.

Online data supplement

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