Revascularisation for the proximal left anterior descending artery: special case or part of the package?

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After the left main, the most important coronary artery is the left anterior descending (LAD), because it subtends the greatest proportion of myocardium. Disease in its proximal part confers the highest risk of myocardial infarction, mortality, left ventricular impairment and ischaemic burden.[1] Therefore, revascularisation of this vessel may provide considerable benefits.

Coronary artery bypass grafting (CABG), including an arterial conduit anastomosed beyond the proximal (p)LAD lesion, diverts blood past the region of vulnerability and obstruction, at the expense of invasiveness and competitive flow through the diseased segment. The internal mammary (thoracic) artery graft is both effective and durable, being virtually immune to atheroma, contributing to excellent surgical outcomes for the last 30 years. The basic operation has therefore remained largely unchanged. The main problems in the longer term relate to premature deterioration in venous grafts, and progression of atheroma and comorbidities.

In contrast, percutaneous coronary intervention (PCI) restores vessel diameter and flow, at the expense of vascular trauma and leaving exposed any mild but potentially vulnerable disease. However, PCI techniques, adjunctive antithrombotic therapy and stents themselves have progressed enormously over the same period. First-generation stents were bare metal and associated with a high rate of restenosis. Second-generation drug-eluting stents had thick struts, thick polymer, a substantial drug load and an accompanying risk of stent thrombosis. But we now have third-generation stents, with thin struts, thin (often only abluminal) polymer and a limited dose of drug, usually of the 'limus' family, virtually eliminating restenosis. Adjunctive therapy has progressed from warfarin and dextran, through aspirin and ticlopidine, to aspirin and clopidogrel or potent $P2Y_{12}$ inhibitor, minimising the risk of thrombosis. In addition, an increasing awareness of the importance of adequate stent deployment, and the adoption of physiological assessment, intravascular imaging, lesion preparation and stent optimisation have made PCI capable and durable. This technological revolution in PCI poses a challenge for assessing historical studies comparing CABG and PCI.

An *isolated* single-vessel lesion in a patient presenting with an acute or chronic coronary syndrome is unusual. When present, it is usually accompanied by disease elsewhere, and the whole ischaemic picture has to be considered when it comes to revascularisation decisions. In the case of one-vessel or two-vessel disease, the majority of patients are treated with PCI, whether or not one of the lesions is located in the pLAD, bearing in mind the efficacy of stenting in the current era; but three-vessel disease, particularly that involving the left main or pLAD, generally stimulates a 'Heart Team' discussion about the relative merits of each form of revascularisation, and particularly an assessment of whether the patient fits the criteria of the 'PCI versus CABG' trials, which are largely based on multivessel disease. Of note, there is no large-scale trial of CABG versus PCI for isolated pLAD disease.[2]

One of the most influential trials in the modern era is the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) Study,[3] now augmented by the 'SYNTAXES' (extended survival) Study of the same patients out to 10 years.[4] In the original study, 1787 patients with de novo three-vessel and/or left main coronary artery disease were randomised to CABG or PCI with Taxus Express paclitaxel-eluting stents.

In this journal, Ono *et al* present a post hoc evaluation of the subset of patients from SYNTAXES whose pattern of disease did (or did not) include the pLAD, but not the left main, with mortality outcomes to 10 years and major adverse cardiac and cardiovascular events (MACCE) to 5 years.[5] There were 559 patients with multi-vessel disease including a pLAD lesion, of which 269 were treated with PCI and 290 with CABG. Five hundred and twenty-nine did not have a pLAD lesion, of which 274 were treated with PCI and 255 with CABG. There were two points of interest: first, any differences in outcomes between pLAD and non-pLAD patients as a whole; and second, any advantage of PCI over CABG, or vice versa, in each group.

The main finding was that 10-year all-cause mortality was identical in the pLAD and non-pLAD groups (24% for each); and even 5-year MACCE was very similar (29% vs 30%, respectively). In both pLAD and non-pLAD groups, mortality was higher after PCI than CABG (pLAD 29% vs 22%, p=0.06; and non-pLAD 29% vs 20%, p=0.03); and MACCE at 5 years was also higher, whether there was a pLAD lesion (42% vs 26%) or not (41% vs 28%).

This study appears to show that revascularisation of patients with a pLAD is not associated with any different results from those without. There are, however, some important limitations of this study. There were generic issues relevant to the original SYNTAX Study. First, this was a rarefied group of patients who were deemed to be suitable for either form of revascularisation. In the 'real world', most patients with MVD tend to fall into one or the other group; an excess of comorbidity or poor 'target' vessels predisposing to PCI, and an excess of complex lesions with good targets predisposing to CABG. Second, this is now an old study (recruitment 2005–2008). The PCI group is therefore disadvantaged, with a thick strut, thick polymer, stent with an old-fashioned drug (paclitaxel). Third, physiological guidance was not used and we know that many cases of visually apparent disease are actually physiologically non-significant. Fourth, the rate of complete revascularisation was disappointing in both PCI and CABG groups, being 50%–53% in the former and 56%–59% in the latter.

In addition, there were specific limitations imposed by a retrospective analysis. The location of a lesion in the pLAD was not prespecified, and therefore the findings are prone to bias. The large majority of patients in both pLAD and non-pLAD groups had triple vessel disease (95% vs 98%, respectively), but there were some potentially important differences; for pLAD versus non-pLAD, respectively, the SYNTAX score was 30 vs 24, the proportion in the lowest SYNTAX tertile was 21% vs 45%, the proportion in the highest tertile was 39% vs 19% (though this was partly a tautological reflection of the pLAD lesion itself), there was a

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previous myocardial infarction in 34% vs 40%, and there was an important bifurcation in 78% vs 71%.

Setting aside the methodological and statistical conundrums, why might there be no difference in mortality if a lesion involves the pLAD or not? First, mortality is not simply a function of a lesion in a particular location in one vessel in a patient with multivessel coronary disease. Second, both modalities, performed in optimal fashion, in a trial setting, would be expected to give excellent results. Third, the difference between proximal and non-proximal LAD depended on whether the lesion was before or after the first septal. In reality, that is a small difference. It is unlikely that the lesions were extremely distal, implying that the difference in the volume of 'protected' myocardium (on the one hand) and residual vulnerable atheroma (on the other) was particularly different. The findings accord with the accepted wisdom that a tight proximal stenosis in a proximal(ish) LAD with a good target will have an excellent outlook following internal mammary artery grafting or stenting.

The superiority in clinical outcomes for CABG versus PCI, whether involving pLAD or not, arose from an aggregate of a marginally statistically significant surfeit of all-cause mortality, and an excess of non-fatal myocardial infarction and repeat revascularisation. This mirrors the findings of the original SYNTAX Study. An excess PCI-related mortality is a potential concern, although only half of the total was contributed by cardiac causes. A relevant factor may be that the mean number of stents was five in both groups, and the mean stent length was >90 (SD >60–>120) mm. Considering the limitations of the Taxus stent outlined above, this could be regarded as excessive compared with 'real-world' contemporary practice.

Where does this leave us? The lack of difference in outcome after revascularisation between patients with and without a pLAD proximal goes some way to resolve a long-held belief that CABG is superior to PCI for patients with a lesion at this location. However, this was a trial of *treatment for* that condition, not of the *natural history of untreated pLAD disease*, and it is important not to conflate those two conditions. Furthermore, in 'real-world' practice, very few patients with a pLAD lesion evince true clinical equipoise for both revascularisation strategies. For them, with a variety of symptoms, diffuseness of disease, quality of distal vessels, degree of left ventricular impairment, diabetic status and comorbid burden, the pLAD lesion will be just one small factor in the 'Heart Team' discussion (see figure 1). A personalised approach is appropriate, and the data from this study contribute to that process.

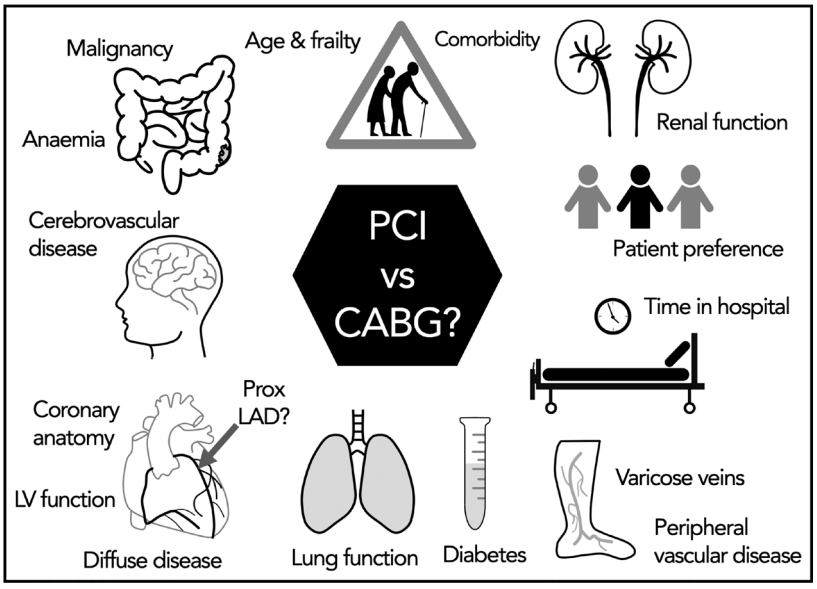

Figure 1 The factors to be considered when deciding on the mode of coronary revascularisation. The location of a lesion in the pLAD is only one of several important clinical factors which may influence the success of the procedure and the chances of a sustained result. Image used with permission, courtesy of Dr Paul Morris. CABG, coronary artery bypass grafting; LAD, left anterior descending; LV, left ventricular; PCI, percutaneous coronary intervention; pLAD, proximal LAD.

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