Does prior PCI increase the risk of subsequent CABG?

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This editorial refers to ‘Impact of previous percutaneous transluminal coronary angioplasty and/or stenting revascularization on outcomes after surgical revascularization: insights from the imagine study’ by S. Chocron et al.,† on page 673

Chocron and colleagues have reported that prior percutaneous coronary intervention (PCI) leads to a worse outcome in patients subsequently undergoing coronary artery bypass graft (CABG). In view of the fact that around one-third of patients with multivessel disease treated with bare metal stents will require re-intervention within a few years, this conclusion is potentially worrying and raises several questions. (i) Is the conclusion justifiable? (ii) Are the findings consistent with other studies in the literature? (iii) If real, what are the likely pathological mechanisms? (iv) Will the findings be different drug-eluting stents? (v) What are the clinical implications for patients and the economic implications for health services?

Is the conclusion justifiable?

The obvious weakness of the study of Chocron et al. is that it is a re-analysis of the primary end-point of the IMAGINE trial according to whether the patients had undergone PCI prior to CABG, a question which the IMAGINE trial was not designed to answer. Rather, IMAGINE was a randomized trial of the angiotensin-converting enzyme (ACE) inhibitor quinapril in 2553 subjects with preserved left ventricular function after CABG, which concluded that there was no difference in time to occurrence of the primary end-point (a composite of cardiovascular death, readmission for unstable angina requiring hospitalization, documented angina not requiring hospitalization, stroke, or congestive heart failure requiring hospitalization) in the active or placebo group. Re-emphasizing that IMAGINE was not actually designed to investigate the effects of prior PCI, the two groups were otherwise relatively similar. Although the 455 patients in the prior PCI group had a higher incidence of previous myocardial infarction, the overall ejection fraction was similar to that in the 2098 patients in the non-PCI group who also had a higher incidence of left main stem stenosis and multivessel disease. In the current analysis, there was a significant increase in the primary end-point in the prior PCI group [hazards ratio (HR) = 1.64, 95% confidence interval (CI) (1.28–2.11) P < 0.0001]. In this group, an increase in the risk of death after CABG just failed to reach statistical significance [adjusted HR = 2.04; 95% CI (0.94–4.46)] but the adjusted HRs for unstable angina requiring hospitalization [HR = 2.43 (1.54–3.83), P = 0.0001] and repeat coronary revascularization [HR = 1.85 (1.17–2.90), P = 0.008] were significantly increased. The authors point out that their findings cannot be explained by more advanced disease or less complete appropriate revascularization in the PCI group.

Are the findings consistent with other studies in the literature?

Other studies have previously reported a worse outcome in prior PCI patients undergoing non-cardiac surgery, but more recently two other large studies addressing precisely the same question as Chocron and colleagues have reached the same conclusions. Hassan et al. compared outcome after CABG in 919 patients with and 5113 without prior PCI. Although the prior PCI group had less severe coronary artery disease and less co-morbidity, multivariate analyses identified prior PCI as an independent predictor of hospital mortality (HR 1.93; P = 0.003). In two groups of 919 propensity-matched patients, the in-hospital mortality was 3.6% in the prior vs. 1.7% in the non-prior PCI group (P = 0.01).

Thielmann and colleagues investigated outcome in 2626 consecutive patients undergoing first time CABG without prior PCI in comparison with 360 after a single and 289 patients with multiple prior PCI. Using risk-adjusted multivariate logistic regression analysis they reported that multiple prior PCI were associated with increased in-hospital mortality [HR = 2.24 (95% CI 1.52–3.21); P < 0.001] and the risk of major adverse cardiovascular events.

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events \( [HR = 2.28; (95\% CI 1.38–3.59); P < 0.001] \). In a subsequent propensity-matched group based on 13 pre-operative risk factors, logistic regression analysis again confirmed multiple prior PCIs to be associated with increased in-hospital mortality \( (HR = 3.01; P < 0.01) \) and major adverse cardiovascular events \( (HR = 2.31; P < 0.01) \). In a subset of 621 of the same group of patients with diabetes there were almost identical findings.7

If real, what are the likely pathophysiological mechanisms?

An explanation for why prior PCI should increase the risk of subsequent CABG is not immediately apparent. Obvious explanations such as differences in age, gender, ventricular function, extent of coronary artery or other vascular disease (often less severe in the prior PCI group), or completeness of appropriate revascularization are not supported by the data.

While the prior PCI group often present with more unstable symptoms, as in the study of Chocron and colleagues,1 it is not clear from the literature whether the ‘new culprit’ lesion is related to the previous PCI or de novo remote disease. Other possibilities might be that prior stents encourage more distal bypass grafting with less favourable graft run off, or may compromise collateral blood flow.8 While it is well recognized that drug-eluting stents (DES) cause dysfunction of the endothelium both overlying the stent and further downstream,9 is it possible that bare metal stents (BMS) also compromise endothelial function overlying the stent which is exaggerated by changes in the inflammatory and coagulation status precipitated by cardiac operations?

Will the findings be different with drug-eluting stents?

A potential criticism of the studies by Chocron, Hassan, and Thielmann is that PCI may have been suboptimal as there was a relatively low use of DES in comparison with BMS. However, as several meta-analyses have consistently demonstrated that while DES reduce the risk of restenosis in low-risk coronary lesions they do not reduce the risk of mortality or subsequent myocardial infarction,10 it is counter-intuitive to believe that they will improve results post-CABG.

There is a further concern with DES: the FDA have warned that their use is ‘associated with increased risks of both early and late stent thrombosis, as well as death and myocardial infarction’,11 DES impair endothelialization, leaving a potentially prothrombotic substrate within the vessel,12 and leave a further conundrum for the surgeon in terms of control of antiplatelet medication and whether to perform bypass grafts to a coronary vessel with a DES without critical restenosis in patients who have multivessel disease. These clinical concerns are compounded by cost implications; not only are DES significantly more expensive than BMS, but new recommendations that patients remain on clopidogrel for at least a year, and possibly indefinitely, add significantly to overall costs.

What are the clinical implications for patients and the economic implications for health services?

In economic terms there is already strong evidence that stenting in multivessel coronary artery disease is not a cost-effective treatment;13 and the studies of Chocron and others will add to these concerns. However, the major implication of the finding that prior PCI increases the risk of subsequent CABG is to add ammunition against the spurious belief that CABG can always be safely deferred in favour of an initial strategy of PCI in multivessel disease, where several large registries already show a consistent survival advantage for CABG over PCI in propensity-matched patients.2,10 These dual observations should be carefully considered in patients with multivessel disease who are likely eventually to require CABG, and underline the importance of the proposed interventions being discussed by a multidisciplinary team including a surgeon rather than by the individual cardiologist.10,14

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References


CLINICAL VIGNETTE

Post-traumatic ventricular septal defect
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A 20-year-old male was admitted to the emergency department with a stab wound in his chest in the cardiac region. Given the haemodynamic instability and suspected cardiac tamponade, urgent thoracotomy was performed with drainage of haemopericardium and cardiac surgery was performed immediately, during which right ventricular free wall laceration was sutured under extracorporeal circulation (Panel A). Before discharge, the patient underwent routine transthoracic echocardiography that revealed defect in the distal third of the interventricular septum, with sharply demarcated edges, 4–5 mm wide, and left to right shunt flow (Panel B). These findings were confirmed by magnetic resonance imaging (MRI) (Panel C and D). Given the asymptomatic course of the patient and size of the shunt, which has been assessed as non-significant (Qp/Qs = 1.4/1, according to MRI), a conservative approach was proposed with the possibility of a future catheter-based treatment. At the 3-month follow-up the patient was asymptomatic.

Panel A. Suture of right ventricular free wall.
Panel B. Transthoracic echocardiography. Apical four-chamber view. Left to right shunt in the distal third of the interventricular septum (white arrow).
Panel C. Magnetic resonance imaging in the short axis showing the ventricular septal defect (white arrow).
Panel D. Magnetic resonance imaging in the long axis showing the ventricular septal defect with shunt flow (white arrow).