

Physiological stenosis assessment for coronary artery surgery: quo vadis?

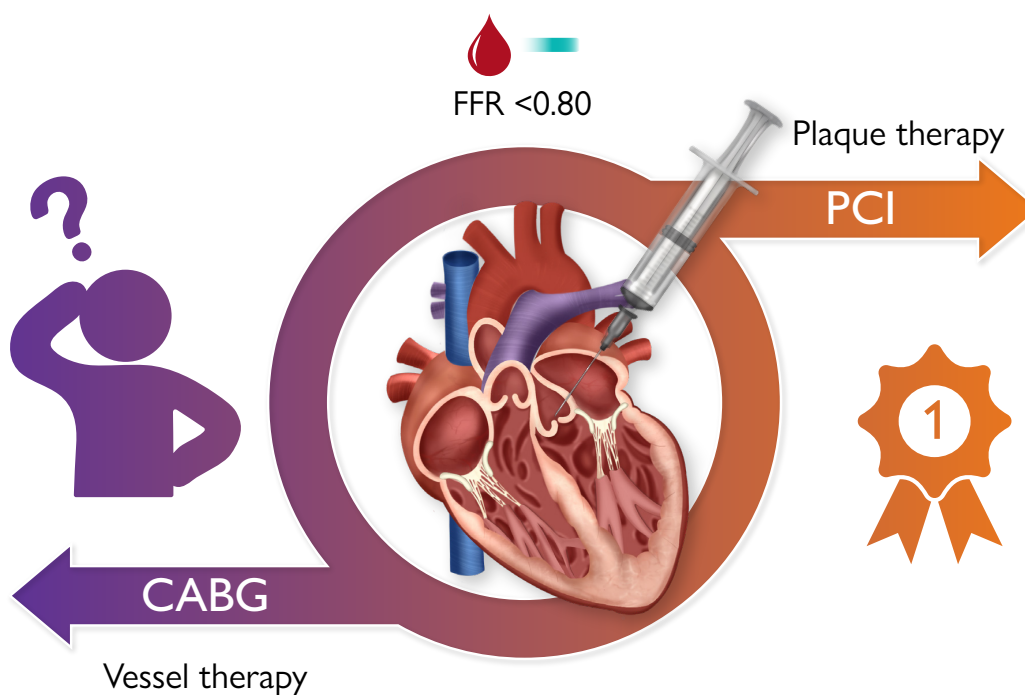
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This editorial refers to ‘Coronary artery bypass grafting with or without preoperative physiological stenosis assessment: a SWEDEHEART study’, by E.C. Hansson *et al.*, <https://doi.org/10.1093/eurheartj/ehaf327>.

Graphical Abstract

Physiological stenosis assessment: CABG vs PCI



The opinions expressed in this article are not necessarily those of the Editors of the *European Heart Journal* or of the European Society of Cardiology.

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'The only true wisdom is in knowing that you know nothing.' Socrates

Debate over whether coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is the best modality to treat patients with stable coronary artery disease (CAD) has divided the cardiovascular community for almost 50 years. During this period, ~20 randomized controlled trials have established that the two treatment modalities are complementary, with distinct mechanisms of action and, for best outcomes, are indicated in patients with different demographics, acuity, and extent of CAD.

Percutaneous coronary intervention addresses haemodynamically significant coronary lesions that are responsible for ischaemic symptoms. Importantly, in patients with stable CAD, these lesions become flow limiting only at times of increased myocardial blood flow demand typically occurring with physical activity. Hence, treating these lesions with PCI resolves ischaemic symptoms but does not improve patient survival or the risk of future myocardial infarction (MI) compared with optimal medical therapy.¹⁻⁴ Given this therapeutic mechanism of PCI, physiological assessment of the lesions to undergo PCI makes logical sense as treatment of those lesions that are not haemodynamically significant, either at rest or at times of peak myocardial oxygen demand, provides no patient benefit and indeed has been shown to cause harm.⁵

Coronary artery bypass grafting, on the other hand, is a treatment modality whereby the bypass grafts not only mitigate symptoms due to flow-limiting lesions at peak myocardial oxygen demand, but also because placement of the distal coronary anastomoses downstream from haemodynamically significant lesions palliates any potential adverse clinical events from non-haemodynamically significant plaques that may become unstable in the future, leading to an acute MI. This CABG therapeutic effect has been termed more appropriately 'collateralization' rather than 'revascularization'.⁶

Given this fundamental distinction between PCI and CABG, the role and value of physiological assessment of coronary lesions in patients undergoing CABG are much less intuitively obvious and, more importantly, remain undefined by the available literature. Only small low-quality studies, probably underpowered to draw meaningful conclusions and with conflicting results, have been published.⁷⁻¹⁰ Yet, despite these limitations, there are ongoing efforts to extend physiological assessment of lesions to drive graft deployment.

What is clear from the literature on physiological stenosis assessment in CABG patients is that fractional flow reserve (FFR) downstages the severity of coronary lesions and results in a lower number of grafts.⁷⁻⁹ Given the protective effects of coronary grafts on future plaque instability, a strong argument might be made that deferring placement of a graft may be injurious. Indeed, it is well recognized that haemodynamically significant lesions cause angina in patients with stable CAD, but they infrequently cause an MI and subsequent death, due to plaque instability and rupture.⁶ The culprit lesion resulting in MI is typically <50% and located in the proximal segment of a coronary artery.¹¹

Measurement of FFR in CABG may be helpful in choosing venous vs. arterial grafts, although even this is unclear as the hypothesized underlying mechanism behind the lower arterial vs. venous graft patency in targets with an FFR-negative lesion is competitive flow.¹² This premise is based on the unproven hypothesis that the flow in the target vessel overwhelms the flow in venous grafts, leading to sluggish flow, and eventual graft failure due to graft thrombosis. Arterial grafts with more robust medial smooth muscle develop a string sign driven by accommodating to downstream flow demands which are minimized due to high flow in the target vessel. Yet the distribution of flow through the native coronary target vs. the graft is also likely to be affected by a

complex interplay between target vessel stenosis, size of the graft and size of the target vessel. Some have argued that the minimal luminal diameter of the native vessel at the site of the most severe stenosis compared with the size of the graft is more important to the durability of the graft than its haemodynamic significance. As we continue to debate and ascertain whether the documented value of physiological stenosis assessment in PCI can be extended to CABG, it is essential to remember that lesions that are commonly classified as haemodynamically significant by physiological criteria are only flow limiting with maximal hyperaemia but with no decrement in flow at rest or a mild increase in coronary flow demand. Hence, almost all lesions bypassed or stented do not cause ischaemia at rest in patients with stable CAD. Therefore, all coronary grafts, whether arterial or venous, are subject to competitive flow under rest conditions. As such, additional elements such as pressure drop across lesions under maximal hyperaemia may be important to graft durability.

Hansson and colleagues¹³ must be applauded for their attempt to clarify the value of physiological assessment of coronary lesions in patients undergoing CABG in their study published in this issue of the *European Heart Journal*. They leveraged the SWEDEHEART registry with linkage to national administrative databases for long-term outcomes. Their large study group of 2869 CABG patients, by far the largest ever studied, underwent pre-operative assessment of the physiological significance of lesions identified on coronary angiography. Compared with 15 342 patients without physiological assessment, the CABG patients with flow assessment had fewer grafts placed, corroborating previous reports.^{7,8,10} At an average of 3.6 years follow-up, there were no differences in the risk-adjusted composite endpoint of mortality, stroke, or MI. The rate of repeat angiography and repeat revascularization at >2 years post-operatively was higher in the flow assessment group which also had fewer grafts. Their study reflects the investigators' well thought out and valiant efforts to clarify the murky waters surrounding the value of physiological stenosis assessment in CABG patients. Despite these ambitious efforts and innovative strategies for database linkage to flow assessment, the value of physiological assessment of lesions in CABG remains as unclear as ever. Indeed, the results of this study lead to more questions than they answer, and all conclusions must be interpreted with caution when administrative databases are used in clinical research. Perhaps the biggest Achilles' heel of this analysis is the underlying assumed premise that surgeons fully incorporated the flow assessment data into their grafting strategy and placed grafts only to haemodynamically significant lesions in the flow assessment group. The authors state that the final decision regarding the grafting strategy was left to the discretion of the operating surgeon. This is a significant limitation as there is no consistent practice pattern regarding this *modus operandi* among the surgical community. Moreover, there are no data on the location of lesions physiologically assessed, the size of the target vessels, the overall complexity of coronary disease (Syntax Score), the amount of myocardium at ischaemic risk, the per patient percentage of lesions with physiological stenosis assessment, and whether the repeat revascularization was driven by graft failure or progression of disease in target vessels that were not revascularized at the index CABG. Although these limitations are acknowledged by the authors in the manuscript, these issues make reaching any definite conclusions nearly impossible.

Although there are no data on the complexity of CAD in either group, one can assume that the physiological stenosis assessment group, by virtue of lower graft number, was incompletely revascularized as per the normal angiographic criteria, a situation well documented to be associated with adverse outcomes. Hence it should not be surprising that

this group had higher reimaging and repeat revascularization rates. Although causality is impossible to ascertain in a retrospective study, one may consider that this repeat revascularization rate contributed to the equivalent clinical outcomes. The mediation analysis confirmed that the increased reimaging rate was driven by the lower number of grafts. This becomes an important consideration, given the previously reported observation that non-FFR-positive targets that were not grafted showed an appreciable progression rate within 6 months of surgery.⁸

Physiological assessment of lesions allows us to more rigorously define the severity of an angiographically documented lesion. Yet one should question its relevance to patient prognosis given the observation that clinical outcomes in patients with stable CAD are not driven by the severity of coronary stenosis but rather by the total atherosclerotic burden affecting the coronary circulation.¹⁴

The future role of physiological stenosis assessment in CABG will probably be impacted by novel non-invasive imaging modalities such as photon counting coronary computed tomography angiography (CTA). The information provided by coronary CTA which includes CT FFR, delta FFR, plaque characterization, and total plaque burden will be likely to further our understanding of CAD far beyond what coronary angiography has been able to provide. These imaging advancements will probably make traditional invasive determination of flow assessment less, if at all, relevant.

The current study adds further weight to the perspective that the efficacy of flow assessment of lesions in PCI cannot and should not be extrapolated to CABG given the very different therapeutic mechanisms of action of these interventions (*Graphical Abstract*). What was once a simple static plumbing problem for coronary surgeons, has become remarkably more complex with our evolving understanding of the dynamic interplay of coronary physiology and anatomy guiding CABG. We need a lot more knowledge regarding the very basic tenants of CABG on the optimal number and location of coronary grafts to maximize the effectiveness of surgical revascularization. Invasive physiological assessment of coronary lesions in its present form will be unlikely to add to this goal.

Declarations

Disclosure of Interest

All authors declare no disclosure of interest for this contribution.

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