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Ischaemic and viability testing for guiding PCI are overrated: pros and cons

Margaret B. McEntegart[1]*, MD, PhD; Anja Oksnes[2], MD; Xavier Carrillo[3], MD, PhD; **Victoria Delgado**[3,4]**, MD, PhD

**Corresponding author: Columbia University Irving Medical Center, 630 West 168th Street, New York, NY, 10032, USA. E-mail: mbm2179@cumc.columbia.edu*

***Corresponding author: Heart Institute, Hospital University Germans Trias i Pujol, Carretera de Canyet s/n, 08916, Badalona, Barcelona, Spain. E-mail: videlga@gmail.com*

The authors' affiliations can be found at the end of this article.

Introduction

Over the years, establishing indications and appropriate candidates for percutaneous coronary intervention (PCI) has been a subject of investigation, with the concepts of "ischaemia" and "viability" playing important roles. Ischaemia, caused by a mismatch between myocardial oxygen demand and supply, has long been a pillar of decision-making in the field of interventional cardiology. Similarly, viability – based on the theory of hibernating myocardium – has been considered a key criterion to avoid futile PCI procedures. However, the main findings and subanalyses of randomised trials that have been published over the last few years have significantly challenged the usefulness of ischaemia and viability testing for guiding PCI. In light of current evidence, whether ischaemia and viability testing maintain an important role, or are limited to selected patients or scenarios, is an area of uncertainty.

Pros

Margaret B. McEntegart, MD, PhD; Anja Oksnes, MD

The concept that ischaemic and viability testing should guide percutaneous coronary intervention has been firmly ingrained in cardiology practice. However, the recent challenge to this paradigm by the ISCHEMIA and REVIVED-BCIS2 trials prompts the need to reconsider the appropriateness of this approach.

The ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial[1], which compared medical therapy to an invasive approach in stable patients with moderate or severe ischaemia, found that severity of coronary artery disease (CAD), but not severity of ischaemia, was associated with 4-year mortality. In addition, while ischaemia severity did not identify a subgroup with treatment benefit, a benefit was seen for cardiovascular death or myocardial infarction in patients with the most severe CAD. The conclusion that assessment of anatomical CAD severity was superior to ischaemia testing is consistent with decades of revascularisation trials demonstrating that CAD severity predicts clinical outcomes.

This finding aligns with previous observations from the STICH (Surgical Treatment for Ischemic Heart Failure) trial's[2] *post hoc* analysis, which found that the presence or extent of ischaemia was not associated with 10-year mortality and that there was no interaction with the trend towards reduced mortality with coronary artery bypass grafting (CABG). Furthermore, a *post hoc* analysis from the COURAGE trial[3] also found that the extent of ischaemia did not predict adverse events or the treatment effectiveness of PCI at 5 years.

It is interesting to consider that while non-invasive ischaemic testing does not predict outcomes following PCI, invasive assessment with coronary physiology has been shown to do so in several trials. This highlights the limitation of non-vessel, non-lesion specific, non-invasive testing and raises the question whether this can be overcome by non-invasive coronary computed tomography angiography and angiography-derived coronary physiology.

In ischaemic cardiomyopathy, the concept that revascularisation should be guided by viability is based on

historical observational data. This was initially challenged by the STICH viability substudy[4], which found no association between viability and mortality and no interaction with the benefit from CABG at 10 years. The more recent REVIVED-BCIS2 trial[5] also found that the extent of viable myocardium was not associated with death or heart failure hospitalisation and that there was no interaction with the effect of PCI at 3.4 years. Whether these findings challenge the theory of hibernating myocardium, illustrate the futility of PCI in stable patients treated with contemporary medical and device therapy, or reflect the limitations of the imaging modalities, viability testing cannot be reliably used to guide PCI.

In conclusion, while ischaemia and viability may still be relevant, current non-invasive testing is inadequate to guide PCI. The evidence consistently and robustly supports the use of coronary anatomy and physiology to guide revascularisation.

Conflict of interest statement

M. McEntegart is a consultant for Boston Scientific, Shockwave Medical, and Teleflex. A. Oknes is a consultant for Boston Scientific.

Cons

Victoria Delgado, MD, PhD; Xavier Carrillo, MD, PhD

Myocardial ischaemia is caused by a mismatch between the oxygen supply and demand of the myocardium, whereas myocardial viability relates to the presence of dysfunctional myocardium that has the potential to recover once the myocardial oxygen supply is restored. In general, both myocardial ischaemia and viability are evaluated when there is coronary artery stenosis that may be revascularised with PCI or surgical CABG. Various functional non-invasive imaging tests can be used to assess different aspects of the ischaemic and viable myocardium **(Table 1)**. The sensitivity and specificity of each imaging modality to detect ischaemia depend on various factors (coronary artery lesion complexity, plaque burden, etc.)[6]. To detect myocardial viability, imaging techniques that assess myocardial perfusion and metabolism are usually the most sensitive, while those evaluating the contractile reserve are the most specific[7]. While the use of non-invasive imaging techniques to detect the presence of myocardial ischaemia prior to revascularisation is well established, the assessment of myocardial viability prior to revascularisation remains controversial.

In patients with stable CAD, recent clinical studies have questioned the role of non-invasive imaging testing to assess myocardial ischaemia[8,9]. The ORBITA trial demonstrated that PCI was not superior to guideline-directed medical therapy (GDMT) in preventing major adverse cardiovascular events (MACE)[8]. However, among patients who had severe myocardial ischaemia, based on stress echocardiography, those treated with PCI had fewer MACE at follow-up as compared to patients under GDMT. In the ISCHEMIA trial, which included 5,159 patients with moderate to severe ischaemia based on an imaging stress test, who were randomised to PCI+GDMT versus GDMT alone, there were no differences in the combined MACE endpoint after 3.3 years of follow-up[9]. However, patients allocated to the PCI+GDMT arm had better control of angina symptoms as compared to those treated with GDMT alone. Subsequent subanalyses have shown that myocardial ischaemia was a weak predictor of left main CAD and was not associated with the severity of the non-obstructive CAD. These results led to the misleading interpretation that non-invasive myocardial ischaemia detection was not needed to indicate PCI, instead of concluding that myocardial ischaemia is multifactorial and that PCI does not treat all those factors (e.g., burden of atherosclerosis, microvascular dysfunction, etc.).

Table 1. Non-invasive imaging tests to assess myocardial ischaemia and viability

Myocardial characteristics	Non-invasive imaging techniques
Myocardial perfusion	Myocardial contrast stress echocardiography Single-photon emission computed tomography Positron emission tomography Stress cardiac magnetic resonance Stress cardiac computed tomography
Coronary flow reserve	Stress echocardiography with interrogation of the epicardial coronary arterial flow Positron emission tomography
Contractile reserve	Dobutamine stress echocardiography
Cellular metabolism and integrity of cellular membrane	Single-photon emission computed tomography Positron emission tomography
Myocardial scar	Single-photon emission computed tomography Positron emission tomography Late gadolinium-enhanced cardiac magnetic resonance

In patients with ischaemic heart failure and CAD who are amenable for revascularisation, assessment of myocardial viability has been used to identify patients whose left ventricular systolic function and clinical outcome would improve, in order to justify the increased risk of the intervention. However, subsequent randomised clinical trials have questioned the role of non-invasive imaging to assess myocardial viability[7]. The recent REVIVED-BCIS2 trial demonstrated that PCI+GDMT did not result in a lower incidence of MACE in patients with a left ventricular ejection fraction <35% and myocardial viability assessed with cardiac magnetic resonance (CMR), compared to patients treated with GDMT alone[10]. Other factors influencing the potential functional recovery of the myocardium may have had an impact on the results of this and previous trials[7]. The use of CMR to assess myocardial viability based on the location and extent of late gadolinium enhancement makes it possible to identify other aetiologies of myocardial scar/fibrosis, such as inflammatory and infiltrative diseases, for which the revascularisation benefits are unknown. PCI is a less invasive procedure than surgical CABG, and it may be difficult to

deny PCI to patients with ischaemic heart failure based on the non-invasive imaging results. However, having myocardial viability information upfront may help to partially understand the potential lack of functional recovery after PCI.

In summary, myocardial ischaemia and viability testing is not overrated when guiding PCI.

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Authors' affiliations

1. Columbia University Irving Medical Center, New York, NY, USA; 2. Haukeland University Hospital, Bergen, Norway; 3. Heart Institute, Germans Trias i Pujol University Hospital, Badalona, Spain; 4. Centre of Comparative Medicine and Bioimaging, Badalona, Spain

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