

Intracoronary imaging: routine precision or reserve for complexity?

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The utility of intracoronary imaging (ICI) to overcome the limitations of angiography in assessing lesion morphology and vessel geometry in percutaneous coronary intervention (PCI) has been studied in numerous trials¹. The accumulated totality of evidence very recently prompted the European Society of Cardiology (ESC) to raise the level of recommendation for ICI-guided PCI to Class 1, Level of Evidence A². Hooray, at long last the uplift we had all been waiting for! However, lost among the celebration is the disclaimer that the recommendation is for complex lesions, in particular left main stem, true bifurcations and long lesions. Should ICI be universally used in PCI, or in selected patients/lesions? Which factors determine the utility of ICI? What makes a lesion complex? Is it the lesion or the patient?

In this issue of EuroIntervention, Lee et al seek to answer some of these outstanding questions³. Combining data from the RENOVATE-COMPLEX-PCI randomised trial (n=1,639) and a registry from a single institution (n=2,972), the authors use a score that integrates nine factors of lesion complexity. Their analysis determines a complexity score ≥ 3 to independently predict target vessel failure (TVF). Using this threshold to dichotomise lesions, they show that ICI confers a larger relative and absolute reduction in TVF, compared with angiography, with increasing complexity. The authors suggest that ICI in lesions with a complexity score ≥ 3 maximises clinical impact, perhaps in the most cost-effective manner, compared to angiography³. The message is clear, simple and believable – the more complex the lesion becomes, the higher the risk of stent failure.

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But is it the chicken or the egg? Patients with complexity scores ≥ 3 were older, presented with more acute coronary syndrome (ACS), were more likely to be diabetic, hypertensive, have a history of stroke, peripheral vascular disease, and had lower ejection fractions. When the individual components of

the TVF endpoint are broken down, the differences are largely driven in number and magnitude by cardiac death, suggesting that complexity scores ≥ 3 were in sicker patients, who were more likely to die. When the results are adjusted for these potential confounders, there is no significant interaction for a reduction in relative risk for any endpoint, including TVF, suggesting that the beneficial effects of ICI actually extend to all patients with complex lesions. So, the more complex the patients, the more complex the lesions, the higher the absolute risk of stent failure.

Separating patient complexity from lesion complexity is challenging. Whilst the rationale for selecting the particular factors of complexity in the current analysis was not specified, it may be gleaned from the available ICI data. Less clear, however, is whether these rather disparate factors – which include lesion location, number of coronary arteries, lesion-specific characteristics such as length or calcification, and in-stent restenosis – would have a meaningful additive effect in all the possible combinations. This issue arises from collating heterogeneous factors with differing mechanistic effects on TVF, e.g., compromise of a side branch in bifurcation lesions versus impact of calcification on stent expansion. Moreover, equal weight has been assumed for each factor without *a priori* prospective determination of their correlation coefficient with TVF despite very clear differences in relative risk amongst the different subgroups in RENOVATE-COMPLEX-PCI⁴. Therefore, it is unclear whether a score of two that is calculated for PCI on simple lesions in two vessels needing a total of three stents is equivalent to the same score for PCI on a bifurcation stenosis in the distal left main artery, or for PCI on a severely calcified aorto-ostial lesion. Likely not.

The authors highlight the differences in their findings with the ILUMIEN IV trial⁵. In the latter trial, the limitation of optical coherence tomography (OCT), which requires blood clearance, led to the exclusion of aorto-ostial and left main coronary lesions, whereas in RENOVATE-COMPLEX-PCI,

these lesions are those in which ICI guidance provided the greatest relative benefit⁴. The inclusion of ACS and diabetic patients in the ILUMIEN IV trial was based on the traditionally higher TVF rates in these conditions⁵. Why? True culprit lesions in ACS are not always decipherable on angiography or ICI, nor can the true vessel dimensions in these often spasmic coronary arteries be determined⁶. While we are accustomed to coronary lesions in patients with diabetes mellitus (DM) being calcified and diffuse, advances in medical management may have hampered the accelerated *de novo*- and neo-atherosclerosis that contribute to lesion complexity⁶. Indeed, when we removed isolated patient risk of ACS or DM from ILUMIEN IV, but maintained lesion risk including ACS and DM, there was a strong benefit for ICI-guided PCI on the hard endpoints of cardiac death, target vessel myocardial infarction or stent thrombosis⁷. On the contrary, a recent randomised trial of PCI in diabetic patients with ACS showed a clear benefit for ICI versus angiography in reducing TVF⁸. Is it the chicken or the egg?

There are inherent limitations of this retrospective *post hoc* non-prespecified analysis, some of which have been rightfully described in the article³, the most glaring being the combining of randomised data with registry data from different eras. Advances in stent design, iterations in adjunctive interventional tools, differences in interventional techniques and the lack of a standardised approach in using ICI to optimise PCI between the two study periods are major limitations, despite sensitivity analyses suggesting similar benefits within the registry and randomised cohorts. Why did the authors pool the data? To increase the sample size, of course. To this avail, would further increasing the sample size not accentuate the beneficial effect of differences seen with even one complex lesion feature?

The lesion complexity score is a useful proof of principle, showing that ICI impacts TVF rates in a continuum³. This lesion-centric score, however, cannot be used practically to select patients/lesions for ICI. ICI is a strategy of assessing the whole vessel anatomy and lesion characteristics within a workflow that, we recommend, should include pre- and post-PCI analysis in all patients⁶. The ESC guidelines, in highlighting certain complex lesions for ICI, recognises this key notion and thus encourages the use of ICI in other clinical scenarios and lesions². So, is it the chicken or the egg? It doesn't matter, ICI improves outcomes in PCI¹.

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Conflict of interest statement

G.W. Stone has received speaker honoraria from Medtronic, Pulnovo, Infraredx, Abiomed, and Abbott; has served as a consultant to Valfix, TherOx, Robocath, HeartFlow, Ablative Solutions, Vectorious, Miracor, Neovasc, Ancora,

Elucid, Occlutech, CorFlow, Apollo Therapeutics, Impulse Dynamics, Cardiomech, Gore, Amgen, Adona Medical, and Millennia Biopharma; and has equity/options from Ancora, Cagent, Applied Therapeutics, Biostar family of funds, SpectraWAVE, Orchestra Biomed, Aria, Cardiac Success, Valfix, and Xenter; his daughter is an employee at IQVIA; his employer, Mount Sinai Hospital, receives research support from Abbott, Abiomed, Bioventrix, Cardiovascular Systems, Inc., Philips, Biosense Webster, Shockwave Medical, Vascular Dynamics, Pulnovo, and V-Wave. Z.A. Ali reports institutional grants from Abbott, Abiomed, Acist Medical, Boston Scientific, Cardiovascular Systems, Inc., Medtronic, Opsens Medical, Philips, Shockwave Medical; personal fees from Amgen, AstraZeneca, and Boston Scientific; equity from Elucid, Lifelink, SpectraWAVE, Shockwave Medical, and Vital Connect. K. Karimi Galougahi has received speaker honoraria from Abbott.

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