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Commentary on the Nordic-Baltic bifurcation study IV (randomised comparison of provisional side branch stenting versus a two-stent strategy for treatment of true coronary bifurcation lesions involving a large side branch)

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Current practice involving bifurcations still recommends a provisional strategy. This stems from two large randomised trials, namely, Nordic bifurcation study (NORDIC I) and the British Bifurcation Coronary Study (BBC ONE).[1 2] In these trials a composite end point of all-cause death, myocardial infarction and target vessel revascularisation demonstrated superiority of a provisional strategy. These trials, however, didn't differentiate true bifurcations in which a large side branch had significant disease and those that were not true bifurcations. Additionally, the final kissing inflation and proximal optimisation was not employed in all cases in the two-stent strategy arm. Both of these may have impacted the outcomes and remain points of significant controversy when discussing these initial trials. Subsequently, trials such as the European Bifurcation Coronary TWO (EBC TWO) trial compared provisional one-stent technique with an upfront two-stent technique in large true bifurcation lesions (with a side branch diameter ≥2.5 mm) and significant ostial disease length (≥5 mm). This study found no difference in major adverse cardiovascular events (MACE) between the two techniques. As such, the investigators still conclude that a provisional strategy should be the default.[3]

The NORDIC IV study follows in the heels of the above study. Briefly, this was a randomised multicentre trial comparing a simple provisional strategy with an upfront complex two-stent strategy in true bifurcation lesions (Medina 1,1,1 or 1,0,1 or 0,1,1) with a large side branch (main vessel diameter ≥3.0 mm and side branch diameter ≥2.75 mm). Randomisation was 1:1 and occurred after wiring both vessels. The primary endpoint was a composite of MACE at 6 months. Secondary endpoints included a composite MACE endpoint at 2 years, all-cause mortality, cardiac death, non-procedural myocardial infarction, clinically indicated target lesion revascularisation or target vessel revascularisation, and definite, probable or possible stent thrombosis. The primary endpoint was 5.5% versus 2.2% for provisional versus complex strategy, respectively. MACE at 2 years was 12.9% versus 8.4% for provisional versus complex strategy. Both endpoints did not meet statistical significance. The difference in MACE at 2 years was primarily driven by target lesion revascularisation. The complex two-stent strategy had a less angiographic stenosis of the side branch with higher procedure time, fluoroscopy time, contrast volume and number of stents. Overall this trial was underpowered to establish superiority.

One limitation that may have confounded outcomes was the use of 'Cypher Select+' (Cordis, USA) in the first 225 patients and the Xience V or Xience Prime, everolimus eluting stents (Abbott, USA) in the remaining 225 patients. Analysis of the subgroup treated with newer generation drug eluting stents demonstrated a MACE rate of 12.0% versus 5.6% with provisional versus complex techniques. This too didn't reach statistical significance. Note, this was not prespecified. Whether these results persist using a variety of different stent platforms including ultrathin stent struts, biodegradable polymers or even dedicated bifurcation

stents remains unknown. Another limitation, which the investigators allude to in their discussion, is the lack of consistency in the use of intracoronary imaging or physiology to guide revascularisation (emphasised at follow-up and not index procedure). A visual assessment of vessel size and per cent stenosis at the index angiogram is no longer contemporary practice. The quantitative coronary analysis of restenosis was binary with a cut-off of 50% and was un-blinded. Both intracoronary imaging and physiological assessment of side branches is current practice and recommended in the 2018 European Bifurcation Club Consensus Statement.[4–6] Despite these recommendations and multiple studies demonstrating the utility of intravascular imaging, it remains underutilised across the spectrum of percutaneous coronary interventions. While lack of strict adherence to intravascular imaging to guide decisions during bifurcation stenting remains a limitation of the current study, it seems to be more reflective of real world practice.[7 8] It is also important to note that proximal optimisation was not standard of practice during the recruitment phase of this trial and once again its utility may have impacted the significance of the results.[9] Another observation is that antiplatelet therapy was limited to aspirin and clopidogrel; therefore, the antiplatelet regimen remains a point of debate with respect to duration and the more liberal use of a potent P2Y12 inhibitors. Finally, with a very small portion of patients enrolled having left main disease (1.7% and 2.3% of total enrolled had left main stenosis in each arm), the results cannot be applied to left main interventions.

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