

Outcomes with intravascular ultrasound-guided stent implantation: a meta-analysis of randomized trials in the era of drug-eluting stents

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Intravascular ultrasound (IVUS) is a useful tool for planning percutaneous coronary intervention (PCI) by informing the operators of lesion severity, reference vessel size, lesion length, and extent of calcification. With validated criteria for stent underexpansion and edge problems, post-stenting IVUS has been used to optimize stent deployment to prevent stent failure (restenosis and early thrombosis). Despite its potential benefits, routine use of IVUS has been restricted by cost and time and questions regarding clinical data. In reality IVUS is used in less than 20% of all PCIs cases in the United States (1).

A recent meta-analysis by Elgendy *et al.* included the seven randomized angiography *vs.* IVUS-guidance trials in the drug-eluting stent (DES) era. It demonstrated a lower rate of major adverse cardiac event associated with IVUS-guidance, primarily driven by a decreased risk of ischemia-driven target lesion revascularization (2). Considering that presumed insufficient scientific evidence is partly responsible for the low penetration of IVUS, this meta-analysis strongly supports the recommendation of IVUS utilization in clinical practice.

Early randomized trials in the DES era showed conflicting results and failed to prove the superiority of an IVUS-guided PCI approach in terms of improving clinical outcomes (3-5). The AVIO trial compared clinical efficacy between IVUS- *vs.* angiography-guided DES implantation in 284 patients with complex coronary lesions (3). Although IVUS optimized DES implantation resulted in a larger post-procedure minimal lumen diameter, there was no significant difference in the rates of 2-year major adverse

cardiac events. In the Real Safety and Efficacy of a 3-month Dual Antiplatelet Therapy Following Zotarolimus-eluting Stents Implantation (RESET) trial based on intention-to-treat analysis, IVUS-guided PCI in a long lesion subset did not significantly reduce the rates of 1-year clinical events (4). In chronic total occlusion (CTO) lesions, the AIR-CTO randomized study showed comparable rates of clinical events between IVUS- *vs.* angiography-guided PCI (5), while the CTO-IVUS trial suggested that IVUS-guidance might improve 1-year clinical outcomes after newer generation DES implantation (6).

At the other end of the spectrum, in the multicenter Impact of Intravascular Ultrasound Guidance on Outcomes of Xience Prime Stents in Long Lesions (IVUS-XPL) evaluating 1,400 patients with long coronary lesions (≥ 28 mm in stent length), IVUS-guidance was proved to be superior to angiography-guidance in terms of improving long-term clinical outcomes (7). IVUS- (*vs.* angiography-) guided everolimus-eluting stent implantation significantly reduced the rate of 1-year major adverse cardiac events (2.9% *vs.* 5.8%), mainly driven by a lower risk of target lesion revascularization (2.5% *vs.* 5.0%).

Including IVUS-XPL, the currently updated, comprehensive meta-analysis of seven randomized trials and 3,192 patients compared long-term clinical outcomes between IVUS-guided *vs.* angiography-guided DES implantation (2). With the mean lesion length of 32 mm, IVUS-guided PCI group showed more frequent postdilatation and a larger post-stenting minimal lumen diameter, and a greater reduction in the diameter stenosis. Routine IVUS-guidance

was associated with a reduction in the risk of major adverse cardiac events (6.5% *vs.* 10.3%) at 15 months, primarily due to a reduction in the risk of ischemia-driven target lesion revascularization (4.1% *vs.* 6.6%). Moreover, the rates of cardiovascular death (0.5% *vs.* 1.2%), and stent thrombosis (0.6% *vs.* 1.3%) appeared to be lower in the IVUS-guided group, which might be owing to the better detection of mechanical factors associated with stent thrombosis, including edge problems, stent malapposition, and stent underexpansion similarly as previously suggested (8).

There still remain unsolved issues. First, the included trials used inconsistent definitions of major adverse cardiac events and arbitrary IVUS criteria for optimizing stent deployment. Particularly, for the treatment of diffuse, complex and CTO lesions, IVUS optimization criteria have not been yet established although the IVUS-XPL trial showed the best results with an MSA greater than the distal reference lumen. Second, the meta-analysis included mixed lesion subsets (such as diffuse, left main, or CTO lesions) with non-identical therapeutic and prognostic implications (5-7,9). Third, based on intention-to-treat analysis, a high rate of crossover especially from angiography-guided to the IVUS-guided CTO intervention (6) and losses of follow-up might have potentially affected the results. By recognizing the use of IVUS (during half of the procedures), the physicians and the patients could not be completely blinded to the assigned randomization. Moreover, even in the angiography-guided PCI group, physicians' knowledge of IVUS might lead to their biased approach. Nevertheless, the IVUS-XPL trial and this current meta-analysis proved the clinical benefit of IVUS-guided PCI, especially in diffuse lesions although the lack of patient-level data made it difficult to determine which other patients would have maximal clinical benefits from IVUS-guidance.

This meta-analysis validated the superiority of IVUS-guided PCI (*vs.* angiography-guided PCI) to improve clinical outcomes even in the DES era, especially the recommendation to expand routine IVUS-guidance for treating complex coronary lesions.

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Footnote

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