

Significance of verification of IVUS-guided stent optimisation



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During percutaneous coronary intervention (PCI), intravascular ultrasound (IVUS) provides anatomic information for the coronary artery lumen, wall, and plaques, which can help the accurate evaluation of the lesion with vessel sizing¹. Moreover, post-PCI stent underexpansion, malapposition, or edge dissections can be detected for stent optimisation, resulting in improved clinical outcomes¹⁻⁴. Recently, much evidence demonstrating the clinical usefulness of IVUS has become available, particularly for complex lesions, such as left main disease, chronic total occlusions, and diffuse long lesions²⁻⁴. According to the recent large randomised study of the IVUS-XPL (Impact of Intravascular Ultrasound Guidance on Outcomes of Xience Prime Stents in Long Lesions) trial, IVUS-guided drug-eluting stent (DES) implantation, particularly for diffuse long lesions, compared with angiography-guided DES implantation resulted in a significantly lower rate of the composite endpoint of major adverse cardiac events (a composite of cardiac death, myocardial infarction, or target lesion revascularisation) at one year (2.9% vs. 5.8%, hazard ratio [HR] 0.48, $p=0.007$)². These differences

were primarily due to a lower risk of target lesion revascularisation (2.5% vs. 5.0%, HR 0.51, $p=0.02$). Also, the results of a meta-analysis with individual patient-level data from 2,345 randomised patients showed that IVUS-guided new-generation DES implantation vs. angiography-guided DES implantation was associated with a favourable outcome, particularly the occurrence of the hard clinical endpoint (the composite of cardiac death, myocardial infarction, or stent thrombosis) for complex lesions³. Of note, the primary endpoint of this meta-analysis did not include target lesion revascularisation. Therefore, different from the IVUS-XPL trial showing the benefit of IVUS due primarily to less frequent TLR events², major adverse cardiac events, even excluding the target lesion revascularisation events in this meta-analysis, were less frequent with IVUS guidance than with angiography guidance³. Lastly, according to the ADAPT-DES (Assessment of Dual AntiPlatelet Therapy With Drug Eluting Stents) study, the largest all-comers observational study ($n=8,583$)⁵, IVUS was utilised in 3,349 patients (39%), and larger-diameter devices, longer stents, and/or higher inflation

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pressure were used in the IVUS-guided cases. At one year, propensity-adjusted multivariable analysis revealed that IVUS guidance vs. angiography guidance was associated with reduced definite/probable stent thrombosis (0.6% vs. 1.0%, $p=0.003$), myocardial infarction (2.5% vs. 3.7%, $p=0.004$), and a composite of adjudicated major cardiac events (cardiac death, myocardial infarction, or stent thrombosis) (3.1% vs. 4.7%, $p=0.002$). The benefits of IVUS were especially evident in patients with acute coronary syndromes and complex lesions⁵.

Contrary to these findings²⁻⁵, in this issue of *AsiaIntervention*, Watanabe et al in their study failed to demonstrate the clinical usefulness of IVUS guidance for target vessel revascularisation in the patients treated with first-generation DES⁶.

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They sought to evaluate the clinical impact of IVUS use in first-generation DES implantation from the Coronary REvascularisation Demonstrating Outcome study in Kyoto (CREDO-Kyoto) PCI/CABG registry cohort-2. As a retrospective cohort study, they selected the patients treated with first-generation DES without acute myocardial infarction, and compared clinical outcomes between the two groups of patients with or without IVUS use (IVUS-guided group [n=2,768] vs. angiography-guided group [n=2,000]). There was no significant difference between the groups in the cumulative incidence of target vessel revascularisation (21.5% vs. 22.2%, $p=0.57$). Even after adjustment for confounders, the risk of IVUS guidance relative to angiography guidance for target vessel revascularisation remained neutral (HR 1.09, 95% CI: 0.90-1.32, $p=0.37$). Thus, they concluded that IVUS-guided PCI as compared with angiography-guided PCI was not associated with a lower risk for target vessel revascularisation in patients treated with first-generation DES.

Failure to demonstrate the clinical usefulness of IVUS-guided DES implantation in this study might be attributed to the following reasons. First, the definition of IVUS usage was too obscure. They did not differentiate the use of IVUS according to the timing of IVUS examination, and included the IVUS usage for pre-stent deployment, post-stent deployment, or both strategies. Thus, the effect of IVUS usage particularly for stent optimisation, which can be most important during PCI, was not accurately addressed. According to the previous IVUS-XPL trial¹, even among the patients with IVUS guidance, the clinical outcomes were totally different between the patients meeting the IVUS criteria for stent optimisation and those who did not meet the IVUS criteria (1.5% vs. 4.6%; HR 0.31, 95% CI: 0.11-0.86, $p=0.02$). Thus, the study evaluating the clinical efficacy of IVUS requires appropriate analyses of the measurements of IVUS parameters after DES implantation. Moreover, the lack of analyses of IVUS parameters raises the question of the extent to which the stent optimisation by IVUS was achieved in the IVUS-guided group. It is not a simple matter of usage or non-usage of IVUS, but whether the improvement of clinical outcomes is accompanied by “appropriate use of IVUS”, i.e., the extent of stent optimisation by IVUS usage. The interpretation of IVUS images

is not intuitive, but requires a careful understanding of what is important¹. Second, this study was not a randomised study but an observational study with a modest sample size. Third, the authors only included patients treated with first-generation DES, which are not widely used in current practice. Fourth, in this study, all-comers treated with DES were included. Patients with chronic total occlusions were only 15.9% in the IVUS group, and the proportion of patients with a larger than 28 mm stent was 52.8%. However, rather than routine use of IVUS for stent optimisation, IVUS usage (particularly for complex lesions) could be more beneficial. Although they tried subgroup analyses, the number of patients could be too small to detect the clinical efficacy of IVUS for each subgroup, something which was different from the previous ADAPT-DES study⁵.

However, it is notable that there was a trend towards a beneficial effect in small vessels in subgroup analyses, indicating the beneficial effect of IVUS particularly for small vessels. Also, the final balloon pressure was statistically greater in the IVUS group at 20 atm vs. 18 atm ($p<0.0001$), although the authors did not include the analyses of quantitative coronary angiography after stent implantation, which would be essential to confirm the differences in angiographic results between the two groups. Lastly, although the authors failed to demonstrate the superiority of the IVUS-guided group for target vessel revascularisation, the superiority of the IVUS-guided group was observed for all-cause death (HR 0.85, 95% CI: 0.73-0.99, $p=0.04$), myocardial infarction (HR 0.75, 95% CI: 0.59-0.95, $p=0.02$), and major adverse cardiac events (HR 0.88, 95% CI: 0.79-0.97, $p=0.01$) for the propensity score-matched cohort.

Taken together, the present study provides valuable lessons in terms of (i) the importance of appropriate IVUS usage in selected patients rather than routine usage along with appropriate interpretation of the IVUS images¹, (ii) the necessity of well-designed randomised trials, (iii) the need for cautious interpretation of negative findings of retrospective analyses with modest sample sizes, and (iv) the requirement for analyses of the parameters of quantitative coronary angiography and IVUS measurements.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Mintz GS, Guagliumi G. Intravascular imaging in coronary artery disease. *Lancet*. 2017;390:793-809.
2. Hong SJ, Kim BK, Shin DH, Nam CM, Kim JS, Ko YG, Choi D, Kang TS, Kang WC, Her AY, Kim YH, Hur SH, Hong BK, Kwon H, Jang Y, Hong MK; IVUS-XPL Investigators. Effect of intravascular ultrasound-guided vs angiography-guided everolimus-eluting stent implantation: The IVUS-XPL randomized clinical trial. *JAMA*. 2015;314:2155-63.
3. Shin DH, Hong SJ, Mintz GS, Kim JS, Kim BK, Ko YG, Choi D, Jang Y, Hong MK. Effects of intravascular ultrasound-

guided versus angiography-guided new-generation drug-eluting stent implantation: meta-analysis with individual patient-level data from 2,345 randomized patients. *JACC Cardiovasc Interv.* 2016;9:2232-2239.

4. Ye Y, Yang M, Zhang S, Zeng Y. Percutaneous coronary intervention in left main coronary artery disease with or without intravascular ultrasound: A meta-analysis. *PLoS One.* 2017;12:e0179756.

5. Witzenbichler B, Machara A, Weisz G, Neumann FJ, Rinaldi MJ, Metzger DC, Henry TD, Cox DA, Duffy PL, Brodie BR, Stuckey TD, Mazzaferri EL Jr, Xu K, Parise H, Mehran R,

Mintz GS, Stone GW. Relationship between intravascular ultrasound guidance and clinical outcomes after drug-eluting stents: the assessment of dual antiplatelet therapy with drug-eluting stents (ADAPT-DES) study. *Circulation.* 2014;129:463-70.

6. Watanabe H, Morimoto T, Shiomi H, Furukawa Y, Nakagawa Y, Ando K, Kadota K, Kimura T; the CREDO-Kyoto PCI/CABG registry investigators. Intravascular ultrasound-guided versus angiography-guided percutaneous coronary intervention with drug-eluting stents: five-year outcomes from the CREDO-Kyoto PCI/CABG registry. *AsiaIntervention.* 2018;4:26-33.