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EDITORIAL COMMENT

IVUS Guidance for Coronary Revascularization

When to Start, When to Stop?*

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Since its introduction more than 40 years ago, angiography-guided percutaneous coronary intervention (PCI) using either plain balloon angioplasty or the implantation of a bare-metal stent or a drug-eluting stent (DES) has dramatically improved quality of life for patients with anatomically obstructive disease. Obviously, the lack of intravascular information (including plaque morphology, vessel diameter, stent expansion, etc.) provided by angiography alone reveals its disadvantage in guiding PCI for complex lesions or in high-risk patients and expedited the development of grayscale intravascular ultrasound (IVUS) more than 30 years ago. Since then, the strength of IVUS guidance over coronary angiographic guidance during PCI procedures has been further enhanced with the development of better IVUS systems, as demonstrated in a recent meta-analysis that included 9 randomized controlled trials (1).

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In this issue of *JACC: Cardiovascular Interventions*, Hong et al. (2) report the 5-year clinical results of the randomized IVUS-XPL (Impact of Intravascular Ultrasound Guidance on the Outcomes of Xience Prime Stents in Long Lesions) trial in 1,400 patients in whom an everolimus-eluting stent (Xience Prime, Abbott Vascular, Santa Clara, California) 28 mm or greater in length was required. Among 1,183 of these patients (85%) who completed 60-month follow-up, the benefit of IVUS guidance was maintained through 5-year follow-up compared with angiographic guidance, driven mainly by the significant reduction of ischemia-driven target lesion revascularization. Furthermore, landmark analysis demonstrated less "catchup" in terms of the primary endpoint (a composite of cardiac death, target lesion-related myocardial infarction, and ischemia-driven target lesion revascularization) if procedures were guided by IVUS.

Although we acknowledge the great contribution of the IVUS-XPL 5-year substudy, caution is warranted in translating the results of this study into practice. First, IVUS-XPL was originally designed for 2-year follow-up. Although the sample size at 5 years was almost equal between the 2 groups, it is clear that this subanalysis has at least partially lost its original feature of randomization. And this may be one reason for the nonsignificant differences seen in cardiac death and myocardial infarction.

Second, an optimal IVUS-guided stenting procedure was defined in this study as the attainment of a minimal stent area greater than the distal reference luminal area (i.e., expansion index >1.0). The aforementioned meta-analysis showed that IVUS criteria to define an optimal stenting procedure varied among studies (1,3). More recently, the ULTIMATE (Intravascular Ultrasound Guided Drug Eluting Stents Implantation in "All-Comers" Coronary Lesions) study (3) included 3 criteria: 1) minimal stent area in the stented segment >5.0 mm^2 or an expansion index of 90% or greater; 2) plaque burden 5 mm proximal or distal to the stent edge <50%; and 3) no edge dissection involving media with length >3 mm. We found that aggressive post-dilation to achieve an optimal expansion index was associated with an increased rate of edge complications, including severe dissection, slow flow, and/or perforation (3). As a

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result, to achieve an expansion index >1.0 may be impossible in most stents after deployment. Additional information about intraprocedural complications from the IVUS-XPL study may enhance our understanding of the safety of more aggressive post-dilation.

Third, the IVUS-XPL study revealed a significant reduction in the rate of major adverse cardiac events at 5-year follow-up in the optimal IVUS group compared with the suboptimal IVUS group. However, the landmark analysis demonstrated a nonsignificant difference in the primary endpoint between 1- and 5-year follow-up between the optimal and suboptimal IVUS groups, which was inconsistent with already known results. Recently, Choi et al. (4) reported among 6,005 patients with complex coronary artery lesions that IVUS-guided PCI was associated with a lower long-term risk for cardiac death (10.2% vs. 16.9%; $p < 0.001$) and adverse cardiac events compared with angiography-guided PCI during 64-month median follow-up. Andell et al. (5) also reported, among 2,468 patients who underwent unprotected left main coronary artery stenting, that compared with angiographic guidance, IVUS guidance resulted in superior clinical outcomes (composite endpoint of all-cause mortality, restenosis, and definite stent thrombosis) (hazard ratio: 0.65; 95% confidence interval: 0.50 to 0.84) during more than 5-year follow-up.

Fourth, both the proximal and distal landing zones were not clearly described in the IVUS-XPL substudy. Patients with plaque burden >50% at stent edge post-PCI would possibly be classified as having undergone optimal IVUS guidance procedures according to the IVUS-XPL protocol, which would in turn lead to a greater grade of residual plaque burden and a higher incidence of in-segment restenosis at long-term follow-up.

Finally, we must consider the profound difference between IVUS use and optimal IVUS criteria for stent implantation (3). In 1 prospective study comparing IVUS-guided versus angiography-guided implantation of second-generation DES (5) for patients with acute coronary syndromes, a suboptimal IVUS-guided PCI procedure was in fact the same as angiographic guidance with regard to revascularization, myocardial infarction, and cardiac death.

In conclusion, the 5-year results of the IVUS-XPL trial revealed the long-term benefits of IVUS guidance in optimizing long DES implantation. With a view to the gradually stronger benefits of IVUS guidance, long-term (3- to 5-year follow-up) results of the all-comers ULTIMATE trial are expected. In contrast, further randomized studies are warranted to identify the difference in clinical relevance among different optimal IVUS criteria during PCI. Furthermore, when the advantages of IVUS guidance have been tested in long lesions, all-comers, chronic total occlusion, and high-risk patients, the net benefit of an IVUS-guided systematic 2-stent strategy for complex bifurcation lesions must be determined in a randomized fashion. In this regard, the randomized DKCRUSH VIII (IVUS-Guided DK Crush Stenting Technique for Patients With Complex Bifurcation Lesions) study comparing IVUS guidance versus angiographic guidance for complex bifurcations is ongoing and is anticipated to report its 1-year clinical results in October 2022. Most important, the STOPDAPT-2 (Short and Optimal Duration of Dual Antiplatelet Therapy-2) trial (6) has shown a lower rate of bleeding in a single-antiplatelet therapy group among patients undergoing PCI compared with dual-antiplatelet therapy. In that study, IVUS was much more commonly used during procedures. Accordingly, IVUS-guided DES implantation may shorten dual-antiplatelet therapy duration by improving stent expansion or accelerating endothelial coverage.

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