Stent Area by Intravascular Ultrasound and Outcomes in Left Main Intervention With Drug-Eluting Stents

Small Stents, More Events

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While the standard revascularization for left main lesions traditionally has been surgical coronary artery bypass grafting, increasingly studies suggest that percutaneous coronary intervention (PCI) with drug-eluting stents (DES) may be an acceptable alternative to surgery for selected patients. In total, the current evidence suggests that rates of death, myocardial infarction, and stroke may be similar between patients managed with PCI and coronary artery bypass grafting, but revascularization occurs less frequently in patients undergoing surgery. This was illustrated in the recently published randomized PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) trial, where the 2-year risk of death, myocardial infarction, or stroke was similar [hazard ratio: 0.92; 95% confidence interval (CI), 0.43 to 1.96; P=0.83] in patients with unprotected left main disease managed with PCI using DES (N=300) and coronary artery bypass grafting (N=300), but revascularizations were more common in patients undergoing PCI (hazard ratio: 2.18; 95% CI, 1.10–4.32; P=0.02). A recent meta-analyses of 1611 patients from 4 randomized trials comparing PCI with coronary artery bypass grafting for unprotected left main lesions found similar results.1

Given the significant consequences associated with stent thrombosis and restenosis in the left main, intravascular ultrasound (IVUS) guidance has been advocated to optimize stent deployment in this important lesion subset. Increasing evidence suggests that IVUS-guidance reduces adverse events in PCI with DES in various clinical settings.3,4 This likely relates to the preintervention assessment of appropriate stent size and interventional strategy, as well as the postintervention detection and correction of suboptimal stent deployment, such as dissections, underexpansion, geographic miss, plaque/tissue prolapse, and incomplete stent apposition. Of these, stent underexpansion most consistently has been associated with adverse events in nonleft main PCI with DES.5,6 However, the optimal cut-off values to define “adequate stent expansion” in left main lesions are unknown.

In the current issue of Circulation: Cardiovascular Interventions, Kang et al investigated the relationship between underexpansion in left main PCI with DES and adverse events.7 Specifically, the authors evaluated the relationship between poststent area by IVUS on 9-month angiographic restenosis, and 2-year clinical outcomes in 403 consecutive patients undergoing left main PCI with DES from a single center. In the study, IVUS measurements were made at 4 locations: proximal left main, at the polygon of confluence, ostial left anterior descending, and ostial left circumflex in order to determine the stent area cut-off values associated with optimal outcomes. Of the patients undergoing PCI in this study, 13% were ostial/midshaft and 87% were bifurcation lesions. Two thirds of the bifurcation lesions were treated with a 1-stent strategy, and one-third was treated with a 2-stent strategy (crush and T-stents).

The authors found that the best IVUS predictors of angiographic restenosis were minimal stent areas (MSA) of <8.2 mm² in the proximal left main, <7.2 mm² in the polygon of confluence, <6.3 mm² in the ostial left anterior descending, and <5.0 mm² in the ostial left circumflex. When adequate expansion was defined as stent areas above these thresholds at all 4 locations, angiographic restenosis was greater with “underexpansion” compared with “adequate expansion” (24.1% versus 5.4%, P<0.001). More importantly, freedom from major adverse events was higher in patients with adequate stent expansion compared with underexpansion (98.1±0.9% versus 90.2±2.6%, P<0.001). Interestingly, the authors noted that acute malapposition by IVUS in the left main was not related to either restenosis or 2-year adverse events, findings that are in line with other IVUS studies from nonleft main lesions.8

The results from the present study are noteworthy as they reinforce the important influence of smaller stent areas by IVUS after PCI on adverse outcomes. Smaller MSA at any 1 of 4 sites in left main lesions were associated with greater angiographic restenosis at 9 months. These findings are in line with similar studies of nonleft main lesions where smaller stent areas (MSA <5.0–5.5 mm²) by IVUS were associated with higher restenosis after PCI with DES.5,6 This is significant because of 2 major mechanisms. First, even with optimal deployment, similar amounts of neo-intimal hyperplasia result in greater area stenosis in smaller diameter stents. Second, smaller stent areas can represent stent under-expansion, which often can be improved with adequate postdilation.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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542
In the present study, the authors determined MSA cut-off values at 4 sites that were associated with “optimal outcomes” in left main PCI with DES. However, there are several limitations to the clinical application of these cut-off values. Because this was a single-site observational study, there was a potential for selection and ascertainment bias as well as an undeterminable influence of routine use of angiography to guide PCI. In addition, whether these MSA values apply to second generation stents is unknown. Most importantly, a single MSA value at any location to define optimal stent expansion fails to take into account the reference vessel size. Underexpansion, by definition, is an area of inadequately expanded stent compared with the adjacent normal reference segment.9 While there is no consensus definition for adequate expansion, studies of nonleft main lesions from the bare-metal stent era demonstrated reduced restenosis with stent expansion >80 to 90% of the reference cross-sectional area.10 Similar studies in the DES era are lacking. Regardless, a single MSA cut-off value at any site is significantly limited in defining expansion in different sized reference vessels. For example, a proximal left main MSA of 8.1 mm² (which is <8.2 mm² cut-off MSA value proposed in the current study), would represent 84% stent expansion for a 3.5 mm reference diameter left main, but only 51% stent expansion for a 4.5 mm diameter reference segment. The former stent may be expanded adequately, while the latter stent is significantly underexpanded.

Even if a consensus definition of adequate stent expansion was available, there is limited evidence in the DES era of high pressure stent deployment that further stent expansion is feasible and safe (mean balloon inflation exceeded 17 atm in this study), or that increasing the stent area with postdilatation improves outcomes. In nonleft main PCI with bare-metal stent, IVUS-guidance did increase postdilatations with larger balloons at higher pressure, and this was associated with lower rates of restenosis.11 However, similar findings have not been demonstrated in PCI with DES. In the only published randomized trial in 210 patients undergoing PCI with DES, IVUS-guidance led to more postdilatations, higher balloon inflation pressures, and larger balloon sizes, but this did not result in lower rates of target vessel revascularization or major adverse cardiac events.12 Similar findings were noted in the recently presented AVIO (Angiographic versus IVUS Optimization) study of 284 patients with complex lesions (long lesions, bifurcations, chronic total occlusions, and small vessels) undergoing PCI with DES.13 Again, IVUS-guidance resulted in larger stent dimensions, but did not improve rates of revascularization. To be fair, these randomized studies have been small and underpowered to detect smaller differences in clinical events.

Contrary to the small randomized trials, larger propensity-matched studies have found that IVUS-guided PCI with DES improves outcomes. Recently, in nonleft main lesions, IVUS-guided PCI with DES reduced both stent thrombosis and the combination of death and myocardial infarction compared with an angiographically-guided strategy.3,4 Similar benefits also have been noted in left main lesions. In 145 propensity-matched patients undergoing unprotected left main PCI with DES from the multicenter MAIN-COMPARE (revascularization for unprotected left MAIN coronary artery stenosis: COMParison of Percutaneous coronary Angioplasty versus surgical Revascularization) registry, the 3-year mortality was lower with IVUS-guidance (4.7% versus 16.0%, P = 0.048).14 While compelling, the mechanisms of benefit of IVUS-guidance in these propensity-matched studies were not elucidated, and whether the benefits relate to better stent expansion remains unknown. Furthermore, it should be noted that target vessel revascularizations were not influenced by IVUS-guidance in any of the above studies.

So how do we understand the results from the current study by Kang et al in context of the current literature? Most importantly, it reinforces that “bigger is better” when it comes to poststent areas after left main PCI with DES. While it may seem intuitive that strategies to improve poststent areas would decrease adverse events, there is little data to support this concept in the DES era. Furthermore, over aggressive stent sizing and very high pressure postdilatation can result in adverse events, such as vessel perforations, balloon rupture, overstretch injury, and edge dissections. As such, the “cut-off” stent area values by IVUS from the current study always should be considered in the context of the reference vessel size, and larger trials investigating IVUS-guidance in left main PCI with current generation DES are warranted to further refine the exact IVUS criteria for optimal stent deployment.

On a different note, the study by Kang et al does further support a 1-stent strategy in left main bifurcation lesions.7 Angiographic restenosis was more common in bifurcation lesions using a 2-stent technique (25.4%), compared with single-stent strategies in bifurcation lesions (6.3%) and non-bifurcation lesions (4.5%), and the ostium of the left circumflex was the most common location for restenosis. In fact, underexpansion may be more common than reported in the 2-stent strategy as the left circumflex was not able to be imaged in all patients because of technical difficulty in passing the IVUS catheter. Whether dedicated bifurcation stents will improve these outcomes in the future remains to be seen.

In conclusion, given the significant risks associated with restenosis and stent thrombosis in unprotected left main lesions, routine IVUS-guidance seems reasonable to assist in the selection of appropriately sized stents and to detect and correct suboptimal stent deployment. While the findings from the study suggest that larger poststent areas are associated with better outcomes, optimal stent areas should be considered in the context of the reference vessel size. Perhaps the completion of the EXCEL (Evaluation of Xience Prime versus Coronary Artery Bypass Surgery of Effectiveness of Left Main Revascularization) trial will provide a better understanding of both the role of PCI in left main revascularization as well as the role of IVUS-guidance in this very important lesion subset.

Disclosures

None.

References


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