## **EDITORIAL**

# **EXCELling in Left Main Intervention** The Right Technique for the Right Patient

### See Article by Kandzari et al

merging clinical evidence from prospective all-comer registries<sup>1</sup> and randomized trials<sup>2</sup> provide a solid basis for percutaneous coronary intervention (PCI) as a treatment option in selected patients with unprotected left main (LM) coronary artery disease. Consequently, current clinical practice guidelines from both sides of the Atlantic have recognized the role of PCI in treating patients with LM disease and low SYNTAX score. In the field of percutaneous LM treatment, defining the optimal stenting technique for distal LM disease is of significant clinical importance because LM bifurcation is affected in the majority of patients<sup>1,2</sup> and PCI of LM bifurcation had been associated with worse outcomes compared with the intervention on isolated ostial/midshaft lesions.

In non-LM bifurcation lesions, initial stent implantation in the main vessel, with provisional stenting of the side branch (SB), is considered the gold standard in most cases.<sup>3</sup> By contrast, the as-yet only published randomized study specifically addressing the issue of 1- versus 2-stent strategy for distal LM lesions, the DK-CRUSH V trial (Double Kissing and Double Crush Versus Provisional T Stenting Technique for the Treatment of Unprotected Distal Left Main True Bifurcation Lesions), showed more favorable clinical outcomes of a planned 2-stent DK-Crush technique, over a provisional SB stenting strategy, in patients with true distal LM bifurcation.<sup>4</sup> These results are reflected in the European Society of Cardiology's recently published recommendation that in true bifurcation lesions of the LM, the DK-Crush technique may be preferred over provisional T stenting (Class IIb, level of evidence B).<sup>3</sup> However, apart from an unusually high reported rate of stent thrombosis in the provisional SB stenting arm (3.3% at 1 year), the trial's unique methodology may limit the scope of its findings in contemporary clinical practice. More specifically, the underlying coronary disease was very diffuse (mean left circumflex artery lesion length ≈16 mm) and the operators were highly experienced and crush-dedicated (each participating operator needed to submit 3 to 5 previous DK-Crush cases for review by the steering committee).<sup>4</sup>

In this issue of *Circulation: Cardiovascular Interventions*, Kandzari et al<sup>5</sup> present the 3-year outcomes of 1-stent provisional versus planned 2-stent techniques in 529 patients with a distal LM bifurcation lesion from the EXCEL trial (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization),<sup>2</sup> and thereby provide a different perspective on distal LM treatment technique, perhaps more reflective of an everyday clinical setting. The analysis included 185 patients treated with planned 2-stent techniques, of which  $\approx$ 40% had at least 1 major distal LM SB free of significant ostial disease and 344 treated with 1-stent provisional strategy ( $\approx$ 20% had significant disease at both distal LM SB ostia). At 3 years, the rate of death, myocardial infarction, or stroke was lower Goran Stankovic, MD, PhD Dejan Milasinovic, MD

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https://www.ahajournals.org/journal/ circinterventions in the provisional arm (14.1% versus 20.7%, *P*=0.01 after adjusting for differences in baseline coronary anatomy and clinical characteristics). Importantly, provisional stenting strategy resulted in lower cumulative occurrence of 3-year death, myocardial infarction, or stoke only in patients with nontrue bifurcations (13.8% versus 23.3%), including the reduction in mortality (6.1% versus 13.0%).

The main limitation of this EXCEL subanalysis<sup>5</sup> is its nonrandomized, observational design, with selection of stenting technique at operator's discretion so that the presence of unmeasured selection bias cannot be excluded. However, despite being exploratory by nature, these findings contribute valuable information to the totality of evidence on distal LM bifurcation treatment, mainly by emphasizing the importance of adapting the stenting strategy to an individual patient's disease complexity. Nevertheless, the following potential outcome modifiers seem to still remain unaddressed.

First, the presented EXCEL subanalysis<sup>5</sup> seems to suggest the extent of the disease at SB ostium to be the main determinant of differential outcomes of provisional single versus planned double stenting for distal LM disease. This finding seems to be further corroborated by the results of the DK-CRUSH V trial, which had even indicated superiority of an elective DK-Crush over provisional stenting in case of very extensive SB disease (>10 mm).<sup>4</sup> However, the extent of the disease at the SB ostium was not specifically addressed in the most recent European Society of Cardiology myocardial revascularization guidelines.<sup>3</sup>

Second, although guideline-recommended intravascular ultrasound was used in  $\approx$ 75% of the patients in the EXCEL trial,<sup>5</sup> the impact of intravascular ultrasound guidance on the observed outcomes of 1- versus 2-stent strategy was not systematically assessed in the current analysis.

Third, longer-term follow-up may be needed to adequately appraise the effects of 1- versus 2-stent technique for distal LM treatment because a recent pooled analysis of 2 randomized trials comparing provisional 1-stent versus systematic 2-stent bifurcation PCI showed lower mortality at 5 years in provisional group, with the survival curves beginning to separate 3 years postprocedure.<sup>6</sup>

Fourth, operator experience and volume have been shown to significantly impact short- and long-term outcomes after LM PCI,<sup>7</sup> which has been recognized by the current clinical practice guidelines that recommend a minimum of 25 LM procedures per year.<sup>3</sup> However, the effect of operator experience pertaining to a specific 2-stent technique has not been studied. This could be important given the considerable differences in the everyday use of different 2-stent techniques. It may also contribute to better understanding of the hitherto collected evidence including a randomized trial showing superiority of DK-Crush over the culotte technique for distal LM disease<sup>8</sup> or the discrepancy in the rate of final kissing in the here-described EXCEL substudy<sup>5</sup> versus the DK-CRUSH V trial<sup>4</sup> (85% versus >99%, respectively, despite >50% T-stenting or T and protrusion [TAP] rate in the EXCEL study).

In summary, while awaiting the results of ongoing randomized trials comparing provisional versus planned 2-stent strategy for distal LM lesions,<sup>9</sup> the current evidence base seems to suggest to align the stenting strategy with an individual patient's coronary anatomy and clinical condition, with an imperative of meticulously performing a 2-stent technique within the experience limits of an individual operator.<sup>10</sup>

#### **ARTICLE INFORMATION**

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#### Disclosures

 ${\rm Dr}$  Stankovic is the current president of the European Bifurcation Club. Dr Milasinovic reports no conflicts.

#### REFERENCES

- Chieffo A, Tanaka A, Giustino G, Briede I, Sawaya FJ, Daemen J, Kawamoto H, Meliga E, D'Ascenzo F, Cerrato E, Stefanini GG, Capodanno D, Mangiameli A, Templin C, Erglis A, Morice MC, Mehran R, Van Mieghem NM, Nakamura S, De Benedictis M, Pavani M, Varbella F, Pisaniello M, Sharma SK, Tamburino C, Tchetche D, Colombo A; DELTA 2 Investigators. The DELTA 2 registry: a multicenter registry evaluating percutaneous coronary intervention with new-generation drug-eluting stents in patients with obstructive left main coronary artery disease. *JACC Cardiovasc Interv*. 2017;10:2401–2410. doi: 10.1016/j.jcin.2017.08.050
- Stone GW, Sabik JF, Serruys PW, Simonton CA, Généreux P, Puskas J, Kandzari DE, Morice MC, Lembo N, Brown WM III, Taggart DP, Banning A, Merkely B, Horkay F, Boonstra PW, van Boven AJ, Ungi I, Bogáts G, Mansour S, Noiseux N, Sabaté M, Pomar J, Hickey M, Gershlick A, Buszman P, Bochenek A, Schampaert E, Pagé P, Dressler O, Kosmidou I, Mehran R, Pocock SJ, Kappetein AP; EXCEL Trial Investigators. Everolimuseluting stents or bypass surgery for left main coronary artery disease. N Engl J Med. 2016;375:2223–2235. doi: 10.1056/NEJMoa1610227
- Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Juni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization [published online August 25, 2018]. *Eur Heart J.* doi: 10.1093/eurheartj/ehy394
- 4. Chen SL, Zhang JJ, Han Y, Kan J, Chen L, Qiu C, Jiang T, Tao L, Zeng H, Li L, Xia Y, Gao C, Santoso T, Paiboon C, Wang Y, Kwan TW, Ye F, Tian N, Liu Z, Lin S, Lu C, Wen S, Hong L, Zhang Q, Sheiban I, Xu Y, Wang L, Rab TS, Li Z, Cheng G, Cui L, Leon MB, Stone GW. Double kissing crush versus provisional stenting for left main distal bifurcation lesions: DKCRUSH-V randomized trial. J Am Coll Cardiol. 2017;70:2605–2617. doi: 10.1016/j.jacc.2017.09.1066
- 5. Kandzari DE, Gershick AH, Serruys PW, Leon MB, Morice MC, Simonton CA, Lembo NJ, Banning AP, Merkely B, Van Boven AJ, Ungi I, Kappetein

AP, Sabik JF III, Généreux P, Dressler O, Stone GW. Outcomes among patients undergoing distal left main percutaneous coronary intervention: technique analysis from the EXCEL trial. *Circ Cardiovasc Interv.* 2018;11:e007007. doi: 10.1161/CIRCINTERVENTIONS.118.007007

- Behan MW, Holm NR, de Belder AJ, Cockburn J, Erglis A, Curzen NP, Niemelä M, Oldroyd KG, Kervinen K, Kumsars I, Gunnes P, Stables RH, Maeng M, Ravkilde J, Jensen JS, Christiansen EH, Cooter N, Steigen TK, Vikman S, Thuesen L, Lassen JF, Hildick-Smith D. Coronary bifurcation lesions treated with simple or complex stenting: 5-year survival from patient-level pooled analysis of the Nordic Bifurcation Study and the British Bifurcation Coronary Study. *Eur Heart J.* 2016;37:1923–1928. doi: 10.1093/eurhearti/ehw170
- Xu B, Redfors B, Yang Y, Qiao S, Wu Y, Chen J, Liu H, Chen J, Xu L, Zhao Y, Guan C, Gao R, Généreux P. Impact of operator experience and volume on outcomes after left main coronary artery percutaneous coronary intervention. *JACC Cardiovasc Interv.* 2016;9:2086–2093. doi: 10.1016/j.jcin.2016.08.011
- Chen SL, Xu B, Han YL, Sheiban I, Zhang JJ, Ye F, Kwan TW, Paiboon C, Zhou YJ, Lv SZ, Dangas GD, Xu YW, Wen SY, Hong L, Zhang RY, Wang HC, Jiang TM, Wang Y, Sansoto T, Chen F, Yuan ZY, Li WM, Leon MB. Clinical outcome after DK crush versus culotte stenting of distal left main bifurcation lesions: the 3-year follow-up results of the DKCRUSH-III study. *JACC Cardiovasc Interv.* 2015;8:1335–1342. doi: 10.1016/j.jcin.2015.05.017
- Chieffo A, Hildick-Smith D. The European Bifurcation Club Left Main Study (EBC MAIN): rationale and design of an international, multicentre, randomised comparison of two stent strategies for the treatment of left main coronary bifurcation disease. *EuroIntervention*. 2016;12:47–52. doi: 10.4244/EIJV1211A8
- Burzotta F, Lassen JF, Banning AP, Lefèvre T, Hildick-Smith D, Chieffo A, Darremont O, Pan M, Chatzizisis YS, Albiero R, Louvard Y, Stankovic G. Percutaneous coronary intervention in left main coronary artery disease: the 13<sup>th</sup> consensus document from the European Bifurcation Club. *EuroIntervention*. 2018;14:112–120. doi: 10.4244/EJ-D-18-00357