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Commentary: Coronary artery bypass grafting versus percutaneous coronary intervention in left main disease: Plausibility does not equal evidence

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The debate between coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) for left main coronary artery disease (LMCAD) has dominated the revascularization field for almost 20 years and led to 6 randomized-controlled trials (RCTs). While the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) score discriminates between most patients better suited for CABG rather than PCI, it remains unclear whether left main disease in general, and lesion location in particular, further influence decision-making.¹ PCI for left main bifurcation lesions involves a greater degree of technical challenge and multiple stents, whereas the effectiveness of bypass is largely independent of lesion location. The 2011 American Heart Association Guidelines vary their recommendation for PCI of the ostium/shaft (Class IIa) versus the bifurcation (Class IIb), whereas the 2018 European Society of Cardiology Guidelines do not discriminate between left main lesion locations when considering revascularization.^{2,3}

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CENTRAL MESSAGE

The notion that CABG outperforms PCI for distal LMCAD but is equivalent in ostial disease appears plausible but remains inconclusive without sufficient evidence from randomized trials.

In this issue of *The Journal*, De Filippo and colleagues⁴ pooled 6296 patients from the EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization), PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery vs Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease), and NOBLE (Nordic-Baltic-British left main revascularisation study) trials along with 6 observational studies that compared PCI with either ostial/shaft or distal LMCAD with CABG. They found no significant difference between PCI and CABG in major adverse cardiovascular events (MACE), all-cause death, myocardial infarction, stroke, or repeat revascularization for LMCAD in the ostium/shaft (n = 2274). For distal LMCAD (n = 4022), however, PCI was associated with an increased risk of MACE (hazard ratio, 1.56; 95% confidence interval, 1.19-2.04) and repeat revascularization (hazard ratio, 2.49; 95% confidence interval, 1.74-3.56) compared with CABG at the longest follow-up. These findings persisted after sensitivity analyses excluding the observational studies.⁴ Unlike stents, bypass grafts address current lesions and future progression of atherosclerosis proximal to the anastomosis. Thus, the authors' findings of greater repeat revascularizations in PCI—which likely drove differences in MACE—are supported by the limitations of contemporary stenting and the pathoanatomy of LMCAD.

Verisimilitude, however, does not equal evidence, and a crucial drawback to De Filippo and colleagues' meta-analysis was the inability to include 3 of the 6 landmark RCTs assessing LMCAD: LEMANS (Study of Unprotected Left Main Stenting vs Bypass Surgery), SYNTAX, and Boudriot 2011.⁵⁻⁷ This is an unfortunate limitation of the

data rather than the methodology, as these landmark RCTs did not report outcomes according to lesion sites. Another potential limitation is that only 2 studies excluded patients with high SYNTAX scores, and most studies did not report them. The average reported SYNTAX score of 32 suggests that multivessel disease may be a confounding factor in this meta-analysis. Additional limitations are that second-generation stents and contemporary bifurcation techniques (eg, double-kissing crush stenting) have increased the success of PCI in LMCAD, but these were not widely represented in the sample population.⁸ Rather, bare metal stents were used in up to 30% of the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty vs Surgical Revascularization) cohort, and more than half of the included studies used first-generation stents—neither of which are used currently.^{4,9}

Overall, De Filippo and colleagues are to be commended on conducting an important meta-analysis, attempting to clarify whether the site of left main stenosis is a revascularization treatment effect modifier. For now, these findings must be viewed as hypothesis-generating,⁹ but including lesion anatomy along with other patient factors in interdisciplinary heart team discussions seems reasonable. Until sufficient randomized evidence can be incorporated, however, we would do well to remember that biological

plausibility does not constitute proof—and that lesion anatomy is only one variable in the algorithm for the optimal revascularization strategy.

References

1. Head SJ, Farooq V, Serruys PW, Kappetein AP. The SYNTAX score and its clinical implications. *Heart*. 2014;100:169-77.
2. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*. 2019;40:87-165.
3. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery. *Circulation*. 2011;124:2610-42.
4. De Filippo O, Di Franco A, Boretto P, Bruno F, Cusenza V, Desalvo P, et al. Percutaneous coronary intervention versus coronary artery surgery for left main disease according to lesion site: a meta-analysis. *J Thorac Cardiovasc Surg*. August 20, 2021 [Epub ahead of print].
5. Boudriot E, Thiele H, Walther T, Liebetrau C, Boeckstegers P, Pohl T, et al. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. *J Am Coll Cardiol*. 2011;57:538-45.
6. Buszman PE, Buszman PP, Banasiewicz-Szkróbka I, Milewski KP, Zurakowski A, Orlik B, et al. Left main stenting in comparison with surgical revascularization: 10-year outcomes of the (Left Main Coronary Artery Stenting) le MANS trial. *JACC Cardiovasc Interv*. 2016;9:318-27.
7. Serruys PW, Morice M-C, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961-72.
8. Chen SL, Zhang JJ, Han Y, Kan J, Chen L, Qiu C, et al. Double kissing crush versus provisional stenting for left main distal bifurcation lesions: DKCRUSH-V randomized trial. *J Am Coll Cardiol*. 2017;70:2605-17.
9. Hyun J, Kim JH, Jeong Y, Choe KJ, Lee J, Yang Y, et al. Long-term outcomes after PCI or CABG for left main coronary artery disease according to lesion location. *JACC Cardiovasc Interv*. 2020;13:2825-36.