## Meta-Analysis of Intravascular Ultrasound-Guided Drug-Eluting Stent Implantation for Left Main Coronary Disease



Percutaneous coronary intervention with drug-eluting stents (DES) has emerged as a reasonable alternative to bypass surgery for select patients with unprotected left main coronary artery (LMCA) disease. 1,2 Meta-analyses of randomized controlled trials (RCTs) documented a reduction in cardiovascular mortality and myocardial infarction with intravascular (IVUS) guidance for DES implantation<sup>3,4</sup>; however, LMCA lesions were excluded from most of these trials. In the most recently published meta-analysis of 4,971 patients with LMCA disease, we found that IVUS-guided DES implantation to treat LMCA disease was associated with improved outcomes.5 Since that meta-analysis, further evidence with a larger number of patients has become available<sup>6,7</sup>; thus, we performed an updated meta-analysis to evaluate the impact of IVUS-guided DES implantation for LMCA on individual outcomes measures.

Details of the previous meta-analysis have been published.<sup>5</sup> Briefly, electronic databases were searched for RCTs and propensity-matched or adjusted observational studies comparing IVUS-guidance or angiography alone for DES implantation for LMCA disease. The following outcomes were assessed: cardiovascular mortality, all-cause mortality, myocardial infarction (MI), target lesion revascularization (TLR), and thrombosis. Summary estimates using the adjusted hazard ratio (HR) were reported for each individual study. Statistical heterogeneity was evaluated using I<sup>2</sup>. A subgroup analysis was performed to compare RCTs vs observational studies. This meta-analysis was registered at the PROSPERO database (CRD42019132938). For the purpose of the present study, the search was updated from April 2019 to March 2020.

The updated search identified 2 new studies (one propensity-matched and a second adjusted analysis). 6.7 A total of 11 studies (2 RCTs and 9 propensity-matched or adjusted observational studies) with 15,083 patients (7,668 in the IVUS group and 7,415 in the angiography group) were included in the present

study. Follow-up in the included studies ranged from 1 to 10 years. Compared with angiography alone, IVUS-guidance was associated with a lower incidence of cardiovascular mortality (HR 0.39, 95% confidence interval [CI] 0.27 to 0.58,  $I^2 = 72\%$ ), all-cause mortality (HR 0.59, 95% CI 0.53 to 0.66,  $I^2 = 0\%$ ), MI (HR 0.66, 95% CI 0.48 to 0.90,  $I^2 = 0\%$ ), TLR (HR 0.51, 95% CI 0.39 to 0.68,  $I^2 = 38\%$ ), and stent thrombosis (HR 0.38, 95% CI 0.26 to 0.56,  $I^2 = 0\%$ ) (Figure 1). The benefit of IVUS-guidance was observed irrespective of the type of study (ie, RCT vs observational studies), all P<sub>interaction</sub> >0.05.

In this updated meta-analysis of 11 studies with >15,000 patients with LMCA disease who underwent DES implantation, we documented that IVUSguidance was associated with a lower incidence of cardiovascular mortality, all-cause mortality, MI, TLR, and stent thrombosis. By using the totality of evidence to date, this meta-analysis provided more refined estimates for individual outcomes measures and showed a benefit for IVUS-guidance in reducing TLR, compared with a previous meta-analysis. Importantly, we found no evidence of statistical heterogeneity for all-cause mortality, MI, and stent thrombosis. In addition,

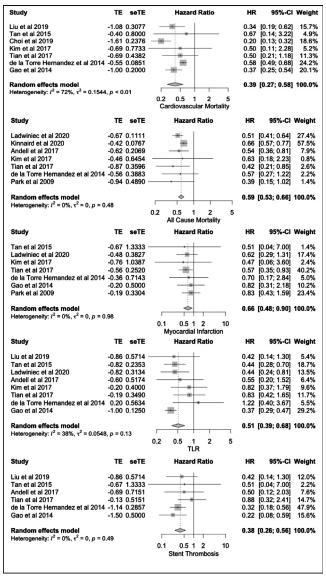


Figure 1. Summary plot for the outcomes.

Summary plot for cardiovascular mortality, all-cause mortality, myocardial infarction, target lesion revascularization, and stent thrombosis.

CI = confidence interval; HR = hazard ratio; TLR = target lesion revascularization.

this benefit was observed across RCTs and observational studies. Although this study is limited by the lack of patient-level data, it confirms the benefit of IVUS-guidance for this high-risk group. These findings justify a large outcome RCT to evaluate the impact of IVUS-guided DES implantation for LMCA.

## **Disclosures**

Dr. Mintz receives honoraria from Boston Scientific and Philips. The other authors have no conflicts of interest to disclose.

Islam Y. Elgendy, MD<sup>a,\*</sup>
Mohamed Gad, MD<sup>b</sup>
Gary S. Mintz, MD<sup>c</sup>

<sup>a</sup> Division of Cardiology, Massachusetts General
Hospital and Harvard Medical School, Boston,
Massachusetts

<sup>b</sup> Department of Medicine, Cleveland Clinic
Foundation, Cleveland, Ohio

<sup>c</sup> Cardiovascular Research Foundation, New York,
New York
28 April 2020

- Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice MC, Puskas J, Kandzari DE, Karmpaliotis D, Brown WM 3rd, Lembo NJ, 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 PE, Bochenek A, Schampaert E, Pagé P, Modolo R, Gregson J, Simonton CA, Mehran R, Kosmidou I, Généreux P, Crowley A, Dressler O, Serruys PW. Five-year outcomes after PCI or CABG for left main coronary disease. N Engl J Med 2019;381:1820–1830.
- Elgendy IY, Mahmoud AN, Gad M, Elgendy AY, Bhatt DL. Long-term outcomes with drug-eluting stents or coronary artery bypass surgery for unprotected left main coronary disease: a meta-analysis and trial sequential analysis of randomized trials. Am J Cardiol 2020. https://doi.org/10.1016/j.amjcard.2020.04.005.
- Malik AH, Yandrapalli S, Aronow WS, Panza JA, Cooper HA. Intravascular ultrasoundguided stent implantation reduces cardiovascular mortality—updated meta-analysis of randomized controlled trials. *Int J Cardiol* 2020; 299:100–105.
- 4. Elgendy IY, Mahmoud AN, Elgendy AY, Mintz GS. Intravascular ultrasound-guidance is associated with lower cardiovascular mortality and myocardial infarction for drug-eluting stent implantation—insights from an updated

- meta-analysis of randomized trials. *Circ J* 2019:83:1410–1413.
- Elgendy IY, Gad M, Jain A, Mahmoud AN, Mintz GS. Outcomes with intravascular ultrasound-guided drug eluting stent implantation for unprotected left main coronary lesions: a meta-analysis. Am J Cardiol 2019;124:1652– 1653.
- Kinnaird T, Johnson T, Anderson R, Gallagher S, Sirker A, Ludman P, de Belder M, Copt S, Oldroyd K, Banning A, Mamas M, Curzen N. Intravascular imaging and 12-month mortality after unprotected left main stem PCI: an analysis from the British Cardiovascular Intervention Society Database. *JACC Cardiovasc Interv* 2020:13:346–357.
- Ladwiniec A, Walsh SJ, Holm NR, Hanratty CG, Mäkikallio T, Kellerth T, Hildick-Smith D, Mogensen LJH, Hartikainen J, Menown IBA, Erglis A, Eriksen E, Spence MS, Thuesen L, Christiansen EH. Intravascular ultrasound to guide left main stem intervention: a sub-study of the NOBLE trial. *EuroInterven*tion 2020. https://doi.org/10.4244/EIJ-D-19-01003. [Epub ahead of print].

https://doi.org/10.1016/j.amjcard.2020.05.013