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Meta-analysis of Percutaneous Coronary Intervention Versus Medical Therapy in the Treatment of Coronary Chronic Total Occlusion

Coronary chronic total occlusion (CTO) is a common finding during coronary angiography and is associated with increased morbidity and mortality.[1] Historically, treating a CTO with percutaneous coronary intervention (PCI) was technically difficult with a low success rate and a high rate of complications.[1,2] Technical and operator skill advancements have led to an increased frequency and procedural success rate of contemporary CTO-PCI.[3] Nevertheless, the benefit of this treatment remains controversial. Therefore, we conducted this meta-analysis to evaluate the efficacy and safety of PCI in CTO.

A search through Pubmed, MEDLINE, and Cochrane Library from inception up to September 2018 was performed by 2 independent reviewers and any discrepancy was resolved by a third reviewer. We included only randomized controlled trials (RCTs) that compared CTO-PCI with medical therapy (MT). Two independent reviewers screened and extracted the data using a predefined table. The primary end point was major adverse cardiac and cerebrovascular events (MACCE). Secondary end points included all-cause mortality, cardiac death, spontaneous myocardial infarction (MI), repeat revascularization, target vessel revascularization (TVR), stent thrombosis, and left ventricle ejection fraction (LVEF) change. We calculated the risk ratios (RRs) and 95% confidence intervals (CIs) using a random-effects model with the aid of RevMan v5.3 and CMA v3 software in an intention-to-treat analysis. The meta-analysis was registered with the International Prospective Register of Systematic Reviews (PROSPERO ID: CRD42019121399).

From a total of 528 screened studies, 5 randomized controlled trials were included, [1,2,4,5,6] with a total of 1,792 patients (mean age 62.7 ± 9.7, 84% male, follow up range 4 to 60 months). The procedural success rate was ~86% (as-treated). The right coronary artery was the most commonly involved artery in the included trials (~54%).

There was no significant difference between CTO-PCI or MT with regard to MACCE (RR 0.83; 95% CI 0.50 to 1.36; $p = 0.45$; $I^2 = 47\%$). In a trial sequential analysis (TSA software)[7] to establish whether the current sample size and events were adequately powered to draw conclusive results (using a 17.8% incidence of MACCE in the MT group, 25% relative risk reduction in the PCI group, 5% type-α error, and 80% power), we found that the optimal information (sample) size was not achieved with the current meta-analysis (1,792 vs 11,895 patients) and the cumulative Z-curve did not cross any trial sequential boundaries, indicating a lack of evidence. A subgroup analysis based on the initial cardiac event (acute coronary syndrome vs stable) showed no evidence of interaction (p for interaction >0.1). Meta-regression analyses based on study-level covariates (SYNTAX score, J-CTO score, LVEF, and left anterior descending [LAD] artery percentages) did not suggest any statistically significant modifier effect. CTO-PCI significantly reduced TVR compared with MT (RR 0.34; 95% CI 0.16 to 0.72; $p < 0.01$; $I^2 = 10\%$). There were no significant differences between both groups with regard to all-cause mortality, cardiac mortality, spontaneous MI, stent thrombosis, repeat revascularization, or LVEF change (Figure 1). Sensitivity analysis by including only the published trials did not change any of the end points results.

A subgroup analysis of the EXPLORE trial showed a better outcome when the target vessel was the LAD.[2] Similarly, a meta-analysis published by Ma et al suggested better outcomes when PCI was done on a CTO involving the left coronary artery or its branches.[3] However, we were not able to demonstrate any effect of LAD CTO-PCI on MACCE.

The complexity of coronary artery disease in the treatment of CTO should always be considered. In the REVASC trial, patients with less complex disease (SYNTAX score ≤13), mainly derived by the CTO lesion itself, had better segmental wall thickening improvement with CTO-PCI.[4] In our meta-regression, there was a nonsignificant trend toward increased MACCE with higher SYNTAX score. Further adequately powered trials are needed to examine the clinical outcomes of CTO-PCI in those with CTO driven ischemia.

In conclusion, in patients with CTO, PCI was not associated with significant reductions in MACCE, all-cause mortality, MI, stent thrombosis, or repeat revascularization, though there was a significantly lower incidence of TVR compared with MT. However, further adequately powered and long-term trials are required to identify the best treatment strategy of CTOs.

Disclosures

DLB discloses the following relations−Advisory Board: Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, PhaseBio, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft; Chair: American Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic, Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo), Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical

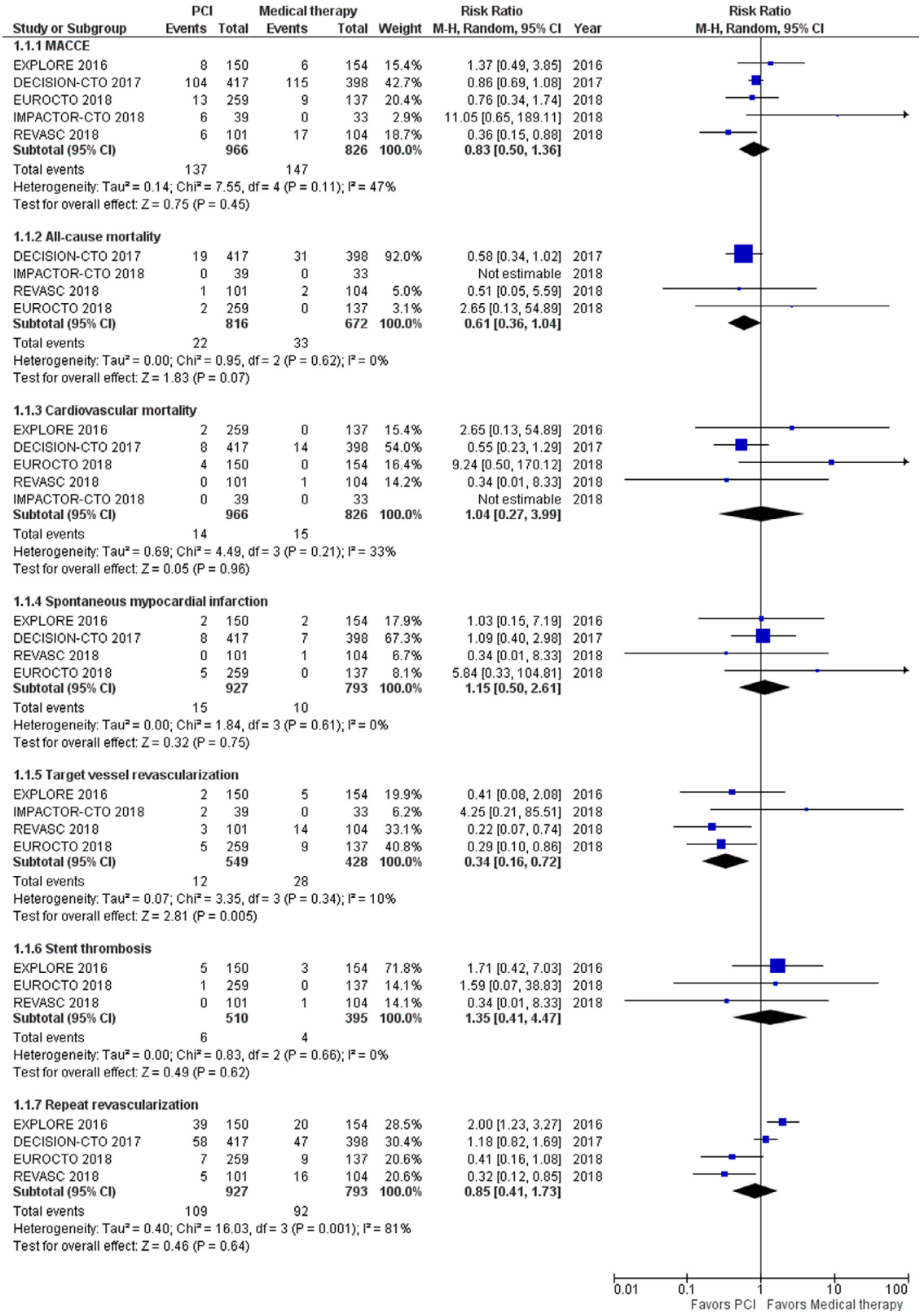

Figure 1. Forest plot for the clinical outcomes. CI = confidence interval. CTO-PCI = chronic total occlusion-percutaneous coronary intervention; DECISION-CTO = Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients With Chronic Total Occlusion; EUROCTO = Evaluate the Utilization of Revascularization or Optimal Medical Therapy for the Treatment of Chronic Total Coronary Occlusions; EXPLORE = Evaluating Xience and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Segment Elevation Myocardial Infarction; IMPACTOR-CTO = Impact on Inducible Myocardial Ischemia of PercutAneous Coronary InTervention versus Optimal Medical TheRapy in Patients with Right Coronary Artery Chronic Total Occlusion; MACCE = major adverse cardiac and cerebrovascular events; REVASC = Recovery of Left Ventricular Function After Stent Implantation in Chronic Total Occlusion of Coronary Arteries; SD = standard deviation.

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