Meta-Analysis of Comparison of 5-Year Outcomes of Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting in Patients With Unprotected Left Main Coronary Artery in the Era of Drug-eluting Stents

Mahin R. Khan, MD[a], Waleed T. Kayani, MD[b], Waqas Ahmad, MBBS[c], Ravi S. Hira, MD[d], Salim S. Virani, MD[b,e], Ihab Hamzeh, MD[b], Hani Jneid, MD[b,e], Nasser Lakkis, MD[b], and Mahboob Alam, MD[b,*]

Patients with unprotected left main coronary artery (ULMCA) disease are increasingly being treated with percutaneous coronary intervention (PCI) using drug-eluting stents (DES), but long-term outcomes comparing PCI with coronary artery bypass grafting (CABG) remain limited. We performed aggregate data meta-analyses of clinical outcomes (all-cause death, nonfatal myocardial infarction, stroke, repeat revascularization, cardiac death, and major adverse cardiac and cerebrovascular events) in studies comparing 5-year outcomes of PCI with DES versus CABG in patients with ULMCA disease. A comprehensive literature search (January 1, 2003 to December 10, 2016) identified 9 studies (6,637 patients). Effect size for individual clinical outcomes was estimated using odds ratio (OR) with 95% confidence intervals (CI) using a random effects model. At 5 years, PCI with DES was associated with equivalent cardiac (OR 0.95, 95% CI 0.62 to 1.46) and all-cause mortality (OR 0.98, 95% CI 0.72 to 1.33), lower rates of stroke (OR 0.50, 95% CI 0.30 to 0.84), and higher rates of repeat revascularization (OR 2.52, 95% CI 1.63 to 3.91); compared with CABG, major adverse cardiac and cerebrovascular events showed a trend favoring CABG but did not reach statistical significance (OR 1.19, 95% CI 0.93 to 1.54). In conclusion, for ULMCA disease, PCI can be considered as a comparably effective and yet less invasive alternative to CABG given the comparable long-term mortality and lower incidences of stroke. **(Am J Cardiol 2017;120:1514–1520)**

Coronary artery bypass grafting (CABG) has been considered the cornerstone of treatment for unprotected left main coronary artery (ULMCA) disease since the early 1980s as compared with medical management,[1–4] with percutaneous coronary intervention (PCI) gradually gaining popularity.[5,6] However, with studies paralleling the outcomes of PCI and CABG,[7–11] including the ground-breaking Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) trial,[12] 2011 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA)/Society for Cardiovascular Angiography and Interventions (SCAI) Guidelines[13] recognized PCI as a class IIa instead of a class III intervention for ULMCA disease in select patient populations. Likewise, 2014 European Guidelines on myocardial revascularization[14] upgraded PCI to a class I intervention for left main disease in patients with SYNTAX score ≤22. With PCI's risk of *late* adverse events like very late stent thrombosis and late target vessel revascularization,[15–17] CABG's upfront risk of stroke and mortality and with conflicting outcomes of randomized controlled trials (RCTs) comparing PCI and CABG, the choice of optimal revascularization remains debatable. Our study is an aggregate data meta-analysis of studies comparing long-term (≥5 year) outcomes of CABG versus PCI in the drug-eluting stents (DES) era.

Methods

We performed a systematic data search from January 1, 2003 to December 10, 2016 in PubMed; only reports published in peer-reviewed and indexed medical journals were included (Figure 1). A meticulous literature search using the keywords "unprotected coronary artery," "percutaneous coronary intervention," and "coronary artery bypass graft" identified 55 studies comparing the outcome of patients with ULMCA disease who had undergone percutaneous or surgical revascularization. However, only 9 studies with a mean or median follow-up of ≥5 years that compared the outcomes of PCI and CABG for patients with ULMCA disease were included in the final systematic analysis, and 46 studies were resultantly excluded (Table 1).

Data pertaining to baseline socio-demographic variables, and variables pertaining to the clinical presentation of the

[a]Resident Internal Medicine, McLaren Flint/Michigan State University, Flint, Michigan; [b]Department of Medicine, Section of Cardiology, Baylor College of Medicine, Houston, Texas; [c]Nishtar Medical College, Multan, Pakistan; [d]University of Washington, Seattle, Washington; and [e]Section of Cardiology, Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas. Manuscript received May 10, 2017; revised manuscript received and accepted July 21, 2017.

See page 1519 for disclosure information.

*Corresponding author: Tel: (713) 798-0280; fax: 844-710-6063.
E-mail address: mahboob.alam@bcm.edu (M. Alam).

0002-9149/
https://doi.org/10.1016/j.amjcard.2017.07.048

Table 1
Summary of all studies included in the meta-analysis

Author	Year	Study Design	DES	PCI(n)	CABG(n)	Region	Mean Follow-up(mo)	BMS(n)
Chieffo et al	2010	Retrospective	100%	107	142	Europe	60	0
Park et al (ASAN MAIN)	2010	Prospective	100%	176	219	Asia	60	0
Park et al (MAIN COMPARE)	2011	Prospective	100%	784	690	Asia	62*	0
Morice et al	2014	RCT	100%	357	348	Europe	60	0
Ahn et al (PRE-COMBAT)	2015	RCT	100%	300	300	Asia	60	0
Shiomi et al	2015	Retrospective	75.83%	364	640	Asia	65.3*	88
Yu et al	2015	Retrospective	100%	465	457	Asia	85.2*	0
Buszman et al	2016	RCT	100%	52	53	Europe	120	0
Makkikalio et al	2016	RCT	100%	592	592	Europe	60	0
Total				**3197**	**3440**			**88**

* Median follow-up.

BMS = bare metal stent; CABG = coronary artery bypass graft; DES = drug-eluting stent; PCI = percutaneous coronary intervention; RCT = randomized controlled trial.

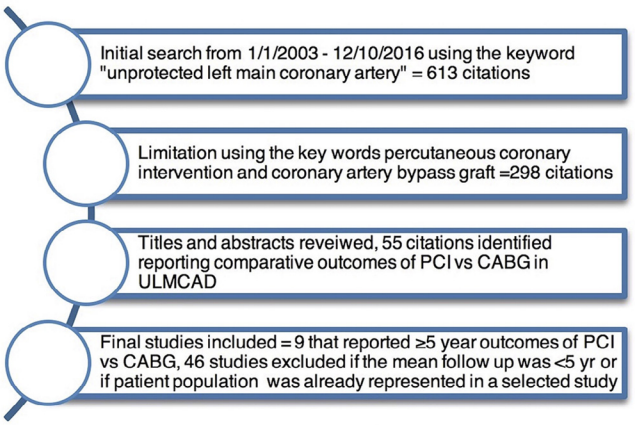

Figure 1. Literature search and review methodology.

patients, risk stratification scores (additive European System for Cardiac Operative Risk Evaluation [EuroSCORE] and SYNTAX score), coronary anatomy, and procedural variables (Table 2) were independently extracted by 2 reviewers. Primary independent variable was the initial revascularization strategy (PCI or CABG). Primary clinical outcome included all-cause mortality at a follow-up period of ≥5 years. Secondary clinical outcomes included major adverse cardiac and cerebrovascular events (MACCE; composite end point of all-cause mortality, nonfatal myocardial infarction [MI], stroke, or repeat revascularization) and individual outcomes of cardiac death, nonfatal cardiac MI, stroke, and repeat revascularization (target vessel revascularization and target lesion revascularization). We used the included studies' defined outcomes for our analysis.

Cochran Q-statistic and I^2 index tests were used as measures of heterogeneity, where an I^2 index of >25% was considered statistically significant. Funnel plot analysis for all-cause mortality was used to assess for publication bias (Figure 2). Only results from the random effects model were reported given the statistically shown variable degrees of heterogeneity of data. We considered p values <0.05 to be statistically significant. Analysis of baseline was performed using SPSS Statistics 23 (IBM Inc, Armonk, NY), and the meta-analyses using Review Manager version 5.0 (Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration 2012).

Results

Our meta-analyses included 9 comparative studies enrolling a total of 6,637 patients (PCI = 3,197, CABG = 3,440). Patients in the PCI and the CABG arms had comparable mean age and left ventricular ejection fraction. In terms of cardiovascular co-morbidities, patients had comparable rates of hypertension, hyperlipidemia, smoking, chronic renal insufficiency, previous MI, and previous stroke. However, the patients in the CABG arm had higher rates of diabetes mellitus, previous congestive heart failure, and peripheral arterial disease than the PCI arm. At the time of revascularization, the 2 study arms had comparable proportions of presentation with acute coronary syndrome. The PCI arm, however, had a higher rate of presentation with stable angina and/or silent myocardial ischemia.

A higher proportion of patients with ULMCA disease with 3-vessel involvement underwent CABG compared with PCI (59.7% vs 32.1%). In contrast, the PCI arm had greater proportions of patients with isolated ULMCA disease, ULMCA disease with 1-vessel involvement, or 2-vessel involvement. Notably, 88 of 3,197 (2.8%) patients in the PCI arm received bare-metal stents.

At 5-year follow-up, PCI with DES was associated with equivalent cardiac (odds ratio [OR] 0.95, 95% confidence interval [CI] 0.62 to 1.46) and all-cause mortality (OR 0.98, 95% CI 0.72 to 1.33), lower rates of stroke (OR 0.50, 95% CI 0.30 to 0.84), and higher rates of repeat revascularization (OR 2.52, 95% CI 1.63 to 3.91). MACCE showed a trend favoring CABG but did not reach statistical significance (OR 1.19, 95% CI 0.93 to 1.54) (Table 3).

Discussion

In our meta-analysis, PCI had an equivalent mortality, lower rates of stroke, and higher rates of repeat revascularization when compared with CABG for revascularization of ULMCA (Figure 3). With major RCTs presenting conflicting comparative outcomes and suggestions that a longer duration of