Outcomes of Coronary Artery Bypass and Stents for Unprotected Left Main Coronary Stenosis

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Background. **This study assessed the short-, medium-, and long-term outcomes of coronary artery bypass grafting vs stenting for patients with unprotected left main coronary artery disease through a meta-analysis of randomized controlled trials.**

Methods. **PubMed, Embase, Scopus, Web of Science, Cochrane Library, and major conference proceedings databases were systematically searched for randomized controlled trials of coronary artery bypass grafting compared with stents in unprotected left main coronary artery disease. End points assessed were all-cause death, myocardial infarction, major adverse cardiac and cerebrovascular events, target vessel revascularization, and cerebral stroke. A meta-analysis was conducted according to predefined clinical end points.**

Results. **All-cause death and stroke were similar between stenting and coronary artery bypass grafting at 1 year and at follow-up beyond 1 year. The incidence of myocardial infarction was similar between stenting and coronary artery bypass grafting at each separate time point. The incidence of repeat revascularization was similar between the two groups at 30 days but was higher for stenting at 1 year and beyond. There was a trend toward fewer major adverse cardiac and cerebrovascular events after stenting compared with coronary artery bypass grafting at 30 days, but this difference was no longer significant at 1 year and reversed at follow-up beyond 1 year.**

Conclusions. **The early advantages of stenting over coronary artery bypass grafting have been shown to progressively shift to coronary artery bypass grafting over time. Further larger sample randomized controlled trials are warranted to confirm the results.**

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For several decades, coronary artery bypass grafting (CABG) was regarded as the standard of care for significant left main disease in patients eligible for surgical intervention [1–4]. In recent years, outcomes after percutaneous coronary intervention (PCI) of the unprotected left main coronary artery disease (ULMCAD) have been shown to be noninferior to CABG [5, 6]. This has been reflected in current guidelines. The 2014 European Society of Cardiology/European Association for Cardio-thoracic Surgery guidelines already endorse that CABG and PCI may both provide effective treatment for LMCAD with an overall low to intermediate anatomic complexity [7]. The guidelines of the American societies recommend CABG for the treatment of LMCAD disease and suggest PCI as an alternative in patients with an increased surgical risk and an amenable anatomy [8].

These recommendations carry a B level of evidence, indicating the lack of data derived from multiple randomized clinical trials (RCTs) or meta-analyses. We therefore performed an up-to-date meta-analysis of data from all RCTs with the aim of assessing the short-, medium-, and long-term outcomes after PCI and CABG for patients with ULMCAD. Specific end points included death, stroke, myocardial infarction (MI), target-vessel revascularization (TVR), and major adverse cardiac and cerebrovascular events (MACCEs).

Material and Methods

Search Strategy and Study Selection

This meta-analysis was conducted and is presented in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [9]. Electronic searches were performed using PubMed, Embase, Scopus, Web of Science, Cochrane Library, and major conference proceedings databases. Search date variables were from dates of inception to May 2016. To achieve the maximum sensitivity of the search strategy and identify all studies, we combined the terms surgery or coronary artery bypass with stenting or percutaneous coronary intervention and left main and randomized clinical trial. The reference lists of key reviews and all potentially relevant studies were hand searched. Two of the

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Abbreviations and Acronyms

ASAN MAIN = ASAN Medical Center-Left MAIN Revascularization
BMS = bare-metal stents
CABG = coronary artery bypass grafting
CI = confidence interval
DES = drug-eluting stent
EES = everolimus-eluting stents
LE MANS = Left Main Coronary Artery Stenting
MACCE = major adverse cardiac and cerebrovascular events
M-H = Mantel-Haenszel test
MI = myocardial infarction
PCI = percutaneous coronary intervention
PES = paclitaxel-eluting stents
PRECOMBAT = Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease
RCT = randomized controlled trial
RR = relative risk
SES = sirolimus-eluting stents
SYNTAX = Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery
TVR = target vessel revascularization
ULMCAD = unprotected left main coronary artery disease

investigators independently screened the title and abstract of records that were identified in the search. Full-text publications were reviewed separately if either investigator considered the article to be potentially eligible. Disagreements regarding final study inclusion were resolved by discussion until consensus was reached.

Eligibility Criteria

Studies were included if the following criteria applied: (1) RCTs of CABG vs stenting, (2) unprotected left main stenosis exceeding 50% narrowing, and (3) outcomes of interest were reported.

Exclusion Criteria

Studies were excluded if any of the following criteria applied: (1) outcomes of interest were not clearly reported or were impossible to extract or calculate from the published results, and (2) single-arm studies. Abstracts, case reports, conference presentations, editorials, and expert opinions were excluded. Review articles were omitted because of the potential for publication bias and duplication of results.

Data Extraction and Study Quality

All data were independently extracted from text, tables, and figures by 2 of the investigators. Discrepancies between the 2 reviewers were resolved by discussion and consensus. The final results were reviewed by a third investigator. The information extracted for each study was first author, year and journal of publication, study period, MACCEs, all-cause death, MI, stroke, and TVR. The studies were grouped into short-term (30 days), medium-term (1 year), and long-term (>1 year) follow-up. The quality of the RCTs included in the meta-analysis was appraised by using Cochrane methods (selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias) [10]. We considered blinding adequate if outcome assessors were blinded. Because of the invasive nature of the interventions, we did not deem blinding of patients or performing physicians relevant. Finally, we judged each trial as a whole to ascertain whether there was low, unclear, or high risk of bias, based on whether the level of bias in each of the defined domains could have led to material biases in the risk estimates.

Statistical Analysis

When pooled effects from fewer than 3 studies were estimated, a fixed-effects model was used to avoid overweighting of small studies [11]. When the number of studies was sufficiently large to reliably estimate the τ^2 statistic, a random-effects model was used to minimize heterogeneity between groups [12]. Statistical significance for the relative ratio (RR) was set at a 2-tailed p of less than 0.05, provided the confidence interval (CI) did not cross 1. A 2-tailed α of 5% was used for hypothesis testing. Statistical heterogeneity was assessed with Cochran Q by the χ^2 test and quantified with the I^2 test [13]. Significant heterogeneity was considered present for p values of less than 0.10 or an I^2 of less than 50%, or both. Statistical analysis was conducted with Review Manager 5.2 (Cochrane Collaboration, Copenhagen, Denmark).

Results

We screened 337 records, of which 71 articles were selected for full-text review. From these 71 articles, 8 articles (5 trials) were selected for inclusion [5, 6, 14–19]. If multiple articles were available for a single study, we only used the most recent or most comprehensive article, unless data for different intervals of follow-up were not reported in these articles. A flow diagram in Figure 1 shows the search and selection process. Two articles reported outcomes at 30 days [6, 14]. Four of the eight articles reported 1-year outcomes [5, 6, 14, 15], and four articles [15–18] reported longer-term outcomes at 1.5, 2, 5, and 10 years. The four articles included longer-term outcomes for 2,343 patients [16–19]. Table 1 summarizes the characteristics of these studies.

Short-Term (30-Day) Results

Outcomes for all clinical end points at 30 days appear in Figure 2. The total MI rate was 2.9% (2 studies) in 306 patients, and the difference in the MI rate between the two groups (3.2% in the CABG group vs 2.6% in the stenting group) was not significant. There was no significant heterogeneity among the studies ($I^2 = 0\%$; $p = 0.64$). The RR in the fixed-effects model was 1.23 (95% CI, 0.34 to