Drug-eluting stents versus coronary artery bypass graft surgery in left main coronary artery disease: A meta-analysis of early outcomes from randomized and nonrandomized studies

Christopher Cao, MBBS, BSc (Med),[a,b] Con Manganas, MBBS,[b] Paul Bannon, MBBS, PhD,[a] Michael Vallely, MBBS, PhD,[a] and Tristan D. Yan, MD, PhD[a]

Objective: The present meta-analysis aimed to compare the short-term safety and efficacy of drug-eluting stents and coronary artery bypass graft surgery for patients with left main coronary artery disease.

Methods: Fourteen relevant studies were identified from 5 electronic databases. End points included mortality, stroke, myocardial infarction, repeat revascularization, and major adverse cardiac and cerebrovascular events.

Results: Results indicate that all-cause mortality was similar between drug-eluting stents and coronary artery bypass grafting at 30 days and at follow-up beyond 1 year. Likewise, the incidence of myocardial infarction was similar between drug-eluting stents and coronary artery bypass grafting at 12 months and at follow-up beyond 1 year. However, drug-eluting stents were associated with a lower incidence of all-cause mortality at 12 months and a higher incidence of myocardial infarction at 30 days compared with coronary artery bypass grafting. Drug-eluting stents were consistently associated with a higher incidence of repeat revascularization, whereas coronary artery bypass grafting had a higher incidence of stroke. The incidence of major adverse cardiac and cerebrovascular events was similar between the 2 groups at 30 days but higher for drug-eluting stents at 12 months and beyond.

Conclusions: Patients treated by drug-eluting stents in randomized controlled trials and observational studies in the current literature are often a preselected subgroup with less complex lesions compared with the overall target population. Results drawn from these studies should be viewed with caution. Coronary artery bypass grafting is associated with a lower incidence of major adverse cardiac and cerebrovascular events at 1 year and beyond, and thus should be regarded as the standard of treatment. However, drug-eluting stents may have a role for selected patients with percutaneously amenable left main disease who are poor surgical candidates. (J Thorac Cardiovasc Surg 2013;145:738-47)

Left main coronary artery disease (LMCAD) is defined as a greater than 50% narrowing of the left main coronary artery and is found in approximately 5% of all patients who undergo angiography.[1] Without revascularization, patients with LMCAD have a relatively poor prognosis, with 3-year survival as low as 34%.[2] Previous studies have demonstrated a clear survival benefit from revascularization over medical management.[2,3] Because of the anatomic complexity and unfavorable characteristics often associated with left main coronary artery lesions, percutaneous coronary intervention (PCI) has been traditionally deferred in preference for coronary artery bypass grafting (CABG).[4] However, with the evolution of drug-eluting stents (DES) in recent years, there has been a renewed interest in expanding the indication for PCI in patients with LMCAD.[5] This shift in paradigm was reflected in recent guidelines that recommended consideration of PCI for selected patients with low risk of PCI-related complications and increased risk of surgical complications.[6] The recent European Society of Cardiology and the European Association for Cardiothoracic Surgery guidelines on myocardial revascularization made level IA recommendations for CABG in all patients with LMCAD, whereas PCI was only recommended for selected patients with less complex disease based on level II or III evidence.[7]

Despite encouraging results for DES from relatively small observational studies with limited follow-up, there was a lack of robust clinical data to compare DES with CABG in patients with LMCAD.[8] In view of this, a number of randomized controlled trials have recently been published to compare these 2 revascularization techniques.[9-12]

From The Baird Institute for Applied Heart and Lung Surgical Research,[a] Sydney, Australia; and the Department of Cardiothoracic Surgery,[b] St George Hospital, Sydney, Australia.

Disclosures: Authors have nothing to disclose with regard to commercial support.
Received for publication Sept 29, 2011; revisions received Jan 15, 2012; accepted for publication Feb 3, 2012; available ahead of print March 12, 2012.

Address for reprints: Tristan D. Yan, MD, PhD, The Baird Institute for Applied Heart and Lung Surgical Research, Sydney, Australia (E-mail: tristan.yan@hotmail.com).

0022-5223/$36.00

doi:10.1016/j.jtcvs.2012.02.004

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
DES = drug-eluting stent
LMCAD = left main coronary artery disease
MACCE = major adverse cardiac and cerebrovascular events
PCI = percutaneous coronary intervention
RR = relative risk
SYNTAX = Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery

The aim of the present meta-analysis is to assess the short-term outcomes after DES or CABG for patients with LMCAD by using data from randomized and nonrandomized comparative studies in the current literature. Specific end points include components of major adverse cardiac and cerebrovascular events (MACCE), including mortality, stroke, myocardial infarction, and repeat revascularization.

PATIENTS AND METHODS

Literature Search Strategy

Electronic searches were performed using Ovid Medline, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ACP Journal Club, and Database of Abstracts of Review of Effectiveness from January 2000 to August 2011. To achieve the maximum sensitivity of the search strategy and identify all studies, we combined the terms *surgery* or *coronary artery bypass* with *angioplasty* or *stent* or *percutaneous coronary intervention* and *left main*. The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies. All relevant articles identified were assessed with application of the inclusion and exclusion criteria.

Selection Criteria

Eligible comparative studies for the present meta-analysis included those in which patients with angiographically proven LMCAD were treated by DES or CABG. All forms of DES were included, as were patients who underwent off-pump CABG. For studies that included patients with LMCAD as a subset of patients who had other types of coronary artery diseases, results for patients with LMCAD who underwent DES or CABG were extracted when possible. Likewise, studies that included DES as a proportion of patients who underwent PCI were only included if outcomes were available for the DES cohort. When centers have published duplicate trials with accumulating numbers of patients or increased lengths of follow-up, only the most complete reports were included for qualitative appraisal at each time interval. To maintain the consistency of measured end points, previous guidelines and definitions were used to assess short-term outcomes when applicable.[13,14] It is acknowledged that patient selection for revascularization varied among institutions and sometimes within an institution at different time periods. All publications were limited to human subjects and in the English language. Abstracts, case reports, conference presentations, editorials, and expert opinions were excluded. Review articles are omitted because of potential publication bias and possible duplication of results. Studies that included fewer than 20 patients or presented data with less than 12 months follow-up were also excluded.

Data Extraction and Critical Appraisal

All data were extracted from article texts, tables, and figures. When insufficient data were available from publications, corresponding authors were contacted to provide additional records. Two investigators (C.Q.C. and T.D.Y.) independently reviewed each retrieved article. Discrepancies between the 2 reviewers were resolved by discussion and consensus. The final results were reviewed by the senior investigators.

Statistical Analysis

Meta-analysis was performed by combining the results of reported incidences of mortality, stroke, myocardial infarction, repeat revascularization, and MACCE. The relative risk (RR) was used as a summary statistic. In the present study, both fixed and random effect models were tested. In a fixed effect model, it was assumed that treatment effect in each study was the same, whereas in a random effect model, it was assumed that there were variations between studies and the calculated ratios thus had more conservative value.[15] Chi-square tests were used to study heterogeneity between trials. I^2 statistic was used to estimate the percentage of total variation across studies due to heterogeneity rather than chance. I^2 can be calculated as $I^2 = 100\% \times (Q - df)/Q$, with Q defined as Cochrane's heterogeneity statistics and *df* defined as degrees of freedom.[16] An I^2 value greater than 50% was considered substantial heterogeneity. If there was substantial heterogeneity, the possible clinical and methodological reasons for this were explored qualitatively. In the present meta-analysis, the results using the random effects model were presented to take into account the possible clinical diversity and methodological variation among studies. Specific analyses considering confounding factors were not possible because raw data were not available. All *P* values were 2-sided. All statistical analysis was conducted with Review Manager Version 5.1.2 (Cochrane Collaboration, Software Update, Oxford, UK).

RESULTS

Quantity and Quality of Trials

A total of 1018 references were identified through the 5 electronic database searches. After exclusion of duplicate or irrelevant references, 570 potentially relevant articles were retrieved for more detailed evaluation. After the selection criteria were applied, 16 comparative studies remained for assessment. Manual search of the reference lists did not identify any additional relevant studies. One study was excluded because of duplicating patients at different follow-up periods. One study was excluded because primary outcome data were not available. Of the 14 studies included for final analysis in the present meta-analysis, 3 were from randomized controlled trials and the remainder were from observational studies, as summarized in Table 1.[9-12,17-26]

In these 14 studies, 5628 patients with LMCAD were compared, including 2490 patients who were treated with DES and 3138 patients who underwent CABG. Baseline characteristics, patient selection, and follow-up periods varied between studies, as summarized in Table 2.

Assessment of Mortality

All-cause mortality was not significantly different between DES and CABG at 30 days (2.3% vs 4.6%; RR, 0.57; 95% confidence interval [CI], 0.22-1.51; $P = .26$; $I^2 = 54\%$). At 12 months, DES was found to be associated with a significantly lower all-cause mortality (3.5% vs 5.7%; RR, 0.71; 95% CI, 0.54-0.95; $P = .02$; $I^2 = 0\%$).