CLINICAL RESEARCH STUDY

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Comprehensive Meta-Analysis on Drug-Eluting Stents versus Bare-Metal Stents during Extended Follow-up

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ABSTRACT

BACKGROUND: Several observational reports have documented both increased and decreased cardiac mortality or Q-wave myocardial infarction with drug-eluting stents compared with bare-metal stents.

METHODS: We sought to evaluate the safety and efficacy of drug-eluting stents compared with bare-metal stents early after intervention (<1 year) and late (>1 year) among a broad population of patients, using a meta-analysis of randomized clinical trials.

RESULTS: We identified 28 trials with a total of 10,727 patients and a mean follow-up of 29.6 months. For early outcomes (<1 year), all-cause mortality for drug-eluting stents versus bare-metal stents was 2.1% versus 2.4% (risk ratio [RR] 0.91, [95% confidence interval (CI), 0.70-1.18]; $P = .47$), non-Q-wave myocardial infarction was 3.3% versus 4.4% (RR 0.78 [95% CI, 0.61-1.00]; $P = .055$), target lesion revascularization was 5.8% versus 18.4% (RR 0.28 [95% CI, 0.21-0.38]; $P < .001$), and stent thrombosis was 1.1% versus 1.3% (RR 0.87 [95% CI, 0.60-1.26]; $P = .47$). For late outcomes (>1 year), all-cause mortality for drug-eluting stents versus bare-metal stents was 5.9% versus 5.7% (RR 1.03 [95% CI, 0.83-1.28]; $P = .79$), target lesion revascularization was 4.0% versus 3.3% (RR 1.22 [95% CI, 0.92-1.60]; $P = .16$), non-Q-wave myocardial infarction was 1.6% versus 1.2% (RR 1.36 [95% CI, 0.74-2.53]; $P = .32$) and stent thrombosis was 0.7% versus 0.1% (RR 4.57 [95% CI, 1.54-13.57]; $P = .006$).

CONCLUSIONS: There was no excess mortality with drug-eluting stents. Within 1 year, drug-eluting stents appear to be safe and efficacious with possibly decreased non-Q-wave myocardial infarction compared with bare-metal stents. After 1 year, drug-eluting stents still have similar mortality, despite increased stent thrombosis. The reduction in target lesion revascularization with drug-eluting stents mainly happens within 1 year, but is sustained thereafter.

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The use of drug-eluting stents has become common practice during coronary interventions, both for stable angina and acute coronary syndromes. Their efficacy in reducing angiographic restenosis and the subsequent need for repeat revascularization procedures has been well established.[1-3] Their ability to reduce target lesion revascularization also has been studied in patients with ST-elevation myocardial infarction.[4-12] On the other hand, several meta-analyses documented increased late stent thrombosis.[2,3,13,14] Subsequent to these reports, several additional reports have raised concerns about increased mortality with drug-eluting stents,[15,16] while more recent studies have reported decreased myocardial infarction,[17] no change in mortality,[2,17,18] or even decreased mortality.[19-21]

This controversy in outcomes associated with drug-eluting stents speaks to the uncertainty with these devices and the need for an updated comprehensive meta-analysis. Furthermore, the differential effect on Q-wave and non-Q-wave myocardial infarction and the early versus late effects of drug-eluting stents on the safety and efficacy outcomes have not been emphasized. We sought to confirm and explore new associations in a comprehensive meta-analysis of all randomized clinical trials that compared the commonly used paclitaxel- and sirolimus-eluting stents with bare-metal stents to assess their efficacy and safety in both short-term and long-term follow-up.

CLINICAL SIGNIFICANCE

- Drug-eluting stents do not increase or decrease mortality compared with bare-metal stents.
- The reduction in subsequent revascularization procedures with drug-eluting stents is mainly observed within 1 year postprocedure, but is sustained up to 5 years of follow-up.
- Drug-eluting stents might decrease non-Q-wave myocardial infarction within 1 year postprocedure.
- After 1 year, drug-eluting stents increase the risk of very late stent thrombosis.

METHODS

Search Strategy

We searched the Medline database for randomized clinical trials in the English language from 2000 to 2007 using the medical subject heading terms "Angioplasty," "Percutaneous," "Coronary," "Bare metal," and "stent," along with "Paclitaxel" or "Sirolimus." The titles and abstracts were reviewed on studies that presented original data from randomized clinical trials and compared paclitaxel-eluting stents or sirolimus-eluting stents with bare-metal stents. We also searched relevant journal supplements for abstracts, obtained abstract presentations from cardiology meetings, and used the Science Citation Index to cross-reference any articles that met our selection criteria.

Selection Criteria

The main inclusion criteria were randomized clinical trials that assigned patients to drug-eluting stents versus bare-metal stents and reported at least 6 months of follow-up. We included trials on a broad population of patients, including exclusively diabetic patients. The indications for stent placement included myocardial infarction, stable or unstable angina, and total coronary occlusion. We excluded studies that used nonpolymeric stent platforms, next-generation drug-eluting stents, venous bypass graft revascularization, treatment of in-stent restenosis, or head to head comparison of paclitaxel stents versus sirolimus stents. We also required that antiplatelet therapy consist of lifelong aspirin and a specified duration of a thienopyridine (clopidogrel or ticlopidine). Studies that used cilostazol instead of a thienopyridine were excluded.

Data Abstraction and Quality Assessment

Two of the 4 reviewers (HR and AAB) independently assessed appropriate treatment allocation and adequacy of analysis in each study. We used intention-to-treat analysis. For each outcome, 3 independent reviewers (HR, MLS, and GM) recorded the interval events. Discrepancies were resolved through a fourth reviewer (AAB). The reviewers also tabulated the baseline patient population and procedural characteristics. When trial results were available in both presentation and peer-reviewed published articles, the latter was considered for abstraction.

Endpoints and Definitions

The endpoints studied were all-cause mortality, cardiovascular mortality, Q-wave myocardial infarction, non-Q-wave myocardial infarction, target lesion revascularization, and stent thrombosis. Cardiovascular mortality was defined as death due to acute myocardial infarction, cardiac perforation or pericardial tamponade, arrhythmia or conduction abnormality, cerebrovascular accident before hospital discharge or suspected of being related to the procedure, and all death in which a cardiac cause could not be excluded. A sudden death of unknown cause was considered a cardiovascular death in the absence of another explanation. A myocardial infarction was defined as an elevation of creatine kinase of at least 2 times the upper normal limit with a positive creatine kinase MB enzyme. A Q-wave myocardial infarction was defined as the development of new pathological Q-waves in 2 or more leads lasting 0.4 second or more. An elevation of creatine kinase levels to at least 2 times normal without new Q-waves was considered a non-Q-wave myocardial infarction. Target lesion revascularization was defined as any repeat percutaneous coronary intervention of the target lesion or bypass surgery of the target vessel driven by a positive functional study, ischemic electrocardiogram