META-ANALYSIS

Meta-analysis of 14 trials comparing bypass grafting vs drug-eluting stents in diabetic patients with multivessel coronary artery disease

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Abstract *Background and aim:* Clinical trials have reported lower mortality and repeated revascularization rate in diabetic patients treated with coronary artery bypass grafting (CABG) as compared to percutaneous revascularization. However, these studies were conducted in the era of bare-metal stents. Therefore, we performed a meta-analysis to compare CABG to PCI with drug-eluting stents (DES) in diabetic patients with multivessel and/or left main disease.
Methods and results: The literature was scanned by formal search of electronic databases (Medline, EMBASE, and Cochrane databases), and major international scientific session abstracts from 2000 to 2013. Primary endpoint was mortality. A total of 14 (4 randomized and 10 non-randomized) trials were finally included, with a total of 7072 patients. Up to 5 years follow-up, CABG was associated with a reduction in mortality (7.3% vs 10.4%, OR[95%CI] = 0.65[0.55−0.77], $p < 0.0001$; phet = 0.00001), with similar results in both RCTs (OR[95%CI] = 0.64[0.50−0.82], $p = 0.0005$) and NRCTs (OR[95%CI] = 0.75[0.6−0.94], $p = 0.01$) (p int = 0.93). A significant relationship was observed between risk profile and benefits in mortality with CABG ($p < 0.001$). CABG reduced target vessel revascularization (TVR; 5.2% vs 15.7%, OR[95%CI] = 0.30[0.25−0.36], $p < 0.00001$, p het = 0.02), with a relationship between risk profile and the benefits from CABG as compared to DES ($p < 0.0001$). CABG was associated with a lower rate of MACCE (14.9% vs 22.9%, OR[95%CI] = 0.59[0.51−0.67], $p < 0.00001$, p het<0.00001) but higher risk of CVA (3.6% vs 1.4%, OR[95%CI] = 2.34[1.63−3.35], $p < 0.00001$, p het = 0.71).
Conclusions: The present meta-analysis demonstrates that among diabetic patients with multivessel disease and/or left main disease, CABG provides benefits in mortality and TVR, especially in high-risk patients but it is counterbalanced by a higher risk of stroke. Future trials are certainly needed in the era of new DES and improved antiplatelet therapies.
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Background

Coronary artery disease currently represents the leading cause of mortality in developed countries. Diabetes mellitus is one of the most common risk factors for cardiovascular disease, accounting for a higher rate of myocardial infarction and cardiovascular mortality [1,2], even after percutaneous revascularization procedures with both bare-metal (BMS) [3–6], or drug-eluting stents (DES) [7,8], especially in the

setting of acute myocardial infarction, where it is associated with higher risk of distal embolization and impaired myocardial perfusion [9–11]. Clinical trials have reported lower mortality rates as well as lower rates of repeated revascularization in patients with diabetes treated with coronary artery bypass grafting (CABG) compared to percutaneous revascularization [12]. However, these studies were conducted in the era of BMS, whereas the recent introduction of DES has been shown to decrease in-stent restenosis and repeat revascularization in patients with diabetes [13–17]. Therefore, we performed a meta-analysis to compare CABG to PCI with DES in diabetic patients with multivessel and/or left main disease.

Methods

Eligibility and search strategy

We conducted a search of Medline, EMBASE, and Cochrane databases for clinical studies and the scientific session abstracts in Circulation, Journal of College of Cardiology, European Heart Journal and American Journal of Cardiology from January 1990 to February 2013. Furthermore, oral presentations and/or expert slide presentations were included (searched on the TCT (www.tctmd.com), EuroPCR (www.europcr.com), ACC (www.acc.org), AHA (www.aha.org), and ESC (www.escardio.org) websites from January 2000 to December 2012). The following key words were used: "coronary artery bypass graft surgery", "drug-eluting stent", "DES", "sirolimus-eluting stent", "SES", "paclitaxel-eluting stent" "PES", "zotarolimus-eluting stent", "ZES", "everolimus-eluting stent", "EES", "biolimus-eluting stent", "BES", "tacrolimus-eluting stent", "diabetes mellitus", "multivessel disease", "left main".

Data extraction and validity assessment

Data were independently abstracted by two investigators. In case of incomplete or unclear data, authors, where possible, were contacted. Disagreements were resolved by consensus. Data were managed according to the intention-to-treat principle.

Outcome measures

Primary endpoint was mortality. Secondary endpoints were: 1) repeated revascularization, defined as target vessel revascularization (TVR) or any urgent revascularization on the basis of clinical condition, including surgical or percutaneous intervention; 2) cerebrovascular events (CVA); 3) major adverse cardiac and cerebrovascular events, MACCE (death, myocardial infarction, repeated revascularization and CVA).

Data analysis

Statistical analysis was performed using the Review Manager 4.27 freeware package, SPSS 11.5 statistical package. Odds ratio (OR) and 95% confidence intervals (95% CI) were used as summary statistics. The pooled odds ratio was calculated by using a random effect model (The DerSimonian and Laird method). The Breslow−Day test was used to examine the statistical evidence of heterogeneity across the studies ($p < 0.1$). Potential publication bias was examined by constructing a "funnel plot", in which sample size was plotted against odds ratios (for the primary endpoint). The study quality was evaluated by the same two investigators according to a score, that, as previously described [18], was expressed on an ordinal scale, allocating 1 point for the presence of each of the following: 1) statement of objectives; 2) explicit inclusion and exclusion criteria; 3) description of intervention; 4) objective means of follow-up; 5) description of adverse events; 6) power analysis; 7) description of statistical methods; 8) multicenter design; 9) discussion of withdrawals; 10) details on medical therapy (e.g. anticoagulation and antithrombotic regimen) during and after the procedure.

A meta-regression analysis was carried out to evaluate the relationship between the absolute difference in outcome for death and TVR between the revascularization strategies and several variables such as the prevalence of 3-vessel disease, left main disease, female gender, age, and the risk profile (rate of death and TVR in PCI group). The study was performed in compliance with the Quality of Reporting of Meta-Analyses (QUOROM) guidelines [19].

Results

Eligible studies

Among 380 potentially relevant publications, a total of 14 trials were finally included [20−33], 4 randomized (RCTs) and 10 non-randomized controlled trials (NRCTs, prospective cohort studies) (Fig. 1). A total of 7072 patients were included (3422 (48.4%) undergoing CABG and 3650 (51.6%) to DES). Of this, 3069 patients (43.3%) were included in 4 RCTs. Study characteristics of included trials are shown in Tables 1 and 2. The vast majority of patients were treated with SES, whereas less than 30% of patients received both internal mammary arteries. Follow-up data
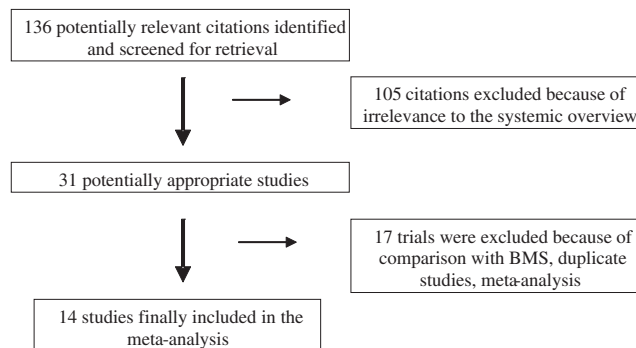

Figure 1 Flow diagram of the systematic overview process. RCT = Randomized controlled trials.