

Drug-eluting Stents versus Coronary Artery Bypass Grafting in Diabetic Patients with Multi-vessel Disease: A Meta-analysis



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Background

Data comparing long-term results after percutaneous intervention with drug-eluting stents (DES/PCI) and coronary artery grafting (CABG) in diabetic patients (pts) with multi-vessel disease is conflicting. We have conducted a systematic review and meta-analysis to help answer this issue.

Methods

MEDLINE, WoS, and Scopus were systematically analysed to yield observational studies (OBS) or randomised controlled trials (RCT) fulfilling search criteria. Odds ratio (OR) for studied end-points were obtained with inverse variance random effects analysis. Results are presented with 95% confidence intervals with significance at $p < 0.05$.

Results

A total of 14 studies (5 RCT; 9 OBS) including more than 5000 pts were selected for review. Early/30-day was lower in the DES/PCI cohort [OR 0.49(0.27, 0.88); $p = 0.02$; $I^2 = 0\%$]. Post-procedural stroke was higher in the CABG (1.8%) cohort compared to DES/PCI (0.17%; $p < 0.01$). A pooled analysis of RCT demonstrated that stroke rate was similar in both cohorts at the end of one year [OR 0.84(0.19, 3.74); $p = 0.82$; $I^2 = 67\%$].

During a follow-up of three to five years, repeat intervention was much higher in the DES/PCI cohort [OR 3.02(2.13, 4.28); $p < 0.01$]. The odds of suffering an adverse cardiovascular / cerebrovascular event were 1.71 (1.27, 2.3) times higher in the DES/PCI cohort compared to CABG.

Conclusion

In diabetic patients with multivessel disease, early mortality is lower in the DES/PCI cohort. While peri-procedural stroke rates are lower with PCI, they are, however, comparable at the end of one year. Use of drug-eluting stents leads to a higher rate of re-intervention and major cardiovascular/cerebrovascular events at three to five years.

Keywords

Coronary artery bypass grafting • Diabetes mellitus • Percutaneous intervention • Re-intervention
• Myocardial infarction • Major adverse cardiovascular and cerebrovascular events

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Introduction

Diabetes Mellitus (DM) is an important factor contributing to cardiovascular disease. It is accompanied by more extensive atherosclerosis and accelerated plaque progression, which may lead to a suboptimal outcome after coronary revascularisation [1–3]. The present era has seen a rapidly increasing use of drug-eluting stents. Observational studies comparing percutaneous intervention with drug eluting stents (DES/PCI) and coronary artery grafting (CABG) report conflicting results [4,5]. The randomised trials in this subset of patients viz. CARDia [6] and FREEDOM trials [7] are powered to detect a composite end-point, rather than individual adverse events. Thus we have conducted a systematic review and meta-analysis comparing DES/PCI and CABG in diabetic patients with multi-vessel disease.

Methods

Eligibility Criteria

We included randomised controlled trials (RCT) or observational studies (OS) which met the following criteria: (1) adult human subjects, (2) English language (3) articles comparing the results of PCI versus CABG in the diabetic patients or in which the analysis for the subset of diabetic patients was included, (4) study reporting either early or late survival, myocardial infarction (MI), the need for repeat revascularisation (NRR), and major adverse cardiovascular and cerebrovascular events (MACCE) during the follow-up period. (5) The study had to implement the use of DES/PCI in at least 80% of the patients undergoing angioplasty.

To obtain the most recent results of included RCTs, proceedings of major international conferences (2011 and 2012) were manually searched. Diabetes mellitus was limited to type 2 diabetes, defined as a fasting plasma glucose level \geq 126 mg/dl. Diabetic patients who were treated with either oral hypoglycaemic agents or insulin were included while excluding those treated with diet only.

Search Strategy

Pubmed, Ovid, and Medline were searched to identify studies meeting our study criteria. The key words used for the search were ‘percutaneous stents or PCI’, ‘drug eluting stents’, ‘heart catheterization’, ‘coronary artery disease’, ‘coronary stenosis’, ‘CABG or coronary artery bypass graft’, ‘myocardial revascularization’, ‘risk assessment’, or ‘treatment outcome’.

Study Selection

Two investigators (JYL, SVD) independently reviewed all abstracts fulfilling search criteria. Thereafter, promising full-text articles were retrieved and reviewed to finalise the articles for inclusion. Differences of opinion were resolved by consensus (JYL, SVD), reaching a Cohen’s kappa of 94%.

Study End-points

End-points studied were mortality, stroke, need for repeat re-intervention, and myocardial infarction. MACCE, a composite end-point was reported by many studies and was also selected for comparison. Results were divided into early (30 day/1year) and late (3-5 year) according to the follow-up period.

Data Abstraction

Data abstracted included study design, study year, country, treatment regimen, duration of follow-up, early/late mortality and other clinical end-points. The quality of included studies was assessed with the Newcastle-Ottawa scale for observational studies. The Newcastle-Ottawa scale [8] assesses the study on three aspects: Selection of the study cohort, comparability of the cases and controls on the basis of study design and the methods used to determine exposure to the event studied. The meta-analysis has been reported according to the PRISMA guidelines [9]. RCT have been analysed for quality using the Jadad scale, a numeric scale from 1-5 [10].

Statistical Analysis

Statistical analysis was conducted using Review Manager 5.1 (RevMan 5.1®, Nordic Cochrane Center and Copenhagen, Denmark). A random effects model using inverse variance weighting was implemented to obtain the pooled effect estimate for the studied end-points [11,12]. All results have been presented using the odds ratio (OR) as the dichotomous effect estimate. A small constant has been added to all the cells of the 2x2 contingency table when a single ‘‘zero’’ event rate was present. [13] Studies where both cohorts had ‘‘zero’’ event rates did not contribute to the pooled effect estimate. Results are shown graphically using forest plots. A forest plot is a representation of the odds ratio of each individual study along with the pooled event rate and odds ratio obtained from the statistical analysis. The square box depicts the weight of each study with the horizontal lines depicting the range of the odds ratio with 95% confidence intervals. The diamond demonstrates the pooled odds ratio. The centre of the diamond is at the obtained odds ratio value with the sides extended to reach the 95% confidence intervals value.

We used the Egger’s I^2 statistic, which estimates the percentage of total variation across studies that is due to heterogeneity rather than chance. Suggested thresholds for heterogeneity were used, with I^2 values of 25-49%, 50-74%, and \geq 75% indicative of low, moderate, and high heterogeneity [14]. Publication bias was investigated analysing funnel plot asymmetry using the rank correlation test [12,15].

Results

The initial search strategy yielded 1574 results. After exclusion of duplicates, non-English language studies, and case

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