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Original Article

Comparison of coronary artery bypass grafting and drug-eluting stents in patients with chronic kidney disease and multivessel disease: A meta-analysis

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ABSTRACT

Background: The optimal revascularization strategy of coronary artery bypass grafting (CABG) versus percutaneous coronary intervention with drug-eluting stent (PCI-DES) in patients with chronic kidney disease (CKD) and multivessel disease (MVD) remains unclear.
Methods: Pubmed, EMBASE and Cochrane Library electronic databases were searched from inception until June 2016. Studies that evaluate the comparative benefits of DES versus CABG in CKD patients with multi-vessel disease were considered for inclusion. We pooled the odds ratios from individual studies and conducted heterogeneity, quality assessment and publication bias analyses.
Results: A total of 11 studies with 29,246 patients were included (17,928 DES patients; 11,318 CABG). Compared with CABG, pooled analysis of studies showed DES had higher long-term all-cause mortality (OR, 1.22; $p < 0.00001$), cardiac mortality (OR, 1.29; $p < 0.00001$), myocardial infarction (OR, 1.89; $p = 0.02$), repeat revascularization (OR, 3.47; $p < 0.00001$) and major adverse cardiac and cerebrovascular events (MACCE) (OR, 2.00; $p = 0.002$), but lower short-term all-cause mortality (OR, 0.33; $p < 0.00001$) and cerebrovascular accident (OR, 0.64; $p = 0.0001$). Subgroup analysis restricted to patients with end-stage renal disease (ESRD) yielded similar results, but no significant differences were found regarding CVA and MACCE.
Conclusions: CABG for patients with CKD and MVD had advantages over PCI-DES in long-term all-cause mortality, MI, repeat revascularization and MACCE, but the substantial disadvantage in short-term mortality and CVA. Future large randomized controlled trials are certainly needed to confirm these findings.

1. Introduction

Chronic kidney disease (CKD) is associated with increased cardiovascular mortality and morbidity [1–2]. Patients with end-stage renal disease (ESRD) have a high prevalence of coronary artery disease (CAD) [3]. Based on data from United States Renal Data System (USRDS), cardiovascular disease accounts for approximately 44% of all-cause mortality in dialysis patients [4].

Currently, coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are two major approaches used for coronary revascularization in CKD patients with CAD. Observational studies comparing PCI and CABG report conflicting results [5–7]. Moreover, many studies were carried out in the era of bare metal stent (BMS), whereas the introduction of drug-eluting stent (DES) has been shown to provide favorable outcomes compared to BMS in CKD patients [8–11].

A previous meta-analysis concluded that DES is associated with lower early mortality but higher rate of reintervention when compared with CABG specifically in patients with end-stage renal disease [12]. Although the results of several recently published studies are available, there are still no prospective randomized trials addressing this important issue. Chan et al. found that CABG was associated with improved early and late clinical outcomes when compared with DES [13]. However, Wang et al. showed similar outcomes between the two procedures in patients with CKD and multi-vessel disease [14]. Thus, the optimal method for coronary revascularization in CKD patients remains to be determined. As small observational studies are underpowered to detect statistical significance, it is reasonable to perform to a meta-analysis of accumulated evidence to evaluate the comparative benefits of DES versus CABG in CKD patients with multi-vessel disease.

2. Methods

2.1. Search strategy

This meta-analysis was compiled with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) guidelines [15]. We systematically searched Pubmed, Embase, and Cochrane

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Library for relevant studies reported from inception until July 2016. MeSH terms and keywords used to identify articles included "coronary artery bypass grafting or CABG", "drug-eluting stents or DES", "percutaneous coronary intervention or PCI", "coronary artery disease or CAD", "multi-vessel disease", "chronic kidney disease", "end-stage renal disease or ESRD" and "dialysis". References of relevant studies have also been checked for articles suitable for our meta-analysis. No language restriction was applied.

2.2. Study selection

Studies were included if they met the following criteria: 1) studies comparing CABG with PCI-DES for CKD with left main (LM) and/or multi-vessel disease (MVD); 2) studies published in peer-reviewed journals with full available text; (3) studies reported at least one outcome of interest: death, myocardial infarction (MI), cerebrovascular accident (CVA), and repeat revascularization. Studies were excluded if they met any of the following criteria: 1) the subjects were not exclusively CKD with LM and/or MVD, 2) using only BMS or combined use of BMS. Two investigators (Y.W. and S.Z) independently reviewed all studies retrieved from the databases according to the prespecified search criteria. Differences of opinion were resolved via consensus.

2.3. Data extraction and quality assessment

Following data were independently extracted by two investigators (Y.W. and P.G) from each study: first author, study design, location of study, sample size, clinical baseline characteristics, the proportion of dialysis patients and duration of follow-up. Primary endpoints were short-term (in-hospital or 30 days) and long-term all-cause mortality. Secondary endpoints were: 1) long-term cardiac mortality; 2) myocardial infarction (MI); 3) repeated revascularization (subsequent to PCI or CABG); 4) cerebrovascular accident (CVA); 5) major adverse cardiac and cerebrovascular events (MACCE), a composite endpoint including death, stroke, MI or repeated revascularization. CKD was defined as an estimated glomerular filtration rate of <60 ml/min/1.73 m^2. End-stage renal disease (ESRD) patients was defined as patients with an estimated glomerular filtration rate < 15 ml/min or dialysis dependence, or both). The study quality was evaluated by the same two investigators according to a nine-item Newcastle-Ottawa Quality scale [16]. High-quality studies were defined as a study with a modified Newcastle-Ottawa score of ≥5 (maximum, 9).

2.4. Statistical analysis

Odds ratio (OR) with 95% confidence intervals (95% CI) were used as summary statistics for categorical variables. We examined heterogeneity across studies by the Cochran's Q statistic and the I^2 statistic. An I^2 < 50% was considered low heterogeneity. The random-effect and fixed-effect model were used, as previously described [17]. Publication bias was investigated by analyzing funnel plot asymmetry and Egger regression asymmetry test [18] ($p < 0.05$ was considered indicative of statistically significant publication bias). For each endpoint we performed subgroup analysis restricted to patients with ESRD, apart from the overall analysis. A sensitivity analysis was performed when the between-study heterogeneity was significant. A p value <0.05 was considered statistically significant. RevMan 5.3 and Stata 12.0 software was used for statistical analysis.

3. Results

3.1. Study selection

A total of 954 articles have been obtained from Pubmed, EMBASE, and Cochrane databases. In addition, 6 suitable articles were obtained from the reference lists. After a careful check, 345 duplicates have been eliminated. Among the remaining 613 articles, 557 articles were eliminated because they were not related to our topic. Fifty-six full-text articles were assessed for eligibility. Forty-five articles were further eliminated because they were meta-analysis, commentary or letter to editors, adverse clinical outcomes were not reported in their clinical endpoints, or there was no comparison group between DES and CABG in CKD patients. A flow-chart of the detailed results of the search strategy was presented in Fig. 1.

3.2. Study characteristics and quality assessment

A total of 11 retrospective studies [13,14,19–27] were identified in this meta-analysis. Of them, two were matched cohort studies [13,20]. Three studies were conducted in America, 1 was conducted in Canada, and 7 studies were performed in Asian countries (3 in Japan, 2 in the China, 2 in Korea). The main characteristics of the included studies were summarized in Table 1. A total number of 29,246 patients with CKD consisting of 17,928 patients from the DES group and 11,318 patients from the CABG group were included in this meta-analysis. Ages, percentage of male participants were comparable between both groups. Patients with single and double vessel disease were more likely undergo DES while triple vessel patients undergo CABG. Shroff et al. [23] used the United States Renal Data System (USRDS) database, which did not provide number of vessel involvement in the cohorts. Three studies [14,20,25] excluded patients with left main artery disease. 5 studies [21–24,26] included all the dialysis patients. Of them, four studies included hemodialysis patients while one study [23] included both hemodialysis and peritoneal dialysis patients. Moreover, all studies included in our meta-analysis were considered to be of high quality.

3.3. Primary outcomes

Six studies reported the short-term all-cause mortality. The pooled result for short-term mortality showed a 67% decrease in the patients who underwent DES instead of CABG (OR, 0.33; 95% CI, 0.29 to 0.38; $p < 0.00001$, $I^2 = 45\%$; Fig. 2a). In the 11 studies from which the available data for long-term all-cause mortality were extracted, there was low heterogeneity among the results ($p = 0.07$, $I^2 = 41\%$). The DES group showed higher long-term all-cause mortality than CABG (OR, 1.22; 95% CI, 1.15 to 1.29; $p < 0.00001$; Fig. 2b).

As demonstrated in Table 2, in the subgroup analysis restricted to ESRD patients, DES was also associated with lower short-term mortality (OR, 0.31; 95% CI, 0.27 to 0.36; $p < 0.00001$, $I^2 = 0\%$) but higher long-term mortality (OR, 1.26; 95% CI, 1.19 to 1.34; $p < 0.00001$, $I^2 = 4\%$) compared with CABG.

3.4. Secondary outcomes

3.4.1. Long-term cardiac mortality

Mild heterogeneity was observed among the results of 6 studies ($p = 0.37$, $I^2 = 7\%$). There was a higher risk for cardiac mortality in patients treated with DES compared with CABG (OR, 1.29; 95% CI, 1.20 to 1.38; $p < 0.00001$; Fig. 3a). In ESDR patients, the overall outcome revealed that DES led to higher long-term cardiac mortality risk than CABG (OR, 1.28; 95% CI, 1.20 to 1.37; $p < 0.00001$, $I^2 = 19\%$; Table 2).

3.4.2. Myocardial infarction

There was substantial heterogeneity among the five studies that provided the relevant data for myocardial infarction in CKD patients with multi-vessel coronary disease ($p < 0.0001$, $I^2 = 76\%$). After pooled analysis, DES showed obviously higher risk of myocardial infarction than CABG (OR, 1.89; 95% CI, 1.11 to 3.21; $p = 0.02$; Fig. 3b). In the subgroup analysis limited to ESDR patients, pooled analysis of five studies yielded similar results with low heterogeneity (OR 1.94; 95% CI 1.30 to 2.91; $p = 0.001$; $I^2 = 14\%$; Table 2).

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