Ther Adv Chronic Dis
2021, Vol. 12: 1–12
DOI: 10.1177/2040622321990273

Coronary artery bypass graft surgery *versus* stenting for patients with chronic kidney disease and complex coronary artery disease: a systematic review and meta-analysis

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Abstract

Background: The relative role of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) with stent implantation in patients with chronic kidney disease (CKD) and complex coronary artery disease (CAD) remains debatable due to the lack of randomized controlled trials (RCTs). We therefore performed this meta-analysis to compare the outcomes of the two strategies in CKD patients with multivessel and/or left main disease.

Methods: Electronic databases including PubMed, EMBASE and Cochrane Library were comprehensively searched to identify the eligible subgroup analysis of RCTs and propensity-matched registries. The primary endpoint was all-cause mortality during the longest follow-up.

Results: Five subgroup analyses of RCTs and six propensity-matched registries involving 26,441 patients were analyzed. Overall, the strategy of CABG was associated with lower risks of long-term mortality [odds ratio (OR) 0.83, 95% confidence interval (CI) 0.74–0.93], myocardial infarction (OR, 0.41; 95% CI, 0.27–0.62), and repeat revascularization (OR, 0.25; 95% CI, 0.16–0.39) compared with PCI in CKD patients with complex CAD. However, CABG was slightly associated with higher risk of stroke than PCI (OR, 1.33; 95% CI, 1.00–1.77). Nonetheless, the higher stroke risk in the CABG group no longer existed during long-term follow-up (OR, 0.92; 95% CI, 0.37–2.25) (>3 years).

Conclusion: This meta-analysis supports the current guideline advising CABG for patients with CKD and complex CAD. At the expense of slightly increased risk of stroke, CABG reduces the incidences of long-term all-cause death, myocardial infarction and repeat revascularization compared with PCI.

Keywords: chronic kidney disease, complex coronary artery disease, coronary artery bypass grafting, outcome, percutaneous coronary intervention

Received: 16 April 2020; revised manuscript accepted: 5 January 2021.

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Introduction

Cardiovascular disease is the leading cause of death in patients with chronic kidney disease (CKD).[1] In clinical scenarios, CKD patients are prone to complex coronary artery disease (CAD) characterized by diffuse lesions, marked calcification, and small vessel diameters, rendering percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) challenging.[2] Unsurprisingly, CKD patients, especially those with multivessel or left main disease, often have an increased risk of unfavorable outcomes after

revascularization compared with patients with preserved renal function.[3,4]

However, the relative role of PCI and CABG on survival in this population remains debatable. Although current the guideline supports CABG over PCI in patients with CKD and multivessel disease, the evidence mainly dates from retrospective registries since this high-risk group of patients is generally excluded or under included by randomized controlled trials (RCTs).[5,6] Actually, patients still prefer PCI over surgery due to fewer complications and quicker recovery in real world practice.[7] The advent of the drug-eluting stent (DES) and more potent antiplatelet strategy has strikingly reduced the incidence of ischemic events, broadening the indications for PCI to include high-risk patients with complex lesions.[8] Although previous meta-analysis with non-randomized trials found that CABG had a survival advantage over PCI in patients with CKD and multivessel disease, the unadjusted confounding factors definitely had an effect on the results.[9] Therefore, we performed this meta-analysis including sub-analysis of RCTs and propensity-matched studies with high quality to compare the two revascularization strategies for patients with complex CAD and CKD.

Methods

This study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement, as well as Meta-analysis Of Observational Studies in Epidemiology checklist.[10,11]

Search strategy

A comprehensive search of the electronic databases including PubMed, EMBASE, and Cochrane Library from inception to 30 November 2019 was conducted by two independent investigators (JFT and DFZ) to identify pertinent articles comparing clinical outcomes of CABG and PCI with stent implantation in CKD patients with multivessel and/or left main disease. The following medical subject headings and search terms were used: "chronic kidney disease", "end-stage renal disease", "dialysis", "percutaneous coronary intervention", "coronary artery bypass", "stent", "revascularization", "outcome", "survival", "mortality", "randomized controlled trial", "clinical trial", "propensity-score matched", and "propensity-score matching". We also examined the references of the identified articles and relevant reviews to include other potentially eligible studies.

Study selection

Studies satisfying the following criteria were eligible: (1) patients with multivessel and/or left main CAD and concomitant CKD with an estimated glomerular filtration rate of <60 ml/min per 1.73 m^2 or creatinine clearance <60 ml/min, or on dialysis; (2) sub-analysis of RCTs and propensity-matched observational studies comparing the two alternative approaches, that is, PCI and CABG; and (3) studies reporting endpoint data of interest. In addition, we did not include studies published as abstracts or conference proceedings. Only studies published in English were taken into account. When several reports overlapped with each other, we selected the largest and the latest one. The studies were reviewed by two investigators independently (WW and MDZ) to determine whether they met the inclusion criteria and any disagreement was resolved by consensus.

Data extraction and quality assessment

The following data was independently extracted by two authors (MZ and FX) through a standardized form for each study: study design, patient characteristics, quality indicators, and clinical outcomes. Differences in assessments were resolved by discussing with a third investigator (FY). The quality of RCTs was assessed by evaluating the following methodological criteria recommended by the Cochrane Collaboration: sequence generation, concealment of allocation, blinding of participants, personnel and outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias,[12] whereas the observational studies were evaluated by the Newcastle–Ottawa Scale criteria.[13] Studies with a Newcastle–Ottawa score of $\geqslant 6$ (maximum, 9) were considered high quality.

Endpoints

The primary endpoint was all-cause mortality during the longest follow-up. Secondary outcomes included short-term mortality (within 30 days), myocardial infarction (MI), stroke, and repeat revascularization. All the endpoints were

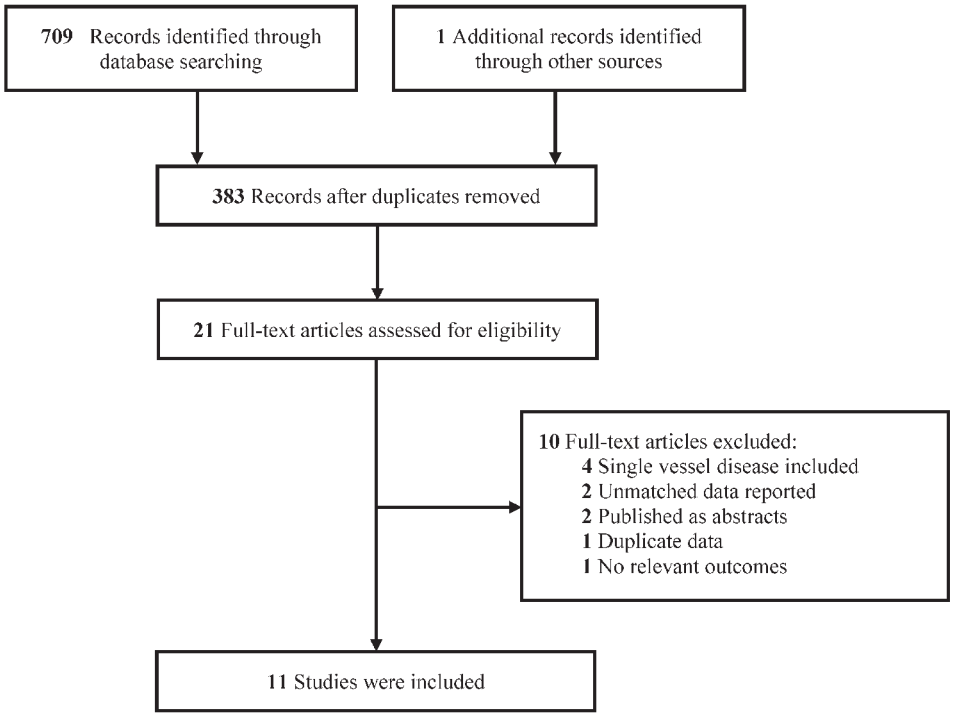

Figure 1. Flow diagram of included studies.

defined as reported in each study (Supplemental material Table S1 online). Of note, we did not analyze cardiac mortality as an endpoint, since few studies reported the incidence of cardiac death.

Statistical analysis

Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated with the Dersimonian and Lair random-effects model to account for heterogeneity. Potential heterogeneity among studies was quantified with the I^2 statistic, which was classified as mild, moderate, and severe according to I^2 values of $<25\%$, $25\% \leqslant I^2 \leqslant 50\%$, and $>50\%$, respectively.[14] To demonstrate the robustness of the results, we investigated the influence of each single study on the overall results by omitting each in turn. Moreover, we performed separate analyses according to the following variables: (1) RCTs or propensity-matched studies; (2) studies with long-term (>3 years) or midterm ($\leqslant 3$ years) follow-up; (3) studies with multivessel disease; (4) studies using DES exclusively. Meta-regression analysis was also conducted to assess the correlation of patient characteristics, that is, age, gender, diabetes, hypertension, dyslipidemia, and previous MI with all the outcomes. The risk of potential publication bias was assessed by visual inspection of funnel plots, and the Begg and the Egger tests.[15,16] All p values were two-sided, and results were considered statistically significant at $p<0.05$. Computations were performed using Stata/SE12.0 (StataCorp, College Station, Texas, USA).

Results

Eligible studies

Eleven studies involving 26,441 patients (PCI group: 13,217; CABG group: 13,224) were included in the final analysis, including five sub-analyses of RCTs and six propensity-matched registries,[17–27] published between 2005 and 2019 (Figure 1). The main characteristics of the eligible studies are presented in Table 1. Of the 11 studies, two compared PCI using bare-metal stent (BMS) *versus* CABG,[17,25] five compared PCI using DES *versus* CABG,[20,21,23,24,26] and the remaining four compared PCI using mixtures of BMS and DES *versus* CABG.[18,19,22,27] Overall, nine studies included multivessel disease with no

Table 1. Main characteristics of the eligible studies in the meta-analysis.

Study	No. patients		Period	Region	Design, center	Inclusion criteria	Stent type	Follow-up, years
	PCI	CABG						
Aoki *et al.*[17]	69	73	1997–1998	19 countries	Post-hoc analysis of RCT, multi	MVD, Ccr <60 ml/min	BMS	5
Chang *et al.*[18]	7049	7049	1997–2009	USA	PSM registry, multi	MVD, on dialysis	BMS/DES	1.7 (median)
Chang *et al.*[19]	1458	1458	1996–2008	USA	PSM registry, multi	MVD, eGFR <60 ml/min per 1.73 m^2, not on dialysis	BMS/DES	3.9 (median)
Bangalore *et al.*[20]	2960	2960	2008–2011	USA	PSM registry, multi	MVD, eGFR <60 ml/min per 1.73 m^2	EES	2.9 (mean)
Chan *et al.*[21]	893	893	2008–2011	Canada	PSM registry, multi	MVD, Ccr <60 ml/min	DES	1.8 (mean)
Komiya *et al.*[22]	77	77	2005–2007	Japan	PSM registry, multi	MVD, eGFR <30 ml/min per 1.73 m^2, not on dialysis	BMS/DES	2.5 (median)
Baber *et al.*[23]	225	226	2005–2010	18 countries	Post-hoc analysis of RCT, multi	MVD, diabetes, eGFR <60 ml/min per 1.73 m^2	PES/SES	3.8 (median)
Giustino *et al.*[24]	177	184	2010–2014	17 countries	Post-hoc analysis of RCT, multi	LM, eGFR <60 ml/min per 1.73 m^2	EES	3 (median)
Lima *et al.*[25]	47	49	1995–2000	Brazil	Post-hoc analysis of RCT, single	MVD, eGFR <60 ml/min per 1.73 m^2	BMS	9.4 (median)
Milojevic *et al.*[26]	158	151	2005–2007	17 countries	Post-hoc analysis of RCT, multi	LM/MVD, eGFR <60 ml/min per 1.73 m^2	PES	5
Gaipov *et al.*[27]	104	104	2007–2014	USA	PSM registry, multi	MVD, on dialysis	BMS/DES	1.5 (median)

BMS, bare-metal stent; CABG, coronary artery bypass grafting; Ccr, creatinine clearance; DES, drug-eluting stent; EES, everolimus-eluting stent; eGFR, estimated glomerular filtration rate; LM, left main; MVD, multivessel disease; PCI, percutaneous coronary intervention; PES, paclitaxel-eluting stent; PSM, propensity-score matching; RCT, randomized controlled trial.

or very few left main disease,[17–23,25,27] one study enrolled both multivessel and left main disease,[26] and the remaining one study enrolled only left main disease.[24] The clinical characteristics of the patients appear in Table 2. Quality assessment results are summarized in Supplemental Tables S2 and S3, and all the observational studies were considered to be of high quality.

Primary endpoint

In summary, all the included studies reported all-cause mortality. CABG was significantly associated with lower risk of long-term mortality *versus* PCI with moderate heterogeneity (OR, 0.83; 95% CI, 0.74–0.93; I^2 = 48.5%) (Figure 2). Subgroup analyses showed that there was mild heterogeneity in the sub-analysis of RCTs (OR, 0.68; 95% CI, 0.51–0.91; I^2 = 4.4%) and no signs of heterogeneity in studies with long-term follow-up (OR, 0.84; 95% CI, 0.72–0.98; I^2 = 0%) (Figure 2 and Table 3). In addition, in the propensity-matched registries (OR, 0.86; 95% CI, 0.77–0.96), in studies with midterm follow-up (OR, 0.81; 95% CI, 0.70–0.95), in studies with multivessel disease (OR, 0.86; 95% CI, 0.77–0.95), and in studies using DES exclusively

Table 2. Clinical characteristics of the patients.

Study	Mean age, years	Male	Current smoker	Diabetes	Hypertension	Dyslipidemia	Prior MI	Mean LVEF, %	Mean SYNTAX score	Mean eGFR, ml/min per 1.73 m^2	Dialysis
Aoki *et al.*[17]	70.5	68.3%	13.4%	18.3%	49.3%	54.9%	N/A	59.5	N/A	52†	N/A
Chang *et al.*[18]	64.3	57.5%	4.3%	66.5%	80.0%	25.5%	17.5%	N/A	N/A	N/A	100%
Chang *et al.*[19]	72.0	69.2%	32.9%*	35.6%	73.2%	88.4%	37.7%	N/A	N/A	N/A	0%
Bangalore *et al.*[20]	69.8	61.7%	26.6%*	48.6%	77.6%	62.9%	21.4%	N/A	N/A	N/A	8.3%
Chan *et al.*[21]	75.1	52.7%	48.8%*	44.3%	84.0%	75.2%	N/A	N/A	N/A	43.5†	6.2%
Komiya *et al.*[22]	72.7	59.7%	21.4%	60.4%	92.9%	48.1%	26.6%	N/A	29.4	21.9	0%
Baber *et al.*[23]	67.9	63.2%	10.6%	100%	93.8%	84.3%	25.7%	N/A	26.9	47.4	0%
Giustino *et al.*[24]	72.7	66.2%	12.3%	40.4%	84.8%	73.9%	21.6%	55.5	26.5	48.6	0.8%
Lima *et al.*[25]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0%
Milojevic *et al.*[26]	71.8	67.6%	10.7%	30.4%	85.1%	78.0%	34.0%	N/A	29.5	47.6	N/A
Gaipov *et al.*[27]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	100%

*Represents current or former smoker.
†Represents creatinine clearance (ml/min).
eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MI, myocardial infarction.

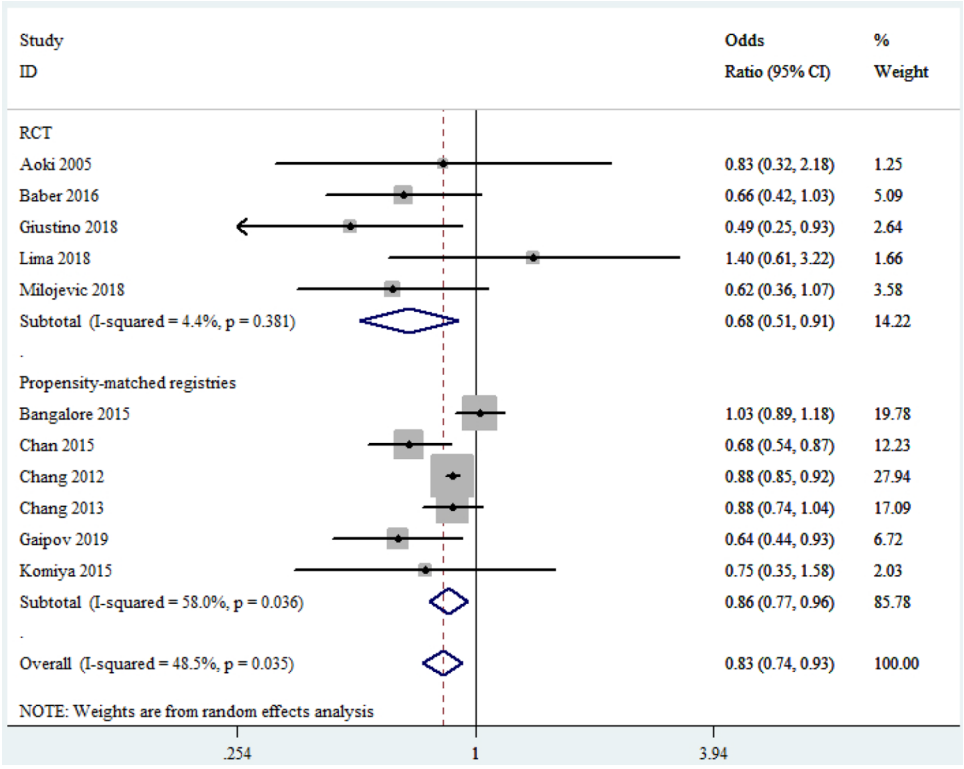

Figure 2. Forest plot of long-term all-cause mortality for coronary artery bypass grafting *versus* percutaneous coronary intervention.
CI, confidence interval; RCT, randomized controlled trial.

(OR, 0.72; 95% CI, 0.54–0.97) the results were consistent with the overall analysis (Table 3). Moreover, sensitivity analysis conducted through the removal of any single trial showed that it did not essentially affect the overall pooled estimate (Supplemental Figure S1).

Secondary endpoints

Four studies provided information regarding short-term death. Overall, short-term mortality did not differ between CABG and PCI with moderate heterogeneity (OR, 0.84; 95% CI, 0.48–1.47; $I^2 = 44.5\%$; Figure 3A). Also, the lack of statistically significant difference was consistent across all the subset analyses (Table 3).

The incidence of MI was reported in nine studies. Compared with the PCI group, patients who received CABG were associated with lower risk of MI (OR, 0.41; 95% CI, 0.27–0.62; $I^2 = 80.9\%$) (Figure 3B). When analyzing the studies with long-term follow-up exclusively, the heterogeneity was significantly reduced (OR, 0.35; 95% CI, 0.23–0.55; $I^2 = 40.6\%$). Additionally, in subset analysis of RCTs (OR, 0.50; 95% CI, 0.26–0.97), in propensity-matched registries (OR, 0.35; 95% CI, 0.20–0.63), in studies with midterm follow-up (OR, 0.46; 95% CI, 0.22–0.96), in studies with multivessel disease (OR, 0.37; 95% CI, 0.23–0.60), and in studies using DES exclusively (OR, 0.42; 95% CI, 0.23–0.74) the results were in line with the overall analysis (Table 3).

Seven studies reported the endpoint of stroke. There was a slightly significant increased risk of stroke in the CABG group compared with the PCI group (OR, 1.33; 95% CI, 1.00–1.77; $I^2 = 15.5\%$), which was largely driven by the results of the propensity-matched registries (OR, 1.49; 95% CI, 1.18–1.90), whereas no difference was found between the two strategies in subset analysis of RCTs (OR, 1.05; 95% CI, 0.55–2.00) (Figure 3C). The higher risk of stroke in the CABG group was consistent in studies with midterm follow-up (OR, 1.49; 95% CI, 1.18–1.88), whereas it was similar between the two therapies

Table 3. Sensitivity analysis.

Outcome	Subgroup	No. studies	OR (95% CI)	I^2	$p_{heterogeneity}$
All-cause death	RCTs	5	0.68 (0.51–0.91)	4.4%	0.381
	PSM studies	6	0.86 (0.77–0.96)	58.0%	0.036
	Long-term	5	0.84 (0.72–0.98)	0%	0.410
	Midterm	6	0.81 (0.70–0.95)	66.9%	0.010
	MVD	9	0.86 (0.77–0.95)	45.6%	0.065
	DES exclusively	5	0.72 (0.54–0.97)	73.8%	0.004
Short-term death	RCTs	2	1.45 (0.27–7.80)	29.7%	0.233
	PSM studies	2	0.77 (0.41–1.44)	69.5%	0.070
	Long-term	1	3.90 (0.43–35.26)	N/A	N/A
	Midterm	3	0.76 (0.46–1.24)	39.2%	0.193
	MVD	2	0.77 (0.41–1.44)	69.5%	0.070
	DES exclusively	4	0.84 (0.48–1.47)	44.5%	0.144
Myocardial infarction	RCTs	5	0.50 (0.26–0.97)	58.1%	0.049
	PSM studies	4	0.35 (0.20–0.63)	90.5%	<0.001
	Long-term	5	0.35 (0.23–0.55)	40.6%	0.151
	Midterm	4	0.46 (0.22–0.96)	86.3%	<0.001
	MVD	7	0.37 (0.23–0.60)	84.1%	<0.001
	DES exclusively	5	0.42 (0.23–0.74)	84.2%	<0.001
Stroke	RCTs	4	1.05 (0.55–2.00)	26.7%	0.251
	PSM studies	3	1.49 (1.18–1.90)	0%	0.368
	Long-term	3	0.92 (0.37–2.25)	49.2%	0.140
	Midterm	4	1.49 (1.18–1.88)	0%	0.567
	MVD	5	1.33 (0.94–1.90)	31.4%	0.212
	DES exclusively	5	1.48 (1.18–1.86)	0%	0.459
Repeat revascularization	RCTs	4	0.33 (0.24–0.47)	0%	0.484
	PSM studies	4	0.19 (0.09–0.38)	94.3%	<0.001
	Long-term	4	0.24 (0.19–0.29)	0%	0.500
	Midterm	4	0.23 (0.08–0.63)	92.1%	<0.001
	MVD	6	0.21 (0.12–0.36)	90.6%	<0.001
	DES exclusively	5	0.27 (0.14–0.53)	89.2%	<0.001

CI, confidence interval; DES, drug-eluting stent; MVD, multivessel disease; OR, odds ratio; PSM, propensity-score matched; RCT, randomized controlled trial.

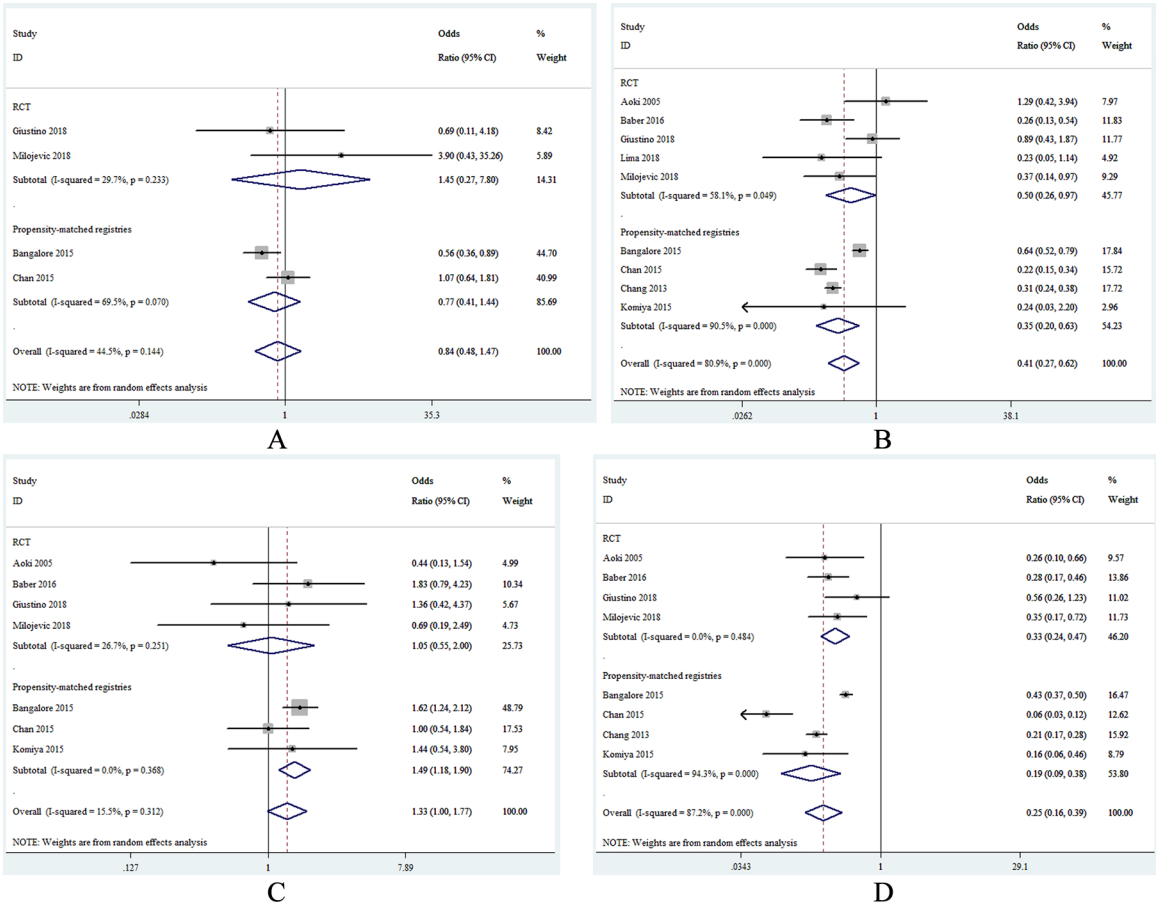

Figure 3. Forest plots of the secondary endpoints for coronary artery bypass grafting *versus* percutaneous coronary intervention. (A) short-term mortality, (B) myocardial infarction, (C) stroke, (D) repeat revascularization. CI, confidence interval; RCT, randomized controlled trial.

in studies with long-term follow-up (OR, 0.92; 95% CI, 0.37–2.25). Notably, the higher risk of stroke in the CABG group was more evident when compared with patients who used DES exclusively in the PCI group (OR, 1.48; 95% CI, 1.18–1.86). Besides, the strategy of CABG tended to be associated with higher risk of stroke *versus* PCI in studies with multivessel disease (OR, 1.33; 95% CI, 0.94–1.90).

As shown in Figure 3D, the use of CABG *versus* BMS produced a 75% significant reduction in the risk of repeat revascularization (OR, 0.25; 95% CI, 0.16–0.39), with severe heterogeneity (I^2 = 87.2%). When analyzing the sub-analysis of RCTs (OR, 0.33; 95% CI, 0.24–0.47; I^2 = 0%) or studies with long-term follow-up (OR, 0.24; 95% CI, 0.19–0.29; I^2 = 0%), no signs of heterogeneity were found and CABG remained to be associated with lower risk of repeat revascularization in comparison with PCI. In the propensity-matched registries (OR, 0.19; 95% CI, 0.09–0.38), in studies with midterm follow-up (OR, 0.23; 95% CI, 0.08–0.63), in studies with multivessel disease (OR, 0.21; 95% CI, 0.12–0.36), and in studies using DES exclusively (OR, 0.27; 95% CI, 0.14–0.53) the results were in concordance with the overall analysis (Table 3).

Meta-regression analysis and publication bias

Funnel plot assessment was performed, and no publication bias was found for all the outcomes (Supplemental Figure S2 and Supplemental Table S4). In addition, meta-regression analyses revealed significant association between previous MI and the endpoints of MI (regression coefficient, –0.045; 95% CI –0.089 to –0.001; p = 0.047) as well as repeat revascularization (regression coefficient, –0.042; 95% CI –0.068 to

–0.016; $p=0.011$). No interaction was found between the aforementioned age, gender, diabetes mellitus, hypertension, dyslipidemia, and all the clinical outcomes (Supplemental Table S5).

Discussion

The present meta-analysis involving 26,441 patients showed that the strategy of CABG reduced the risk of long-term mortality, MI, and repeat revascularization compared with PCI in CKD patients with multivessel and/or left main disease. However, CABG was slightly associated with higher risk of stroke than PCI and the short-term mortality was similar between the two treatment strategies. Subgroup analysis of RCTs, propensity-matched registries, studies with long-term or midterm follow-up, studies with multivessel disease, and studies using DES exclusively obtained mostly similar results compared with the overall analysis.

It is well-recognized that complex CAD characterized by diffuse lesions, extensive calcification, and small vessel diameters is more common in CKD patients, making coronary revascularization difficult.[2] During PCI, stents cannot expand adequately in heavily calcified lesions. The increasingly used rotational atherectomy is sufficient to modify physical attributes of calcified plaque to facilitate balloon dilatation and stent implantation.[28] Although it is associated with greater acute diameter gain, less final residual stenosis after stent implantation, and higher procedural success, routine use of rotational atherectomy did not reduce the long-term ischemic events in randomized trials.[29,30] Likewise, calcified vessels also pose technical challenges during the performance of distal anastomoses. Not surprisingly, patients with CKD often have an increased risk of unfavorable outcomes after revascularization compared with those without CKD.[3,4]

However, the relative role of the two revascularization approaches has not been fully demonstrated in this population. Until now, no randomized trial has been performed to address this issue. Current observational studies have shown conflicting results: some reported better outcomes in patients who underwent CABG, whereas others reported similar survival rates between the two groups. Previous meta-analysis conducted by Wang *et al.* showed that CABG could reduce the all-cause mortality compared with PCI in CKD patients with multivessel disease.[9] Nonetheless, our study has several strengths. First of all, all the available subanalysis of RCTs and propensity-matched registries were included in our analysis to improve the power and reliability of the results. Contrarily, that review did not include the recently published data from large-scale RCTs and high quality registries, and most of the included studies reported unmatched data severely influenced by confounding factors. Second, we included only complex disease including multivessel disease and/or left main disease in our study, whereas four of the 11 studies enrolled patients with single-vessel disease (17.9–59%) in that review. Moreover, the study by Shroff *et al.*, which accounted for over 60% of the sample size in that meta-analysis, did not report the data of diseased vessel number. Third, more diverse subgroup analyses were performed in our study, and the results of all the outcomes were largely consistent with the overall analysis, confirming the robustness of our findings.

Similar to the recently published meta-analysis of five randomized trials conducted by Gallo *et al.* in patients with left main disease not stratified for CKD,[31] our study found that CABG reduced the risk of long-term MI and repeat revascularization compared with PCI in CKD patients with multivessel and/or left main disease. Moreover, CABG was also associated with lower long-term all-cause mortality than PCI in the current meta-analysis. Furthermore, this conclusion was reinforced by the fact that the results of subgroup analyses based on different study design, follow-up time, type of stent, and type of disease were totally consistent with the overall population. Theoretically, CABG offers prophylactic protection by virtue of bypassing a larger extent of obstructive lesions or vulnerable plaques, minimizing the effect of progressive disease in the entire upstream proximal vessel. Meanwhile, the use of internal mammary artery ensures the long-term patency of the conduits.[32] In contrast, PCI addresses short segments of severe stenosis where progressive atherosclerosis forms new severe significant stenosis and plaque ruptures. Moreover, the advantage of CABG over PCI may be partially due to the completeness of revascularization, since complete revascularization is more often achieved in patients who underwent CABG rather than PCI, especially in complex disease.[33]

Of note, the predominantly applied first-generation DES or BMS and the suboptimal antiplatelet therapies may contribute to the poor outcomes in patients who underwent PCI than those who received CABG. New-generation DESs with novel stent platforms and more biocompatible polymers are associated with enhanced endothelialization, fewer stent fractures and less endothelial dysfunction.[34–36] In fact, robust evidence has confirmed the superiority of new-generation DESs regarding lower risks of stent thrombosis, MI, and repeat revascularization compared with first-generation DES and BMS.[37] Also, new antiplatelet drugs have a particular advantage over clopidogrel regarding MI and stent thrombosis.[38] Previous studies have illustrated the more beneficial effect of intravascular ultrasound or fractional flow reserve on prognosis than routine PCI in complex disease. Thus, the use of new-generation DESs, more potent antiplatelet drugs, and new interventional techniques will likely reduce the incidence of ischemic events for patients who received PCI.

The benefit of CABG over PCI with DES comes at the expense of slightly increased stroke risk. Given the serious consequences of stroke, this finding may have important clinical implications. It is generally believed that aortic manipulation and consequent atherosclerotic debris embolization are the most common mechanisms of stroke in on-pump CABG.[39] Hopefully, off-pump CABG with the "aortic no-touch" technique appears to be of special value for patients with CKD.[40] Also, the lower incidence of dual antiplatelet therapy after revascularization might also contribute to the bad result of CABG. Similar to prior observations from the NOBLE and the SYNTAX trials,[41,42] our study demonstrated that PCI was associated with an increase in late stroke (>3 years), which might completely counteract the early benefit of PCI.

Limitations

Our study presents several limitations that cannot be ignored. First, considering the lack of RCTs, we included both sub-analysis of RCTs and propensity-matched registries in our study, thus the results should be considered exploratory and hypothesis generating. Second, trials included in this meta-analysis were varied in study design, inclusion criteria, stent type, and follow-up time. Not surprisingly, heterogeneity was noted in the analyses of certain endpoints. Thus, a random-effect model was applied all across the study, and subgroup analyses as well as meta-regression analyses were conducted to explore the heterogeneity. Third, subgroup analysis according to CKD stages was not performed due to lack of data. In fact, our meta-analysis mainly included patients with stage 3–4 CKD, with only two study enrolled patients on dialysis. Thus, the results should be extrapolated carefully to patients on dialysis. Finally, first-generation DES, applied mostly in the original studies, could not fully reflect the clinical practice in the new-generation DES era.

Conclusion

This meta-analysis supports current guideline advising CABG for patients with complex CAD and CKD. At the expense of slightly increased risk of stroke, CABG reduces the incidences of long-term all-cause death, MI, and repeat revascularization compared with PCI. More importantly, the results of all the subgroup analyses were mostly consistent with the overall population. Randomized trials are warranted to investigate the relative benefit of CABG and PCI with new-generation DESs, more potent antiplatelet therapy and new interventional techniques in the future.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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Supplemental material

Supplemental material for this article is available online.

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