

Survival outcomes and adverse events in patients with chronic kidney disease after coronary artery bypass grafting and percutaneous coronary intervention: a meta-analysis of propensity score-matching studies

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ABSTRACT

Background: The present meta-analysis of propensity score-matching studies aimed to compare the long-term survival outcomes and adverse events associated with coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) in patients with chronic kidney disease (CKD).

Methods: Electronic databases were searched for studies comparing CABG and PCI in patients with CKD. The search period extended to 13 February 2021. The primary outcome was all-cause mortality, and the secondary endpoints included myocardial infarction, revascularization, and stroke. Odds ratios (ORs) and hazard ratios (HRs) with 95% confidence intervals (CIs) were used to express the pooled effect. Study quality was assessed using the Newcastle–Ottawa scale. The analyses were performed using RevMan 5.3.

Results: Thirteen studies involving 18,005 patients were included in the meta-analysis. Long-term mortality risk was significantly lower in the CABG group than in the PCI group (HR: 0.76, 95% CI: 0.70–0.83, $p < .001$), and similar results were observed in the subgroup analysis of patients undergoing dialysis and for different estimated glomerular filtration rate ranges. The incidence rates of myocardial infarction (OR: 0.25, 95% CI: 0.12–0.54, $p < .001$) and revascularization (OR: 0.17, 95% CI: 0.08–0.35, $p < .001$) were lower in the CABG group than in the PCI group, although there were no significant differences in the incidence of stroke between the two groups (OR: 1.24; 95% CI: 0.89–1.73, $p > .05$). Subgroup analysis among patients on dialysis yielded similar results.

Conclusions: Our propensity score matching analysis revealed that, based on long-term follow-up outcomes, CABG remains superior to PCI in patients with CKD.

Abbreviations: CABG: coronary artery bypass grafting; CHD: coronary heart disease; CAD: coronary artery disease; CI: confidence interval; CKD: chronic kidney disease; eGFRs: estimated glomerular filtration rates; FFM: functional form misspecification; HR: hazard ratio; MI: myocardium infarction; MR:: multiple regression; NOS: Newcastle–Ottawa Quality scale; OR: odds ratio; PCI: percutaneous coronary intervention; PRISMA: preferred reporting items for systematic reviews and meta-analyses; RCTs: randomized controlled trials

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Introduction

Previous large-scale randomized controlled trials (RCTs) have compared the prognosis of patients with coronary artery disease (CAD) following percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). However, most trials included only a small subgroup of patients with chronic kidney disease (CKD) [1] and did not conduct a subgroup analysis on these

patients [2], with some even listing CKD as an exclusion criterion [3]. When we make clinical decisions for patients with CKD, it is inappropriate to make conclusions based on the analysis of a cohort including both patients with and without CKD. Moreover, the three current RCTs included only 1121 patients with CKD in total. Of the three trials, two studies suggested that the long-term mortality risk did not significantly differ

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between PCI and CABG in patients with CKD [4, 5], while Milojevic et al. reported a remarkably higher risk of death in those after PCI [6]. As such, further evidence that provides convincing insights into the optimal revascularization strategy for patients with CKD is required.

Cohort studies usually report clinical characteristics for both groups, but several factors that influence the results do not match before the consequent comparison. A proper comparison of groups with balanced background characteristics is necessary. Randomization is an ideal method for balancing characteristics between groups. However, RCTs comparing the effects of PCI and CABG in patients with CKD are limited. On the other hand, propensity score-matching is an alternative method for cohort studies to ensure the homogeneity of clinical characteristics between groups, making the extrapolation more accurate [7]. Multiple systematic reviews in other fields have suggested that the results from PSM studies are representative of RCT efficacy [8, 9] and are widely utilized for comparisons [10, 11].

Several recent studies have focused on this topic. However, no meta-analysis has analyzed the results of propensity score-matching studies comparing prognosis between PCI and CABG in patients with CKD. Furthermore, previous meta-analyses have failed to conduct a subgroup analysis of long-term survival outcomes stratified by different estimated glomerular filtration rates (eGFRs) [12, 13]. Therefore, we conducted an updated meta-analysis to obtain more persuasive results.

Methods

The present analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Five online databases (PubMed, Embase, Cochrane Library, Scopus, and Web of Science) were searched to compare PCI and CABG in patients with CKD. We used the Mesh Terms 'coronary artery bypass', 'percutaneous coronary intervention', 'renal insufficiency, chronic', 'renal insufficiency', 'renal dialysis', 'kidney failure, chronic', 'peritoneal dialysis', and their entry items to search the relative references. The search period extended to 13 February 2021. The search strings are detailed in the [Supplementary file](#).

Inclusion and exclusion criteria

Studies were included upon meeting the following criteria:

- a. Data comparing CABG and PCI.
- b. Patients involved in the study had CKD.

- c. They were written in English.
- d. They are cohort studies using propensity score matching.

Studies were excluded under the following conditions:

- a. They were found to be duplicate studies.
- b. They were meta-analyses, reviews, meeting abstracts, or protocols.
- c. The authors did not present any data regarding the comparison between CABG and PCI.
- d. They are not cohort study.
- e. Propensity score matching was not used before outcome analysis.

The primary outcome of interest was mortality (all-cause death). Secondary outcomes included myocardial infarction, revascularization including target vessel revascularization and target lesion revascularization, and stroke. The long-term follow-up period was defined as a follow-up period of ≥ 1 year.

Data extraction and review

Two authors (YGY and NL) independently searched the databases for eligible studies. The following information and relevant data were extracted by the two authors: the number of patients, study type, follow-up period, and baseline clinical features. Disagreements on certain studies and data were discussed and resolved via consensus. If a consensus could not be reached, a final decision was made by MHC. Study quality was evaluated by the same two investigators according to the Newcastle–Ottawa Quality scale (NOS). High-quality studies were defined as those with a modified NOS score of ≥ 5 (maximum, 9) [14].

Statistical analysis

Heterogeneity was assessed using the I^2 statistic, in which the results range from 0% to 100%. If I^2 was $>50\%$, heterogeneity was considered significant; otherwise, the opposite was considered. Pooled results were calculated using the random-effects model. In addition, a sensitivity analysis was conducted to identify the sources of heterogeneity. A funnel plot was used to evaluate publication bias. Hazard ratios (HRs) and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and the pooled analyses were performed using RevMan 5.3 software.

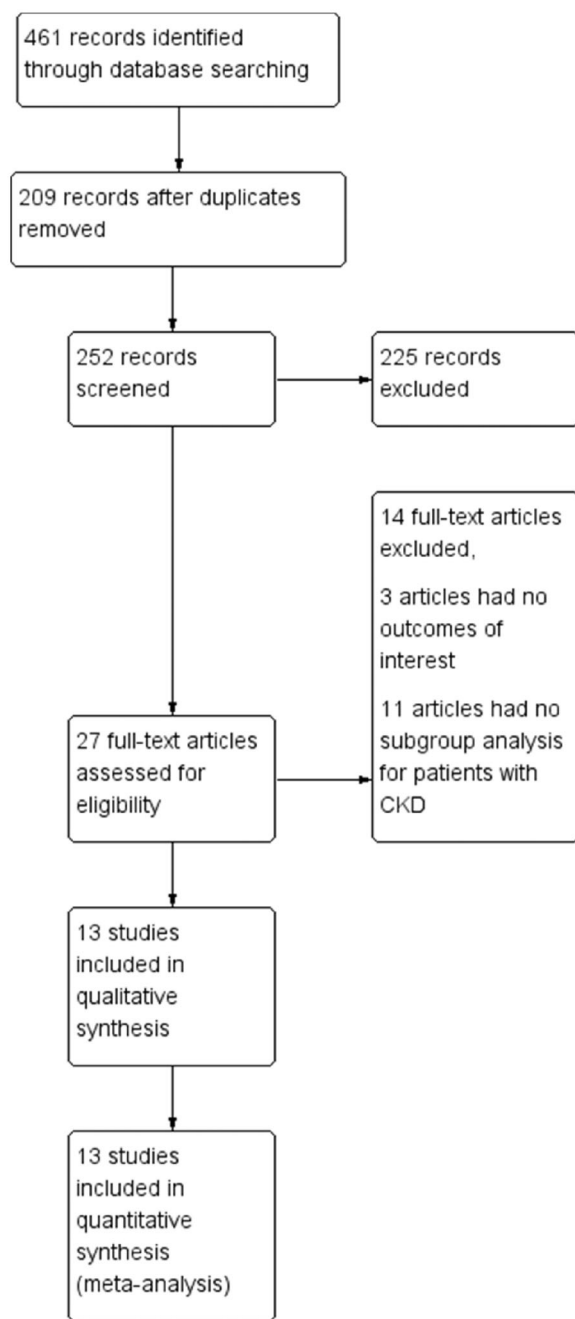


Figure 1. Flow diagram of study selection. CKD: chronic kidney disease.

Results

Four hundred and sixty-one records were retrieved from five online databases (PubMed = 43; Embase = 187; Web of Science = 60; Scopus = 156; Cochrane Library Center = 15). Two hundred and nine (209) duplicates were removed. After careful screening, 252 articles were excluded. Of the 252 articles, 61 were conference abstracts, 21 were reviews or editorials, and 143 were not related to our topic. Twenty-seven (27) articles were assessed for eligibility. After assessment, 14

articles were excluded because three articles did not report the outcomes of interest, and 11 articles did not conduct a subgroup analysis including patients with CKD. Finally, 13 articles including 18,005 patients were included in the meta-analysis. The flow diagram of the study selection procedure is depicted in [Figure 1](#). The characteristics of the included studies are listed in [Table 1](#). The details of the study quality assessment (NOS), matching variables, medical treatment, and dialysis type in each study are shown in the [supplementary file](#).

Long-term hazard risks in patients with CKD

The overall long-term mortality risk was significantly lower in the CABG group than in the PCI group (HR: 0.76, 95% CI: 0.70–0.83), with moderate heterogeneity ($I^2=21%$). The results are shown in [Figure 2](#).

When the subgroup analysis was restricted to patients on dialysis, long-term mortality was still lower in the CABG group than in the PCI group (HR: 0.74; 95% CI: 0.60–0.91), with moderate heterogeneity ($I^2=24%$). This result is shown in [Figure 3](#).

When the subgroup analysis was conducted among patients with different eGFR levels, the CABG group still exhibited a lower risk of mortality than the PCI group when eGFR ranged from 0 to 30 (HR: 0.56, 95% CI: 0.41–0.77) and from 30 to 59 (HR: 0.75, 95% CI: 0.63–0.89). These results are shown in [Figure 4](#).

When the subgroup analysis was conducted among patients with eGFRs ranging from 0 to 45, mortality risk was significantly lower in the CABG group than in the PCI group (HR: 0.73; 95% CI: 0.55–0.97; $I^2=69%$). After the removal of Bangalore 2015, the heterogeneity decreased ($I^2=0$), and the advantage of CABG over PCI remained unchanged (HR: 0.82; 95% CI: 0.68–0.98). The details of the sensitivity analysis are shown in the [supplementary file](#). CABG was also associated with a lower mortality risk than PCI for eGFRs ranging from 45 to 59 (HR: 0.85; 95% CI: 0.73–0.99; $I^2=0$). These results are shown in [Figure 5](#).

Secondary outcomes between PCI and CABG

Myocardial infarction

Patients who underwent CABG exhibited an obviously lower risk of myocardial infarction than those who underwent PCI (OR: 0.25; 95% CI: 0.12–0.54), with substantial heterogeneity ($I^2=78%$, [Figure 4\(A\)](#)). This result is shown in [Figure 6](#). After the removal of Bangalore 2015, the heterogeneity decreased ($I^2=0%$), while the significance of the result remained unchanged (OR: 0.19; 95% CI: 0.13–0.30). The details of the sensitivity

Table 1. Characteristics of included studies.

Study	Country	Study type	Sample size		Patients on dialysis (%)		Follow-up (years)	Quality of study
			PCI	CABG	PCI	CABG		
Baek et al. [15]	Republic of Korea	Cohort study	44	43	100	100	5	7
Bangalore et al. [16]	USA	Cohort study	2960	2960	8.2	8.2	5	8
Chan et al. [17]	USA	Cohort study	893	893	6.2	6.3	2	7
Kilic et al. [18]	USA	Cohort study	352	352	11.1	10.2	5	7
Komiya et al. [19]	Japan	Cohort study	77	77	0	0	4	8
Kumada et al. [20]	Japan	Cohort study	787	210	100	100	10	7
Kumada et al. [21]	Japan	Cohort study	92	92	100	100	5	7
Lautamäki et al. [22]	Finland	Cohort study	54	54	11.1	16.7	3	7
Marui et al. [23]	Japan	Cohort study	258	130	100	100	5	7
Roberts et al. [24]	USA	Cohort study	39	30	1.4	2.1	5	8
Sugumar et al. [25]	Australia	Cohort study	263	526	23	35	3.1	7
Chang et al. [26]	USA	Cohort study	1458	1458	<i>n</i>	<i>n</i>	8	7
Vuurmans et al. [27]	Canada	Cohort study	135	135	<i>n</i>	<i>n</i>	2	7

PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery.

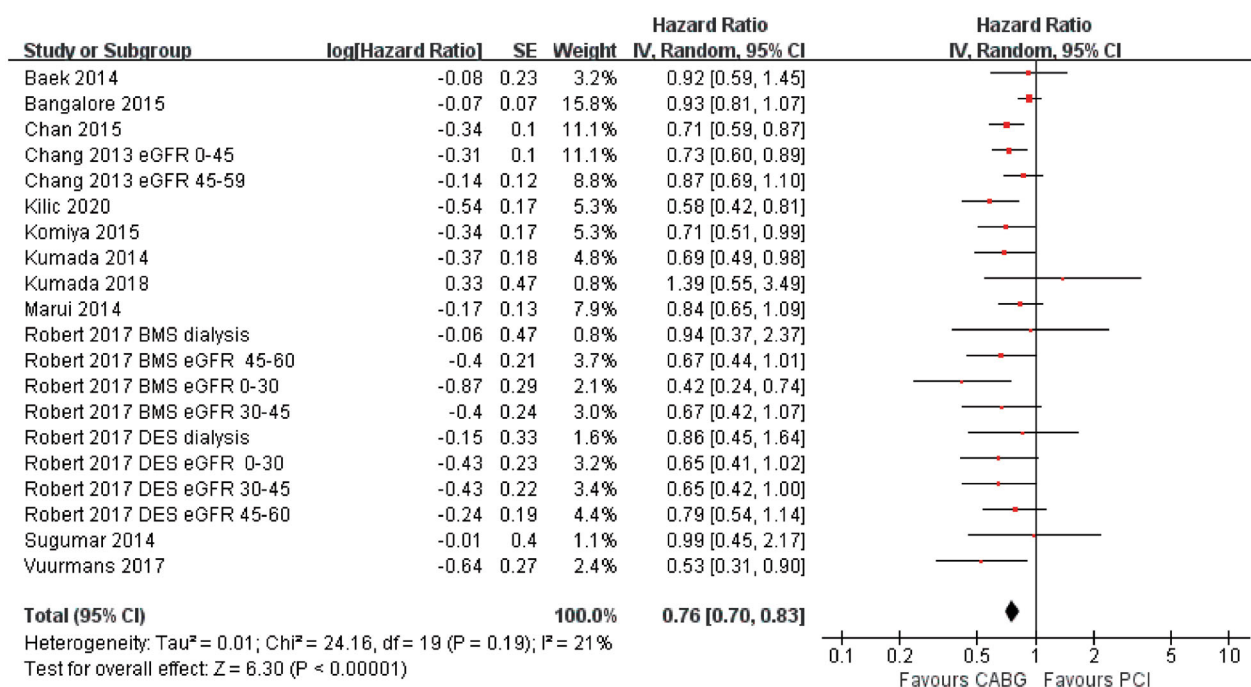


Figure 2. Hazard ratios of overall long-term mortality between PCI and CABG in patients with chronic kidney disease. PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery; SE: standard error; CI: confidence interval.

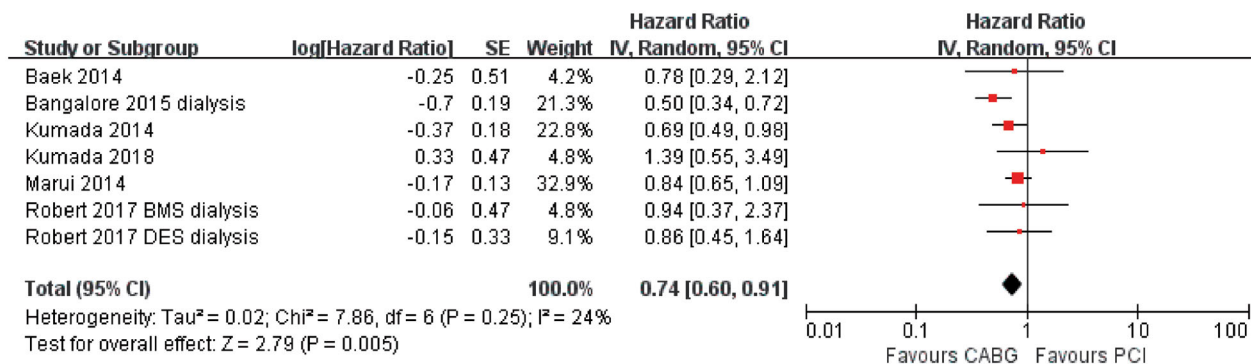


Figure 3. Hazard ratios of overall long-term mortality between PCI and CABG in patients on dialysis. PCI: percutaneous coronary intervention. CABG: coronary artery bypass surgery; SE: standard error; CI: confidence interval.

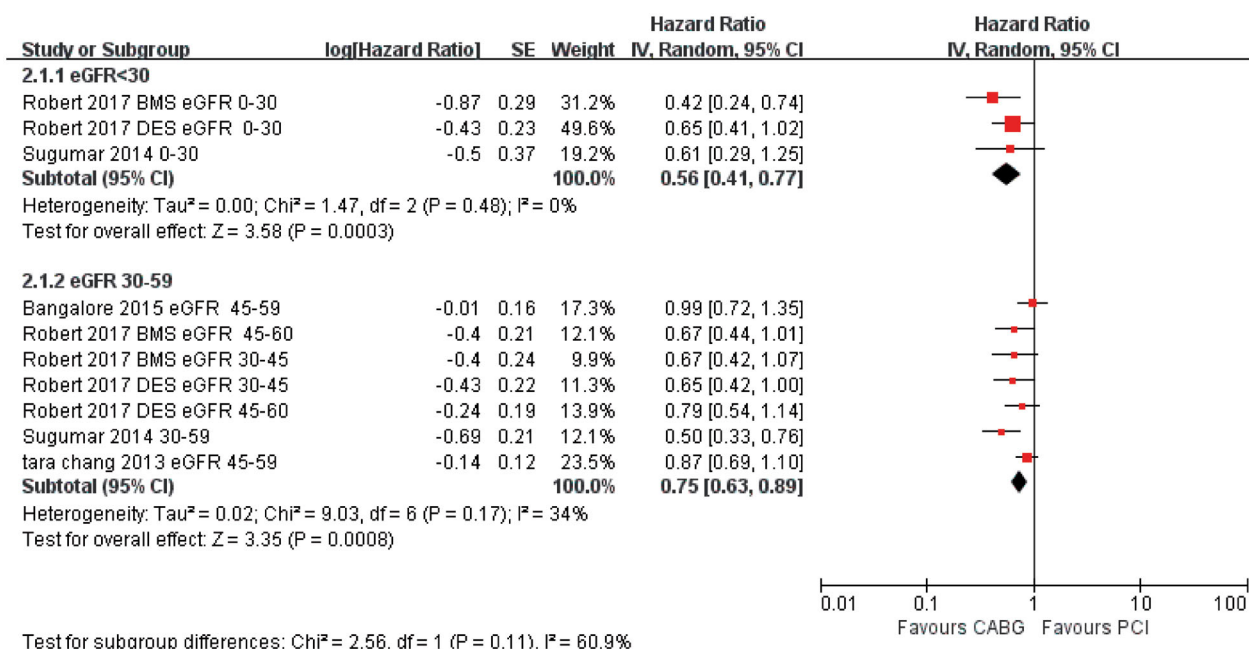


Figure 4. Hazard ratios of overall long-term mortality between CABG and PCI in patients with eGFR < 30 and eGFR > 30. PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery; eGFR: estimated glomerular filtration rate; SE: standard error; CI: confidence interval.

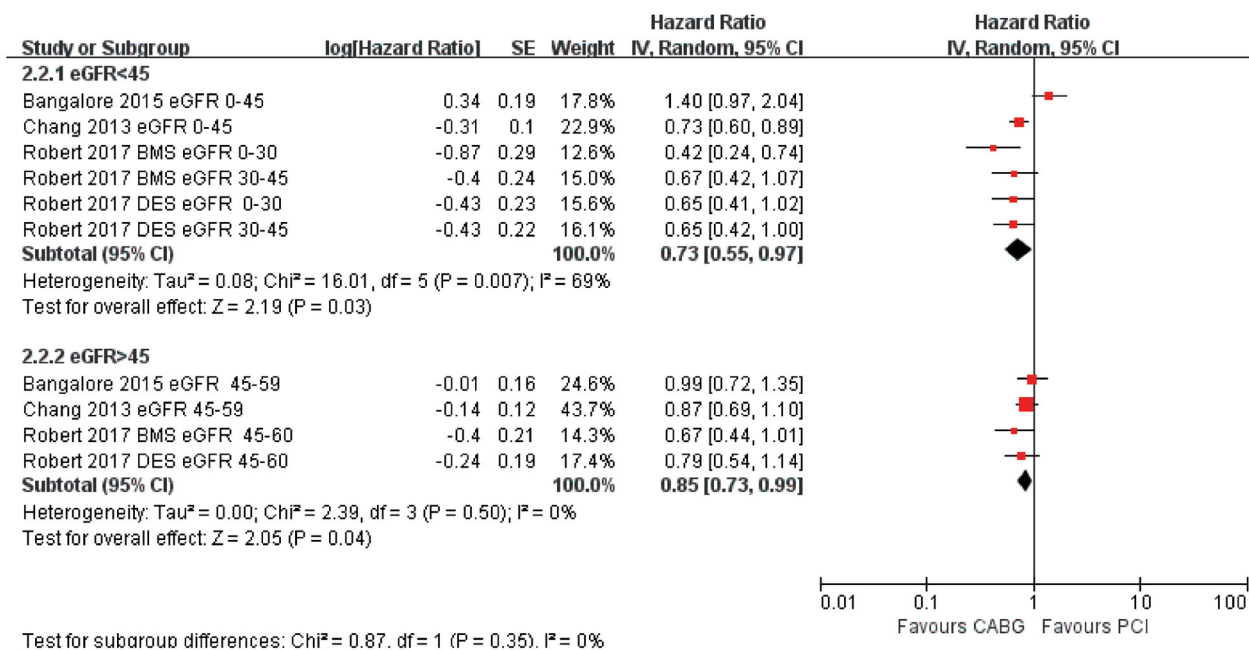


Figure 5. Hazard ratios for overall long-term mortality between CABG and PCI in patients with eGFR < 45 and eGFR > 45. PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery; eGFR: estimated glomerular filtration rate; SE: standard error; CI: confidence interval.

analysis are shown in the [supplementary file](#). When the subgroup analysis was conducted among patients on dialysis, the pooled results were similar (OR: 0.46, 95% CI: 0.30–0.72), without heterogeneity ($I^2=0\%$) This result is shown in [Figure 7](#).

Revascularization

Patients who underwent CABG exhibited an obviously lower incidence of revascularization than those who underwent PCI (OR: 0.17; 95% CI: 0.08–0.35), with substantial heterogeneity ($I^2=87\%$, [Figure 4\(B\)](#)). After the

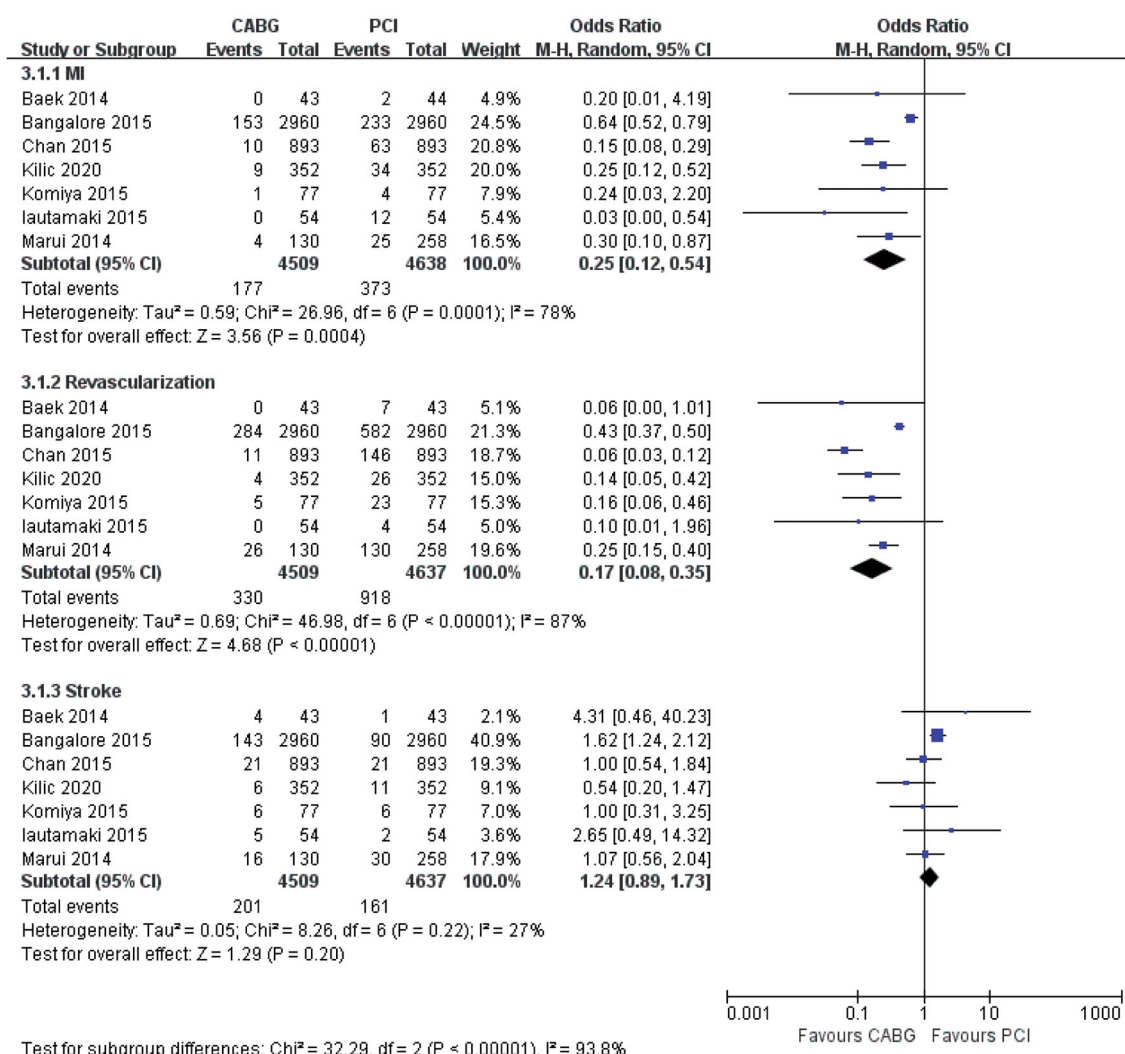


Figure 6. Comparison of secondary outcomes (myocardial infarction (MI), revascularization, and stroke) between CABG and PCI in patients with chronic kidney disease. PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery; CI: confidence interval.

removal of Bangalore 2015, the heterogeneity decreased ($I^2=59$), and the OR was 0.13 (95% CI: 0.07, 0.25). The results are shown in Figure 6. After the removal of Bangalore 2015 and Chan 2015, the heterogeneity decreased ($I^2=0\%$), and the OR was 0.20 (95% CI: 0.14–0.31). The details are provided in the [supplementary file](#). The obvious advantage of CABG over PCI in terms of revascularization remained significant after removing the studies that contributed to the remarkable heterogeneity. When the subgroup analysis was conducted among patients on dialysis, the pooled analysis yielded similar results (OR: 0.30; 95% CI: 0.18–0.51), with moderate heterogeneity ($I^2=44\%$). The results are shown in Figure 7.

Stroke

Stroke incidence was similar in patients with CKD undergoing CABG and PCI (OR, 1.24, 95% CI, 0.89–1.73,

$I^2=27\%$) and in the subgroup of patients undergoing dialysis (OR: 0.97, 95% CI: 0.47–2.00, $I^2=33$). These results are shown in Figures 6 and 7, respectively.

All the results were summarized in Table 2.

The funnel plots for publication bias evaluation were shown in Figures 8 and 9.

Discussion

In the present study, we aimed to compare long-term outcomes between patients with CKD undergoing CABG and PCI by performing a meta-analysis of propensity score-matching studies. Our findings indicated that CABG was associated with lower long-term mortality risk than PCI. In addition, the incidences of myocardial infarction and revascularization were lower in the CABG group than in the PCI group. We also observed an advantage of CABG over PCI in terms of long-term

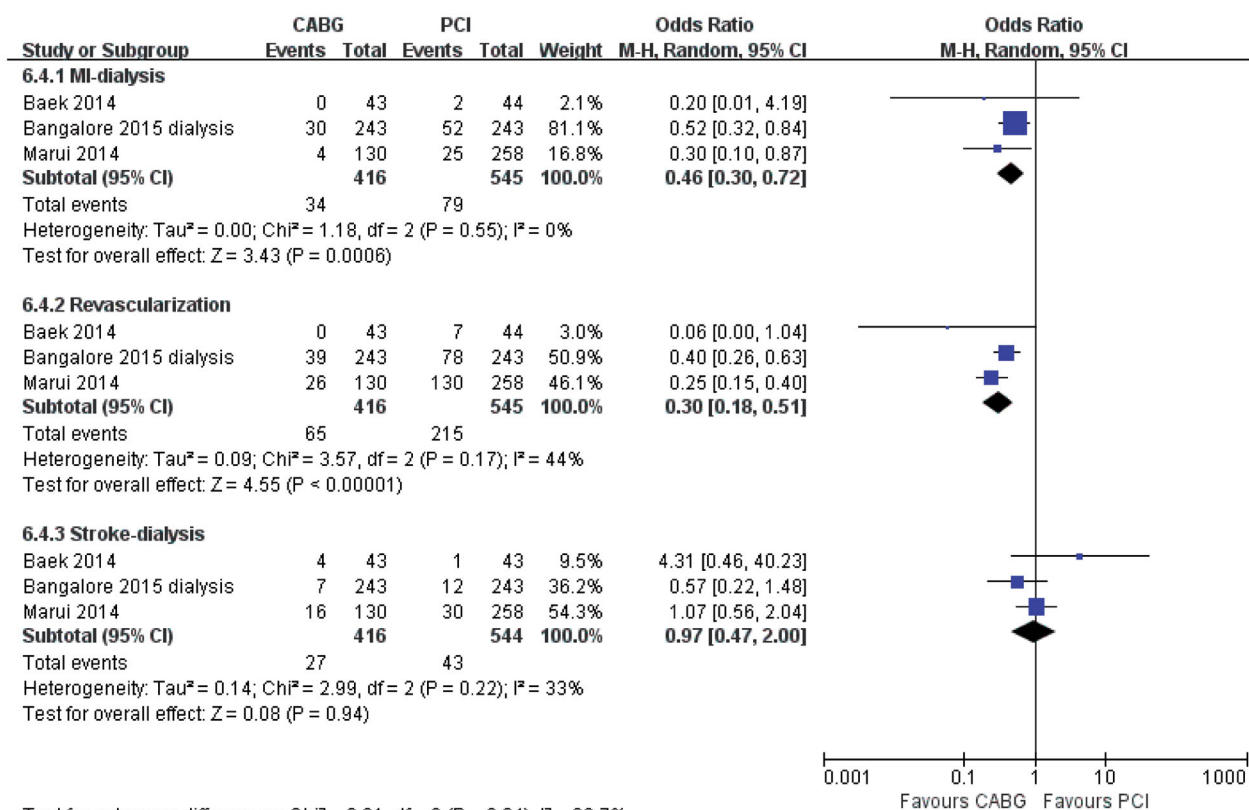


Figure 7. Secondary outcomes (myocardial infarction (MI), revascularization, and stroke) between CABG and PCI in patients on dialysis. PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery; CI: confidence interval.

Table 2. Results of the main analysis.

Outcomes	Reported study number	OR/HR with 95% CI	p Value	I ² (%)
<i>Patients with CKD (CABG vs. PCI)</i>				
Mortality risk (HR)				
Full cohort	12	0.76 (0.70–0.83)	<.001	21
eGFR 0–30	2	0.56 (0.41–0.77)	<.001	0
eGFR 30–59	4	0.75 (0.63–0.89)	<.001	34
eGFR 0–45	3	0.73 (0.55–0.97)	.03	69
eGFR 45–59	3	0.85 (0.73–0.99)	.04	0
MI (OR)	7	0.25 (0.12–0.54)	<.001	78
Revascularization (OR)	7	0.17 (0.08–0.35)	<.001	87
Stroke (OR)	7	1.24 (0.89–1.73)	>.05	27
Patients on dialysis				
Mortality risk (HR)	6	0.74 (0.60–0.91)	.005	24
MI (OR)	3	0.46 (0.30–0.72)	<.001	0
Revascularization (OR)	3	0.30 (0.18–0.51)	<.001	44
Stroke (OR)	3	0.97 (0.47–2.00)	p > .05	33

OR: odd ratio; HR: hazard ratio; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery.

survival and the incidence of myocardial infarction and revascularization in the subgroup analyses of patients on dialysis and those with different eGFRs. However, the CABG and PCI cohorts had similar stroke rates.

Three RCTs on this topic have been published [4–6]. A meta-analysis including these three trials, which included a total of 1121 patients with CKD, reported that CABG was associated with a lower risk of mortality, MACCE, myocardial infarction, and repeat revascularization than PCI [13]. These results

are consistent with the findings of the present meta-analysis.

We noticed that the heterogeneity for the HR of patients with an eGFR range of 0–45 and for the ORs for myocardial infarction and revascularization were high. We believe that these unexpected results may be due to the nature of the cohort design and differences in the inclusion and exclusion criteria among studies. In a study by Bangalore et al., the subgroup of patients with an eGFR ranging from 0 to 45 did not include

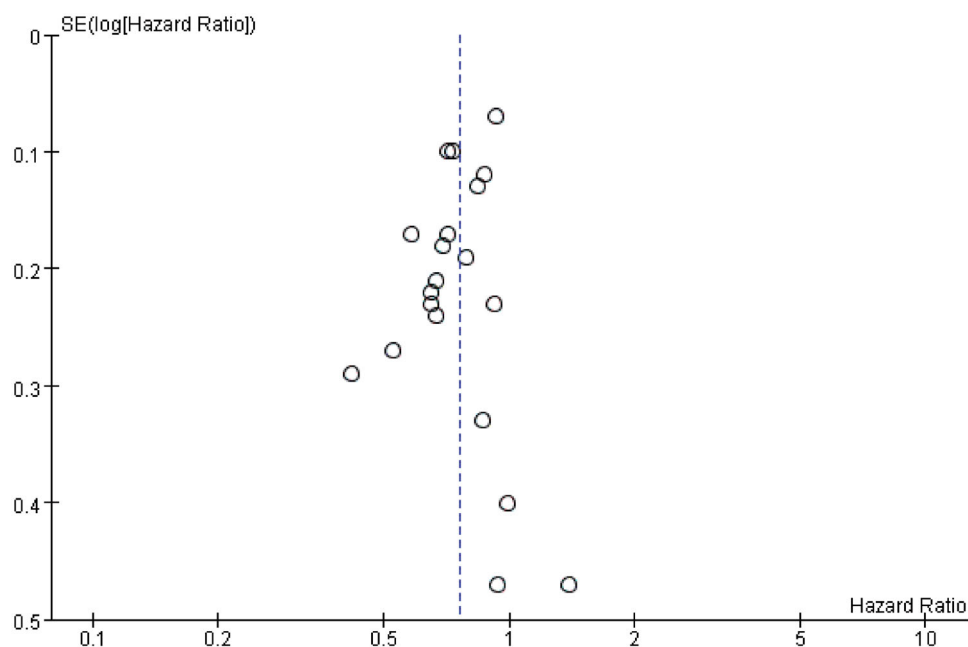


Figure 8. Funnel plot for the survival hazard ratio.

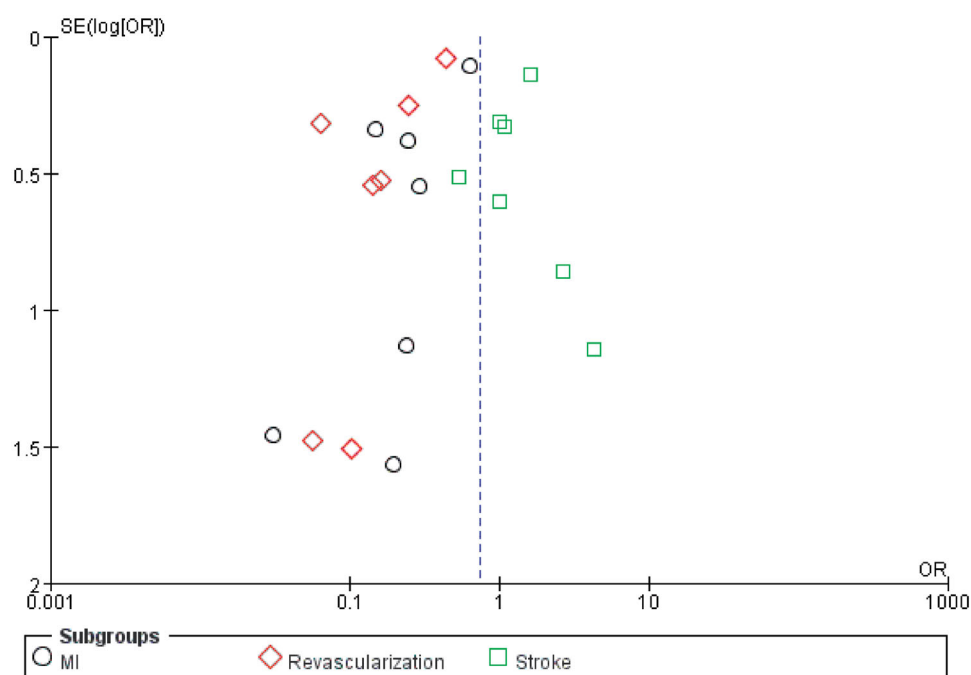


Figure 9. Funnel plot for odds ratios for myocardial infarction (MI), revascularization, and stroke.

those on dialysis. Therefore, the mortality risk may be lower than that reported in other studies involving this subgroup analysis. We performed several sensitivity analyses. After removing Bangalore 2015, the heterogeneity (I^2) was reduced from 60% to 0% for the HR of patients with an eGFR range of 0–45. Removal of this study also reduced the heterogeneity (I^2) of the OR for MI from 78% to 0% and the OR for revascularization from 87% to 59%. After removing both Bangalore 2015 and Chan 2015, the heterogeneity (I^2) of the OR for

revascularization further decreased from 87% to 0%. The significantly lower HR for mortality and lower incidence of MI and revascularization in the CABG group remained unchanged after the removal of Bangalore 2015 and Chan 2015.

There are several explanations for these results. PCI usually treats specific culprit lesions, which are responsible for clinical symptoms. However, many residual vessel stenoses can develop after PCI, resulting in incomplete revascularization. The increased incidence

of incomplete revascularization is considered the major cause of adverse cardiovascular events, such as myocardial infarction, repeated revascularization, and even death [20]. In contrast, CABG provides new vessels to replace the culprit vessels exhibiting stenosis, thereby ensuring a higher frequency of complete revascularization than PCI [28]. In addition, routine coronary angiographic follow-up, which is associated with an increased need for repeat revascularization, is more frequently performed in patients who undergo PCI than in those who undergo CABG [29], and an adverse clinical prognosis may be induced by repeated revascularization [30]. Recent studies have suggested that the risk of stroke may decrease in the CABG group due to the increased use of off-pump surgery and the avoidance of aortic cross-clamping [16]. A meta-analysis pooling three cohort studies and three RCTs together reported that CABG was associated with a higher risk of stroke than PCI, in contrast to our findings [13]. Thus, further studies are required to confirm whether PCI and CABG are associated with a similar risk of stroke.

Patients with CKD usually have worse outcomes after PCI or CABG than those with normal kidney function. In a study by Baber et al., patients with CKD exhibited a significantly higher risk of mortality, main adverse cardiovascular and cerebrovascular events, myocardial infarction, and stroke than patients without CKD [4]. In a trial by Giustino et al., obviously higher risks of mortality and major adverse cardiovascular events were observed in patients with CKD than in those without CKD [5]. In contrast, a large-scale RCT including patients with CKD and non-CKD reported no significant differences in the rate of the composite outcome of death, stroke, or myocardial infarction between PCI and CABG [2]. Given that RCTs including patients with CKD are limited, it is reasonable to conduct a new meta-analysis including cohort studies that have performed propensity score-matching.

Although the long-term prognosis of PCI is inferior to that of CABG, there are still advantages of PCI over CABG, such as a lower frequency of infection and a shorter period to hospital discharge. Importantly, patients who are either unsuitable for surgery or need emergency revascularization must choose PCI rather than CABG.

Novelty

The present study is novel in that we included several newly published cohort studies that involved propensity score-matching analyses. In addition, we only included propensity score-matching studies to ensure

that the patient characteristics remained balanced. Furthermore, we performed a subgroup analysis of survival outcomes between PCI and CABG for different eGFR levels.

Limitations

This study had several limitations. First, the total number of participants in the study was still limited. Second, multiple regression (MR) was used to alleviate some endogenous problems. The unbiased estimation of MR depends on the correct setting of the function forms of Y and X. Otherwise, functional form misspecification (FFM) will occur, leading to a biased estimate. Propensity score-matching relieves the FFM problem by reducing the dependence on the function form setting. However, it cannot solve more general endogenous problems, such as self-selection and missing variables. Therefore, propensity score-matching cannot completely replace RCTs. Third, the SYNTAX score, a unique tool proposed in the Synergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) trial, can be used to evaluate the complexity of CAD. Due to a shortage of SYNTAX score data in the most involved studies, we could not perform a subgroup analysis stratified by the different SYNTAX score ranges. A study by Zhang et al. [9] demonstrated that patients who underwent peritoneal dialysis had a lower risk of developing hemorrhagic stroke than those receiving hemodialysis. However, we could not conduct a subgroup analysis stratified by different types of dialysis (peritoneal dialysis versus hemodialysis) because the included studies did not provide sufficient data on dialysis type, and we were unable to access the patient-level data.

Medical treatments were not evaluated in many included studies. It could be a factor influencing the long-term outcomes.

Conclusions

The present results demonstrate that, based on long-term follow-up outcomes, CABG remains superior to PCI in patients with CKD.

Disclosure statement

The authors declare that they have no conflicts of interest relevant to this work.

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Data availability statement

All data and materials used in this research are freely available. References have been provided.

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