Original Paper

Multivessel Coronary Revascularization Strategies in Patients with Chronic Kidney Disease: A Meta-Analysis

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Keywords

Multivessel coronary artery disease · Chronic kidney disease · Revascularization strategy

Abstract

Background: Early revascularization can lead to better prognosis in multivessel coronary artery disease (CAD) patients with chronic kidney disease (CKD). However, whether coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is better remains unknown. **Methods:** We searched PubMed and the Cochrane Library database from inception until December 9, 2017, for articles that compare outcomes of CABG and PCI in multivessel CAD patients with CKD. We pooled the odds ratios with a fixed-effects model when $I^2 < 50\%$ or a random-effects model when $I^2 > 75\%$ and conducted heterogeneity and quality assessments as well as publication bias analyses. **Results:** A total of 17 studies with 62,343 patients were included. Compared with CABG, the pooled analysis showed that PCI had a lower risk of short-term all-cause death (OR, 0.56; 95% CI, 0.37–0.84) and cerebrovascular accidents (OR, 0.65; 95% CI, 0.53–0.79) but a higher risk of cardiac death (OR, 1.29; 95% CI, 1.21–1.37), myocardial infarction (MI) (OR, 1.73; 95% CI, 1.35–2.21), and repeat revascularization (RR) (OR, 3.9; 95% CI, 2.99–5.09). There was no significant difference in the risk of long-term all-cause death (OR, 1.08; 95% CI, 0.95–1.23) and major adverse cardiac and cerebrovascular events (MACCE) (OR, 1.58; 95% CI, 0.99–2.52) between the PCI and CABG groups. A subgroup analysis restricted to patients treated with dialysis or with PCI-drug-eluting stent yielded similar results. **Conclusions:** PCI for patients with CKD and multivessel disease (multivessel CAD) had advantages over CABG with regard to short-term all-cause death and cerebrovascular accidents, but disadvantages regarding the risk of myocardial death, MI, and RR; there was no significant difference in the risk of long-term all-cause death and MACCE. Large randomized controlled trials are needed to confirm our findings.

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Introduction

Coronary artery disease (CAD) is the leading cause of cardiovascular death among patients with chronic kidney disease (CKD) [1]. In patients with CAD and CKD, i.e., with decreasing renal function, coronary vessel lesions are complex and serious, which leads to a worse prognosis and greater financial burden [2–4]. Therefore, we should pay more attention to finding an effective treatment strategy for this subset of patients. Recently, some researchers reported that for CAD patients with CKD, early invasive therapy with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) results in lower mortality compared with medical therapy [5, 6]. Nevertheless, some articles reported that CABG is a better strategy for multivessel CAD patients with CKD, while others did not. Previous studies reported that patients treated with CABG have better survival than those treated with PCI [7–10], although CABG will increase the risk of short-term acute kidney injury. However, Kang et al. [11] followed up 2,108 CKD patients with multivessel CAD and found that PCI with drug-eluting stent (DES) resulted in similar rates of the composite outcome of any-cause mortality, myocardial infarction (MI), or stroke when compared with CABG.

Which revascularization strategy is better remains to be seen; thus, we made a meta-analysis of the accumulated evidence to choose a more suitable therapy for multivessel CAD with CKD.

Methods

Search Strategy

A systematic review of published data on outcomes of PCI and CABG in CKD patients with multivessel CAD was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12]. A broad computerized search was performed to identify relevant studies from PubMed and the Cochrane Library from inception until December 9, 2017. The following keywords and MeSH terms were used: coronary artery bypass, coronary artery bypass grafting, coronary artery bypass graft, CABG, percutaneous coronary intervention, percutaneous coronary revascularization, PCI, stent, chronic kidney disease, chronic renal disease, end-stage kidney disease, chronic kidney failure, chronic renal failure, dialysis, CKD, and ESRD.

Inclusion and Exclusion Criteria

We included all studies of original design that compared PCI and CABG for multivessel CAD patients with CKD. We included studies from which quantitative raw data were available that enabled the calculation of odds ratios (ORs) for the outcomes of interest. If there were potentially overlapping groups of study patients, the publication with the most information of interest was included in the article. We excluded studies in which the number of patients was <50 in total. All case reports, editorials, review articles, and non-English-language articles were excluded. Two of the authors (P.W. and F.L.) independently reviewed all studies, evaluated the studies' quality, and extracted data. If there was disagreement, Z.F. resolved it according to the prespecified criteria.

Data Extraction and Quality Assessment

We extracted information with standardized data sheets. The following study-, patient-, and outcome-related data were extracted: authors, published year, trial design, country, recruitment time, sample size, age, sex, smoking, diabetes, hypertension, hyperlipidemia, dialysis, type of stent, vessel involvement, mean follow-up period, long-term all-cause death, short-term all-cause death, major adverse cardiac and cerebrovascular events (MACCE), cardiac death, MI, repeat revascularization (RR), and cerebrovascular accidents. We used the Newcastle-Ottawa scale for retrospective observational studies with a numeric scale of 1–10 and the Jadad scale for randomized controlled trials (RCTs) with a numeric scale of 1–5 to evaluate study quality [13, 14].

Fig. 1. Flow diagram of study selection.

Definitions and Outcomes

CKD was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m². Multivessel CAD disease was defined as severe stenosis ($\geq 50\%$) in at least 2 major epicardial coronary arteries. The outcomes included long-term all-cause death, short-term all-cause death, MACCE, cardiac death, MI, RR, and cerebrovascular accidents. Given the considerable heterogeneity in reporting outcomes across the relevant studies, we used the following prespecified definitions to define the outcome. Long-term all-cause death was defined as all-cause death during a period of >1 year. Short-term all-cause death was defined as all-cause death during a period of 30 days. MACCE was defined as a composite endpoint including all-cause death, nonfatal MI, stroke, and any RR. MI was defined as any typical variation in cardiac biomarkers in the setting of clinical signs or symptoms consistent with cardiac ischemia. Cerebrovascular accidents were defined as neurological deficits which were diagnosed by a neurologist on the basis of imaging study, including stroke, transient ischemic attack, and reversible ischemic neurological deficit. The outcomes were analyzed within different subgroups: one subgroup was restricted to dialysis patients, while the other one was restricted to patients with DES-only PCI.

Statistical Analysis

Statistical analyses were performed with RevMan 5.3 and Stata 12.0 software. ORs with 95% confidence intervals (CIs) were calculated. A $p < 0.05$ was considered statistically significant. The I^2 statistic was used to examine heterogeneity across studies, with an I^2 of 25–50, 50–75, and $>75\%$ equal to low, moderate, and high heterogeneity [15]. Provided that I^2 was $<50\%$, the M-H fixed-effects model was used, but if I^2 was $>50\%$, we used the M-H random-effects model in the course of the statistical analysis. A sensitivity analysis was performed after excluding studies one by one when heterogeneity was high. We evaluated funnel plot asymmetry and Egger regression asymmetry tests to assess the potential effect of publication bias. If the number of studies was <5 , we did not evaluate publication bias [16]. We made two subgroup analyses apart from the overall analysis.

Results

Study Selection and Quality Assessment

A total of 2,699 articles from PubMed and the Cochrane Library database were screened, of which 89 stood out because they showed to be closely related to our subject after title and abstract review. Of these 89 studies, the full texts were assessed for applicability. Seventy-two

Table 1. Baseline characteristics of the studies included in the meta-analysis

a Study parameters as well as sample size, age, and gender (PCI vs. CABG)

Study	Year	De- sign	Country	Recruitment period	Sample size, <i>n</i>			Age, years		Male, %	
					PCI	CABG	overall	PCI	CABG	PCI	CABG
Li [27]	2017	ROS	China	Jan 2004–Dec 2010	46	53	99	73±9	72±11	89	74
Kang [11]	2017	ROS	Korea	Jan 2003–Dec 2013	1,165	943	2,108	67±10	66.4±8.4	67	70
Milojevic [10]	2018	RCT	Multinational	Mar 2005–Apr 2007	158	151	309	72±7	72±8	68	67
Pan [24]	2016	ROS	China	Jan 2005–Mar 2010	147	206	353	69±6	68±6	74	75
Chan [25]	2015	ROS	Canada	Oct 2008–Sep 2011	893	893	1,786	75±9	75±8	53	52
Bangalore [17]	2015	ROS	USA	Jan 2008–Dec 2011	2,960	2,960	5,920	70±11	70±11	62	62
Kumada [20]	2014	ROS	Japan	Apr 1999–Dec 2010	787	210	997	67±10	66±9	70	74
Baek [21]	2014	ROS	South Korea	Jan 2003–Feb 2006	44	43	87	60±11	61±7	64	63
Shroff [18]	2013	ROS	USA	2004–2009	16,855	6,178	23,033	45–74; 75%	45–74; 66%	55	62
Chang [29]	2013	ROS	USA	Jan 1996–Dec 2008	1,458	1,458	2,916	62–74	62–75	69	69
Chang [9]	2012	ROS	USA	1997–2009	7,665	14,316	21,981	65	63	56	63
Terazawa [22]	2012	ROS	Japan	2004–2007	67	58	125	64±9	65±8	76	78
Sunagawa [23]	2010	ROS	Japan	Jan 2002–Dec 2006	75	29	104	65±13	63±10	73	87
Ashrith [8]	2010	ROS	USA	May 2003–Dec 2006	517	295	812	>65:70	>65:60	58	60
Wang [19]	2009	ROS	China	Jan 2004–Jun 2006	724	345	1,069	NR	NR	67	70
Na [28]	2009	ROS	South Korea	May 2003–Jan 2006	401	101	502	NR	NR	57	57
Aoki [26]	2005	RCT	Multinational	Apr 1997–Jun 1998	69	73	142	70±6	71±6	64	73

articles were further eliminated because they were reviews or meta-analyses, they were overlapping studies, they did not report relevant data, or they did not include enough patients. Finally, 17 studies that satisfied all the inclusion and none of the exclusion criteria were analyzed. Figure 1 shows the flow diagram of study selection.

Study Characteristics and Quality Assessment

Of the included studies, 2 were RCTs and 15 were retrospective observational studies. Subject enrollment occurred between January 1996 and December 2013. The sample sizes varied from 87 to 23,033 patients and the follow-up period ranged from 7 months to >5 years.

A total of 62,343 patients (34,031 patients treated with PCI and 28,312 patients treated with CABG) were included in this analysis. All the patients had their eGFR assessed, and all the eGFRs were <60 mL/min/1.73 m². The baseline characteristics of the studies are listed in Table 1. Most characteristics were similar between the two groups (PCI and CABG), but patients with more complex coronary lesions were more likely to choose CABG. Three studies excluded patients with left main artery disease, and 1 study did not report the number of vessel involvements [8, 17–19]. Although some studies included single-vessel disease patients, the small number did not influence our analysis. Six studies included all types of dialysis patients [9, 18, 20–23], 10 studies included DES-only patients, and 1 study included bare-metal stent-only patients [8, 10, 11, 17, 19, 21–26]. Four studies included both DES and bare-metal stent patients [18, 20, 27, 28], and 2 studies did not report the type of stent used [9, 29]. Moreover, all studies included in our meta-analysis were considered to be of high quality.

Outcome Analysis

Long-Term All-Cause Death

Seventeen studies reported on long-term all-cause death, but there was great heterogeneity ($I^2 = 77\%$, $p < 0.00001$) across the studies. No significant difference between the PCI and the CABG group was found (OR, 1.08; 95% CI, 0.95–1.23; $p = 0.23$; Fig. 2a) by the random-

Table 1 (continued)

b Sample characteristics by eGFR value, smoking rate, and disease (PCI vs. CABG)

Study	Subgroups				Smoking, %		Diabetes, %		Hyper-tension, %		Hyperlip-idemia, %	
	PCI	%	CABG	%	PCI	CABG	PCI	CABG	PCI	CABG	PCI	CABG
Li [27]	eGFR (30–59)	60.9	eGFR (30–59)	54.7								
	eGFR (15–29)	10.9	eGFR (15–29)	22.6	41	68	NR	NR	91	89	54	50
	eGFR (<15)	28.3	eGFR (<15)	22.6								
Kang [11]	eGFR (30–59)	75.3	eGFR (30–59)	70.3								
	eGFR (15–29)	5.3	eGFR (15–29)	9.1	42	44	49	58	76	76	35	35
	eGFR (<15)	19.4	eGFR (<15)	20.6								
Milojevic [10]	mean eGFR	47.6±10.8	mean eGFR	47.6±10.8	10	12	28	33	86	85	78	79
Pan [24]	eGFR (45–59)	54.4	eGFR (45–59)	59.7								
	eGFR (<45)	45.6	eGFR (<45)	40.3	36	50	41	36	65	70	10	26
Chan [25]	eGFR (30–59)	85.2	eGFR (30–59)	83.2								
	eGFR (<30)	14.8	eGFR (<30)	16.8	49	49	43	45	83	85	75	75
Bangalore [17]	eGFR (30–59)	83.38	eGFR (30–59)	82.91								
	eGFR (15–29)	7.53	eGFR (15–29)	7.84								
	eGFR (<15)	0.78	eGFR (<15)	0.88	26	27	49	48	77	78	62	63
	dialysis	8.31	dialysis	8.38								
Kumada [20]	dialysis	100	dialysis	100	28	24	58	66	61	63	24	22
Baek [21]	dialysis	100	dialysis	100	7	10	59	79	91	88	NR	NR
Shroff [18]	dialysis	100	dialysis	100	NR	NR	76	75	NR	NR	NR	NR
Chang [29]	eGFR (45–59)	64.5	eGFR (45–59)	64.5								
	eGFR (<45)	35.5	eGFR (<45)	35.5	33	33	36	36	73	74	88	89
Chang [9]	dialysis	100	dialysis	100	4	5	68	64	81	80	26	25
Terazawa [22]	dialysis	100	dialysis	100	14	9	64	52	78	78	NR	NR
Sunagawa [23]	dialysis	100	dialysis	100	NR	NR	43	43	77	80	20	20
Ashrith [8]	eGFR (15–59)	93.6	eGFR (15–59)	81.7								
	eGFR (<15 or dialysis)	6.4	eGFR (<15 or dialysis)	18.3	47	52	13	17	NR	NR	NR	NR
Wang [19]	eGFR (<60)	100	eGFR (<60)	100	45	42	26	35	59	59	23	24
Na [28]	eGFR (<60)	100	eGFR (<60)	100	34	34	29	29	57	57	21	21
Aoki [26]	Ccr (<60 mL/min)	100	Ccr (<60 mL/min)	100	16	11	22	15	52	47	58	52

effects model. When looking at the subgroup analyses which were restricted to the dialysis group or the PCI-DES group, neither subgroup showed any significant difference (OR, 0.97; 95% CI, 0.80–1.18; $p = 0.79$; $I^2 = 89\%$; OR, 1.14; 95% CI, 0.91–1.43; $p = 0.26$; $I^2 = 64\%$). Furthermore, we performed a sensitivity analysis after excluding studies one by one, but we did not find any significant results either.

Short-Term All-Cause Death

Nine studies were pooled for short-term all-cause death. The result showed moderate heterogeneity ($I^2 = 65\%$, $p = 0.005$), so we used the M-H random-effects model. After pooled analysis, PCI showed a visibly lower risk of short-term all-cause death than CABG (OR, 0.56;

Table 1 (continued)

c Study subgroups, presence of vessel involvement, follow-up period, and study quality (PCI vs. CABG)

Study	Dialysis, %		DES, %	Vessel involvement, %		Mean follow-up period, months		Quality of study
	PCI	CABG		PCI	CABG	PCI	CABG	
Li [27]	NR	NR	65.2	LM only 10.9 LM+1v 17.4 LM+2v 28.3 LM+3v 43.5	LM only 1.9 LM+1v 3.8 LM+2v 11.3 LM+3v 83	45.6		8
Kang [11]	11	13	100	2v 56.7 3v 43.3	2v 19.3 3v 80.7	41.4		8
Milojevic [10]	NR	NR	100	LM only 42.4 2v 75.0 3v 12.2	LM only 39.7 2v 71.8 3v 5.4	60		4 ^d
Pan [24]	NR	NR	100	LM 100 MVD 96.7	LM 100 MVD 96.7	30.74±15.05		9
Chan [25]	6	6	100	LM 14.8 2v 67.7 3v 32.3	LM 14.7 2v 66.2 3v 33.8	21.12±11.52	23.04±11.52	7
Bangalore [17]	8	8	100	LM excluded 2v 54.1 3v 45.9	LM excluded 2v 53.9 3v 46.1	32.4	38.4	8
Kumada [20]	100	100	43.8	LM 4.3 2v 30.2 3v 26.6	LM 16.2 2v 29.1 3v 54.8	44±25	52±41	8
Baek [21]	100	100	100	1v 29.6 2v 25.0 3v 45.5	1v 4.65 2v 16.3 3v 79.1	50.8		8
Shroff [18]	100	100	70.3	NR	NR	19.2 ^a	19.56 ^a	6
Chang [29]	0	0	NR	MVD 100	MVD 100	45.6	46.8	8
Chang [9]	100	100	NR	MVD 100	MVD 100	16.8	22.8	7
Terazawa [22]	100	100	100	LM only 0 1v 7 2v 26 3v 67	LM only 2 1v 49 2v 43 3v 6	39.0±20.4	34.1±17.9	9
Sunagawa [23]	100	100	100	LM only 19 1v 36 2v 32 3v 13	LM only 52 1v 0 2v 7 3v 42	23.5±14.8	32.0±22.0	7
Ashrith [8]	6	18	100	LM excluded 2v 53 3v 47	LM excluded 2v 25.8 3v 74.2	non-HD CKD: 27.4 ^a ESRD: 27.0 ^a	non-HD CKD: 27.6 ^a ESRD: 24.8 ^a	7
Wang [19]	NR	NR	100	LM excluded 2v 60.1 3v 39.9	LM excluded 2v 28.1 3v 71.9	24 ^b		8
Na [28]	3	3	77.8	LM 9.5 1v 17.9 2v 24.3 3v 32.3	LM 9.5 1v 17.9 2v 24.3 3v 32.3	7		5
Aoki [26]	NR	NR	0	MVD 100	MVD 100	60 ^c		4 ^d

eGFR values in parentheses are given as mL/min/1.73 m². CABG, coronary artery bypass grafting; Ccr, creatinine clearance rate; CKD, chronic kidney disease; DES, drug-eluting stent; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HD, hemodialysis; LM, left main; MVD, multivessel disease; NR, not reported; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; ROS, retrospective observational study; 1v, 1 vessel; 2v, 2 vessels; 3v, 3 vessels. ^a Median. ^b Longest follow-up duration. ^c Shortest follow-up duration. ^d Jadad score.

Fig. 2. Forest plots for long-term all-cause death (**a**) and short-term all-cause death (**b**) for the pooled data from the studies, showing the odds ratios for the outcomes of coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) for multivessel coronary artery disease patients with chronic kidney disease.

95% CI, 0.37–0.84; $p = 0.006$; Fig. 2b); the dialysis subgroup showed the same result (OR, 0.39; 95% CI, 0.35–0.45; $p < 0.00001$; $I^2 = 0\%$). The PCI-DES subgroup showed no statistical difference (OR, 0.73; 95% CI, 0.42–1.24; $p = 0.24$; $I^2 = 52\%$) by the random-effects model, but when we used the fixed-effects model, PCI also showed a visibly lower risk.

Fig. 3. Forest plots for major adverse cardiac and cerebrovascular events (**a**), cardiac mortality (**b**), myocardial infarction (**c**), repeat revascularization (**d**), and cerebrovascular accidents (**e**) for the pooled data from the studies, showing the odds ratios for the outcomes of coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) for multivessel coronary artery disease patients with chronic kidney disease.

(Figure continued on next pages.)

Major Adverse Cardiac and Cerebrovascular Events

Eleven studies reported on MACCE at the end of follow-up. We applied the random-effects model to the analysis because of the high heterogeneity ($I^2 = 93\%$, $p < 0.00001$). The pooled result showed no difference between the PCI and the CABG group (OR, 1.58; 95% CI, 0.99–2.52; $p = 0.05$; Fig. 3a). Both the dialysis subgroup (OR, 2.17; 95% CI, 0.73–6.47; $p = 0.16$; $I^2 = 92\%$) and the PCI-DES subgroup (OR, 1.6; 95% CI, 0.87–2.94; $p = 0.13$; $I^2 = 95\%$) showed the same result. A sensitivity analysis showed that PCI led to a higher risk of MACCE after excluding the study by Ashrith et al. [8] (OR, 1.85; 95% CI, 1.19–2.88; $p < 0.006$; $I^2 = 91\%$) or that by Kang et al. [11] (OR, 1.72; 95% CI, 1.08–2.76; $p < 0.02$; $I^2 = 89\%$).

Cardiac Mortality

Cardiac mortality was significantly lower among patients undergoing CABG when compared with patients treated with PCI (OR, 1.29; 95% CI, 1.21–1.37; $p < 0.00001$; $I^2 = 40\%$; Fig. 3b) based on the results of the pooled analysis of 8 studies by the fixed-effects model. In the subgroup analyses of the dialysis group and the PCI-DES group, CABG was also associated with lower cardiac mortality (OR, 1.28; 95% CI, 1.20–1.36; $p < 0.00001$, $I^2 = 19\%$; OR, 2.26; 95% CI, 1.43–3.57; $p = 0.0005$, $I^2 = 8\%$) in comparison with PCI.

Myocardial Infarction

Thirteen studies were pooled for MI, and the studies showed moderate heterogeneity ($I^2 = 63\%$, $p = 0.001$); thus, we used the random-effects model. After pooled analysis, PCI showed a visibly higher risk of MI than CABG (OR, 1.73; 95% CI, 1.35–2.21; $p < 0.0001$; Fig. 3c). The subgroup analyses of the dialysis group, using the fixed-effects model (OR, 1.59; 95% CI, 1.49–1.70; $p < 0.00001$; $I^2 = 0\%$), and the PCI-DES group, using the random-effects model (OR, 2.26; 95% CI, 1.36–3.76; $p = 0.002$; $I^2 = 74\%$), showed the same result.

Repeat Revascularization

Fifteen studies reported on RR, and they showed high heterogeneity ($p < 0.00001$, $I^2 = 82\%$); thus, we used the random-effects model. After pooled analysis, PCI showed a visibly higher risk of RR than CABG (OR, 3.9; 95% CI, 2.99–5.09; $p < 0.00001$; Fig. 3d). The subgroup analyses of the dialysis group (OR, 4.10; 95% CI, 2.54–6.62; $p < 0.00001$; $I^2 = 69\%$) and the PCI-DES group (OR, 5.1; 95% CI, 3.03–8.59; $p < 0.00001$; $I^2 = 84\%$) showed the same result. A sensitivity analysis showed the same result.

Cerebrovascular Accidents

We pooled 9 studies on cerebrovascular accidents, and they showed no heterogeneity ($I^2 = 0\%$, $p = 0.65$); thus, we used the fixed-effects model. After pooled analysis, PCI showed a visibly lower risk of cerebrovascular accidents than CABG (OR, 0.65; 95% CI, 0.53–0.79; $p < 0.0001$; Fig. 3e). The subgroup analyses of the dialysis group (OR, 0.6; 95% CI, 0.39–0.92; $p = 0.02$; $I^2 = 0\%$) and the PCI-DES group (OR, 0.65; 95% CI, 0.53–0.79; $p < 0.0001$; $I^2 = 0\%$) showed the same result.

Visual inspection of the funnel graphs did not show the asymmetry typically associated with publication bias (Fig. 4).

Fig. 4. Funnel plot for cardiac death of coronary artery bypass grafting versus percutaneous coronary intervention for multivessel coronary artery disease patients with chronic kidney disease. OR, odds ratio; SE, standard error.

Discussion

Recently, with stent technology and pharmacotherapy development, some researchers found that PCI with second DES led to a 5-year mortality comparable to that with CABG ($\Delta = 0.9$; 95% CI, -9.6 to 7.9 ; $p = 0.844$) among patients without CKD [30, 31]. Since CKD is an independent risk factor, patients with CKD have significantly poorer outcomes (including death and other adverse events) after either PCI or CABG than patients without CKD [32–38]. RCTs comparing CABG with PCI for multivessel CAD have largely excluded patients with CKD, so it is still unclear whether CABG or PCI leads to better outcomes in this group.

Our meta-analysis of multivessel CAD patients with CKD indicated that the risk of cardiac death, MI, and RR was lower in the CABG group; however, the risk of short-term all-cause death and cerebrovascular accidents was lower in the PCI group. There was no significant difference in the risk of long-term all-cause death and MACCE between the CABG and the PCI group. Although great heterogeneity in the results for long-term all-cause death, MACCE, and RR was observed, this probably was due to varying clinical characteristics as well as different types of intervention procedures and follow-up periods. In order to trace the origin of the heterogeneity, subgroup analyses were made. In the dialysis group, which was restricted to dialysis patients receiving PCI versus CABG, the studies kept consistency in the results for all outcomes, but the heterogeneity was obviously reduced. In the other subgroup analysis, restricted to patients receiving PCI-DES versus CABG, the pooled studies kept good consistency in the results for all outcomes except short-term all-cause death. No significant difference in the risk of short-term all-cause death was observed between the two strategies among those subsets of patients by the random-effects model, but there was a lower risk of short-term all-cause death in the PCI-DES group by the fixed-effects model. Our meta-analysis included the study by Shroff et al. [18], which did not mention any information on vessel disease; however, we did a sensitivity analysis to confirm that it did not influence the results.

Previous studies have reported that CABG led to a lower rate of mortality and MACCE [10, 25], but most of these studies were observational and included only small samples, which entailed bias. For example, patients who had a severe underlying disease which may have influenced the effectiveness of surgery were more likely to choose PCI, which may have favored CABG outcomes. Thus, our pooled analysis collected all related research including RCTs to amplify the sample size in order to reduce errors and selection bias. We found that

compared with CABG, PCI showed lower short-term all-cause mortality but no significant difference in long-term all-cause death and MACCE. The advantages of PCI are a reduced operation time, minimal invasion, local anesthesia, mechanical ventilation, fewer infections, and shorter hospital stays [39, 40], which provides a benefit for short-term prognosis. In addition, in the SYNTAX trial, the only RCT assessing PCI-DES versus CABG in multivessel CAD patients with CKD, the patients were randomly assigned to undergo PCI ($n = 158$) or CABG ($n = 151$), and the authors found no significant difference in 5-year all-cause mortality (26.7 vs. 21.2%; $p = 0.14$) but a higher rate of MACCE (42.1 vs. 31.5%; $p = 0.019$), mainly driven by RR. However, this research used paclitaxel-eluting stents, which have already been identified to induce the risk of RR compared with everolimus-eluting stents [41–43].

Our results showed higher rates of cardiac mortality, MI, and RR in the PCI group than in the CABG group. A meta-analysis including 11,318 patients undergoing CABG and 17,928 patients undergoing DES-only PCI, where all the patients had multivessel CAD with CKD, showed the same result as ours [44]. Some studies revealed that the high risk of MI, cardiac death, and RR should account for incomplete revascularization (IR), because patients with IR have more calcified lesions and more residual stenosis after PCI. Comparing complete revascularization ($n = 1,188$) with IR ($n = 2,053$) among patients with multivessel CAD, Gao et al. [45] found that IR was leading to a significantly higher rate of cardiac death. Chung et al. [46] also reported that in comparison with IR, the adjusted hazard ratio of complete revascularization for cardiac death and MI was 0.39 (95% CI, 0.16–0.96). Furthermore, CAD patients with CKD have a higher risk of late restenosis, especially hemodialysis patients [47], which may lead to worse outcome. Thus, preventing restenosis may be an effective way to reduce cardiac mortality, MI, and RR after PCI.

Our pooled results showed that compared with the PCI group, the CABG group had a higher risk of cerebrovascular accidents (OR, 0.65; 95% CI, 0.53–0.79; $p < 0.0001$). Yang et al. [48] came to the same conclusion as we did regarding patients with unprotected left main coronary artery with bifurcation lesions after a median follow-up of 7.2 years. A greater severity of coronary artery lesions and a more traumatic procedure may be related to a higher risk of stroke associated with CABG [49]. Fortunately, some technical procedural improvements and preventive measures can reduce the risk of cerebrovascular accidents, such as CABG and the single-clamp technique, aorta no-touch techniques, measures during cardiopulmonary bypass, prophylactic carotid intervention, utilization of internal mammary artery grafting, prevention of emboli from aortic plaque, intraoperative monitoring, and pharmaceutical therapies [37, 49–51]. However, whether off-pump procedures can reduce the risk of stroke is under debate [40, 52]. Furthermore, we should pay attention to acute kidney injury, even though our research did not demonstrate any incidence of acute kidney injury. Shen et al. [53] found that the incidence of AKI after CABG was higher than after PCI (8.9 vs. 4.5%; OR, 2.05; 95% CI, 1.99–2.12; $p < 0.001$), which reminded us to pay more attention to protecting the kidneys during the perioperative period.

Our results show that both PCI and CABG have their respective advantages, but based on the existing evidence, it is hard to say which revascularization strategy is best for multivessel CAD patients with CKD. However, from the perspective of social economics, some studies have reported that CABG is costly [50, 54]. In Ohlow's [55] hypothetical scenario, based on patients' personal experience, 15% of the participants elected CABG and 67% chose staged PCI; thus, the majority of the participants preferred staged PCI over CABG.

Considering the financial burden and patients' preference, PCI may be the favored strategy for multivessel CAD patients with CKD. Because of the high heterogeneity, our conclusion needs future large RCTs to confirm it.

Limitations

There are several limitations to our pooled analysis. First, most of our data were extracted from observational studies, which inevitably contributed to bias. Second, the patients' and studies' clinical conditions were variable, which led to high heterogeneity and might have influenced our results. Finally, we were unable to analyze the specific stent type and CABG procedure used, a factor which is closely related to the outcome. Although there are some limitations to our research, it is still the most comprehensive analysis, including all related studies up to now. We hope it can provide some guidance to doctors and patients for choosing the most suitable revascularization method for multivessel CAD patients with CKD.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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