

Effects of chronic kidney disease on mid- and long-term clinical outcomes after off-pump coronary artery bypass grafting-a retrospective study

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Abstract

Background: To investigate the effect of chronic kidney disease (CKD) on mid- and long-term clinical outcomes after off-pump coronary artery bypass grafting (CABG).

Methods: This was a retrospective analysis of data of 1141 patients discharged from the Department of Cardiac Surgery, Peking University First Hospital from January 2010 to June 2018 after undergoing off-pump CABG. Preoperative baseline, operative, and follow-up data obtained at regular outpatient visits or by telephone calls were collected. Follow-up endpoints included stroke, nonfatal myocardial infarction, heart failure, revascularization, and all-cause death. Patients with preoperative estimated glomerular filtration rate calculated, using the Chronic Kidney Disease Epidemiology equation of ≥ 60 mL/min/1.73 m² and < 60 mL/min/1.73m², were assigned to normal Group (1, 910 cases) and CKD group (231 cases), respectively. The effects of CKD on selected endpoint events were compared and analyzed.

Results: There was a higher proportion of women, more preoperative complications, and a higher incidence of early postoperative complications in patients with CKD than in those with normal renal function. After 1–9 years of follow-up (mean 5.0 ± 2.2 years), the incidences of stroke, non-fatal myocardial infarction, and all-cause mortality were significantly higher in the CKD than in the normal renal function group, whereas incidences of revascularization and heart failure were not. Logistic regression analysis showed that preoperative CKD was a risk factor for stroke, non-fatal myocardial infarction, and all-cause death during follow-up. After correcting for common confounding factors, such as sex, age, and left ventricular ejection fraction, preoperative CKD was a risk factor for non-fatal myocardial infarction (OR 2.675, 95% CI 1.023–6.995, $P=0.045$) and all-cause death (OR 1.833, 95% CI 1.079–3.114, $P=0.025$).

Conclusions: In patients undergoing off-pump CABG, preoperative CKD is associated with increases in the incidences of mid- and long-term non-fatal myocardial infarction and all-cause mortality.

Background

Chronic kidney disease (CKD) is a major risk factor for coronary artery disease (CAD) (1), and the risk of death, cardiovascular events, and hospitalization increase with decreasing estimated glomerular filtration rate (EGFR)(2). Coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are effective treatments for severe coronary heart disease. A meta-analysis found that CABG is associated with significantly lower long-term mortality in patients with CKD and end-stage renal disease than is PCI (3).

Whether off-pump or on-pump CABG is preferable for patients with coronary heart disease with CKD is controversial. Current studies have shown that off-pump CABG may be superior, possibly because off-pump obviates the need for cardiopulmonary bypass and protects renal function in the perioperative period. It is also associated with fewer complications, including allogeneic blood transfusion, postoperative thoracotomy hemostasis, acute kidney injury, and respiratory system dysfunction (4). In

particular, off-pump CABG significantly reduces operative mortality and risk of postoperative dialysis in patients with moderate or severe renal insufficiency (5). Off-pump CABG is currently preferred in mainland China, accounting for approximately 95% of total CABG procedures in our department. Management of such patients is very complicated, and the impact of the comorbidity of CKD on mid- and long-term clinical outcomes of off-pump CABG has rarely been studied. We therefore conducted a retrospective study of the mid-and long-term outcomes of 1141 patients, who had undergone off-pump CABG from January 2010 to June 2018 in the Department of Cardiac Surgery, Peking University First Hospital.

Methods

Inclusion criteria were as follows: consecutive, first-time patients undergoing off-pump CABG discharged from our hospital from January 2010 to June 2018. Exclusion criteria were as follows: acute renal insufficiency, preoperative end-stage renal disease dependent on dialysis, intraoperative transfer to on-pump, death within 30 days after surgery, incomplete data, and refusal to attend for follow-up. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to calculate eGFR (6). Patients with $eGFR_{CKD-EPI} > 60$ mL/min/1.73 m² were classified as having normal renal function and those with < 60 mL/min/1.73 m² as having CKD. Baseline and operative data during hospitalization and postoperative outpatient or telephone follow-up data were collected for statistical analysis. Clinical outcomes included stroke, nonfatal myocardial infarction, heart failure, revascularization, and all-cause death.

SPSS21.0 software (IBM Corp., Armonk, NY, USA) was used for analysis; the χ^2 or Fisher's exact test for analyzing count data between two groups and a group *t*-test for measurement data. The effect of preoperative CKD on all clinical outcome events during follow-up was analyzed by logistic regression. Odds ratios (ORs) and 95% confidence intervals were calculated by univariate analysis and corrected for common confounding factors, such as sex, age, and left ventricular ejection fraction (LVEF). $P < 0.05$ was considered to denote a significant difference (two-sided test).

Results

A total of 1141 patients were included in the study: 910 in the normal Group and 231 in the CKD group. Comparisons of baseline and operative data during hospitalization are shown in Table 1. There was a higher proportion of women, older mean age, and higher incidence of preoperative and postoperative complications in the CKD group than in the normal renal function group.

All patients underwent outpatient or telephone follow-up for 1–9 years (mean 5.0 ± 2.2 years). The incidences of stroke, non-fatal myocardial infarction, and all-cause mortality were significantly higher in the CKD than the normal renal function group, whereas the incidences of revascularization and heart failure were not. Clinical endpoints according to study group are shown in Table 2.

Results of logistic regression analysis on the effect of preoperative CKD on clinical outcome events are shown in Table 3. Preoperative CKD was found to be a risk factor for stroke, non-fatal myocardial infarction, and all-cause mortality. After correction for common confounding factors, such as sex, age, and LVEF, preoperative CKD was identified as a risk factor for non-fatal myocardial infarction and all-cause mortality.

Discussion

Patients with CKD have a significantly increased risk of coronary heart disease, not only because of traditionally recognized CAD risk factors such as diabetes and hypertension, but also because of other non-traditionally recognized cardiovascular disease risk factors associated with uremia, including inflammation, oxidative stress, and abnormal calcium-phosphorus metabolism (1). Lipid metabolism disorders, mainly hypertriglyceridemia, are risk factors for coronary heart disease in patients with CKD. This accounts for a prevalence of coronary heart disease of approximately 12% in patients with Stage 3 or greater CKD, compared with only 5% in those with normal renal function (7). CKD is often accompanied by disorders of mineral bone metabolism, hypocalcemia, hyperphosphatemia, and secondary hyperparathyroidism, all of which can accelerate systemic atherosclerosis and vascular calcification (8). Inflammatory responses, oxidative stress, impaired endothelial cell function, coronary artery calcification, hyperhomocysteinemia, immunosuppression, and other mechanisms can contribute to significant acceleration of atherosclerosis, leading to a poor prognosis in this patient group. Complications of coronary heart disease, such as myocardial infarction and heart failure, are the main causes of death (9). Particularly in dialysis-dependent patients with advanced CKD, the death rate is as high as 40–50% (10). A 2012 epidemiological survey reported an incidence of CKD in mainland China of 10.8% and estimated that there were 119.5 million patients with CKD in that country (11). Increasing numbers of these patients will require CABG in the future. There is an urgent need to improve postoperative long-term survival rate.

In patients with severe coronary heart disease and non-dialysis-requiring CKD, CABG achieves significantly lower mortality, re-infarction, and revascularization rates than do PCI and drug therapy (12, 13). In one study 2108 patients with CKD who underwent PCI using drug-eluting stents, (n = 1165) or CABG (n = 943) were prospectively analyzed in a nonrandomized study with an average follow-up of 41.4 months. Although no significant differences in all-cause death, stroke, and myocardial infarction were observed between the two groups, the revascularization rate was significantly higher in the PCI group (14). A meta-analysis of 29,246 patients enrolled in 11 studies showed that CABG achieved lower long-term all-cause mortality, cardiac mortality, and incidences of myocardial infarction and revascularization, and fewer major adverse cardiac and cerebrovascular events (MACCE) than did drug-eluting stents for revascularization in patients with multivessel coronary heart disease and CKD. However, mortality and risk of cerebrovascular events have recently increased (15). Although CABG can significantly improve the survival rate, it also increases the incidence of postoperative renal failure, especially in high-risk patients (16).

Off-pump CABG reportedly has a protective effect on renal function in the perioperative period because of it does not entail cardiopulmonary bypass; it also reduces the incidences of complications, such as allogeneic blood transfusion, post-operative thoracotomy hemostasis, acute kidney injury, and respiratory system dysfunction (4). However, in the CORONARY study, no significant difference was observed between on-pump and off-pump CABG in effects on renal function at the 1 year follow-up, and off-pump had no demonstrable long-term renal protective effect (17). In the present study, there was a higher proportion of women, older mean age, and higher incidences of preoperative and postoperative complications in the CKD than in the normal group. The follow-up period ranged from 1 to 9 years, with an average of 5.0 ± 2.2 years. The incidences of stroke, non-fatal myocardial infarction, and all-cause mortality were significantly higher in the CKD than in the normal renal function group; however, those of revascularization and heart failure were not. Logistic regression analysis showed that preoperative CKD was a risk factor for stroke, non-fatal myocardial infarction, and all-cause mortality. After correcting for common confounding factors such as sex, age, and LVEF, preoperative CKD was identified as a risk factor for non-fatal myocardial infarction and all-cause mortality in the off-pump CABG over a mid- to long-term follow-up.

CKD and end-stage renal disease not only increase the risk of CAD, but also change its clinical manifestations and main symptoms. Management of patients with CAD and CKD is complex because of the possibility of complications and adverse effects during interventions (1). Protection of renal function and improvement in postoperative survival are critical for discharged patients with CKD not undergoing dialysis who have undergone CABG. There is a need for cooperation among cardiac surgeons, cardiologists, nephrologists, and endocrinologists to enhance postoperative management and construct comprehensive strategies, to improve prognosis and reduce complications and mortality in high-risk patients.

First, the identification of high-risk patients facilitates rational allocation of medical resources, targeted prevention, and management. As renal function worsens, the length of hospital stay and medical costs and the number of complications increase. Decreases in creatinine clearance to 80, 60, and 20 mL/min reportedly lead to cost increases of 10%, 20%, and 30%, respectively. Additionally, the incidence of need for dialysis and mortality increase postoperatively (18). Grouping of CKD severity on the basis of eGFR calculated by the CKD-EPI equation effectively predicts postoperative complications and mortality in both the short- and long-term (23). $eGFR_{CKD-EPI} < 30 \text{ mL/min/1.73 m}^2$, $< 41 \text{ mL/min/1.73 m}^2$, $< 27 \text{ mL/min/1.73 m}^2$, and $< 29 \text{ mL/min/1.73 m}^2$ are predictors of early mortality, stroke, prolonged length of hospital stay, and postoperative dialysis substitution, respectively. Additionally, $eGFR_{CKD-EPI} < 26 \text{ mL/min/1.73 m}^2$, $< 25 \text{ mL/min/1.73 m}^2$, $< 35 \text{ mL/min/1.73 m}^2$, and $< 29 \text{ mL/min/1.73 m}^2$ are predictors of all-cause death, cardiovascular death, myocardial infarction, and heart failure, respectively, during follow-up (average follow-up time 66 months) (19). Therefore, the management of high-risk patients needs to be further strengthened.

Second, active treatment of comorbidities such as hypertension, diabetes, and anemia is vital. Hypertension and diabetes are the two commonest comorbidities in patients with CKD. Recommendations for treatment of diabetic nephropathy include control of Hb1Ac < 7%, blood pressure < 140/90 mmHg, and treatment with renin-angiotensin system blockers (20). Patients with CKD have a high incidence of hypertension that may lead to or originate from CKD. Hypertension aggravates CKD, resulting in uncontrollable hypertension (21). The 2017 American College of Cardiology/American Heart Association Hypertension Guidelines set a BP target of < 130/80 mm Hg for patients with CKD and other strong cardiovascular risk factors to reduce mortality in patients with CKD. However, few data are available for patients with diabetes or Stage 4–5 CKD (22). Anemia, another common manifestation of renal insufficiency, causes decreased erythropoietin secretion and renal anemia. Anemia predicts the risk of cardiovascular events and death in patients with coronary heart disease (23). It is also an independent risk factor for increased mortality of coronary heart disease in CKD patients with blood hemoglobin below 12 g/dL (24).

Third, measures for secondary prevention of coronary heart disease should be actively continued postoperatively, including oral antiplatelet drugs, statin treatment, and good living habits.

In conclusion, patients with CKD undergoing CABG are older preoperatively, have more complications, and more early postoperative complications than those with normal renal function. Mid- and long-term follow-up after CABG revealed associations between preoperative CKD and higher incidences of nonfatal MI and all-cause mortality (after correcting for common confounding factors such as sex, age, and LVEF). Among patients with CKD undergoing off-pump CABG, it is necessary to identify high-risk patients and strengthen comprehensive management to reduce complications and improve long-term survival.

Abbreviations

chronic kidney disease

CKD

coronary artery disease

CAD

coronary artery bypass grafting

CABG

estimated glomerular filtration rate

EGFR

percutaneous coronary intervention

PCI

Chronic Kidney Disease Epidemiology Collaboration

CKD-EPI

left ventricular ejection fraction

LVEF

major adverse cardiac and cerebrovascular events

Declarations

Ethics Approval and consent to participate

This study was approved by the biomedical research ethics committee of Peking University First Hospital (approval No. 2018, scientific research 242). And consent was waived.

Consent for Publication

Not applicable

Availability of supporting data

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors have no conflict of interest to declare.

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Author Contributions

Bo Song and Xihui Li Literature search; shiyong Dong and Siyu zhang Data collection. . All authors read and approved the final manuscript.

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Tables

Table 1. Comparison of baseline and operative data between the CKD and normal groups

	normal Group 1 (n=910)	CKD Group 2 (n=231)	<i>t</i> / χ^2	<i>p</i>
Age(ys)	63.4±9.2	69.7±8.9	9.328	0.000
Female sex(%)	228(25.1)	111(48.1)	46.656	0.000
Hypertension(%)	595(65.4)	194(84.0)	29.871	0.00
Diabetes(%)	347(38.1)	120(51.9)	14.546	0.000
Stroke before operation(%)	90(21.1)	67(28.5)	6.970	0.008
Hyperlipemia(%)	384(42.1)	113(47.4)	3.384	0.066
OMI(%)	345(37.9)	92(39.8)	0.286	0.593
LVEF(%)	61.2±13.3	57.8±15.0	3.380	0.001
Hemoglobin (g/L)	135.1±15.4	123.1±17.9	10.211	0.000
AF before operation(%)	40(4.3)	21(8.4)	6.704	0.01
BNP(pg/mL)	243±415	428±625	4.270	0.000
Left main involved(%)	246(27.0)	78(33.8)	4.108	0.043
Emergency(%)	17(1.9)	4(1.7)	-	1.000
LIMA use(%)	788(86.6)	169(73.2)	25.693	0.000
LCOS	58(6.4)	22(9.5)	2.804	0.094
IABP use	58(6.4)	30(13.0)	11.321	0.001
Grafts	2.7±0.8	2.5±0.8	2.143	0.032
Re-open	8(0.9)	4(1.7)	-	0.276
Re intubation	10(1.1)	7(3.0)	4.682	0.030
AKI	239(26.3)	102(44.2)	28.146	0.000
ARDS	90(9.9)	29(12.6)	1.400	0.237
Stroke peri-operative	13(1.4)	9(3.9)	5.932	0.015
UGH	12(1.3)	9(3.9)	6.774	0.029
AFperi-operative	153(16.8)	52(22.5)	4.058	0.044

AF: atria fibrillation; AKI: acute renal injury; ARDS: acute respiratory distress syndrome; BNP: brain natriuretic peptide; COPD: chronic obstructive pulmonary disease; IABP: intra-aortic balloon pump; LCOS: low cardiac output syndrome; LIMA: left internal mammary artery; LVEF: left ventricular ejection fraction; OMI: old myocardial infarction; UGH: upper gastrointestinal hemorrhage.

Table 2. Comparison of clinical outcome events between CKD and normal groups

	Normal Group (n=910)	CKD Group 2 (n=231)	<i>t/X²</i>	<i>p</i>
Stroke(%)	52(5.7)	22(9.5)	4.408	0.036
Nonfatal MI(%)	12(1.3)	9(3.9)	6.774	0.009
Revascularization(%)	37(4.1)	12(5.2)	0.571	0.450
Heart failure(%)	14(1.5)	4(1.7)	--	0.771
All-cause mortality(%)	50(5.5)	27(11.7)	11.231	0.001

Nonfatal MI: nonfatal myocardial infarction

Table 3. Logistic regression analysis of the effect of CKD on clinical outcome events (before and after adjusted)

	Unadjusted				adjusted			
	OR	95% CI		<i>p</i>	OR	95% CI		<i>p</i>
Stroke(%)	1.737	1.032	2.924	0.038	1.694	0.967	2.966	0.065
Nonfatal MI(%)	3.034	1.263	7.290	0.013	2.675	1.023	6.995	0.045
Revascularization(%)	1.293	0.663	2.521	0.451	1.664	0.808	3.427	0.167
Heart failure(%)	1.128	0.368	3.459	0.833	1.399	0.418	4.682	0.586
All- cause mortality(%)	2.276	1.391	3.725	0.001	1.833	1.079	3.114	0.025

Nonfatal MI: nonfatal myocardial infarction