Multi-vessel disease percutaneous coronary intervention versus coronary artery bypass grafting in patients with chronic kidney disease.

Abstract:

Background:

Coronary revascularization is associated with better prognosis in multivessel coronary artery disease (MV-CAD) chronic kidney disease (CKD) patients. However, whether coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is better remains unknown.

Objectives:

To compare outcome of multi-vessel PCI versus CABG in the group of patients with CKD regarding in-hospital and one-year major adverse cardiovascular and cerebrovascular events (MACCE).

Methods:

A retrospective analysis of the data of patients with established CKD with eGFR less than 60 ml/min with MV-CAD who underwent PCI or CABG were compared as regards in-hospital and one-year MAACE.

Results:

A total number of 565 patients were reviewed, 230 patients had PCI while 335 patients had CABG. Comparing both groups regarding in-hospital MACCE, patients who had mutli-vessel PCI had significantly lower in-hospital death, cerebrovascular events and total MACCE than patients who had CABG (P-value = 0.03, 0.01, 0.04 respectively). While comparing both groups regarding one-year MACCE, patients who had mutli-vessel PCI had significantly lower

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cerebrovascular events and total MACCE than patients who had CABG (P-value = 0.02, 0.03 respectively).

Conclusion:

This is a retrospective study to determine which is the better strategy for revascularization of CKD MV-CAD patients; we can conclude that multi-vessel PCI for CKD patients and MV-CAD had advantages over CABG as regards in-hospital and one-year cerebrovascular accidents (stroke/TIA) and total MACCE. Large randomized controlled trials are needed to confirm our findings.

Keywords: Multivessel coronary artery disease, chronic kidney disease, percutaneous coronary intervention, coronary artery bypass grafting.

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Introduction:

Coronary artery disease (CAD) is the leading cause of cardiovascular morbidity and mortality among patients with chronic kidney disease (CKD) [1]. In patients with CAD and CKD, coronary artery lesions are complex and calcific, which leads to a worse prognosis with higher morbidity and mortality [2-4].

Some clinical studies reported that for CAD patients with CKD, early management of CAD with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) results in lower mortality and better outcomes compared to medical therapy alone [5,6].

There is a paucity of data comparing the effectiveness of percutaneous coronary intervention using drug-eluting stent compared to coronary artery bypass graft surgery in patients with chronic kidney disease. Although there have been 2 large randomized controlled trials (RCTs) comparing PCI using DES versus CABG in patients with multivessel disease (Synergy Between PCI With Taxus and Cardiac Surgery trial [SYNTAX]) [7] and in patients with diabetes mellitus Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease [FREEDOM]) [8], there are no RCTs comparing or evaluating different revascularization strategies in patients with CKD.

Some studies reported that CABG may be a better option for multivessel CAD patients with CKD, however others did not. Other studies reported that treatment with CABG have better survival outcome than multivessel PCI in those CKD patients [9-12], although CABG will increase the short term risk of acute kidney failure. However, one study [13] conducted on CKD patients with multivessel CAD, found that multivessel PCI with drug-eluting stents (DES) resulted in similar outcomes of mortality, myocardial infarction (MI), and stroke in comparison to CABG.

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Objectives:

To compare the outcomes of treating patients with CKD with multi-vessel PCI versus CABG, regarding in-hospital and one-year major adverse cardiovascular and cerebrovascular events (MACCE).

Methods:

A retrospective analysis of the data of patients with established CKD with MV-CAD who underwent PCI or CABG from January 2016 to January 2020, in two tertiary well equipped hospitals. The study was approved by the local ethics committee. Outcomes were compared as regards in-hospital and one-year MAACE.

All consecutive adult patients aged ≥18 years undergoing cardiac catheterization during the study period for suspected coronary artery disease were eligible for inclusion. We excluded patients with missing renal functions, single-coronary artery disease, any previous revascularization, patients undergoing emergency revascularization (primary PCI) or cardiogenic shock, patients with preserved renal function, and nonisolated CABG.

The following data were collected: age, sex, smoking, diabetes, hypertension, hyperlipidemia, dialysis, type of stent, vessel involvement, mean follow-up period, long-term all-cause mortality, short-term all-cause mortality, major adverse cardiac and cerebrovascular events (MACCE), cardiac death, MI, and cerebrovascular accidents.

Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2. Multivessel CAD disease was defined as severe stenosis (≥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, and cerebrovascular accidents. Long-term all-cause mortality was defined as all-cause death during a period of one year. MACCE was defined as a

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composite endpoint including all-cause death, nonfatal MI, stroke, and any revascularization. MI was defined as any typical elevation in cardiac biomarkers in the setting of clinical symptoms or signs consistent with cardiac ischemia. Cerebrovascular accidents were defined as neurological deficits which were diagnosed by a neurologist based on imaging study, including stroke, transient ischemic attack, and reversible ischemic neurological deficit.

Statistical Analysis: Continuous variables are reported as mean±SD. Categorical variables are reported as proportions. Between-group univariate comparisons were performed using χ^2 tests for categorical variables, and *t* tests for continuous variables.

Results:

This study included 565 patients having MVD and CKD, indicated for revascularization. 230 CKD patients underwent multivessel PCI, and 335 CKD patients were treated with CABG. There was no statistically significant difference between both groups regarding eGFR. 5.2% of PCI group were on maintenance hemodialysis, while 3% of CABG group were on HD (table 1).

Regarding patients' demographics and risk factors, no significant difference was found between both groups of CKD patients with MVD treated by CABG or PCI (table 1).

Regarding CKD patients managed by PCI, the mean number of stents used was 4.3 stents, left main intervention was done in 140 patients (61%). Regarding CABG patents, LIMA was used in the majority of the included patients (98.3%) (table 1).

In-hospital MACE was significantly higher in CABG group (7.2%) than PCI group (5.2%), p=0.04. Cerebrovascular stroke was also significantly more in CKD patients who had CABG (1.5%) than those patients who had PCI (0.4%), p=0.01. Also, in-hospital mortality was significantly higher in CABG group (2.7%) versus 1.2% in PCI group, p=0.03 (table 2 & figure 1).

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Upon one year follow up, total MACE was also significantly higher in CABG group (18.2%) than PCI group (12.6%), with P value of 0.03, cerebrovascular stroke occurred more in CABG patients than PCI group (3% versus 1.3%, p=0.02) which was statistically significant (table 2 & figure 1).

Discussion:

With the recent advances in stent technology, it was found that PCI with DES had comparable 5-year outcomes to CABG among patients without CKD [14,15]. Since CKD is an independent risk factor for cardiovascular outcomes and mortality, patients with CKD might have worse outcomes after PCI or CABG [16-19]. Most of RCTs comparing CABG with PCI for revascularization of multivessel CAD have excluded patients with advanced CKD, so it may be uncertain whether CABG or PCI has better outcomes in this subset of patients.

Our study of multivessel CAD patients with CKD indicated that 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 between the CABG and the PCI groups. The overall short term and long-term MACCE was lower in the PCI group than CABG group. Previous studies have reported that CABG led to a lower rate of mortality and MACCE [12,20], but most of these studies were observational and included only small samples, which may entail bias. For example, patients who had a severe underlying disease which may have influenced the effectiveness of surgery were more likely to have PCI, which may have favored CABG outcomes. We found that compared with CABG, PCI showed lower short-term all-cause mortality and 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 [21,22], which provides a benefit for short-term prognosis. In the

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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 no significant difference was found 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. It is notable that this research used paclitaxel-eluting stents, which were found to have more risk of RR compared with everolimus-eluting stents [23-25].

Our results showed that the CABG group suffered significantly higher cerebrovascular accidents than the PCI group, both in-hospital (7.2%, versus 5.2%, P=0.04) and with one year follow up (3%, versus 1.3%, P=0.02). Yang et al. [26] had similar results to ours 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 [27]. However, whether off-pump procedures can reduce the risk of stroke is under debate [22,28]. Shen et al. [29] found that the incidence of development of AKI after CABG was higher than after PCI (8.9 vs. 4.5%; OR, 2.05; 95% CI, 1.99–2.12; $p < 0.001$).

Our results showed that multi-vessel PCI for CKD patients and multivessel CAD had advantages over CABG as regards in-hospital and 1-year cerebrovascular accidents (stroke/TIA) and total MACCE, 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 [30,31]. In Ohlow's [32] 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.

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Considering our findings together with the financial burden and patients' preference, PCI may be the favored strategy for patients with multivessel CAD and CKD. But to validate this, our conclusions need further larger RCTs to confirm it.

Study limitations:

There are some limitations to our study. First, relatively small number of patients in each study group. Second, although all patients in the PCI group were treated with drug eluting stents, the types of stents were not the same. Also, the CABG procedure used, either on-pump or off-pump, a factor which is closely related to the outcome. Although all patients who were referred for either multivessel PCI or CABG had an informed Heart Team discussion between noninterventional cardiologists, interventional cardiologists, cardiac surgeons, nephrologists, and also the patient themselves, we could not find the documentation in all cases regarding these discussions and decisions. Therefore, the potential for selection and referral bias may exist because the PCI cohort might have included patients who were considered not eligible for CABG. Although there are some limitations to our research, it is still beneficial regarding the results and outcomes we found.

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Conclusions:

In this retrospective study to determine which is better in CKD MV-CAD patients, we can conclude that multi-vessel PCI for CKD patients and MV-CAD had advantages over CABG as regards in-hospital and 1-year cerebrovascular accidents (stroke/TIA) and total MACCE.

Abbreviations:

CABG Coronary artery bypass grafting
CAD Coronary artery disease
CKD Chronic kidney disease
DES Drug eluting stents

eGFR	Estimated glomerular filtration rate
MACCE	Major adverse cardiovascular and cerebrovascular events
MI	Myocardial infarction
MV-CAD	Multivessel coronary artery disease
PCI	Percutaneous coronary intervention
RCTs	Randomized controlled trials

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Table 1. Baseline Patient Characteristics (n=1130)

	Total (n=565)	PCI (n=230)	CABG (n=335)	P value
History	**Age, years**	53 (±11.1)	59 (±10.3)	0.62
	Male Sex, n (%)	138 (60%)	180 (53.7 %)	0.21
	HTN, n (%)	126 (54.78 %)	199 (59.4%)	0.14
	Smoking, n (%)	113 (49.13 %)	150 (44.78%)	0.07
	Diabetes, n (%)	58 (25.2%)	101 (30.15%)	0.31
	Old MI, n (%)	50 (21.73%)	59 (17.61%)	0.11
PCI data	**Number of vessels,** mean (SD)	4.05 (±0.8)		
	Number of stents, mean (SD)	4.34 (±0.78)		
	Left Main PCI, n (%)	140 (60.9%)		
CABG data	**LIMA, n (%)**		329 (98.3%)	
	RIMA, n (%)		5 (1.5%)	
	Venous Grafts, n (%)		180 (53.7%)	
	Radial Grafts, n (%)		67 (20%)	
eGFR, ml/min, mean (SD)		38.7 (±12.2)	36.9 (±10.9)	0.8
On HD, n (%)		12 (5.22%)	10 (2.99%)	0.078

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Table 2: In-hospital MACCE and all-cause mortality at 1-year (n=1130)

		PCI (n=230)	**CABG (n=335)**	**P value**
In-hospital MACCE	**Mortality**	3 (1.2 %)	9 (2.7 %)	**0.03**
	MI	4 (1.7 %)	5 (1.5 %)	**0.5**
	TVR	4 (1.7 %)	5 (1.5 %)	**0.5**
	CVS/TIA	1 (0.4 %)	5 (1.5 %)	**0.01**
	Total	12 (5.2 %)	39 (7.2 %)	**0.04**
1-year MACCE	**Mortality**	9 (3.9 %)	15 (4.5 %)	0.06
	MI	10 (4.3 %)	18 (5.4 %)	0.09
	TVR	7 (3.04 %)	18 (5.4 %)	0.06
	CVS/TIA	3 (1.3 %)	10 (3 %)	**0.02**
	Total	29 (12.6 %)	61 (18.2 %)	**0.03**

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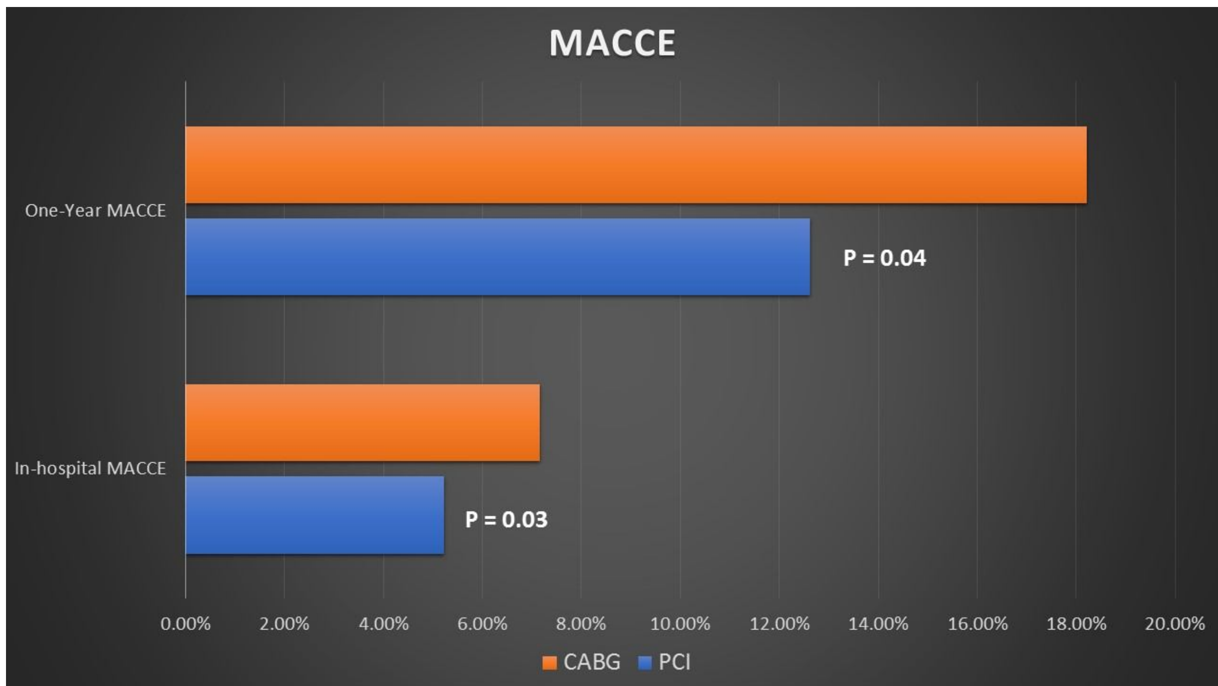

Figure 1: Comparison between in-hospital and 1-year MACCE in PCI and CABG groups

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