

Manuscript type: Original Research Article.

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

Abstract:

Background:

Revascularization of the coronary arteries is associated with better short term and long term prognosis in patients having multivessel coronary artery disease (MV-CAD) and chronic kidney disease (CKD). However, whether revascularization using coronary artery bypass grafting (CABG) surgery or percutaneous coronary intervention (PCI) using drug eluting stents (DES) is better remains unknown.

Objectives:

To compare the outcomes of revascularization by multi-vessel PCI using DES versus revascularization by CABG in patients with CKD having multivessel CAD, regarding in-hospital and one-year major adverse cardiovascular and cerebrovascular events (MACCE).

Methods:

This was a retrospective analysis of the data of a group of patients having CKD with eGFR less than 60 ml/min with multivessel CAD who underwent revascularization by PCI or revascularization by CABG and were compared as regards in-hospital and one-year MAACE.

Results:

A total of 565 patients were reviewed in this study, 230 patients had multivessel PCI using DES while 335 patients had CABG. Comparing both revascularization groups regarding in-hospital MACCE, patients who had mutli-vessel PCI had significantly lower in-hospital mortality, cerebrovascular events (stroke/TIA) and lower total MACCE than patients who had CABG (P-value = 0.03 & 0.01 & 0.04 respectively). When comparing both revascularization groups regarding one-year MACCE, patients who had mutli-vessel PCI had significantly lower cerebrovascular events and total MACCE than those patients who had CABG (P-value = 0.02 & 0.03 respectively).

Conclusion:

This is a retrospective study to determine which strategy is better for revascularization of CKD patients having multivessel CAD; we can conclude that multi-vessel PCI using DES for CKD patients and multivessel CAD had advantages over CABG regarding in-hospital and one-year cerebrovascular accidents (TIA/stroke) and regarding total MACCE. Larger randomized controlled trials are required to confirm our findings.

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

Introduction:

“Coronary artery disease (CAD) is one of the most common causes of cardiovascular morbidity and mortality among patients with established chronic kidney disease (CKD)” [1]. “In patients with CAD and CKD, coronary artery lesions are more complex and calcific, which may lead to a worse prognosis with higher morbidity and mortality” [2-4].

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

“There is a scarcity of data which compare the effectiveness of percutaneous coronary interventions using drug-eluting stents (DES) compared to CABG surgery in CAD patients with established CKD. Two large randomized controlled trials (RCTs) compared revascularization by PCI using DES versus CABG surgery in patients with multivessel coronary artery disease (SYNTAX trial) [7] and in patients with having CAD and diabetes mellitus (FREEDOM trial) [8], however, there are no RCTs to compare or evaluate different revascularization strategies in CAD patients with CKD”.

“Some studies have reported that CABG may be a better option for CKD patients having multivessel CAD, however other studies didn't. It was reported in some studies that treatment with CABG may have better survival outcome than multivessel PCI in CKD patients [9-12], although CABG may increase the short-term risk of acute kidney injury or failure”. “However, one of the studies [13] conducted on CKD patients having multivessel CAD, found that multivessel PCI with DES resulted in similar outcomes of mortality, myocardial infarction (MI), and stroke in comparison to CABG”.

Although there are recent advances in both fields of cardiac surgery and interventional cardiology, which helped to reduce adverse cardiac events, there is always a need for sound clinical judgment for selecting the most appropriate revascularization strategy for CKD patients with multivessel coronary disease. For these reasons, we tried in this research to outline the main differences in the outcomes of revascularization of multivessel CAD in CKD patients.

Objectives:

To compare the outcomes of treating patients with CKD with multi-vessel PCI using DES 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 having MV-CAD who underwent PCI or CABG from January 2016 to January 2020, in two tertiary well equipped hospitals. We compared the outcomes as regards in-hospital and one-year MAACE.

All adult patients aged 18 years or older undergoing elective coronary catheterization during the study period for suspected coronary artery disease were eligible for inclusion in this study. We excluded patients with unknown renal functions, single-coronary artery disease, history of previous revascularization, patients undergoing emergency coronary revascularization (primary PCI), patients with cardiogenic shock, patients with normal renal functions, and nonisolated CABG.

The following data were collected: age, gender, smoking status, history of diabetes mellitus, history of hypertension, history of hyperlipidemia, dialysis, type of stent used, vessel involvement, short-term, and long-term all-cause mortality, major adverse cardiac and

cerebrovascular events (MACCE), cardiac death, MI, and cerebrovascular accidents (TIA/stroke).

Chronic kidney disease was defined as an eGFR (estimated glomerular filtration rate) < 60 mL/min/1.73 m². Multivessel CAD disease was defined as significant (≥50%) stenosis in at least 2 major epicardial coronary arteries. The outcomes included short-term, and long-term all-cause mortality, MACCE, cardiac death, MI, and cerebrovascular accidents. Long-term all-cause mortality was defined as all-cause mortality during a period of one year. MACCE was defined as a composite endpoint including all-cause mortality, nonfatal MI, stroke, or TIA (cerebrovascular accidents), and any revascularization. MI was defined as 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 based on imaging studies, and included stroke, TIA (transient ischemic attack), and any reversible ischemic neurological deficits.

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

Results:

This study included 565 patients having MVD and CKD, indicated for coronary 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' demographic data and risk factors, we found no significant differences between both groups of CKD patients with multivessel CAD who were 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 patients, LIMA was used in most 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).

Upon one year follow up, total MACE was 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).

Discussion:

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

Our study of multivessel CAD patients with CKD indicated that the risk of short-term all-cause mortality and cerebrovascular accidents or stroke were lower in the PCI group. No significant

difference in the overall risk of long-term all-cause mortality was found between the CABG and the PCI groups. The overall short term and long-term MACCE were lower in the PCI group than CABG group.

“Previous studies and trials have reported that CABG in patients with MVD, might have a lower rate of mortality and MACCE [12,20], but most of these studies were observational trials and included only small samples of CKD patients, which may entail bias in selection, patients who had a severe underlying comorbid disease which may influence the effectiveness of surgery were more likely to have PCI rather than surgery, which may have favored the outcomes of CABG”.

“We found that compared with CABG, PCI showed lower short-term all-cause mortality and lower long-term all-cause death and MACCE. The main advantages of PCI are a reduced procedural time, minimal invasion with the use of local anesthesia, absence of mechanical ventilation, fewer local or systemic infections, and shorter hospital stays [21,22], which provides a better benefit for short-term prognosis. In the SYNTAX trial, the only RCT assessing revascularization by PCI with DES versus CABG surgery in patients with multivessel CAD having CKD, the patients were randomly assigned to undergo either PCI with DES or CABG, and no significant difference was found in 5-year all-cause mortality but a higher rate of MACCE, mainly driven by repeat revascularization (RR)”. It is notable that SYNTAX trial used paclitaxel-eluting stents, which have more risk of RR compared with everolimus-eluting stents [23-26].

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. [27] had similar results to ours after a mean follow-up of about 7 years. “A greater severity of atherosclerotic coronary artery stenotic plaques and a more

traumatic, and invasive procedure may be related to a higher risk of occurrence of cerebrovascular stroke associated with CABG” [28]. “However, whether using off-pump CABG procedures can reduce the risk of cerebrovascular accidents is still debatable” [22,29]. Shen et al. [30] found that “the incidence of development of ARF after CABG was higher than after PCI in CKD patients (8.9 vs. 4.5%, $p < 0.001$)”.

“Our study 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 current evidence, it is still hard to figure out which revascularization strategy is better for multivessel CAD patients with CKD. However, from the perspective of social or personal economics, some studies have reported that CABG may be more costly” [31-34]. In Ohlow’s study [35], “based on patients’ personal preference, 15% of the patients chose CABG and 67% chose staged PCI; thus, most of the participants preferred staged PCI over CABG”.

Considering our findings together with the economic burden and patients’ own preference, PCI may be a more favorable strategy for patients with multivessel CAD and CKD. But to validate this, our conclusions need further larger RCTs to confirm it.

Conclusions:

In this retrospective study to determine which is better in CKD multivessel CAD patients, we can conclude 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.

Study limitations:

There are some limitations to our study. First, relatively small number of patients in each study group. Second, although all CKD 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 clinical outcome. Although all patients who were referred for either multivessel PCI or CABG had an informed complete Heart Team discussion between clinical cardiologists, interventional cardiologists, cardiothoracic 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 or referral bias may exist because the PCI cohort might have included some 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.

Ethical Approval:

The study was approved by the local ethics committee (ethics committee of Alexandria faculty of medicine, and ethics committee of the Egyptian ministry of health).

Conference disclaimer:

Title and Abstract part of this manuscript was previously presented and published in the conference: European Society of Cardiology (ESC) Congress 2020- The Digital Experience on Date: 29 August to 01 September 2020 in Paris, France Web Link of the proceeding: <https://www.escardio.org/Congresses-Events/World-cardio-agenda/esc-congress-2020>

Disclosures:

The authors report no financial relationships or conflicts of interest regarding the content herein.

Abbreviations:

ARF	Acute renal failure
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CKD	Chronic kidney disease
DES	Drug eluting stents
eGFR	Estimated glomerular filtration rate
FREEDOM trial	Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease trial
MACCE	Major adverse cardiovascular and cerebrovascular events
MI	Myocardial infarction
MV-CAD	Multivessel coronary artery disease
SYNTAX trial	Synergy Between PCI With Taxus and Cardiac Surgery trial
PCI	Percutaneous coronary intervention
RCTs	Randomized controlled trials

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Table 1. Baseline Patient Characteristics (n=565)

	Total (n=565)	PCI (n=230)	CABG (n=335)	P value
History	Age, years	53 (\pm 11.1)	59 (\pm 10.3)	0.62
	Male Sex, n (%)	138 (60%)	180 (53.7 %)	0.21
	Hypertension, 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 (\pm 0.8)		
	Number of stents, mean (SD)	4.34 (\pm 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 (\pm 12.2)	36.9 (\pm 10.9)	0.8
On HD, n (%)		12 (5.22%)	10 (2.99%)	0.078

CABG=Coronary artery bypass grafting surgery, eGFR= estimated glomerular filtration rate, HD= hemodialysis,

LIMA= left internal mammary artery graft, MI= myocardial infarction, SD= standard deviation, PCI= percutaneous

coronary intervention, RIMA= right internal mammary artery graft.

Table 2: In-hospital MACCE and all-cause mortality at 1-year (n=565)

		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*

CVS= Cerebrovascular stroke, MACCE= Major adverse cardiovascular and cerebrovascular events, MI= Myocardial infarction, TIA= Transient ischemic attacks, TVR= Target vessel revascularization.

* Statistically significant.