Mortality of Patients with Chronic Kidney Disease Post Percutaneous Coronary Intervention Compared with Coronary Artery Bypass Graft: An Evidence Based Case Report

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Abstract:

Background: Chronic kidney disease (CKD) is a disease that causes permanent kidney damage requiring dialysis or transplantation as a follow-up treatment. CKD is a common condition that has a high risk of coronary artery disease (CAD). In CKD patients with CAD, percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) is able to reduce mortality compared with conservative management. However, which method has the most influence on CKD patient mortality is unclear. **Objective:** To find out the prognosis of mortality in post-PCI CKD patients versus CABG. **Methods**: Literature search was done by using three electronic databases (Pubmed, Cochrane, and SCOPUS) using specific keywords. Keywords used were based on the authors' clinical questions. Inclusion and exclusion criteria were applied to the selected studies. **Results**: A total of seven literatures were selected for critical appraisal. These literatures consist of systematic review, meta-analysis, and cohort study. All of these literature demonstrated that mortality in CKD patients underwent PCI is significantly higher than CKD patients underwent CABG. **Conclusion:** PCI performed in patients with CKD causes a significantly higher mortality rate than patients who underwent CABG.

Keywords : chronic kidney disease, coronary artery bypass graft, mortality, percutaneous coronary intervention

Introduction:

Chronic kidney disease (CKD) is a condition characterized by decreased glomerular filtration function that has occurred for years. CKD can cause permanent kidney damage requiring dialysis or a transplant as follow-up treatment. Based on the Kidney Disease Improving Global Outcomes (KDIGO), CKD is defined as kidney damage or decreased glomerular filtration rate (GFR) <60 mL / minute / 1.73 m^2 over three months.[1,2] CKD is a common condition that can have a high risk of cardiovascular mortality and morbidity.[3] Kidney disease also has an association with systemic inflammation that accelerates the incidence of cardiovascular atherosclerosis and thrombosis. Furthermore, coronary artery disease (CAD) is the most common cause of death in CKD patients.[5]

CAD is initiated by calcification of the blood vessels or atherosclerosis. Atherosclerosis can cause three effects, namely arterial stiffness, endothelial dysfunction, and unstable plaque. Endothelial dysfunction and arterial stiffness can cause coronary circulation disorders that can lead to myocardial infarcts. However, in patients with CKD, most myocardial damage is caused by unstable plaque. These processes can increase mortality in patients with CAD.[6]

Percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) are the most common intervention to treat CAD.[7] PCI is a procedure for placing a stent on blocked blood vessels. CABG is a procedure for inserting a new pathway so that blood is able to flow other than through the obstructed vessel, this procedure is a surgical procedure, so it is more invasive than PCI. These two procedures are capable of providing revascularization of the heart.[8] In CKD patients with CAD, these two approaches are able to reduce the mortality rate compared to conservative management.[9] The CABG procedure is performed only once on indications of triple or more severe vessel occlusion, ventricular dysfunction, or comorbidity such as diabetes mellitus. PCI is indicated for patients who have had a sudden cardiac arrest. PCI needs to be done several times to reach complete revascularization.[10] However, which method has the most significant impact to increase CKD patients mortality is still unclear.[11]

Case Illustration:

A 63 year old male patient came for routine control because of the depleted medication. Twenty one

years ago the patient was diagnosed with hypertension. Before being diagnosed, patients often experienced dizziness.

Three years before being admitted to the hospital, the patient experienced continuous shortness of breath so he was taken to the emergency room. Initially, the patient complained of shortness of breath and fatigue when doing activities, such as walking and climbing dates. Shortness of breath gets worse when the patient sleeps so that the patient has to use two pillows.

In Cipto Mangunkusumo Hospital, electrocardiography (ECG) was performed and it was found that the patient had a heart attack accompanied by a heart rhythm disturbance. Therefore, the patient was catheterized and found vessel blockage. Two rings were placed inside the occluded vessels in August 2018 and other two rings were placed in November 2018.

Ten years before being admitted to the hospital, the patient had epistaxis. The bleeding did not stop for eight hours, so he was rushed to the emergency room. At the hospital, the patient was diagnosed with diabetes mellitus. Before being diagnosed, there were complaints of frequent hunger, frequent drinking, frequent urination. The patient was prescribed oral antidiabetic drugs. However, the patient admitted that he did not regularly take the medication.

Six years before being admitted to the hospital, the patient experienced foamy urine, intermittent urinary flow, and a feeling of incomplete urine. The patient admitted that he urinated frequently with a large volume. Patients often wake up from sleep to urinate with a frequency of urinating four times at night. There was no bloody urine, pain while urinating, bed-wetting, and abdominal pain. The patient was checked for a laboratory test at Depok Hospital. The result is high blood creatinine, which is 2.1 mg / dL. The patient was diagnosed with chronic kidney disease (CKD).

Clinical Question

Patient in this case had CABG indication such as CAD with involvement of four blood vessels and comorbid diabetes mellitus, but the patient also had an indication of PCI, a heart attack that brought him to the emergency room. The patient underwent a PCI method that was not as invasive as CABG. Therefore, the authors formulated a clinical question "is there a significant difference

between the prognosis of mortality in patients with CKD who received PCI procedure compared with CKD patients who received CABG?" The description of the authors' clinical question is presented in table 1

Table 1. Clinical Question

Parameter	Population	Intervention	Comparison	Outcome
	CKD patient	PCI	CABG	Mortality
Clinical aspects	Prognosis			
Study design	meta-analysis, systematic review, randomized controlled trial (RCT), cohort			

Methods

Literature Search

The literature search was conducted on January 6, 2021 to June 6, 2021 with keywords that match the author's clinical questions. Literature search used the 'OR' and 'AND' booleans. Literature search was performed on three electronic databases, namely PubMed, Cochrane, and SCOPUS. The search strategy and keywords used can be seen in Table 2.

Table 2. Searching Strategy

Database	Keywords	Obtained	Be chosen
PubMed	("chronic kidney disease" [All Fields]) AND ("PCI" [All Fields]) AND ("CABG" [All Fields]) AND ("mortality" [All Fields])	65	7
Cochrane	"chronic kidney disease" in Title Abstract Keyword AND "percutaneous coronary intervention" in Title Abstract Keyword AND "coronary artery bypass graft" in Title Abstract Keyword AND "mortality" in Title Abstract Keyword	26	0
SCOPUS	(TITLE-ABS-KEY (chronic AND kidney AND disease) AND TITLE-ABS KEY (pci) AND TITLE-ABS KEY (cabg) AND TITLE-ABS-KEY (mortality))	140	1

Selection of Articles

A total of 228 articles were obtained from search results in the PubMed, Cochrane, and SCOPUS databases. The title screening was carried out based on the study design that matched the authors' clinical questions. File selection was carried out based on exclusion criteria. Articles not written in English and not PICO-compliant were excluded. Double screening was performed to exclude duplicate articles. Full text selection is done based on the availability of full text articles. After going through the process of searching and selecting articles, there were three systematic review articles involved in the critical review process. The search and selection process is presented in the PRISMA diagram in Figure 1.

Results

Based on the results of search and selection of articles, there are seven articles that are suitable and can be continued for critical analysis. These articles are systematic review, meta-analysis, and cohort study.

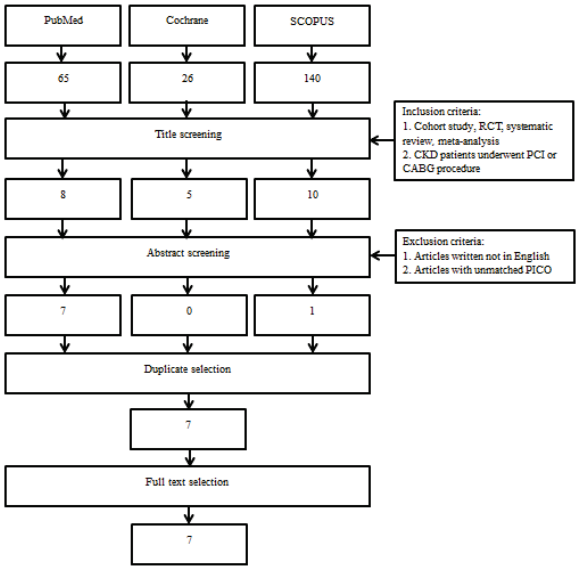

Figure 1. PRISMA Flowchart

The author selected seven articles according to the author's PICO. A summary of the study can be seen in Table 3.

The critical analysis is carried out using the critical analysis instrument from the University of Oxford's Center of Evidence Based Medicine. The results of the critical review of the study of each article are presented in Table 4.

The observed parameter in this study was the mortality of post-PCI CKD patients compared with post-CABG CKD patients. The mortality rate is presented in the form of odds ratios and hazard ratios. The results of the study of each article can be seen in Table 5.

Table 3. Study Summary

Author	Title	Total Population
Doulamis et al	*Percutaneous Coronary Intervention with Drug Eluting Stents Versus Coronary Artery Bypass Graft Surgery in Patients with Advanced Chronic Kidney Disease: A Systematic Review and Meta-Analysis*	A total of 16 articles for a total of 15.313 patients (7.157 patients underwent CABG and 8.156 patients underwent PCI)
Barbarawi et al	*Comparison of Coronary Artery Bypass Grafting and Drug-eluting Stents in Patients with Left Main Coronary Disease: A Systematic Review and Meta-analysis*	Total of 5 articles for a total of 1.212 patients (557 patients underwent PCI and 655 patients underwent CABG)
Bundhun et al	*Impact of Coronary Artery Bypass Surgery and Percutaneous Coronary Intervention on Mortality in Patients with Chronic Kidney Disease and on Dialysis. A Systematic Review and Meta-Analysis*	A total of 18 articles for a total of 69.456 patients (29.239 patients underwent CABG and 40.217 patients underwent PCI)
Yang et al	*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*	A total of 13 articles for a total of 18.005 patients
Chang et al	*Comparative effectiveness of coronary artery bypass grafting and percutaneous coronary intervention for multivessel coronary disease in a community-based population with chronic kidney disease*	Total of 8.172 patients (4.086 patients underwent CABG and 4.086 patients underwent PCI)
Kilic et al	*Surgical versus percutaneous multivessel coronary revascularization in patients with chronic kidney disease*	Total of 1.853 patients (1.269 patients underwent CABG and 584 patients underwent PCI)

Lautamaki et al	*Outcome after coronary artery bypass grafting and percutaneous coronary intervention in patients with stage 3b–5 chronic kidney disease*	Total of 258 patients (148 patients underwent CABG and 110 patients underwent PCI)

Table 4. Critical analysis

Critical analysis	Doulamis et al	Barbarawi et al	Bundhun et al	Yang et al	Chang et al	Kilic et al	Lautamaki et al
Clear PICO and PICO-compliant inclusion criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Evidence found according to the search	Yes	Yes	Yes, but PRISMA is not suitable	Yes	No (cohort design)	No (cohort design)	No (cohort design)
The studies listed have been critically examined	Yes	Yes	Yes	Yes	No (cohort design)	No (cohort design)	No (cohort design)
The studies used were of high quality	Yes	Not stated	Not stated	Yes	No (cohort design)	No (cohort design)	No (cohort design)
Study results are presented in tables and appropriate forest plots	Yes	Yes	Yes	Yes	Yes	Yes for tables, no forest plot	Yes for tables, no forest plot
The heterogeneity between studies is clearly stated	Yes	Yes	Yes	Yes	No (cohort design)	No (cohort design)	No (cohort design)

Table 5. Study Results

Studies	Study results
Doulamis et al	The overall mortality of PCI was higher than that of CABG (HR: 1.28, 95% CI: 1.13 - 1.46; P = 0.00; I^2 = 35.77%).
Barbarawi et al	There was no significant difference in overall mortality in patients undergoing PCI compared to CABG (OR: 0.9, 95% CI: 0.55 - 1.49; P = 0.68; I^2 = 54%)
Bundhun et al	Long-term follow-up mortality of more than one year was higher in PCI patients compared with CABG (OR: 0.81, 95% CI: 0.70–0.94; P = 0.007; I2 = 75%). Mortality after more than three years was also higher for PCI compared with CABG (OR: 0.82, 95% CI: 0.70–0.95; P = 0.01; I^2 = 48.4%)
Yang et al	Long-term follow-up mortality was significantly lower in the CABG group than in the PCI group (HR: 0.76, 95% CI: 0.70 – 0.83; P < 0.001; I^2 = 21%)
Chang et al	CABG was associated with a significantly lower mortality than PCI across all groups of estimated glomerular filtration rate (in mL/min/1.73 m^2): the adjusted HR was 0.81; 95% CI: 0.68 – 1.00 for patients with eGFR ≥60; HR 0.73; 95% CI: 0.56 – 0.95 for eGFR of 45 – 59; and HR 0.87; 95% CI: 0.67 – 1.14) for eGFR<45.
Kilic et al	CKD patients survival with one year follow up was higher in CABG groups than in PCI groups (88.92% vs 82.67%, P<0.0001). In five years follow up, CKD patients survival was also higher in CABG groups than in PCI groups (73.93% vs 52.28%, P<0.0001).
Lautamaki et al	PCI was associated with a significantly higher risk of mortality than CABG in three years follow up (50.4 vs 32.9, HR: 1.77; 95% CI: 1.13–2.77).

Discussion

Various studies have been conducted to determine the mortality of CKD patients undergoing PCI compared to CABG. Mortality in these studies is also described based on the duration of follow-up, so as to indicate the short-term and long-term mortality.[9,11,12] Results presented in those studies are not only useful to identify patients prognosis but also to choose the best suited intervention to patient characteristics.

Doulamis et al's study entitled *Percutaneous Coronary Intervention with Drug Eluting Stents Versus Coronary Artery Bypass Graft Surgery in Patients*

with Advanced Chronic Kidney Disease: A Systematic Review and Meta-Analysis examined 16 articles with a patient population of 15.313 patients consisting of 7.157 CKD patients who underwent PCI and 8.156 patients who underwent CABG. The mortality in this study was divided into two, namely mortality with a follow-up duration of 30 days or while the patient was in hospital and mortality with a follow-up duration of one year. Mortality with a follow-up of 30 days was higher in CABG patients (2.4%) than in PCI (1.7%), with a value of P = 0.39. However, in mortality within one year of follow-up, PCI had a higher mortality rate (8.9%) than CABG (7.4%). with a value of P = 0.83. This study conducted a pooled analysis showing that PCI increased the risk of mortality in CKD patients compared to CABG (HR: 1.28, 95% CI: 1.13 - 1.46; P <0.01; I^2 = 35.77%). In addition, this study also compares the incidence of MACCE (major adverse cardiac and cerebrovascular events) occurring in patients with PCI with CABG. In this study, the incidence of MACCE after PCI was more frequent than in CABG patients (HR: 1.44, 95% CI: 1.17 - 1.79; p <0.01; I^2 = 82.6%).[12]

It was also stated that end stage renal disease (ESRD) can accelerate the formation of atherosclerosis due to increased inflammatory mediators and oxidative stress. In addition, the morphology of atherosclerotic plaque in CKD patients is different from that of patients without CKD. In patients with CKD, the plaque that forms has unstable medial and intimal microcalcifications.[13] This process may lead to a high incidence of restenosis in the PCI stent. In CKD patients undergoing PCI, the use of antiplatelet and anticoagulants has also been associated with a high risk of bleeding and cardiovascular mortality.[14]

The study of Doulamis et al. has limitations that need to be considered in a critical study. Because this study is a meta-analysis study, this study does not have access to detailed patient data, so the data used is data that has not been adjusted. It is this difference that causes the difference in the short-term and long-term mortality rates in CABG patients compared to PCI patients. This study also did not explain the adherence to medical therapy. The severity of CAD and the degree of

revascularization also differed among the included studies.[12]

Barbarawi et al's study entitled *Comparison of Coronary Bypass Grafting and Drug-Eluting Stents in Patients with Left Main Coronary Artery Disease and Chronic Kidney Disease: A Systematic Review and Meta-Analysis* examined five articles with a total of 1.212 patients consisting of 557 patients who underwent PCI and 655 patients underwent CABG. All the follow-ups for these five articles were more than one year long. This study showed that there was no significant difference between mortality in patients with PCI and CABG (OR 0.90; 95% CI 0.55-1.49; P = 0.68; I^2 = 54%). A value of I^2 = 54% indicates high heterogeneity, so that there is excessive variation between the study population.[9]

Apart from being stated in this study that there is no significant difference between mortality in PCI patients with CABG, this study also does not show an excess of survival in patients who received CABG treatment. However, one of the articles used in this study, namely the study by Giustino et al, showed that PCI had a significantly higher mortality rate than CABG (OR 0.49; 95% CI 0.25 - 0.93). It was also explained that the most common cause of death was sepsis, which occurred one month after the procedure.[1]

The study of Barbarawi et al. has several limitations that need to be considered when conducting a critical analysis. The primary outcome in this study was MACCE (major adverse cardiac and cerebrovascular events), whereas mortality was the secondary outcome. The primary outcome in this study was considered to have greater analytical power. Meanwhile, secondary outcomes (including mortality) were considered to have low analytical power. In addition, due to the lack of RCT studies most of the studies included in this analysis were observational, thus increasing the risk of high selection bias and intervention bias.[15] It was also stated in this study that the clinical data of patients were considered inadequate, so that the clinical outcome of each procedure could not be explained in detail.[9]

Bundhun et al's study entitled *Impact of Coronary Artery Bypass Surgery and Percutaneous Coronary Intervention on Mortality in Patients with Chronic Kidney Disease and on Dialysis. A*

Systematic Review and Meta-Analysis examined 18 articles with a total of 69.456 patients consisting of 29.239 CKD patients who had undergone CABG and 40.127 CKD patients who had undergone PCI. The mortality in this study was grouped into three periods of follow-up duration, namely mortality with follow-up while the patient was hospitalized, mortality with a short-term follow-up duration of one month, mortality with one-year follow-up duration, mortality with long-term follow-up duration more than one year, and mortality with long-term follow-up duration greater than three years.[11]

In mortality with inpatient follow-up, CABG showed a higher rate (7.16%) compared to PCI (3.87%), with an OR value of 1.55, 95% CI 0.82-292; P = 0.17, I^2 = 51%. Short-term mortality with the follow-up period also showed a higher rate of CKD patients undergoing CABG (2.45%) compared to PCI (1.72%), with an OR value of 1.24, 95% CI 0.93 - 1.65; P = 0.15, I^2 = 40%. In addition, in mortality with a follow-up duration of one year, CABG and PCI did not show significantly different rates (18.8% and 19.4%) with OR 0.99, 95% CI 0.91 - 1.08; P = 0.86, I^2 = 38%. However, it should be noted that these three results were not statistically significant. In addition, this study also compares the incidence of MAE (major adverse events) occurring in patients with PCI with CABG. MAE consists of MACE (major adverse cardiac events) and MACCE (major adverse cardiovascular and cerebrovascular events). In this study, the incidence of MAE after CABG (18.2%) was less frequent than in PCI patients (29.2%), with OR: 0.51, 95% CI: 0.28 - 0.92; p = 0.03.[11]

The mortality rate that was statistically significant was found in mortality with a longer follow-up duration. However, it was not stated in the study whether there was repeated PCI procedure and the progress of the patient's CKD. When followed up with a duration of more than one year, it was shown that the mortality rate for CABG was lower (18.4%) compared to PCI (23.8%), with an OR of 0.81, 98% CI 0.70 - 0.94; P = 0.007, I^2 = 75%. At a follow-up duration of more than three years, it was also seen that the mortality rate for CABG was lower (18.8%) compared to PCI (24.7%), with an OR value of 0.82, 95% CI 0.70 - 0.95; P = 0.01, I^2 = 79%.

However, it should also be noted that the I^2 value is high, thus indicating high heterogeneity.[11]

On these results, Bundhun et al. explained that the higher long-term mortality in PCI might be due to restenosis and incomplete revascularization of PCI. In addition, another possibility is contrast-induced acute nephropathy which may lead to other complications following PCI. The use of the internal mammary artery for CABG may be the reason why CABG produces a better outcome than PCI.[11] One of the studies included in this study, Chen et al, who studied 38.740 patients showed that PCI had a higher long-term mortality rate. compared with CABG (OR 1.29, 95% CI: 1.23 - 1.35; P <0.01) so this study supports the results of the analysis in the study of Bundhun et al.[16]

The study of Bundhun et al. has several limitations that need to be considered when conducting a critical analysis. The limited number of patients in this study may not show strong results. All studies involved in this study were observational studies, so the data obtained were not as good as the data in the RCT study. The high heterogeneity is a major limitation in this study. In addition, the studies that were involved were those taken after 2012 so there may be selection bias and publication bias. This study also only involved studies written in English, so the results of this study were also influenced by language bias.[11]

Yang et al's study entitled *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* examined 13 articles with a total of 18.005 patients. All the follow-ups for these 13 articles were more than one year long. Long-term follow-up mortality was significantly lower in the CABG group than in the PCI group (HR: 0.76, 95% CI: 0.70 – 0.83; P < 0.001; I^2 = 21%). A value of I^2 = 21% indicates low heterogeneity.[17]

The study of Yang et al. has several limitations that need to be considered when conducting a critical analysis. There was still a limited number of total participants in this study. Medical treatments were also not evaluated in many included studies, this could influence the long-term outcomes.[17]

Besides systematic review and meta-analysis articles, cohort studies were also included in this study. Chang et al cohort study demonstrated that CABG was associated with a significantly lower mortality than PCI across all groups of estimated glomerular filtration rate (eGFR) (in mL/min/1.73 m^2): They divided the subjects into three groups of patients based on eGFR.[18] The adjusted HR was 0.81; 95% CI: 0.68 – 1.00 for patients with eGFR ≥60; HR 0.73; 95% CI: 0.56 – 0.95 for eGFR of 45 – 59; and HR 0.87; 95% CI: 0.67 – 1.14) for eGFR<45. Kilic et al also demonstrated that CKD patients survival with one year follow up was higher in CABG groups than in PCI groups (88.92% vs 82.67%, P<0.0001). In five years follow up, CKD patients survival was also higher in CABG groups than in PCI groups (73.93% vs 52.28%, P<0.0001).[19] Another cohort study was conducted by Lautamaki et al which demonstrated that PCI was associated with a significantly higher risk of mortality than CABG in three years follow up (50.4 vs 32.9, HR: 1.77; 95% CI: 1.13–2.77).[20]

Conclusion

Based on these seven studies, six studies concluded that post-PCI CKD patients had a significantly higher mortality rate than those with CABG. One other study concluded that there was no significant difference in mortality rates between post-PCI and CABG patients. However, when viewed from the critical review and the limitations of each study, the authors conclude that PCI performed in patients with CKD resulted in a significantly higher mortality rate compared to patients who underwent CABG.

Recommendation

It is recommended to conduct a further review of existing studies without limiting publication time. Further investigation is also needed regarding the number of PCI procedures performed during the follow-up period, severity of blood vessels, and progression of CKD. It also needs to be confirmed regarding patients undergoing hemodialysis and non-hemodialysis. and the characteristics of CKD used in selected studies. Further studies regarding morbidity such as MACE or cardiac symptoms that occur during the study observation period also need to be done. Therefore, based on the results of the study in this report, CKD patients who meet the indications

for CABG and PCI are recommended to undergo CABG treatment because of the lower mortality and morbidity compared to PCI.

Declarations

Ethics approval and consent to participate

Not applicable.

Availability of data and material

Not applicable.

Conflict of interests

Not applicable.

Funding

Not applicable.-

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