Percutaneous Coronary Intervention With a Drug-Eluting Stent Versus Coronary Artery Bypass Grafting in Patients Receiving Dialysis: A National Study From Taiwan

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Rationale & Objective: We aimed to study the comparative effectiveness of percutaneous coronary intervention with drug-eluting stent and coronary artery bypass grafting in patients receiving dialysis.

Study Design: This was a retrospective observational cohort study.

Setting & Participants: This population-based study identified patients receiving dialysis hospitalized for coronary revascularization between January 1, 2009 and December 31, 2015, in the Taiwan National Health Insurance Research Database.

Exposures: Patients received percutaneous coronary intervention with drug-eluting stent versus coronary artery bypass grafting.

Outcomes: The study outcomes were all-cause mortality, in-hospital mortality, and repeat revascularization.

Analytical Approach: Propensity scores were used to match patients. Cox proportional hazards models and logistic regression models were constructed to examine associations between revascularization strategies and mortality. Interval Cox models were fitted to estimate time-varying hazards during different periods.

Results: A total of 1,840 propensity score-matched patients receiving dialysis were analyzed. Coronary artery bypass grafting was associated with higher in-hospital mortality (coronary artery bypass grafting vs percutaneous coronary intervention with drug-eluting stent; crude mortality rate 12.5% vs 3.3%; adjusted OR, 5.22; 95% CI, 3.42-7.97; $P < 0.001$) and longer hospitalization duration (median [IQR], 20 [14-30] days vs 3 [2-8] days; $P < 0.001$). After discharge, repeat revascularization, acute coronary syndrome, and repeat hospitalization all occurred more frequently in the percutaneous coronary intervention with drug-eluting stent group. Importantly, with a median follow-up of 2.8 years, coronary artery bypass grafting was significantly associated with a higher risk of all-cause overall mortality (adjusted HR, 1.19; 95% CI, 1.05-1.35; $P = 0.006$) in the multivariable Cox proportional hazard model. Sensitivity and subgroup analyses yielded consistent results.

Limitations: This was an observational study with mainly Asian ethnicity.

Conclusions: Percutaneous coronary intervention with drug-eluting stent may be associated with better survival than coronary artery bypass grafting in patients receiving dialysis. Future studies are warranted to confirm this finding.

Visual Abstract included

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In patients receiving kidney replacement therapy, cardiovascular mortality is the leading cause of death.[1] Coronary artery disease (CAD) is an important etiology of cardiovascular mortality. Coronary revascularization with either coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is a critical therapeutic strategy in addition to medical treatment.

Editorial, • • •

In the context of nonemergent multivessel CAD among the general population, CABG is associated with better long-term outcomes than PCI.[2-5] However, the uremic milieu exposes patients receiving dialysis to several nontraditional cardiovascular risk factors, and the benefit of CABG over PCI is less clear.[6,7] In patients with chronic kidney disease (CKD), a pooled analysis of patient-level data from randomized control trials (RCTs) reported that CABG did not improve survival compared with PCI, although both subsequent myocardial infarction and revascularization were reduced.[8] However, none of the included patients with CKD were receiving dialysis. One observational study performed by Chang et al[9] using data from the United States Renal Data System (USRDS) reported a worse in-hospital survival for dialysis patients receiving CABG compared with those receiving PCI between 1997 and 2009. However, the long-term outcome was better with CABG.[9] Mainly based on this study, the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery (ESC/EACTS) guidelines suggest a possibly favorable role of CABG over PCI in patients receiving dialysis with CAD.[10,11]

Importantly, studies in patients receiving dialysis from the United States and Taiwan reported that PCI with drug-eluting stents (DES) was associated with not only reduced revascularization but also decreased mortality compared

PLAIN-LANGUAGE SUMMARY

Although coronary artery bypass grafting offers better long-term survival in the general population than percutaneous coronary intervention with drug-eluting stent, patients receiving dialysis may be too frail to tolerate the increased perioperative mortality risk of coronary artery bypass grafting. In this retrospective study in a national cohort of patients receiving dialysis from Taiwan, percutaneous coronary intervention with drug-eluting stent is associated with lower in-hospital mortality and better long-term survival when compared with coronary artery bypass grafting. Subsequent acute coronary syndrome, repeat revascularization, and rehospitalization were noted more frequently in the percutaneous coronary intervention with drug-eluting stent group. These findings may suggest percutaneous coronary intervention with drug-eluting stent as a safe revascularization strategy for patients receiving dialysis.

with PCI with bare metal stent (BMS), and the 2018 ESC/EACTS guideline suggested a superior role of DES to BMS in patients with CKD.[12,13] It is thus desirable to examine the comparative effectiveness of CABG and PCI with DES in patients receiving dialysis. However, to date, there has been no large-scale RCT demonstrating the unequivocal advantage of CABG over PCI with DES in patients receiving dialysis. The landmark SYNTAX and EXCEL trials included only 6 and 3 patients receiving dialysis, respectively.[14-16] One large observational study using the URSRDS database reported epidemiologic data of survival and repeat revascularization after CABG, BMS, and DES, but did compare between these strategies.[17] Another large USRDS study compared CABG with PCI, but the stent types used for PCI were not specified.[9] A recent meta-analysis of observational studies and post hoc analyses of RCTs identified 801 patients receiving dialysis and reported no difference in all-cause mortality between CABG and PCI with DES.[18] However, the single largest observational study, including 486 propensity score-matched patients receiving dialysis, reported that CABG was associated with a lower risk for mortality and revascularization.[19] Considering the paucity of evidence, a study on this issue is urgently needed.

To analyze the outcome of CABG versus PCI with DES in patients receiving dialysis, we used the Taiwan National Health Insurance Research Database (NHIRD).[20] The Taiwan National Health Insurance (NHI) program has coverage of up to 99% of all citizens, and the database is representative of the national population. We included 4,165 patients receiving dialysis and analyzed 1,840 propensity score-matched participants for comparison of CABG versus PCI with DES performed between January 1, 2009 to December 31, 2015. Surprisingly, CABG was associated with increased both in-hospital and long-term mortality; however, repeat revascularization and subsequent acute coronary syndrome (ACS) were reduced.

METHODS

Study Population

Our study used the NHIRD through the Applied Health Research Data Integration Service from Taiwan's National Health Insurance Administration. This retrospective cohort study was approved by the Institutional Review Board of National Health Research Institutes, Taiwan (EC1060402-E). Individual information in the NHIRD was encrypted; therefore, the requirement to obtain informed consent was waived. We used the data obtained between January 1, 2008 and December 31, 2017, in the database to identify patients receiving dialysis hospitalized for revascularization using CABG or PCI with DES in Taiwan (Fig S1). The NHIRD has been successfully used to analyze outcomes of specified populations, such as patients receiving dialysis.[13,21] We set the cohort entry date between January 1, 2009 and December 31, 2015, to ensure an observation period of at least 1 year before cohort entry and 2 years after revascularization. The index hospitalization was defined as the first admission for coronary revascularization using either CABG or PCI with DES in patients receiving dialysis, and the index date was the date of revascularization. To avoid the coding error frequently encountered in database study, we defined the dialysis population and revascularization intervention using procedure codes, which are directly linked to reimbursement in NHI and less prone to miscoding. The use of procedure codes and material codes in Taiwan NHI was briefly introduced in the Supplementary Methods (Item S1).

Outcome

The primary outcome of interest was survival after revascularization. Survival was determined from the index date to death or a censoring date. Patients were censored if they received kidney or heart transplant after the index date, were lost to follow-up, or survived through December 31, 2017. To estimate the short-term and long-term effects of revascularization on crude all-cause mortality, we calculated the in-hospital mortality rate and cumulative mortality rates at 1, 2, 3, 4, and 5 years. Kaplan-Meier plots were used to visualize the difference in unadjusted survival between groups. The adjusted odds ratio (OR) of CABG over PCI with DES for in-hospital mortality was estimated in the logistic regression model. Adjusted hazard ratios (HRs) for 1-, 2-, 3-, 4-, and 5-year mortality and overall mortality were estimated in the Cox proportional hazard model.[22] Adjusted survival curves based on a Cox model using baseline statement were used to demonstrate adjusted survival probabilities after revascularization. As secondary outcomes, we analyzed the frequency of repeat revascularization, ACS after the index hospitalization, and repeat hospitalization. Repeat revascularization procedures included CABG and PCI with or without DES. ACS included ST-elevation myocardial infarction, non–ST-elevation myocardial infarction (NSTEMI), and unstable angina (UA).

In the Supplementary Methods (Item S1), we provide details on the description of the selection of patients included in the analysis as covariates or for propensity score matching and statistical analyses.

RESULTS

Patients, Crude Mortality Rate, and Duration of Hospitalization

We identified 4,165 patients receiving dialysis receiving revascularization using either CABG or PCI with DES during the index hospitalization (Fig S1). Among the 4,165 patients, 1,023 received CABG, and 3,142 received PCI with DES. Compared with patients receiving PCI with DES, patients receiving CABG were younger; more likely to be male; less likely to have an intervention on only 1 vessel; more likely to have comorbid CAD, congestive heart failure (CHF), and dyslipidemia; less likely to have comorbid cancer; and less likely to have UA or NSTEMI during the index hospitalization (Table 1). Notably, shock or respiratory failure within 24 hours before revascularization was more likely to develop in patients receiving CABG than PCI with DES. In addition, patients were more likely to receive CABG than PCI with DES in hospitals with a high volume of CABG or medical centers. To minimize the inequity of baseline characteristics, we performed a 1:1 propensity score matching and identified 920 matched pairs. After matching, all the covariates were well balanced (Table 1).

The medians (interquartile range) of follow-up duration were 2.7 (0.9-4.4), 2.9 (1.5-4.4), and 2.8 (1.2-4.4) years in the CABG, PCI with DES, and the whole cohort, respectively. The crude mortality rates of matched patients, including mortality rates at the index hospitalization as well as at 1, 2, 3, 4, and 5 years, were calculated. Surprisingly, the cumulative mortality rates were significantly higher in the CABG group than the PCI with DES group at all the analyzed time points (Table S1). Kaplan-Meier plot also showed a significant survival advantage in the PCI with DES group (Fig 1). The duration of the index hospitalization was longer in the CABG group (CABG 20 [14-30] days vs PCI with DES 3 [2-8] days; $P < 0.001$, Table S1).

Association Between Different Revascularization Strategies and Survival

We analyzed in-hospital mortality in the logistic regression model and long-term mortality in the Cox proportional hazard model. Covariates adjusted in the models included age, sex, number of treated coronary vessels, clinical condition before revascularization, UA and NSTEMI during the index hospitalization, utilization of medical resource before the index hospitalization (frailty), comorbid conditions, medication, hospital type, and hospital volume for CABG. In the adjusted logistic regression model, CABG was strongly associated with increased in-hospital mortality compared with PCI with DES (adjusted OR, 5.22; 95% CI, 3.42-7.97; $P < 0.001$, Table 2 and Table S2). Importantly, in the adjusted Cox proportional hazard model, CABG was also associated with increased overall all-cause mortality over PCI with DES (adjusted HR, 1.19; 95% CI, 1.05-1.35; $P = 0.006$; Table 2 and Table S3) during a median follow-up of 2.8 years. The HRs for all-cause mortality at 1, 2, 3, 4, and 5 years were also increased in the CABG group (Table 2). The adjusted survival curves for overall survival also showed superior survival in the PCI with DES group (Fig S2).

Notably, although CABG was associated with higher overall mortality, PCI with DES was associated with more subsequent ACS, more repeat revascularization, and more repeat hospitalization (Table S4).

Sensitivity and Subgroup Analyses

With regard to overall mortality (Table 3) and in-hospital mortality (Table S5), similar results were obtained in the sensitivity analyses of the unmatched cohort, after exclusion of mortality within 3 days after revascularization, after exclusion of patients with UA or NSTEMI during the index hospitalization, after exclusion of patients with unstable clinical conditions within 24 hours before revascularization, and after exclusion of patients receiving intervention on only 1 coronary artery. Because in-hospital mortality negatively impacted long-term survival in patients receiving CABG, we analyzed overall mortality in patients who survived the index hospitalization and set the date of discharge from index hospitalization as day 0 in the Cox model. Surprisingly, CABG was not associated with better long-term survival over PCI with DES even after the exclusion of patients who died during the hospitalization (HR, 1.02; 95% CI, 0.89-1.17; $P = 0.74$). The result was also consistent when day 0 was set as 90 days after the index revascularization (HR, 1.03; 95% CI, 0.90-1.18, $P = 0.65$). The interval Cox model also showed that PCI with DES was noninferior to CABG during different time periods, and CABG was associated with higher mortality hazard in the first 2 years after revascularization, likely because of higher perioperatively in-hospital mortality risk (Table 3). In addition, survival 90 days after the index revascularization was similar in 2 groups in a 2-slope Cox model (HR, 1.02; 95% CI, 0.89-1.17; $P = 0.75$). Notably, when repeat revascularization was included in the composite outcomes, CABG was significantly associated with decreased HR risks compared with PCI with DES (Table 3).

We performed several predefined subgroup analyses to test the heterogeneity among subgroups. With regard to the overall mortality, the results were consistent across most subgroups (Fig 2). Notably, a significant interaction between the revascularization strategy and the existence of prior CAD was identified. With regard to in-hospital

Table 1. Baseline Characteristics of Dialysis Patients Receiving CABG or PCI with DES in the Full and PSM Cohorts

	Full Cohort			PSM Cohort		
	CABG	PCI With DES[a]	STD	CABG	PCI With DES[a]	STD
No.	1,023	3,142		920	920	
Age (y), mean (SD)	61.2 (9.4)	64.5 (9.3)	0.35	61.7 (9.3)	62.2 (9.8)	0.05
Male sex	707 (69.1)	1,900 (60.5)	0.18	621 (67.5)	628 (68.3)	0.02
Vessels treated[b]						
1	127 (12.4)	1,850 (58.9)	1.11	127 (13.8)	125 (13.6)	0.01
≥2	896 (87.6)	1,292 (41.1)	1.11	793 (86.2)	795 (86.4)	0.01
Comorbid condition, n (%)[c]						
Prior CAD	752 (73.5)	1,784 (56.8)	0.36	655 (71.2)	629 (68.4)	0.06
Heart failure	278 (27.2)	714 (22.7)	0.10	238 (25.9)	236 (25.7)	0.01
Peripheral artery disease	36 (3.5)	122 (3.9)	0.02	35 (3.8)	34 (3.7)	0.01
Stroke	147 (14.4)	401 (12.8)	0.05	129 (14.0)	122 (13.3)	0.02
Diabetes mellitus	546 (53.4)	1,750 (55.7)	0.05	506 (55.0)	502 (54.6)	0.01
Hypertension	808 (79.0)	2,434 (77.5)	0.04	716 (77.8)	715 (77.7)	<0.01
Dyslipidemia	330 (32.3)	828 (26.4)	0.13	281 (30.5)	265 (28.8)	0.04
Cancer	34 (3.3)	173 (5.5)	0.11	32 (3.5)	38 (4.1)	0.03
Cirrhosis	23 (2.3)	63 (2.0)	0.02	20 (2.2)	18 (2.0)	0.02
Medication[d]						
Antiplatelet	571 (55.8)	1,700 (54.1)	0.03	511 (55.5)	523 (56.9)	0.03
β-Blocker	438 (42.8)	1,288 (41.0)	0.04	388 (42.2)	390 (42.4)	<0.01
RAAS blockade	314 (30.7)	1,026 (32.7)	0.04	289 (31.4)	288 (31.3)	<0.01
Statin	271 (26.5)	811 (25.8)	0.02	245 (26.6)	237 (25.8)	0.02
Oral antidiabetic drug	351 (34.3)	1,062 (33.8)	0.01	327 (35.5)	330 (35.9)	0.01
Insulin	281 (27.5)	1,017 (32.4)	0.11	260 (28.3)	258 (28.0)	<0.01
Dialysis vintage (y), mean (SD)	5.1 (4.6)	4.9 (4.5)	0.06	5.1 (4.6)	5.0 (4.6)	0.03
Frailty[e]						
Outpatient department visit, mean (SD)	27.9 (13.9)	29.6 (14.0)	0.12	28.0 (14.2)	28.3 (13.4)	0.02
Hospitalization duration (d), mean (SD)	7.6 (13.0)	6.0 (13.1)	0.12	7.2 (11.8)	7.0 (15.6)	0.02
Charlson comorbidity index, mean (SD)[c]	4.8 (1.8)	4.6 (1.8)	0.07	4.7 (1.7)	4.7 (1.8)	0.03
NSTEMI or UA[f]	314 (30.7)	1,357 (43.2)	0.26	295 (32.1)	319 (34.7)	0.05
Clinical condition[g]						
Cardiopulmonary resuscitation	6 (0.6)	14 (0.5)	0.02	6 (0.7)	6 (0.7)	0.02
Cardiogenic shock	26 (2.5)	9 (0.3)	0.19	10 (1.1)	9 (1.0)	0.01
Respiratory failure or unstable hemodynamics	154 (15.1)	199 (6.3)	0.29	111 (12.1)	98 (10.7)	0.05
Stable	837 (81.8)	2,920 (92.9)	0.34	793 (86.2)	808 (87.8)	0.05
Hospital volume[h]						
≥200	197 (19.3)	289 (9.2)	0.29	151 (16.4)	125 (13.6)	0.08
100-199	254 (24.8)	483 (15.4)	0.24	219 (23.8)	204 (22.2)	0.04
50-99	294 (28.7)	1,187 (37.8)	0.19	280 (30.4)	298 (32.4)	0.04
≤49	278 (27.2)	1,183 (37.7)	0.23	270 (29.4)	293 (31.9)	0.05
Hospital type						
Medical center	713 (69.7)	1,921 (61.1)	0.18	624 (67.8)	601 (65.3)	0.05
Regional hospital	310 (30.3)	1,221 (38.9)	0.18	296 (32.2)	319 (34.7)	0.05

Abbreviations: CABG, coronary artery bypass graft; CAD, coronary artery disease; DES, drug-eluting stent; NSTEMI, non–ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; PSM, propensity score matching; RAAS, renin-angiotensin-aldosterone system; SD, standard deviation; STD, standardized difference; UA, unstable angina.
[a]DES was identified by codes listed in Table S7.
[b]Number of the coronary arteries treated during the index revascularization.
[c]Cormorbid condition was defined by the presence of the diagnosis codes for at least 1 inpatient (including the index hospitalization) or 3 outpatient encounters within 1 year before the index date. Diagnosis codes selected to define comorbid conditions are listed in Table S6.
[d]The medications investigated were listed in Table S8. The use of medication was defined as a medication possession ratio of ≥50%.
[e]The sum of outpatient department visits and the total duration of hospitalization days within 6 months before the index date were calculated.
[f]The development of NSTEMI or UA during the index hospitalization according to codes presented in Table S6.
[g]The clinical condition within 24 hours before revascularization was defined by the procedure codes or medications listed in Table S9.
[h]The total number of CABG performed within 1 year in the hospital.

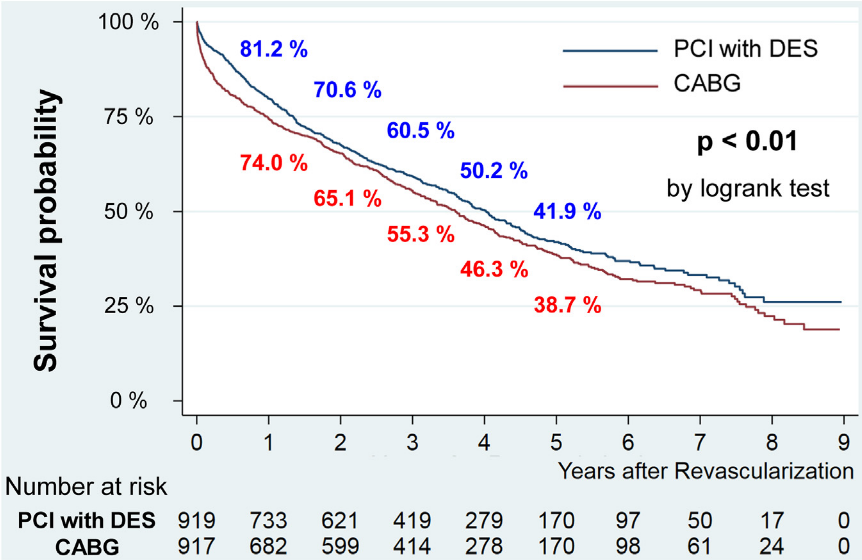

Figure 1. Kaplan-Meier plot of survival in the matched cohort. The Kaplan-Meier plot of survival probabilities in the matched CABG (red line) and PCI with DES (blue line) groups during the study period. In the CABG group, the survival probabilities at 1, 2, 3, 4, and 5 years were 74.0%, 65.1%, 55.3%, 46.3%, and 38.7%, respectively. In the PCI with DES group, the survival probabilities at 1, 2, 3, 4, and 5 years were 81.2%, 70.6%, 60.5%, 50.2%, and 41.9%, respectively. In total, 3 patients in the CABG group and 1 patient in the PCI with DES group died within 1 day after revascularization, and the number at risk were 917 (CABG group) and 919 (PCI with DES group) at day 0. $P = 0.007$ by log-rank test. Abbreviations: CABG, coronary artery bypass graft; DES, drug-eluting stent; PCI, percutaneous coronary intervention

mortality, the results in most subgroups were largely consistent (Fig S3). Interestingly, possible heterogeneity of treatment effect was identified according to clinical condition within 24 hours before revascularization and prior hospitalization duration (as a proxy for frailty).

Discussion

In our cohort of patients receiving dialysis from Taiwan, in contrast to prior observed long-term survival benefits with CABG, we found that PCI with DES is associated with lower in-hospital mortality and better long-term survival.[9]

Compared with PCI with DES, patients receiving CABG had increased in-hospital mortality and increased length of hospitalization. The findings are consistent with prior observational studies.[17,23-26] In our cohort, the crude in-hospital mortality rates in the unmatched cohort were 11.8% and 2.3% in the CABG and PCI with DES groups, respectively (Table S1). The duration of hospitalization was 20 (14-30) and 3 (2-8) days in the CABG and PCI with DES groups, respectively. The in-hospital mortality rate and duration of hospitalization in our study were comparable to prior reports of dialysis patients receiving CABG in the United States (in-hospital mortality rate, 5.4%-31%; duration of hospitalization 13-25 days).[25] It is likely that the increased in-hospital mortality and hospitalization duration arose from surgery-related perioperative mortality and complications in frail and heavily comorbid patients receiving dialysis.

We found that PCI with DES was associated with better long-term survival than CABG in patients receiving dialysis from Taiwan. Even after excluding patients who died during the index hospitalization in the sensitivity analysis (Table 3), PCI with DES was noninferior to CABG based on long-term survival. The interval Cox model suggested that the survival benefit in the PCI with DES group may be largely derived from the reduction of early mortality after revascularization. However, PCI with DES was associated with higher risks for composite outcomes comprising death and repeat revascularization.

Notably, the cumulative 5-year survival probability of patients receiving dialysis after revascularization was much higher in our cohort (38.7% for CABG and 41.9% for PCI

Table 2. Comparison of Mortality Risks Between the 2 Treatment Groups

	OR or HR	95% CI	*P* Value
In-hospital mortality	5.22	3.42-7.97	<0.001
1-y mortality	1.54	1.26-1.87	<0.001
2-y mortality	1.31	1.11-1.54	0.001
3-y mortality	1.24	1.08-1.44	0.003
4-y mortality	1.20	1.05-1.37	0.008
5-y mortality	1.18	1.04-1.34	0.01
Overall mortality	1.19	1.05-1.35	0.006

Notes: The adjusted OR for in-hospital mortality was estimated by the multivariable logistic regression. The adjusted HRs for 1-, 2-, 3-, 4-, and 5-year mortality rates and overall mortality were estimated using the multivariable Cox proportional hazard model. percutaneous coronary intervention with drug-eluting stent served as the reference group.
Abbreviations: CI, confidence interval; HR, hazard ratio; OR, odds ratio.

Table 3. Comparison of Overall Mortality in the Sensitivity Analyses

	No.	HR	95% CI	*P* Value
Original model	1,840	1.19	1.05-1.35	0.006
Additional models				
Patient samples[a]				
Full cohort	4,165	1.16	1.04-1.29	0.008
Excluding deaths within 3 d[b]	1,038	1.08	0.95-1.22	0.24
Excluding ACS cases[c]	1,184	1.12	0.96-1.31	0.14
Excluding cases with an unstable clinical condition[d]	1,590	1.20	1.05-1.37	0.007
Excluding cases with only one vessel treated[e]	1,484	1.13	0.99-1.30	0.08
Excluding deaths before discharge[f]	1,604	1.02	0.89-1.17	0.74
Interval Cox model[g]				
0-2 y	1,840	1.32	1.12-1.55	0.001
2-4 y	1,246	1.00	0.79-1.26	0.98
4-6 y	955	1.13	0.79-1.60	0.51
6-9 y	831	1.12	0.58-2.16	0.74
Survival 90 d after the index revascularization				
Observation since 90 d after the index date	1,628	1.03	0.90-1.18	0.65
Two-slope model[h]	1,840	1.02	0.89-1.17	0.75
Composite outcome measures				
Death, ACS, or repeat revascularization	1,840	0.76	0.68-0.84	<0.001
Death or ACS	1,840	0.99	0.88-1.10	0.82
Death or repeat revascularization	1,840	0.73	0.66-0.81	<0.001

Abbreviation: ACS, acute coronary syndrome.
[a]Separate propensity score matching (1:1) was performed on the included patients each time after modification of the selection criteria.
[b]Patients passing away within 3 days after the index date were excluded.
[c,b,c]Patients who had ACS, unstable clinical condition, or only one coronary artery treated (as defined in Table 1) during the index hospitalization were excluded.
[f]Patients passing away during the index hospitalization were excluded. In this sensitivity analysis, the date of discharge from index hospitalization (instead of the date of revascularization) was set as day 0 of the Cox survival analysis. The proportional hazard assumption was valid in this Cox model (global test, $P = 0.95$).
[g]The time-varying hazard ratios in different time periods were estimated in the interval Cox model. The number of patients (n) who remained alive at the start of the time period is also shown. The proportional hazard assumption was valid in each time period (Schoenfeld residual test, $P = 0.28$, 0.90, 0.68, and 0.47 in the 0-2 years, 2-4 years, 4-6 years, and 6-9 years, respectively).
[h]The hazard ratio in the second slope (90 days after the index revascularization) is shown.

with DES in the matched cohort, Fig 1) compared with reports from URSRD (28% for CABG and 24% for PCI with DES).[17] Interestingly, in one Japanese cohort investigating mortality risk after revascularization in patients receiving dialysis, the cumulative 5-year all-cause mortality (49.9% after CABG vs 52.3% after PCI with DES) was very similar to that noted in our study (55.0% after CABG vs 50.0% after PCI with DES, Table S1).[23] The cause of improved long-term survival in patients receiving dialysis from Taiwan and Japan is not clear. The reason for the absence of long-term survival benefits associated with CABG is also unclear. Both biological and nonbiological factors may contribute.

International comparison indicates a marked variation in overall survival in patients receiving dialysis, which may influence the comparative effectiveness of CABG and PCI with DES.[27-29] According to Dialysis Outcomes and Practice Patterns Study (DOPPS), the crude mortality rate from 2002 to 2008 was 18.1, 15.6, and 5.2 deaths per 100 patient-years in the United States, the United Kingdom, and Japan, respectively.[28] Taiwan had a crude mortality rate of approximately 11.6-11.7 deaths per 100 patient-years during the same time period.[30] Studies reported that ethnic differences may influence the treatment effect and outcome of cardiovascular diseases.[31-33] Although CABG is associated with better long-term survival than PCI in patients receiving dialysis according to the USRDS, it is possible that different ethnic backgrounds may modify the outcomes.[9] Interestingly, in the aforementioned USRDS study, the authors reported in their subgroup analyses that non-White non–African American race was associated with a reduced benefit of CABG.[9] In Japan, similar to our findings, cohort study and registry analysis showed that CABG was not associated with a better 5-year all-cause mortality rate than PCI in patients receiving dialysis.[23,26]

Notably, although PCI with DES was associated with better long-term survival in our study, repeat revascularization, subsequent ACS, and repeat hospitalization developed more frequently, probably indicating incomplete revascularization. Consistent with these findings, in Japanese patients receiving dialysis, although the long-term risks for all-cause mortality were not different in the PCI and CABG groups, the risk for repeat coronary revascularization was significantly higher in the PCI group.[23,26] Interestingly, in our cohort, the survival of patients after discharge from the index hospitalization in the PCI with DES group is not worse than that noted for patients in the CABG group (Table 3). According to statistics from the Organization for Economic Co-operation and Development and the Ministry of Health and Welfare in Taiwan,

Subgroup	CABG (n = 920) % of patients	PCI with DES (n = 920) % of patients	HR (95% CI)	P for interactin
Age				0.74
18-64	63.2	59.8	1.16 (0.98, 1.37)	
65-74	29.0	30.4	1.21 (0.97, 1.49)	
more than 75	7.8	9.8	1.31 (0.87, 1.98)	
Sex				0.64
male	67.5	68.3	1.22 (1.05, 1.42)	
female	32.5	31.7	1.12 (0.90, 1.39)	
DM				0.10
yes	55.0	54.6	1.09 (0.93, 1.39)	
no	45.0	45.4	1.32 (1.09, 1.60)	
Hypertension				0.56
yes	77.8	77.7	1.22 (1.06, 1.40)	
no	22.2	22.3	1.15 (0.88, 1.50)	
Dyslipidemia				0.54
yes	30.5	28.8	1.33 (1.04, 1.69)	
no	69.5	71.2	1.16 (1.01, 1.35)	
Stroke				0.50
yes	14.0	13.3	1.15 (0.82, 1.63)	
no	86.0	86.7	1.21 (1.06, 1.38)	
Prior CAD				0.02
yes	71.2	68.4	1.09 (0.94, 1.27)	
no	28.8	31.6	1.52 (1.20, 1.91)	
CHF				0.51
yes	25.9	25.7	1.35 (1.07, 1.71)	
no	74.1	74.3	1.15 (1.00, 1.34)	
Clinical condition				0.29
Unstable	13.8	12.2	0.87 (0.62, 1.22)	
Stable	86.2	87.8	1.23 (1.08, 1.41)	
Hospital volume for CABG				0.76
more than 200	16.4	13.6	1.15 (0.80, 1.64)	
100-199	23.8	22.2	1.38 (1.06, 1.81)	
50-99	30.4	32.4	1.12 (0.90, 1.40)	
less than 50	29.3	31.8	1.22 (0.98, 1.52)	
Medical center				0.71
yes	67.8	65.3	1.20 (1.03, 1.40)	
no	32.2	34.7	1.15 (0.93, 1.42)	
NSTEMI or UA				0.41
yes	32.1	34.7	1.10 (0.89, 1.36)	
no	67.9	65.3	1.22 (1.04, 1.42)	
Number of vessels treated				0.11
1	13.8	13.6	1.77 (1.20, 2.59)	
2	15.5	73.2	1.27 (1.00, 1.61)	
3	70.7	13.3	1.24 (0.94, 1.64)	
CCI score				0.70
0-3	28.8	29.8	1.21 (0.94, 1.57)	
4-5	36.6	38.9	1.25 (1.02, 1.53)	
more than 6	34.6	31.3	1.15 (0.93, 1.41)	
OPD visit				0.58
0-20	33.2	31.1	1.36 (1.09, 1.70)	
21-30	33.7	33.0	0.94 (0.76, 1.17)	
more than 31	33.2	35.9	1.28 (1.03, 1.57)	
Hospital duration				0.24
0	37.3	52.4	1.35 (1.12, 1.63)	
1-7	33.8	22.9	1.13 (0.87, 1.49)	
more than 8	28.9	24.7	1.13 (0.90, 1.42)	
Dialysis modality				0.15
HD	91.8	91.1	1.18 (1.04, 1.34)	
PD	8.2	8.9	2.06 (1.31, 3.23)	
Incident HD				0.31
yes	6.5	5.8	2.13 (1.06, 4.30)	
no	93.5	94.2	1.17 (1.03, 1.33)	
Insurance area				0.20
Taipei	42.7	36.5	1.25 (1.02, 1.53)	
Northern area	15.8	14.6	1.27 (0.89, 1.81)	
Central area	11.6	15.8	1.39 (0.98, 1.98)	
Southern area	16.0	17.1	1.01 (0.74, 1.38)	
Kao-Ping/Eastern area	13.9	16.1	1.03 (0.74, 1.43)	

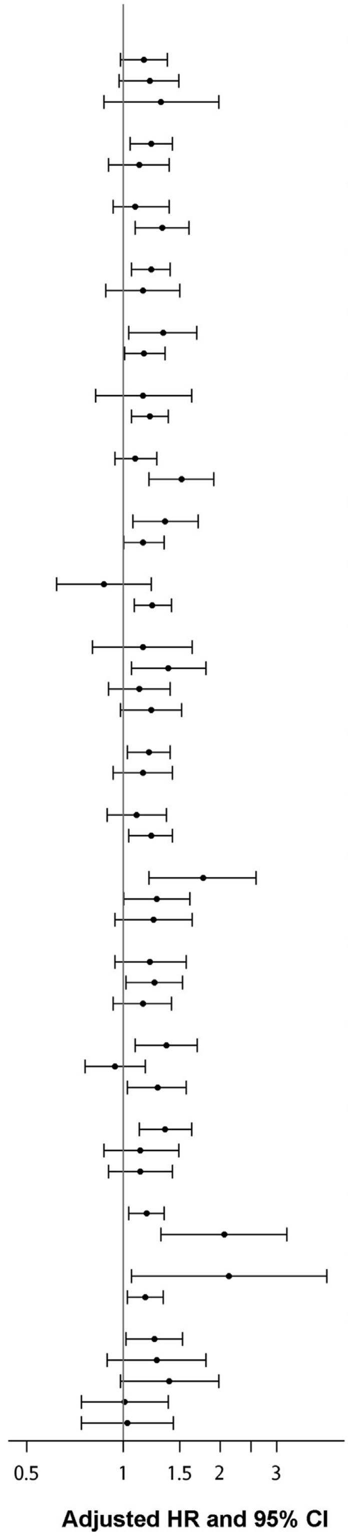

Figure 2. Subgroup analysis of overall survival in the matched cohort. The adjusted HRs for overall survival in the multivariable Cox proportional hazard model according to prespecified subgroups are shown. In each subgroup, the percentage of patients from the CABG (n = 920) and PCI with DES (n = 920) groups were specified. A significant heterogeneity of effect was identified according to the existence of prior CAD and the frequency of prior OPD visits. Abbreviations: CAD, coronary artery disease; CCI, Charlson comorbidity index; CHF, congestive heart failure; CI, confidence interval; DM, diabetes mellitus; HD, hemodialysis; HR, hazard ratio; NSTEMI, non–ST-elevation myocardial infarction; OPD, outpatient department; PD, peritoneal dialysis; UA, unstable angina.

the number of acute care beds per 1,000 population was 8.0, 3.4, and 2.5 for Japan, the United States, and Taiwan, respectively.[34,35] Given that the population density (people per square kilometer of land area) in 2020 is much higher in Taiwan (673) and Japan (345) than in the United States (36), the acute care bed density (number of acute care beds per square kilometer of land area) is also much higher in Taiwan and Japan than in the United States, which may affect the accessibility to timely coronary revascularization.[36,37] Because the risk of mortality associated with recurrent ACS and incompletely treated CAD may be mitigated by timely repeated revascularization, the higher acute care accessibility in Japan and Taiwan compared with the United States may also contribute to improved survival in the PCI with DES group. It should also be noted that CABG might be less commonly performed in Taiwan and Japan than in the United States. According to the USRDS, more than 50% of patients receiving dialysis with multivessel CAD received CABG for revascularization.[9] However, in our study, only 41.0% of patients receiving dialysis received multivessel revascularization with CABG (Table 1). Similarly, in Japan's dialysis cohort, CABG was used as a multivessel revascularization strategy in only 27%-28% of patients receiving dialysis.[23,26] As a result, only 19.3% of CABG in Taiwan was performed at high-volume hospitals compared with 85.1% in the United States (Table 1).[38] Whether the increased utilization of PCI over CABG in Taiwanese and Japanese patients receiving dialysis influenced clinical outcomes remains unclear.

Several limitations should be mentioned. First, the observational nature precludes a definite conclusion. The selection biases and unmeasured confounders both may contribute to error. Second, clinical condition (Killip stage), vessel condition including the distribution of vascular territories (Syntax score), and arterial graft utilization were important predictors of survival in patients with CAD.[14,39,40] However, these parameters were not available in the NHIRD, and we had to adjust for other available surrogate covariates, such as clinical conditions before revascularization and the number of coronary arteries treated. Third, we did not analyze the impacts of BMS employed during PCI. However, studies have shown the benefits of DES over BMS in both non-CKD patients and patients receiving dialysis.[12,13,41-43] Fourth, we included almost exclusively the Asian population, and the results might not be able to be generalized to other ethnic groups. Finally, we did not compare medical treatment with revascularization. However, in the database study, the indication bias for the comparison of conservative treatment versus intervention may be much higher than that of different revascularization strategies.

In conclusion, in Taiwan, in patients receiving dialysis, PCI with DES was associated with lower in-hospital mortality and better long-term survival but increased repeat revascularization and subsequent ACS compared with CABG. Future population-based studies in other countries and ethnic groups are warranted to confirm the comparative effectiveness between CABG and PCI with DES in the contemporary era.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1: Flow diagram of selecting dialysis patients receiving CABG or PCI with DES.

Figure S2: Adjusted survival curves for overall survival in the matched cohorts.

Figure S3: Subgroup analysis of in-hospital mortality in the matched cohort.

Item S1: Supplementary Methods.

Table S1: Crude Mortality Rates and Length of Stay for the Index Hospitalization.

Table S2: The Fully Adjusted Logistic Regression Model for In-Hospital Mortality.

Table S3: The Fully Adjusted Multivariable Cox Model for Overall All-Cause Mortality.

Table S4: Repeat Revascularization, Subsequent ACS, and Repeat Hospitalization After the Index Hospitalization.

Table S5: Comparison of In-Hospital Mortality in the Sensitivity Analyses.

Table S6: List of Procedure Codes and ICD-9-CM Diagnosis Codes.

Table S7: List of Material Codes Used to Identify DES.

Table S8: List of Medications Investigated in This Study.

Table S9: Procedures and Medications Selected to Define Clinical Severity Within 24 Hours Before Revascularization.

Table S10: Multivariable Cox Models Adjusted for Different Covariates.

ARTICLE INFORMATION

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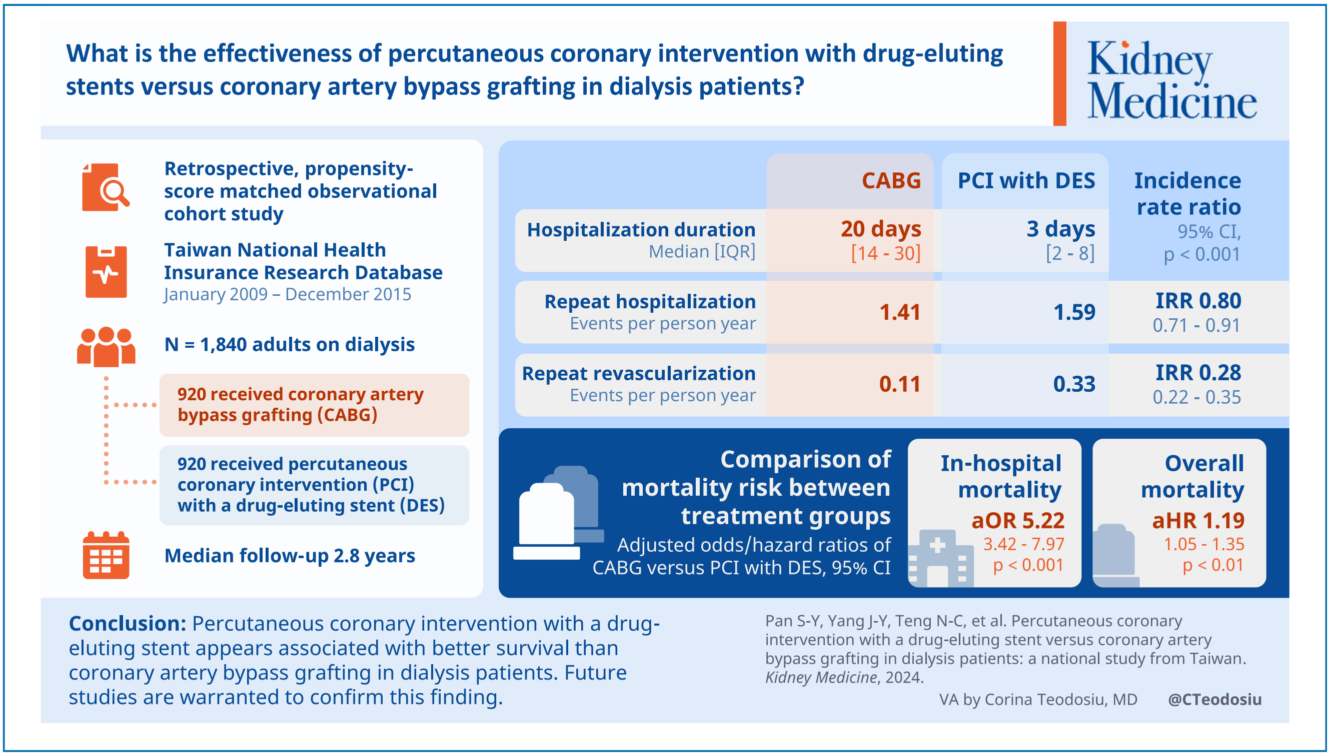
What is the effectiveness of percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in dialysis patients?
Kidney Medicine
Retrospective, propensity-score matched observational cohort study
Taiwan National Health Insurance Research Database
January 2009 – December 2015
N = 1,840 adults on dialysis
920 received coronary artery bypass grafting (CABG)
920 received percutaneous coronary intervention (PCI) with a drug-eluting stent (DES)
Median follow-up 2.8 years
CABG
PCI with DES
Incidence rate ratio
95% CI, p < 0.001
Hospitalization duration
Median [IQR]
20 days
[14 - 30]
3 days
[2 - 8]
Repeat hospitalization
Events per person year
1.41
1.59
IRR 0.80
0.71 - 0.91
Repeat revascularization
Events per person year
0.11
0.33
IRR 0.28
0.22 - 0.35
Comparison of mortality risk between treatment groups
Adjusted odds/hazard ratios of CABG versus PCI with DES, 95% CI
In-hospital mortality
aOR 5.22
3.42 - 7.97
p < 0.001
Overall mortality
aHR 1.19
1.05 - 1.35
p < 0.01
Conclusion: Percutaneous coronary intervention with a drug-eluting stent appears associated with better survival than coronary artery bypass grafting in dialysis patients. Future studies are warranted to confirm this finding.
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