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Comparative Effectiveness Analysis of Percutaneous Coronary Intervention vs. Coronary Artery Bypass Grafting in Patients with Chronic Kidney Disease and Unprotected Left Main Coronary Artery Disease :

Insights From a Large-Sized All-Comers Registry

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Short title: CKD and outcome in LMCAD

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CONDENSED ABSTRACT

Among 4894 patients with LMCAD, renal insufficiency was graded according to the estimated glomerular filtration rate (eGFR). The primary outcome was major adverse cardiocerebrovascular event (MACCE), defined as death, myocardial infarction, stroke, or any revascularization.

At 2 years, after adjustment, the adjusted risk of MACCE was similar between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) in patients with preserved or moderate renal dysfunction. However, PCI was associated with a significantly higher risk of MACCE compared to CABG (HR 1.88, 95% CI 1.08-3.25, P=0.02) in patients with severe renal dysfunction

ABSTRACT

Aims: Outcomes according to the status of renal insufficiency were not fully evaluated in left main coronary artery disease (LMCAD).

Methods and results: Among 4894 patients with LMCAD, renal insufficiency was graded according to the estimated glomerular filtration rate (eGFR). The primary outcome was major adverse cardiocerebrovascular event (MACCE), defined as death, myocardial infarction, stroke, or any revascularization. 3,824 (78%) had group 1 (eGFR ≥60 ml·min -1·1.73m^2), 838 (17%) had group 2 (eGFR ≥ 30 and <60), and 232 (5%) had group 3 (eGFR <30). At 2 years, after adjustment, compared with group 1, the risk of MACCE was significantly higher in group 2 (hazard ratio [HR] 1.46, 95% confidence interval [CI] 1.18-1.79) and in group 3 (HR 3.39, 95% CI 2.61-4.40). Meanwhile, the P interaction for MACCE across groups was 0.20. The adjusted risk of MACCE was similar between percutaneous coronary intervention (PCI) and coronary

artery bypass grafting (CABG) in group 1 or 2. However, PCI was associated with a significantly higher risk of MACCE compared to CABG (HR 1.88, 95% CI 1.08-3.25) in group 3.

Conclusions: The degree of renal insufficiency was proportionately associated with unfavorable outcomes in patients with LMCAD. In group 3, PCI was associated with a higher risk of MACCE compared with CABG. Also, the effect of PCI vs. CABG on MACCE was consistent, with PCI being associated less bleeding and CABG being associated with less repeat revascularization

Keywords: left main, death, renal insufficiency

ABBREVIATIONS

LMCAD left main coronary artery disease

CABG coronary artery bypass graft

PCI percutaneous coronary intervention

CKD chronic kidney disease

IRIS-MAIN Interventional Research Incorporation Society-Left MAIN Revascularization

MACCE major adverse cardiocerebrovascular event

INTRODUCTION

Among several anatomical types of obstructive coronary artery disease (CAD), left main coronary artery disease (LMCAD) is associated with worst clinical outcomes[1]. Coronary-artery bypass graft surgery (CABG) has traditionally been the standard of care for revascularization treatment of unprotected LMCAD. Over the last two decades, however, percutaneous coronary intervention (PCI) has become an alternative strategy for selected patients with LMCA disease[2,3]. Owing to a higher rate of major cardiovascular events and mortality in patients with significant LMCA disease, identification of clinical factors associated with worse clinical outcomes and risk stratification is clinically important in the real-world.

The relationship between the chronic kidney disease (CKD) and an increased risk of cardiovascular events has been shown by many epidemiologic studies[4,5]. Furthermore, several studies suggested that patients with CKD have poor outcomes after coronary revascularization[6,7]. Previous studies identified clinical risk factors associated with poorer outcomes in patients with LMCAD[8-10]. However, little is known about the effect of the renal insufficiency on clinical outcomes in patients with LMCAD. In the present study, we therefore evaluated clinical outcomes in patients with significant LMCAD stratified by the degree of renal insufficiency and the relative clinical outcomes after PCI and CABG stratified by the differential levels of renal function using data from the large multinational "all-comers" Interventional Research Incorporation Society-Left MAIN Revascularization (IRIS-MAIN) registry.

METHODS

Study Population

The study population was part of the IRIS-MAIN registry (ClinicalTrials.govnumber, NCT01341327). The IRIS-MAIN is a nonrandomized, multinational, observational registry which consists of a cohort of consecutive patients with significant unprotected LMCAD who were treated with PCI, CABG, or medication alone. Data were collected on patients who were diagnosed as significant LMCAD (> 50% by visual estimation) at approximately 65 centers in the Asia-Pacific region. From the registry, 5,566 consecutive patients from January 2003 to September 2017 were evaluated. Among them, 118 patients who had incomplete data, 145 patients who did not have the creatinine level, and 164 patients who did not have the angiographic data were excluded. After further excluding patients who had cardiogenic shock, prior CABG, or valvular heart disease, 4,894 patients were included in the current analysis (**Figure 1**). The institutional review board at each hospital approved the use of clinical information in those patients for this study.

Variables and outcome data were collected by specialized personnel using a electronic case report form at each center. Monitoring and verification of registry data were periodically performed in participating hospitals by the staff of the coordinating center (Clinical Research Center, Asan Medical Center, Seoul, Korea). Follow-up was conducted during hospitalization and at 1, 6, 12 months after the index treatment and annually thereafter via an office visit or telephone contact.

Outcomes and Definitions

The primary outcome was a major adverse cardiocerebrovascular event (MACCE), which was

defined as a composite of death from any cause, myocardial infarction (MI), stroke, or any revascularization. Death was considered as cardiac unless an unequivocal noncardiac cause could be established. MI was defined as follows; if occurring within 48 hours following the index treatment, a combination of at least 5 fold increase in the CK-MB with either new pathological Q waves or new bundle branch block, with either new graft or native coronary occlusion documented on angiography, new regional wall motion abnormality or loss of viable myocardium on imaging studies[11,12]. Stroke was defined as a loss of neurological function caused by an ischemic or hemorrhagic event with residual symptoms at least 24 hours after the onset or leading to death and was confirmed by a neurologist on the basis of imaging modalities. Any revascularization included any type of percutaneous or surgical revascularization procedure, regardless of whether the procedure was performed on a target or non-target lesion. Thrombolysis in Myocardial Infarction (TIMI) major bleeding was defined as overt clinical bleeding associated with a drop in hemoglobin of greater than 5 g/dL or in hematocrit of greater than 15% (absolute). All events were based on the clinical diagnoses assigned by the patient's physician and were centrally adjudicated by an independent group of clinicians.

Statistical Analysis

Continuous variables were expressed as median (interquartile range), and categorical variables were presented as numbers and percentages. Differences between the groups, categorized according to the estimated glomerular filtration rate (eGFR), were compared using analysis of variance (ANOVA) or Kruskal-Wallis test for continuous variables, and chi-square test or Fisher's exact test for categorical variables as appropriate. Post-hoc tests were performed using ANOVA with Tukey method or Kruskal-Wallis test with Bonferroni method. Cumulative rates of clinical events were calculated using Kaplan-Meier survival analysis, and log-rank test was

used for comparisons across the groups.

A univariate Cox proportional hazard regression model was used to evaluate potential predictors of clinical outcomes. The proportional hazard assumption was checked for all screened covariates, and no relevant violations were found. To assess the independent association of eGFR category to clinical outcome, multivariate Cox proportional hazard regression was performed using variables with p value of < 0.10 in univariate analysis. Using the group of eGFR ≥ 60 ml/min/1.73m2 as the reference category, we estimated the hazard ratios and 95% confidence intervals for the groups of 30 ≤ eGFR < 60 and eGFR < 30 ml/min/1.73m2. Finally, we compared the rates of primary outcome after PCI and CABG according to the eGFR at baseline. To adjust the differences in baseline characteristics, multivariate Cox proportional hazard regression model was performed using clinically relevant variables and statistically significant variables with a P value <0.10 by univariate analysis. All reported p values were two-sided and were not adjusted for multiple testing. All statistical analyses were performed using IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Baseline Characteristics

Patients were divided into 3 groups according to the eGFR at baseline; group 1 including patients with eGFR ≥60 ml·min -1·1.73m-2 (n=3824, 78.1%), group 2 with 30≤eGFR< 60 (n=838, 17.1%), and group 3 with eGFR < 30 (n=232, 4.7%). 121 patients (52%) in group 3 were on dialysis. Baseline clinical characteristics were substantially different across the three groups (**Table 1**). Group 3 had higher risk-factor profiles. With regard to treatment strategy, PCI was most frequently used in three groups, whereas medical therapy alone was most

frequently selected in group 3. Regarding the information related to PCI, the group 3 tended to have a higher proportion of 2nd generation of DES. The use of intravascular ultrasound (IVUS) during PCI was less frequent in group 3. There was no significant difference in the stent technique at left main lesion among three groups on the whole, while bifurcation stenting was more prevalent in the group 1 and 2 compared to group 3 in part. In terms of drug therapy, antiplatelet agents and statins were less frequently used in group 3 at baseline as well as during follow-up (**Supplemental Table 1**).

Clinical Outcomes

During the median follow-up duration of 1,289 (interquartile range, 729-1,913) days, there were 314 deaths, 39 MIs, 70 cerebrovascular events, and 205 any revascularization. Overall, the cumulative incidence of MACCE at 2 years was lowest in group 1 (9.1%) and highest in group 3 (36.2%), and this trend was consistent regardless whether the patient received CABG, PCI or medical therapy (**Figure 2**). The incidences of individual outcome of death, MI, or stroke were significantly higher in patients with higher degree of renal insufficiency, whereas the rate of any revascularization was comparable between the three groups (4.2% in group 1 vs. 3.8% in group 2 vs. 4.7% in group 3, p=0.79). The incidence of major bleeding events (8.5% in the group 1 vs. 10.3% in the group 2, 12.5% in the group 3, p=0.043) was also associated in proportion to the severity of renal insufficiency (**Supplemental Table 2**).

The landmark analysis revealed that the difference of MACCE according to the eGFR occurred mostly within 1 year. According to the 30 days landmark analysis, there was no significant difference in the rate of MACCE between the group 2 and 3. However, after 1 year, patients in the group 3 consistently had a highest risk of MACCE, whereas there was no significant difference between the group 1 and 2 (**Figure 3**). After multivariate adjustment for

the baseline differences between the three groups, the adjusted risk of MACCE was significantly higher in group 3 compared with group 1 or 2 and was driven mainly by the higher risks of death and MI (**Table 2**).

PCI vs. CABG According to the Status of Renal Function

The Kaplan-Meier 2-year survival estimates for MACCE after PCI and CABG stratified by the status of baseline renal function are shown in **Figure 4.** The cumulative rates of MACCE did not differ between PCI and CABG among patients with group 1 or group 2. In contrast, there was a significantly higher rate of MACCE with PCI than with CABG in group 3 (38.5% vs. 24.7% at 2 years, P=0.01, P for interaction=0.08). Clinical outcomes after adjusting for possible confounders using Cox regression model are summarized in **Table 3.** The risk of MACCE was significantly higher with PCI than with CABG in group 3 (adjusted hazard ratio 1.88, 95% confidence interval 1.08-3.25, P=0.02), whereas it was similar between PCI and CABG in patients with group 1 or group 2. Statistical interaction was not found between the status of renal function and revascularization modality on MACCE (P for interaction=0.20). The risk of any revascularization tended to be higher with PCI whereas the risk of TIMI major bleeding was higher with CABG regardless of eGFR level. The results of the sensitivity analysis excluding patients who received first-generation DESs were largely consistent (**Supplemental Table 3**).

DISCUSSION

From this large, all-comers registry involving patients with LMCAD, we found that the severity of renal insufficiency was proportionately associated with an increased risk of serious adverse

events, regardless of the initial treatment strategy. Among patients with preserved or moderate renal dysfunction, the risk of MACCE after PCI and CABG was comparable, whereas the MACCE risk was significantly higher with PCI than with CABG in patients with severe renal dysfunction. Although a statistically significant interaction was not observed, further studies are required to confirm this observation and to help guide decision making between CABG and PCI in LMCAD patients with CKD.

Although some studies suggested less association between the renal function and clinical outcomes after PCI in patients with obstructive CAD[13,14], the majority of studies showed that patients with renal insufficiency were significantly associated with unfavorable outcomes[7,15,16]. However, patients with LMCAD were mostly excluded in prior studies, thus still lacking of the clinical relevance of renal impairment in patients with such complex lesions. In our study involving this high-risk group of patients, we found that renal insufficiency had a detrimental effect on outcomes including death and MACCE which was proportional to the levels of eGFR. Of note, patients with severe renal insufficiency showed higher cumulative event rates sustained beyond 1 year in the landmark analysis. An association between the severities of renal dysfunction and ischemic cardiovascular events shown in our study is not surprising given the well-known biopathologic features of renal dysfunction such as negative plaque characteristics, heightened states of arterial inflammation, or sympathetic nervous system activation[17-20]. However, our study adds on a more real-world explanation of this observation. Patients with lower eGFR received suboptimal medical therapies of antiplatelet agents and statin, possibly because of the concerns of pharmacokinetic issues of the drugs related to renal excretion and increased bleeding tendency. This treatment pattern seems to be in line with the preferential selection of medical therapy alone rather than PCI or CABG in LMCAD patients with severe renal insufficiency. Furthermore, less frequent use of

intravascular ultrasound-supported PCI in patients with lower eGFR may imply a more complicated or suboptimal procedure which may have related with a worse prognosis.

A comparison between PCI and CABG in patients with LMCAD and CKD has been recently reported in the subgroup analysis of randomized EXCEL trial.[21] There were no significant differences between PCI and CABG in terms of death, stroke, or MI at 3 years after the procedures in patients with and without CKD. However, the results should be interpreted with caution as the number of CKD patients was relatively small (n=361) and the majority of the CKD patients had a moderate degree of renal impairment. The addition of our study was to include larger number of real-world patients and to demonstrate the comparative effectiveness between PCI and CABG in LMCAD patients with severe renal dysfunction, who were usually excluded from randomized trials. This higher-risk subgroup seemed to benefit more after CABG than after PCI regarding serious ischemic adverse events. A plausible explanation would be that patients with advanced renal impairment may hold severe coronary artery characteristics including a higher degree of calcification and atherosclerotic plaque burden, and consequently may distinctly benefit from bypass grafts which provide more durable and protective role against future ischemic events. Because the presence of poor renal function is frequently encountered in the daily clinical practice during heart team discussion to opt for PCI or CABG, subsequent studies will be critical for the development of optimal treatment strategies according to the degree of CKD for high-risk patients with LMCAD.

LIMITATIONS

This study has several limitations. First, there were different risk profiles, comorbidities, and anatomical disease extent or complexity among each CKD group as well as PCI vs. CABG group (**Supplemental Tables 4 to 7**). Although confounding covariates were adjusted in the multivariable models, the results are vulnerable to unmeasured confounders. Second, variables

that are known in clinical practice to have a profound influence on the choice of revascularization (e.g., SYNTAX score or patient frailty) were not available for this analysis. A lack of such information could have penalized the CABG group relative to the PCI group. Third, the number of patients included in group 3 was relatively small. Although the different outcome after PCI and CABG in these patients was one major finding of our study, interpretation of the results should be cautious, and the findings should be considered hypothesis generating only. Fourth, the impact of incomplete revascularization on outcome between PCI and CABG could not be assessed as the registry does not capture this variable for CABG. Finally, relevant information regarding the renal outcomes such as acute renal failure or new requirement of dialysis was not available in our study.

CONCLUSIONS

The presence and severity of renal dysfunction were associated with an increased risk of serious adverse events in real-world patients with LMCAD. Among LMCAD patients with severe renal dysfunction, CABG was associated with a lower risk of MACCE as compared with PCI. Also, the effect of PCI vs. CABG on MACCE was consistent, with PCI being associated less bleeding and CABG being associated with less repeat revascularization. Further studies are required to confirm the differential effect of PCI and CABG by degrees of renal function, which may help guide decision making in patients with LMCAD.

Impact on daily practice

The analysis of the IRIS-MAIN registry showed clinical implications of renal insufficiency in LMCAD patients. Patients with decreasing levels of renal function had a higher risk-profiles of baseline clinical, anatomical, and procedural characteristics and also had unfavorable clinical outcomes. According to the eGFR levels, CABG showed favorable results in patients with advanced renal insufficiency compared with PCI in LMCAD patients, while PCI and CABG had no significant difference in patients with less severe renal insufficiency.

Conflicts of interest statement

None of the authors have any conflicts of interest to declare.

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Figure legends

Figure 1. Study Population

Figure 2. Kaplan-Meier curves of the Primary Composite Outcome According to the Levels of Baseline Renal Function

Figure 3. Kaplan-Meier Curves with 30 Days and 1-Year Landmark Analyses of the Primary Composite Outcome According to the Levels of Baseline Renal Function

Figure 4. Kaplan-Meier curves of the Primary Composite Outcome Between PCI and CABG According to the Levels of Baseline Renal Function

Table 1. Baseline Characteristics

Variable	eGFR≥60 (N=3824)	30≤eGFR<60 (N=838)	eGFR<30 (N=232)	P value
Demographics and laboratory findings				
Age (years)	64 (56, 70)	71 (64, 76)	69 (62, 74)	<0.001
Male sex	2969 (77.6)	622 (74.2)	163 (70.3)	0.01
BMI (kg/m2)	24.5 (22.7, 26.2)	24.6 (22.7, 26.4)	23.4 (21.4, 25.7)	<0.001
Diabetes	1244 (32.5)	388 (46.3)	180 (77.6)	<0.001
Hypertension	2264 (59.2)	636 (75.9)	215 (92.7)	<0.001
Dyslipidemia	2376 (62.1)	487 (58.1)	125 (53.9)	0.01
Current/recent smoker	1008 (26.4)	177 (21.1)	36 (15.5)	<0.001
Prior myocardial infarction	324 (8.5)	104 (12.4)	27 (11.6)	<0.001
Prior CHF	65 (1.7)	45 (5.4)	27 (11.6)	<0.001
Prior PCI	583 (15.3)	158 (18.9)	47 (20.3)	0.01
Atrial fibrillation/flutter	63 (1.7)	42 (5.0)	12 (5.2)	<0.001
Cerebrovascular disease	271 (7.1)	100 (11.9)	36 (15.5)	<0.001
PAD	163 (4.3)	83 (9.9)	25 (10.8)	<0.001
Chronic lung disease	106 (2.8)	24 (2.9)	13 (5.6)	0.05
Dialysis	0	0	121 (52)	<0.001
HDL-C (mg/dL)	41 (35, 48)	39 (32, 47)	35 (28, 43)	<0.001
LDL-C (mg/dL)	97 (73, 123)	90.35 (69, 117)	84 (63, 106)	<0.001
CRP (mg/dL)	0.14 (0.06, 0.44)	0.22 (0.08, 0.65)	0.62 (0.21, 2.00)	<0.001

Clinical diagnosis				0.004
Stable angina	1607 (42.0)	316 (37.7)	77 (33.2)	
Acute coronary syndrome	2217 (58.0)	522 (62.3)	155 (66.8)	
Angiographic finding (%)				
LAD	1770 (46.3)	334 (39.9)	92 (39.7)	<0.001
LCX	866 (22.7)	188 (22.4)	51 (22.0)	0.97
RCA	481 (12.6)	104 (12.4)	22 (9.5)	0.38
Medications (%)				
Aspirin	3706 (97.2)	785 (94.1)	204 (88.3)	<0.001
Clopidogrel	3322 (87.2)	690 (82.9)	178 (77.4)	<0.001
Ticagrelor	102 (2.7)	20 (2.4)	4 (1.7)	0.63
Prasugrel	45 (1.2)	7 (0.8)	3 (1.3)	0.66
Beta blocker	2363 (63.1)	485 (59.2)	138 (59.7)	0.08
Calcium channel blocker	2173 (58.2)	465 (56.8)	111 (48.5)	0.02
ACEi/ARB	1234 (33.2)	333 (41.1)	117 (51.1)	<0.001
Statin	3612 (95.3)	757 (91.3)	174 (75.0)	<0.001
Initial Treatment (%)				<0.001
Medical therapy	437 (11.4)	137 (16.4)	42 (18.1)	
PCI	2289 (59.9)	419 (50.0)	117 (50.4)	
CABG	1098 (28.7)	282 (33.6)	73 (31.5)	
Stent generation				0.02
1st-DES	540 (23.7)	95 (22.9)	15 (12.8)	
2nd-DES	1736 (76.3)	320 (77.1)	102 (87.2)	

IVUS use during PCI (%)	1850 (80.7)	306 (72.9)	85 (71.4)	<0.001
GpIIb-IIIa inhibitor during PCI (%)	199 (8.7)	33 (7.9)	5 (4.2)	0.22
Stent technique at LM (%)				0.81
LM only	440 (19.3)	76 (18.2)	23 (19.5)	
LM to LAD crossover	1219 (53.5)	218 (52.3)	68 (57.6)	
LM to LCX crossover	93 (4.1)	22 (5.3)	4 (3.4)	
2-stent technique	525 (23.1)	101 (24.2)	23 (19.5)	0.04
Crush	336 (64.5)	63 (62.4)	12 (52.2)	
Culotte	12 (2.3)	0	3 (13.0)	
Other techniques	64 (33.2)	13 (37.6)	5 (34.8)	

Values are median (interquartile range) or n (%).

ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; BMI: body mass index; CHF: congestive heart failure; CABG: coronary artery bypass grafting; CRP: C-reactive protein; DES: drug-eluting stent; eGFR: estimated glomerular filtration rate; HDL-C: high density lipoprotein cholesterol; IVUS: intravascular ultrasound; LDL-C: low density lipoprotein cholesterol; LAD: left anterior descending artery; LCX: left circumflex artery; LM: left main; PCI: percutaneous coronary intervention; PAD: peripheral artery disease

Table 2. Adjusted Hazard Ratios of Clinical Outcomes

	2-Year		Multivariate analysis[1]			Multivariate analysis[2]			
	Event	Rate, %	HR	95% CI		P value	HR	95% CI		P value
MACCE										
≥60*	347	9.1	1.00			<0.001	1.00			<0.001
≥30, <60	134	16.0	1.46	1.18	1.79	0.0004	1.43	1.16	1.77	0.0008
<30	84	36.2	3.39	2.61	4.40	<0.001	2.73	1.91	3.92	<0.001
Death										
≥60	154	4.0	1.00			<0.001	1.00			
≥30, <60	89	10.6	1.78	1.36	2.34	<0.001	1.83	1.39	2.40	<0.001
<30	71	30.6	4.23	2.78	6.41	<0.001	4.36	2.85	6.67	<0.001
Myocardial Infarction										
≥60	25	0.7	1.00			<0.001	1.00			
≥30, <60	5	0.6	0.87	0.33	2.28	0.78	0.69	0.26	1.87	0.47

<30	9	3.9	5.98	2.73	13.05	<0.001	3.97	1.28	12.33	0.017
Any revascularization										
≥60	162	4.2	1.00			0.74	1.00			
≥30, <60	32	3.8	0.87	0.59	1.27	0.47	0.91	0.62	1.36	0.66
<30	11	4.7	1.06	0.57	1.98	0.86	0.84	0.32	2.15	0.71
Stroke										
≥60	44	1.2	1.00			0.15	1.00			
≥30, <60	20	2.4	1.64	0.94	2.85	0.08	1.58	0.90	2.77	0.11
<30	6	2.6	1.79	0.74	4.31	0.20	2.30	0.86	6.19	0.10
TIMI major bleeding										
≥60	325	8.5	1.00			0.03	1.00			0.18
≥30, <60	86	10.3	1.23	0.97	1.56	0.09	1.23	0.95	1.58	0.11
<30	29	12.5	1.58	1.08	2.32	0.02	1.41	0.80	2.49	0.23

CI : confidence interval; HR : hazard ratio; MACCE: major adverse cardiocerebrovascular event; TIMI: thrombolysis in myocardial infarction

*Values of estimated glomerular filtration rate

Multivariate analysis[1]: Cox proportional hazards model with backward elimination method

Multivariate analysis[2]: All baseline covariate were adjusted

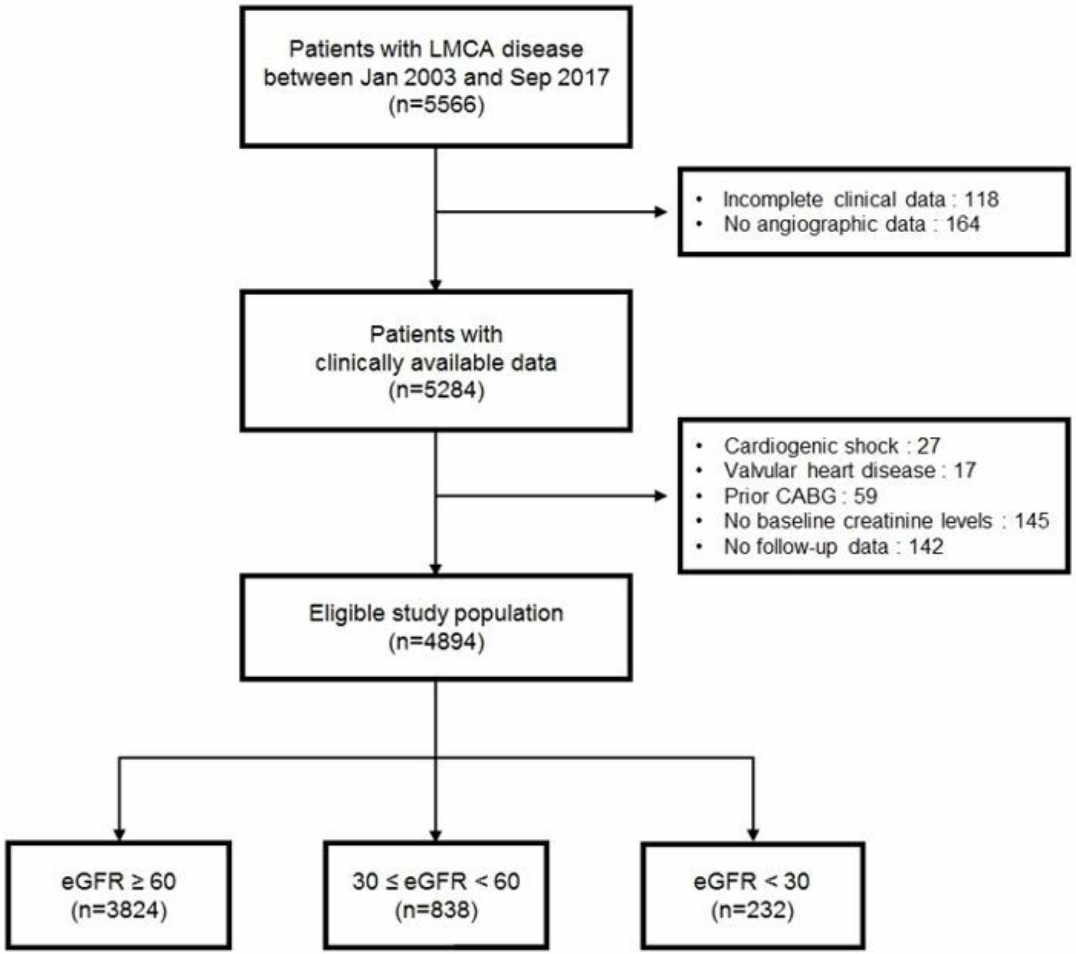
Table 3. Risk of Primary Composite Outcome After PCI and CABG According to the Status of Baseline Renal Function.

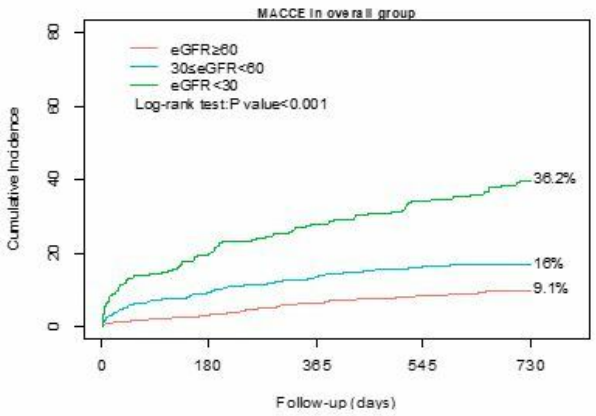
Patient Groups	2-Year Event Rate, n (%)		Crude Risk			Adjusted Risk*			
	Revascularization type								
	PCI	CABG (reference)	HR	95% CI	P value	HR	95% CI	P value	P for interaction
Preserved renal function (eGFR >60)									
MACCE	190 (8.3)	89 (8.1)	1.07	0.83-1.38	0.58	1.11	0.86-1.43	0.42	0.20
Death	50 (2.2)	55 (5.0)	0.45	0.31-0.66	<0.001	0.48	0.33-0.70	<0.001	0.01
Myocardial infarction	11 (0.48)	6 (0.55)	0.91	0.34-2.47	0.85	0.86	0.32-2.32	0.75	0.33
Any revascularizatic	124 (5.4)	21 (1.9)	3.02	1.90-4.80	<0.001	3.10	1.95-4.94	<0.001	0.67
Stroke	22 (1.0)	16 (1.5)	0.67	0.35-1.28	0.23	0.74	0.39-1.41	0.35	0.76
TIMI major bleeding	28 (1.2)	289 (26.3)	0.04	0.03-0.06	<0.001	0.04	0.03-0.06	<0.001	<0.001
Moderate renal dysfunction (eGFR ≥ 30 and <60)									
MACCE	71 (16.9)	37 (13.1)	1.43	0.96-2.13	0.08	1.38	0.92-2.05	0.12	
Death	40 (9.5)	28 (9.9)	1.03	0.64-1.67	0.90	0.93	0.57-1.51	0.79	
Myocardial infarction	4 (1.0)	0	-	-	0.99	-	-	0.99	
Any revascularizatic	24	4 (1.4)	4.5	1.57-	0.005	4.42	1.53-	0.00	

	(5.7)		3	13.1			12.8	6
Stroke	11 (2.6)	8 (2.8)	0.98	0.39-2.44	0.97	0.94	0.38-2.35	0.90
TIMI major bleeding	15 (3.6)	69 (24.5)	0.13	0.08-0.23	<0.001	0.13	0.08-0.23	<0.001
Severe renal dysfunction (eGFR <30)								
MACCE	45 (38.5)	18 (24.7)	2.06	1.19-3.56	0.01	1.88	1.08-3.25	0.02
Death	35 (29.9)	17 (23.3)	1.55	0.87-2.77	0.14	1.30	0.72-2.34	0.37
Myocardial infarction	7 (6.0)	1 (1.4)	5.47	0.67-44.5	0.11	4.99	0.61-40.7	0.13
Any revascularizatic	8 (6.8)	1 (1.4)	6.81	0.85-54.4	0.07	6.77	0.85-54.1	0.07
Stroke	2 (1.7)	3 (4.1)	0.49	0.08-2.93	0.43	0.45	0.08-2.70	0.38
TIMI major bleeding	7 (6.0)	20 (27.4)	0.21	0.09-0.49	<0.001	0.20	0.08-0.47	<0.001

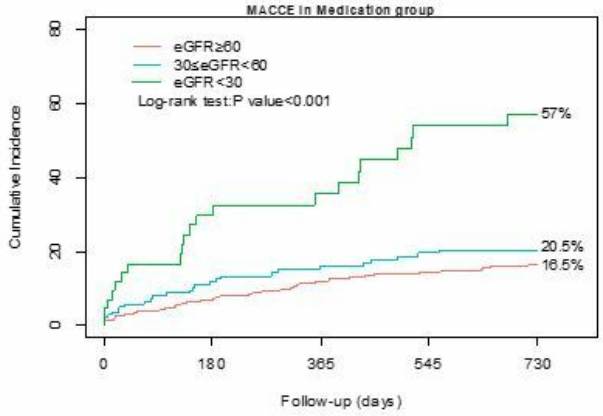
Abbreviations as in Table 1 and 2

*Cox proportional hazards model with backward elimination method

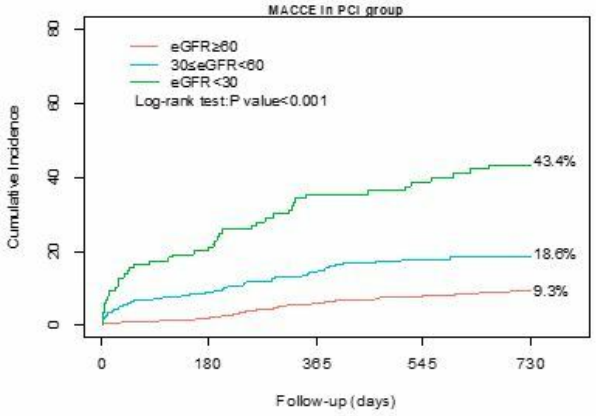




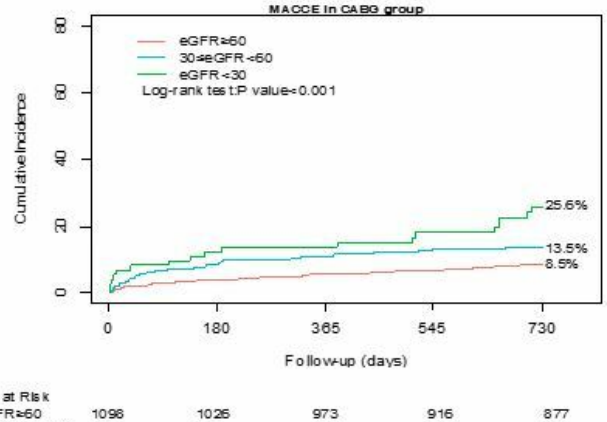
No. at Risk					
eGFR≥60	3824	3527	3193	2973	2796
30≤eGFR<60	838	725	636	578	552
eGFR<30	232	175	142	125	103



No. at Risk					
eGFR≥60	437	393	355	327	310
30≤eGFR<60	137	116	98	89	86
eGFR<30	42	27	21	15	12

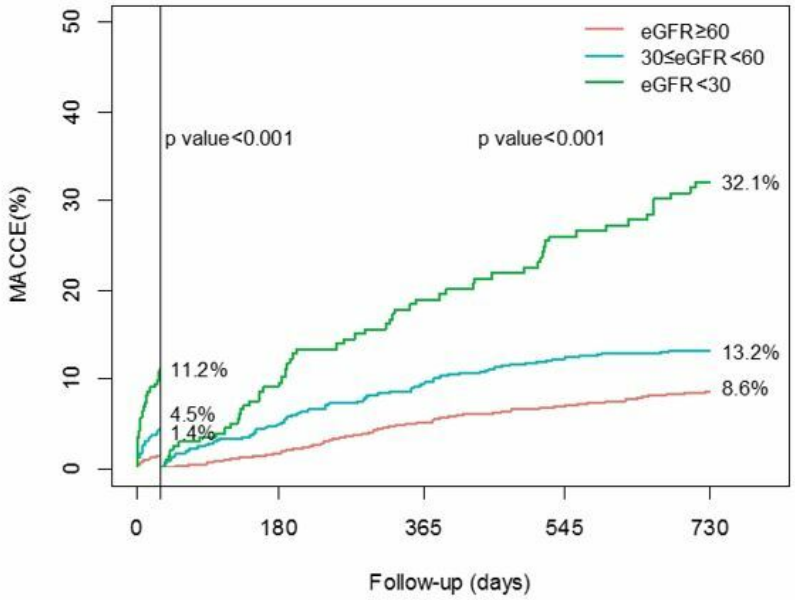


No. at Risk					
eGFR≥60	2289	2108	1865	1730	1609
30≤eGFR<60	419	358	299	266	250
eGFR<30	117	85	60	54	43



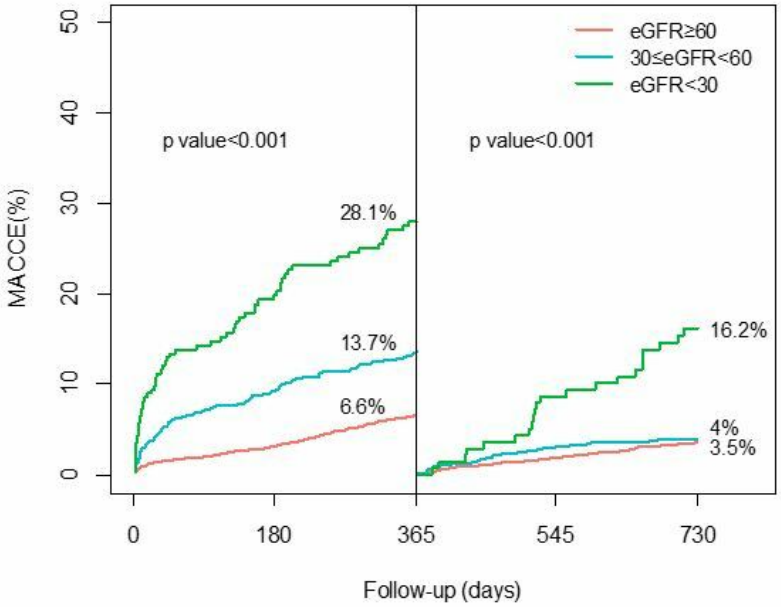
No. at Risk					
eGFR≥60	1098	1026	973	916	877
30≤eGFR<60	282	251	239	223	216
eGFR<30	73	63	61	56	48

A (30 days)

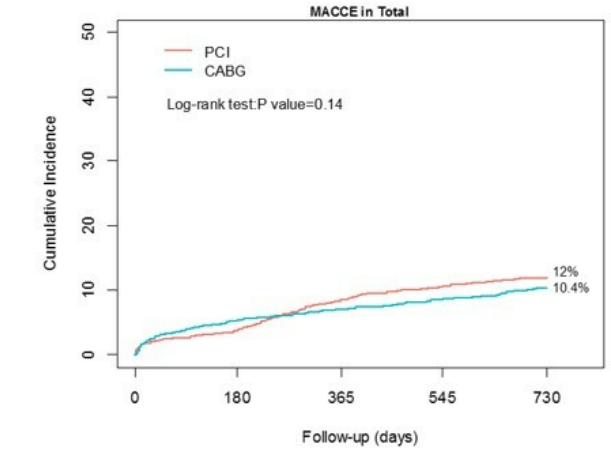


No. at Risk					
eGFR≥60	3824	3527	3193	2973	2796
30≤eGFR<60	838	725	636	578	552
eGFR<30	232	175	142	125	103

B (1 year)

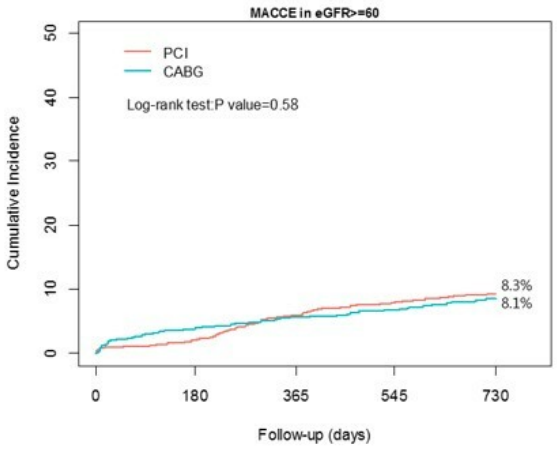


No. at Risk					
eGFR≥60	3824	3527	3193	2973	2796
30≤eGFR<60	838	725	636	578	552
eGFR<30	232	175	142	125	103



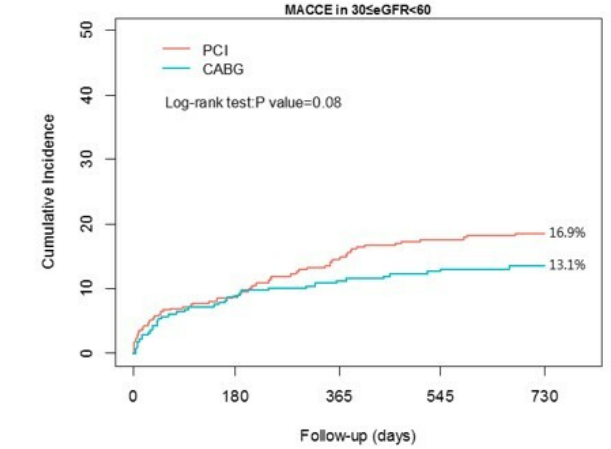
No. at Risk

PCI	2825	2551	2224	2050	1902
CABG	1453	1340	1273	1195	1141



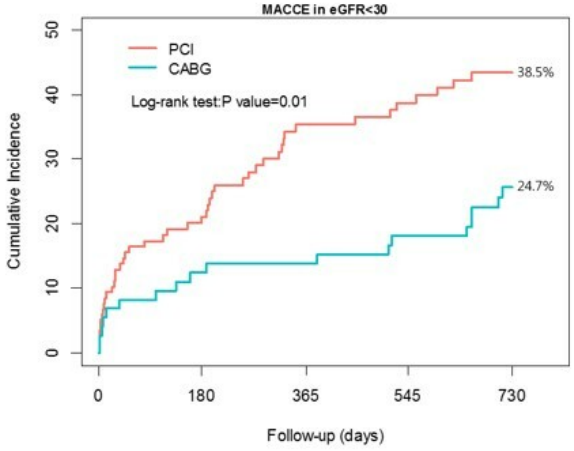
No. at Risk

PCI	2289	2108	1865	1730	1609
CABG	1098	1026	973	916	877



No. at Risk

PCI	419	358	299	266	250
CABG	282	251	239	223	216



No. at Risk

PCI	117	85	60	54	43
CABG	73	63	61	56	48

Supplemental Table 1. Medication Use

Variable	Total			eGFR≥60			30≤eGFR<60			eGFR<30		
	PCI (N=2825)	CABG (N=1453)	P value	PCI (N=2289)	CABG (N=1098)	P value	PCI (N=419)	CABG (N=282)	P value	PCI (N=117)	CABG (N=73)	P value
At discharge												
Aspirin	2767 (98.1)	1393 (96.4)	0.001	2262 (99)	1062 (97.1)	<0.001	400 (95.7)	268 (96.1)	0.81	105 (89.7)	63 (87.5)	0.63
Statins	2599 (93)	1382 (95.5)	0.001	2142 (94.6)	1058 (96.7)	0.007	375 (90.6)	262 (93.6)	0.16	82 (70.1)	62 (84.9)	0.02
ACE inhibitors	1095 (40.3)	335 (23.4)	<0.001	855 (38.8)	218 (20.1)	<0.001	176 (44)	86 (31.3)	0.001	64 (56.1)	31 (42.5)	0.07
Clopidogrel	2568 (91.4)	1229 (84.9)	<0.001	2098 (92)	946 (86.4)	<0.001	370 (89.2)	230 (81.9)	0.006	100 (86.2)	53 (73.6)	0.03
CCB	1493	903	<0.001	1218	697	<0.001	219	167	0.10	56	39	0.57

	(54.5)	(62.9)		(54.8)	(64.2)		(53.9)	(60.3)		(49.1)	(53.4)	
Beta blocker	1855 (67.3)	723 (50.6)	<0.001	1525 (68.2)	549 (50.9)	<0.001	262 (64.7)	129 (46.6)	<0.001	68 (58.6)	45 (61.6)	0.68
At 12 months												
Aspirin	2185 (89.6)	1144 (88.6)	0.36	1827 (91.4)	892 (90)	0.23	296 (83.6)	208 (87)	0.25	62 (72.9)	44 (72.1)	0.91
Statins	2595 (93.4)	1392 (96.5)	<0.001	2149 (95.3)	1066 (97.6)	0.001	366 (89.3)	262 (94.2)	0.02	80 (70.8)	64 (87.7)	0.007
ACE inhibitors	945 (38.8)	370 (27.8)	<0.001	775 (38.9)	253 (25.1)	<0.001	139 (39.7)	90 (35.4)	0.28	31 (33.7)	27 (38.6)	0.52
Clopidogrel	1923 (79)	709 (55.1)	<0.001	1595 (79.9)	562 (56.8)	<0.001	268 (75.7)	119 (50)	<0.001	60 (71.4)	28 (45.9)	0.002
CCB	1306 (53.8)	719 (55.2)	0.40	1091 (55.1)	558 (56.9)	0.36	175 (49.3)	132 (52.2)	0.48	40 (43.0)	29 (42.6)	0.96
Beta blocker	1571	677	<0.001	1308	525 (52.9)	<0.001	217	119	<0.001	46	33	0.89

	(64.8)	(51.3)		(66.1)			(61.8)	(45.9)		(48.9)	(47.8)	
At 24 months												
Aspirin	1757 (81.4)	973 (84.1)	0.051	1477 (83)	763 (86.2)	0.03	236 (78.4)	177 (82.7)	0.23	44 (55.7)	33 (56.9)	0.89
Statins	2580 (93.3)	1394 (96.3)	<0.001	2140 (95.3)	1064 (97.3)	0.008	365 (89.9)	266 (95)	0.02	75 (65.8)	64 (87.7)	0.001
ACE inhibitors	822 (37.4)	347 (28.2)	<0.001	682 (37.8)	248 (26.7)	<0.001	118 (37.9)	83 (35.5)	0.55	22 (25.9)	16 (24.6)	0.86
Clopidogrel	1431 (66.3)	452 (39.1)	<0.001	1200 (67.5)	359 (40.7)	<0.001	192 (63.6)	71 (33)	<0.001	39 (49.4)	22 (37.9)	0.18
CCB	1129 (51.9)	604 (50.8)	0.53	943 (53.2)	470 (52.5)	0.75	153 (48.9)	112 (48.5)	0.93	33 (37.9)	22 (34.9)	0.71
Beta blocker	1295 (60.1)	588 (48.4)	<0.001	1085 (61.5)	454 (49.9)	<0.001	178 (58.2)	110 (45.8)	0.004	32 (37.2)	24 (37.5)	0.97

Values are n (%).

ACE: angiotensin-converting enzyme, CABG: coronary artery bypass grafting, CCB: calcium channel blocker, PCI: percutaneous coronary intervention

Supplemental Table 2. Two-Year Clinical Outcomes According to the Categories of Baseline eGFR

	eGFR≥60 (N=3824)	30≤eGFR<60 (N=838)	eGFR<30 (N=232)	P value
MACCE	347 (9.1)	134 (16.0)	84 (36.2)	<0.001
Death from any cause	154 (4.0)	89 (10.6)	71 (30.6)	<0.001
Cardiac death	122 (3.2)	73 (8.7)	53 (22.8)	<0.001
Myocardial infarction	25 (0.7)	5 (0.6)	9 (3.9)	<0.001
Stroke	44 (1.2)	20 (2.4)	6 (2.6)	0.008
Any revascularization	162 (4.2)	32 (3.8)	11 (4.7)	0.79
TIMI major bleeding	325 (8.5)	86 (10.3)	29 (12.5)	0.04
TIMI minor bleeding	490 (12.8)	118 (14.1)	27 (11.6)	0.51

Values are shown as Kaplan-Meier estimates (number and percentage of events).

MACCE was defined as a composite of death, myocardial infarction, stroke, or any revascularization.

eGFR: estimated glomerular filtration rate; MACCE: major adverse cardiocerebrovascular event; TIMI: thrombolysis in myocardial infarction

Supplemental Table 3. Sensitivity Analysis Excluding Patients With 1st Generation Drug-Eluting Stents

Patient Groups	2-Year Event Rate, n (%)		Crude Risk			Adjusted Risk*		
	Revascularization type							
	PCI	CABG (reference)	HR	95% CI	P value	HR	95% CI	P value
Preserved renal function (eGFR >60)								
MACCE	136 (7.8)	89 (8.1)	1.04	0.80-1.36	0.77	1.05	0.81-1.38	0.70
Death	37 (2.1)	55 (5.0)	0.45	0.30-0.68	<0.001	0.45	0.30-0.69	<0.001
Myocardial infarction	8 (0.5)	6 (0.5)	0.90	0.31-2.61	0.85	0.90	0.31-2.61	0.86
Any revascularization	86 (5.0)	21 (1.9)	2.87	1.78-4.62	<0.001	3.00	1.86-4.84	<0.001
Stroke	19 (1.1)	16 (1.5)	0.79	0.40-1.53	0.48	0.83	0.43-1.62	0.59
TIMI major bleeding	21 (1.2)	289 (26.3)	0.04	0.03-0.06	<0.001	0.04	0.03-0.06	<0.001
Moderate renal dysfunction (eGFR ≥ 30 and <60)								
MACCE	50 (15.6)	37 (13.1)	1.35	0.88-2.07	0.17	1.26	0.82-1.93	0.30
Death	29 (9.1)	28 (9.9)	1.01	0.60-1.69	0.99	0.84	0.49-1.41	0.50
Myocardial infarction	3 (0.9)	0 (0)	-	-	0.99	-	-	0.99
Any revascularization	14 (4.4)	4 (1.4)	3.58	1.18-10.88	0.02	3.73	1.23-11.34	0.02
Stroke	10 (3.1)	8 (2.8)	1.19	0.47-3.03	0.71	1.18	0.47-3.01	0.72
TIMI major bleeding	9 (2.8)	69 (24.5)	0.10	0.05-0.21	<0.001	0.10	0.05-0.21	<0.001

Severe renal dysfunction (eGFR <30)								
MACCE	39 (38.2)	18 (24.7)	2.10	1.20-3.67	0.01	1.74	0.99-3.06	0.06
Death	32 (31.4)	17 (23.3)	1.70	0.94-3.06	0.08	1.30	0.71-2.37	0.39
Myocardial infarction	7 (6.9)	1 (1.4)	6.65	0.82-54.16	0.08	6.65	0.82-54.2	0.08
Any revascularization	6 (5.9)	1 (1.4)	6.19	0.75-51.4	0.09	6.26	0.75-52.1	0.09
Stroke	1 (1.0)	3 (4.1)	0.29	0.03-2.78	0.28	0.26	0.03-2.52	0.25
TIMI major bleeding	7 (6.9)	20 (27.4)	0.24	0.10-0.56	0.001	0.22	0.09-0.52	0.001

CABG: coronary artery bypass grafting; CI: confidence interval; HR : hazard ratio; MACCE: major adverse cardiocerebrovascular event; PCI: percutaneous coronary intervention; TIMI: thrombolysis in myocardial infarction

*Multivariate analysis: Cox proportional hazards model with backward elimination method

Supplemental Table 4. Baseline Characteristics in the Overall Population with PCI and CABG

Variable	PCI (N=2825)	CABG (N=1453)	P value
Demographic and laboratory findings			
Age (years)	63.8±10.7	64.7±9.0	0.003
Male sex	2185 (77.4)	1138 (78.3)	0.47
BMI (kg/m2)	24.5±3.0	24.6±3.0	0.23
Diabetes	966 (34.2)	616 (42.4)	<0.001
Hypertension	1767 (62.5)	938 (64.6)	0.20
Dyslipidemia	1834 (64.9)	793 (54.6)	<0.001
Current/recent smoker	686 (24.3)	384 (26.4)	0.13
Prior myocardial infarction	210 (7.4)	192 (13.2)	<0.001
Prior CHF	62 (2.2)	49 (3.4)	0.02
Prior PCI	481 (17)	190 (13.1)	0.001
Atrial fibrillation/flutter	67 (2.4)	24 (1.7)	0.12
Cerebrovascular disease	221 (7.8)	119 (8.2)	0.67
PAD	106 (3.8)	113 (7.8)	<0.001
Chronic lung disease	67 (2.4)	51 (3.5)	0.03
Dialysis	68 (2.4)	38 (2.6)	0.68
HDL-C (mg/dL)	41 (34.8,48)	39 (33,46)	<0.001
LDL-C (mg/dL)	95 (71,120)	97 (72,123)	0.33
CRP (mg/dL)	0.15 (0.06,0.5)	0.16 (0.07,0.485)	0.06
Clinical diagnosis			
Stable angina	1237 (43.8)	490 (33.7)	<0.001

Acute coronary syndrome	1588 (56.2)	963 (66.3)	
Baseline eGFR			
eGFR (>60 *ml·min -1·1.73m*$^{-2}$)	2289 (81)	1098 (75.6)	<0.001
eGFR (≥ 30 and <60)	419 (14.8)	282 (19.4)	
eGFR (<30)	117 (4.1)	73 (5)	

Values are mean ± SD or n (%).

BMI: body mass index; CHF: congestive heart failure; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; PCI: percutaneous coronary intervention; PAD: peripheral artery disease

Supplemental Table 5. Baseline Characteristics in Patients with Preserved Renal Function

Variable	PCI (N=2289)	CABG (N=1098)	P value
Demographic and laboratory findings			
Age (years)	62.3±10.5	63.6±8.9	<0.001
Male sex	1787 (78.1)	870 (79.2)	0.44
BMI (kg/m2)	24.6±3.0	24.7±3.0	0.34
Diabetes	689 (30.1)	422 (38.4)	<0.001
Hypertension	1333 (58.2)	668 (60.8)	0.15
Dyslipidemia	1499 (65.5)	613 (55.8)	<0.001
Current/recent smoker	578 (25.3)	312 (28.4)	0.05
Prior myocardial infarction	153 (6.7)	142 (12.9)	<0.001
Prior CHF	29 (1.3)	22 (2)	0.10
Prior PCI	369 (16.1)	137 (12.5)	0.005
Atrial fibrillation/flutter	38 (1.7)	14 (1.3)	0.39
Cerebrovascular disease	152 (6.6)	76 (6.9)	0.76
PAD	63 (2.8)	71 (6.5)	<0.001
Chronic lung disease	54 (2.4)	38 (3.5)	0.07
HDL-C (mg/dL)	42.9±13.2	41.2±15.2	<0.001
LDL-C (mg/dL)	99.7±40.4	101.2±37	0.21
CRP (mg/dL)	0.6±1.4	0.6±1.4	0.08
Clinical diagnosis			
Stable angina	1024 (44.7)	382 (34.8)	<0.001
Acute coronary syndrome	1265 (55.3)	716 (65.2)	

Values are mean ± SD or n (%).

BMI: body mass index; CHF: congestive heart failure; CRP: C-reactive protein; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; PCI: percutaneous coronary intervention; PAD: peripheral artery disease

Supplemental Table 6. Baseline Characteristics in Patients with Moderate Renal Dysfunction

Variable	PCI (N=419)	CABG (N=282)	P value
Demographic and laboratory findings			
Age (years)	70.4±9.5	68.7±8.3	0.01
Male sex	312 (74.5)	218 (77.3)	0.39
BMI (kg/m2)	24.6±3.0	24.7±3.2	0.72
Diabetes	188 (44.9)	140 (49.6)	0.21
Hypertension	322 (76.8)	203 (72)	0.15
Dyslipidemia	264 (63)	145 (51.4)	0.002
Current/recent smoker	91 (21.7)	58 (20.6)	0.72
Prior myocardial infarction	44 (10.5)	41 (14.5)	0.11
Prior CHF	19 (4.5)	19 (6.7)	0.21
Prior PCI	87 (20.8)	39 (13.8)	0.02
Atrial fibrillation/flutter	22 (5.3)	8 (2.8)	0.12
Cerebrovascular disease	51 (12.2)	32 (11.3)	0.74
PAD	32 (7.6)	35 (12.4)	0.04
Chronic lung disease	10 (2.4)	8 (2.8)	0.71
HDL-C (mg/dL)	40.8±11.5	38.6±9.8	0.05
LDL-C (mg/dL)	93.3±33.7	95.4±39.9	0.66
CRP (mg/dL)	0.9±1.7	0.7±1.4	0.68
Clinical diagnosis			
Stable angina	174 (41.5)	88 (31.2)	0.006
Acute coronary syndrome	245 (58.5)	194 (68.8)	

Values are mean ± SD or n (%).

BMI: body mass index; CHF: congestive heart failure; CRP: C-reactive protein; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; PCI: percutaneous coronary intervention; PAD: peripheral artery disease

Supplemental Table 7. Baseline Characteristics in Patients with Severe Renal Dysfunction

Variable	PCI (N=117)	CABG (N=73)	P value
Demographic and laboratory findings			
Age (years)	68.9±9.0	66.2±8.2	0.04
Male sex	86 (73.5)	50 (68.5)	0.46
BMI (kg/m2)	23.3±2.9	24±3.1	0.17
Diabetes	89 (76.1)	54 (74)	0.75
Hypertension	112 (95.7)	67 (91.8)	0.34
Dyslipidemia	71 (60.7)	35 (48)	0.09
Current/recent smoker	17 (14.5)	14 (19.2)	0.40
Prior myocardial infarction	13 (11.1)	9 (12.3)	0.80
Prior CHF	14 (12)	8 (11)	0.83
Prior PCI	25 (21.4)	14 (19.2)	0.72
Atrial fibrillation/flutter	7 (6)	2 (2.7)	0.49

Cerebrovascular disease	18 (15.4)	11 (15.1)	0.95
PAD	11 (9.4)	7 (9.6)	0.97
Chronic lung disease	3 (2.6)	5 (6.8)	0.26
Dialysis	64 (54.7)	37 (50.7)	0.59
HDL-C (mg/dL)	41.7±52.8	35.7±11	0.81
LDL-C (mg/dL)	87.4±32.9	87.5±31.5	0.80
CRP (mg/dL)	1.4±1.9	1.2±1.8	0.52
Clinical diagnosis			
Stable angina	39 (33.3)	20 (27.4)	0.39
Acute coronary syndrome	78 (66.7)	53 (72.6)	

Values are mean ± SD or n (%).

BMI: body mass index; CHF: congestive heart failure; CRP: C-reactive protein; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; PCI: percutaneous coronary intervention; PAD: peripheral artery disease