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Effect of Late Revascularization of a Totally Occluded Coronary Artery After Myocardial Infarction on Mortality Rates in Patients with Renal Impairment

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Abstract

Renal dysfunction is an independent predictor of cardiovascular events and a negative prognostic indicator after myocardial infarction (MI). Randomized data comparing percutaneous coronary intervention (PCI) to medical therapy in MI patients with renal insufficiency are needed. The Occluded Artery Trial (OAT) compared optimal medical therapy alone to PCI with optimal medical therapy in 2201 high risk patients with an occluded infarct artery >24 hours post-MI with serum creatinine ≥ 2.5 mg/dl. The primary endpoint was a composite of death, MI, and class IV heart failure (HF). Analyses were carried out utilizing estimated glomerular filtration rates (eGFR) as a continuous variable and by eGFR categories. Long term follow up data (maximum 9 years) were used for this analysis. Lower eGFR (ml/min/1.73m²) was associated with development of the primary outcome (6-year life-table rate 16.9% in eGFR>90; 19.2% in eGFR 60–89; 34.9% in eGFR<60; p-value <0.0001), death, and class IV HF, with no difference in rates of reinfarction. On multivariable analysis, eGFR was an independent predictor of death and HF. There was no effect of treatment assignment on the primary endpoint regardless of eGFR, and there was no significant interaction between eGFR and treatment assignment on any outcome. In conclusion, lower eGFR at enrollment was independently associated with death and HF in OAT participants. Despite this increased risk, the lack of benefit from PCI in the overall trial was also seen in patients with renal dysfunction and persistent occlusion of the infarct artery in the subacute phase post MI.

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Keywords

Myocardial Infarction; Stents and Kidney Disease

Introduction

Many studies that have compared medical therapy to percutaneous coronary intervention (PCI) have either excluded patients with renal dysfunction or did not comment on renal function. Data regarding the potential benefit of PCI in patients with coronary artery disease and chronic kidney disease (CKD) are limited, particularly post-myocardial infarction (MI)^{1–4}. Recent data have shown that these patients are often not treated with guideline-recommended therapies, including revascularization⁵. The Occluded Artery Trial (OAT) was an international, randomized, controlled trial comparing the use of PCI and optimal medical therapy (OMT) against OMT alone for patients with a totally occluded infarct-related artery >24 hours (calendar days 3–28) after MI⁶. We analyzed outcomes and effects of randomized treatment among patients in OAT who had abnormal versus normal renal function at baseline. We hypothesized that patients with lower eGFR would have higher rates of the primary outcome, and given that higher risk, might derive more benefit from revascularization compared to those who have normal renal function.

Methods

The full methods and results of OAT have been published elsewhere^{6–8}. Briefly, OAT included patients with persistent occlusion of the infarct related artery >24 hours after symptom onset, who were stable and at high risk based on future event rates, defined by ejection fraction <50% and/or proximal occlusion of a major epicardial vessel. Participants were randomized to receive PCI plus OMT (PCI group) or OMT alone (MED group). Relevant exclusion criteria included serum creatinine >2.5 mg/dL (221 μ mol/L), NYHA class III/IV HF, shock, left main or three-vessel coronary disease, and severe ischemia on stress testing. Patients were to receive OMT including aspirin, angiotensin-converting-enzyme inhibitor or angiotensin receptor blocker, beta-blocker, lipid-lowering medication unless contraindicated, as well as anti-coagulation if indicated. Thienopyridine therapy was initiated before PCI and continued for 2–4 weeks until 2003, at which time the treatment was recommended for 1 year⁷. PCI technical success was defined centrally as <50% residual in-segment stenosis⁹. The primary end-point was a composite of death, re-infarction, and hospitalizations for NYHA class IV HF. Secondary end points included the components of the primary end point, hospitalization for any class of HF, and cardiovascular death. Data presented here include long-term follow up of the OAT cohort and assessment of reinfarction according to the universal definition of MI¹⁰.

The four-component (simplified) MDRD study equation was used to calculate eGFR (in ml/min/1.73m²)¹¹. This estimate of GFR has been shown to provide superior prognostic information to the Cockcroft-Gault formula among patients with chest pain syndromes¹². The creatinine level used in this analysis was the pre-randomization value. The National Kidney Foundation CKD stages were used to divide the patients into normal renal function (eGFR >90), mild renal dysfunction (eGFR 60–89), and moderate renal dysfunction (eGFR <60)¹³. It was anticipated that very few patients enrolled in OAT have eGFR <30 based on the creatinine exclusion criterion. All deaths were categorized by an independent morbidity and mortality classification committee, which was blinded to treatment assignment, with reporting of the primary and immediate causes using standardized definitions. Death from cancer was a subset of non-cardiovascular death.

Baseline demographic differences between the three groups were analyzed utilizing a one-way analysis of variance (ANOVA) for continuous variables and chi-square for categorical variables. The effects of eGFR on outcomes were assessed both modeling eGFR as a continuous variable and categorizing renal function by eGFR category. The analyses of eGFR as a continuous variable predicting outcomes data were performed utilizing a Cox regression analysis, with calculation of hazard ratios for PCI vs. MED. Separating the participants into eGFR categories, estimates of cumulative 6-year event rates were calculated by the Kaplan-Meier product-limit method. Hazard ratios were calculated utilizing Cox regression analysis. Since the eGFR groups differ in many baseline characteristics, and several of these have been shown to affect outcomes for the OAT population¹⁴, we generated covariate-adjusted hazard ratios utilizing a Cox proportional-hazards regression model with the covariates of interest. The covariates were significantly associated with the primary outcome in OAT (LVEF, time to randomization, diabetes, peripheral vascular disease (PVD), prior HF, rates on examination at time of randomization)¹⁴. All analyses were by intention-to-treat. The pre-determined significant p-value for all post-hoc analyses in OAT is <0.01 with p-values <0.05 labeled as a strong trend toward statistical significance.

Results

Baseline serum creatinine was available for 2160 (98.1%) of the 2201 OAT participants, of whom 624 (28.9%) had normal renal function (eGFR >90), 1216 (56.3%) had mild renal dysfunction (eGFR 60–90), and 320 (14.8%) had moderate renal dysfunction (eGFR <60). Baseline clinical and angiographic variables by eGFR category are shown in Table 1. As expected, there was a small number ($n=8$) of patients categorized as CKD stage 4 (eGFR <30). The average follow up was 5.6 years (standard error 17 days, no difference between the PCI and MED groups). Patients with more severe renal impairment were older, more likely to be female and more likely to have history of diabetes, hypertension, HF, and cerebrovascular disease. On presentation, participants with lower eGFR were more likely to have rales.¹⁵ There was a strong trend toward more multi-vessel disease among patients with lower eGFR. PCI technical success rates were similar in all eGFR groups, however there was a strong trend toward higher frequency of post-PCI TIMI 0 or 1 flow among patients with lower eGFR. The treatment groups were balanced for baseline and angiographic characteristics for all eGFR categories. Discharge medications are shown in Table 1. There was no difference in thienopyridine (clopidogrel or ticlodipine) use between the three eGFR categories. Patients assigned to PCI were more likely to be discharged on thienopyridines in all eGFR categories.

When examined as a continuous function, lower eGFR was associated with higher primary endpoint composite event rates, and with death, class IV HF, and cardiovascular death (Table 2). There was no relationship between eGFR and re-infarction. On multivariable analysis, eGFR remained a significant predictor of all cause mortality and class IV HF. The relationship between eGFR and cardiovascular death was not significant in the multivariable analysis.

Kaplan-Meier survival curves for primary and secondary outcomes divided by eGFR categories are depicted in Figure 1. The group with poorest renal function (eGFR <60) had higher risk of the primary endpoint compared with patients with higher eGFR (HR 2.15, 99% CI 1.60–2.89, $p<0.0001$). Patients with eGFR <60 also had higher rates of death (HR 2.47, 99% CI 1.74–3.51, $p<0.0001$), class IV HF (HR 3.53, 99% CI 2.06–6.03, $p<0.001$), and cardiovascular death (HR 2.00, 99% CI 1.22–3.27, $p=0.0003$). In the multivariable analysis, patients with eGFR <60 had significantly higher rates of the primary outcome (HR 1.79, 99% CI 1.32–2.43, adjusted $p<0.0001$), death (HR 2.01, 99% CI 1.40–2.89, adjusted

$p < 0.0001$), and class IV HF (HR 2.68, 99% CI 1.54–4.67, adjusted $p < 0.0001$), while cardiovascular death showed a trend toward significance (HR 1.55, 99% CI 0.93–2.57, adjusted $p = 0.03$). The group with moderate renal dysfunction had similar rates of re-infarction to those with eGFR > 60 (HR 1.28, 99% CI 0.71–2.32, $p = 0.28$).

Lower eGFR was associated with a higher rate of non-cardiovascular death, including a higher rate of death due to malignancy (Table 2). The difference was due to increased risk in patients with the poorest renal function (eGFR < 60), who had more non-cardiovascular death (HR 3.57, 99% CI 2.06–6.19, adjusted $p < 0.0001$) and death from malignancy (HR 3.75, 99% CI 1.58–8.92, adjusted $p = 0.0002$) when compared to those with eGFR > 60 .

There were no significant differences in primary or secondary endpoint rates between the PCI and MED groups for any eGFR category (Table 3). There was no significant interaction between eGFR category and treatment assignment for the primary outcome ($p = 0.18$) or any secondary outcome (death $p = 0.06$; re-infarction $p = 0.99$; class IV HF $p = 0.83$). As in the trial overall, reinfarction events were mostly of the spontaneous type¹⁰. There was no difference in the distribution of type of reinfarction based on eGFR categories (data not shown). In particular, type 3 reinfarction (sudden death) was equally common among participants with normal eGFR, mild renal dysfunction or moderate renal dysfunction (0.5% 6-year rate vs. 0.7% vs. 0.3%, respectively).

There were very few adverse events related to PCI, such as vascular complications. There was no relationship between eGFR and these adverse events. Two participants were noted to have renal complications within 48 hours of randomization; one with normal renal function and one in the eGFR < 60 group.

Discussion

The moderate renal dysfunction group (eGFR < 60) described here represents the largest published randomized trial experience with PCI vs. medical therapy in a subgroup of post-MI patients with renal impairment. Patients with renal insufficiency in OAT were at higher risk of death¹⁴ and HF, but not reinfarction. Long-term outcomes in patients with eGFR consistent with stage 3+ CKD were not statistically different between PCI and MED groups despite the higher risk of events in this subset. There was no signal of an increase in PCI complications based on lower eGFR. Our study agrees with similarly sized COURAGE analysis which also found no benefit of PCI in CKD patients or those with normal renal function in the setting of stable coronary disease over a shorter duration of follow up⁴. Both of these studies found no increase in complications related to revascularization in participants with renal insufficiency. While there have been few randomized trials comparing revascularization to medical therapy in patients with CKD, our results, combined with the COURAGE results, suggest that a routine strategy of revascularization does not reduce long term clinical events in patients with renal insufficiency despite a low rate of procedural complications, at least in the stable patients studied in these two trials.

PCI success rates were high in participants with decreased renal function and similar to those with normal renal function, as in previous studies^{16,17}. However, there was a trend toward lower TIMI flow grade post PCI related to renal dysfunction. Analyses of data from primary PCI studies have shown similar trends in patients with acute MI, with lower post-procedure TIMI flow¹⁸ and lower TIMI myocardial perfusion grades¹⁹ in patients with renal insufficiency. However, the relationship between post-PCI TIMI grades and long-term outcomes in this subset is still unclear.

Renal impairment is increasingly recognized not only as an independent risk factor for cardiovascular events but as a marker of worse prognosis after cardiovascular events occur.

The present study extends observations on the prognostic impact of CKD to a high-risk cohort of post-MI patients. Patients enrolled in OAT with eGFR consistent with moderate renal dysfunction had higher rates of death and HF, including advanced HF, but not re-infarction. CKD has been consistently associated with death^{20–22} and HF²¹ after MI. Though low eGFR is a risk factor for MI, prior studies have not shown low eGFR to be a risk factor for reinfarction after an MI^{5,22–25}.

Poor outcomes were mostly noted in participants with eGFR <60, while patients with mild renal impairment had similar outcomes to those with normal renal function. Our findings are consistent with prior studies which have shown that moderate renal dysfunction (eGFR <60) is an independent predictor of adverse outcomes after myocardial infarction^{20–22}.

Prior OAT analyses have found a high rate of early post-MI HF in patients with renal insufficiency, many with preserved systolic function¹⁵. The increase in early post-MI HF persisted through the OAT follow up period. The explanation for this increase in death and HF is likely multi-factorial. CKD patients have signs of ongoing inflammation, endothelial dysfunction, anemia, increased coagulability, elevated homocysteine levels, and impaired ability of the kidney to excrete sodium and water loads^{15,26}. How these factors interact to increase cardiovascular morbidity and mortality has yet to be elucidated.

We also found a higher risk of non-cardiovascular death among patients with lower eGFR. This is consistent with data demonstrating excess in both cardiovascular (38 per 1000 person years) and non-cardiovascular death (50 per 1000 person years) among patients starting dialysis as compared with the general population²⁷. End stage renal disease (ESRD) has also been associated with an increased risk of malignancy²⁸. However, few data exist with respect to the relationship between kidney disease other than ESRD and malignancy. While our study was not designed for this comparison, our results showing an increase in non-cardiovascular deaths, mostly from malignancy, are intriguing in light of an observational report of higher malignancy rates in men with renal insufficiency²⁹. The link between renal disease and cancer, like the link with HF, may be multi-factorial. Chronic inflammation, which is known to complicate CKD²⁶ and to be important in the development of malignancy³⁰, may play a role.

This study has several limitations. OAT was powered for detection of the effects of PCI in the whole study population, and not in subsets of the population. Further studies of interventions are needed to reduce the high risk of death and HF in CKD. As is true of all studies on the impact of renal insufficiency on clinical outcomes, there are measured and unmeasured confounders which may have affected our results. This study used creatinine on presentation to classify the patients into CKD stages. Estimation of GFR using the MDRD equation assumes the creatinine to be in steady state, which may not have been true of all patients. New classification schemes for renal dysfunction incorporate the presence of micro-albuminuria; however urine protein was not checked in OAT patients. There was no standardized creatinine measurement at >48 hours after PCI and renal complications post-PCI may have been underestimated.

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Figure 1.

Kaplan-Meier survival curves for the primary (death, re-infarction, and hospitalizations for class IV heart failure) and secondary endpoints of both treatments in the eGFR <60 and eGFR >60 groups. PCI-percutaneous coronary intervention plus medical therapy group (solid lines); MED-optimal medical therapy alone group (dashed lines)

Table 1

Demographic Data; PCI-percutaneous intervention; eGFR-estimated glomerular filtration rate; CAD-Coronary artery disease; Values are number (percent) or mean $\pm$ one standard deviation.

Variable	eGFR > 90 N = 624 (28.9%)	eGFR 60–90 N = 1216 (56.3%)	eGFR < 60 N = 320 (14.8%)	p-value *
Assigned to PCI	316 (50.6%)	591 (48.6%)	169 (52.8%)	0.77
eGFR (mL/min/1.73m ²)	106 $\pm$ 16.6	75.5 $\pm$ 8.1	50.4 $\pm$ 7.7	N/A
Age (years)	54.2 $\pm$ 9.7	58.7 $\pm$ 10.5	67.2 $\pm$ 9.6	<0.0001
Men	533 (85.4%)	969 (79.7%)	181 (56.6%)	<0.0001
White	492 (78.8%)	983 (80.8%)	257 (80.3%)	0.60
Diabetes Mellitus	127 (20.4%)	222 (18.3%)	96 (30%)	0.009
Prior Myocardial Infarction	59 (9.5%)	149 (12.3%)	35 (10.9%)	0.28
Hypertension	245 (39.3%)	589 (48.4%)	221 (69.1%)	<0.0001
Heart Failure	7 (1.1%)	27 (2.2%)	18 (5.6%)	<0.0001
Cerebrovascular disease	11 (1.8%)	50 (4.1%)	20 (6.3%)	0.0003
Peripheral Vascular Disease	26 (4.2%)	37 (3%)	16 (5%)	0.84
Previous PCI	26 (4.2%)	56 (4.6%)	19 (5.9%)	0.26
Hyperlipidemia [†]	316 (50.6%)	629 (51.7%)	177 (55.5%)	0.19
Family History of CAD	266 (42.6%)	496 (40.8%)	105 (32.8%)	0.008
Cigarette smoker	324 (51.9%)	449 (36.9%)	72 (22.5%)	<0.0001
Body Mass Index (kg/m ²)	28.4 $\pm$ 5.1	28.6 $\pm$ 4.9	28.5 $\pm$ 5.3	0.77
At randomization				
Rales on exam	25 (4%)	69 (5.7%)	40 (12.5%)	<0.0001
NYHA Heart Failure class II–IV	107 (17.1%)	249 (20.5%)	93 (29.1%)	<0.0001
Thrombolytic in first 24 hours	103 (16.5%)	245 (20.2%)	65 (20.3%)	0.09
Heart Rate (beats/min)	72.1 $\pm$ 11.5	71.4 $\pm$ 11.9	72.7 $\pm$ 12.7	0.13
Systolic Blood Pressure (mmHg)	119.4 $\pm$ 17.4	120.7 $\pm$ 17.7	123.9 $\pm$ 19.7	0.001
Diastolic Blood Pressure (mmHg)	72.6 $\pm$ 11.1	72.3 $\pm$ 11.4	71.8 $\pm$ 11.6	0.63
Heart Rate	72.1 $\pm$ 11.5	71.4 $\pm$ 11.9	72.7 $\pm$ 12.7	0.13
Blood Glucose (mg/dL)	122.8 $\pm$ 47.2	116.5 $\pm$ 36.8	126.9 $\pm$ 48.4	0.0001
Time to randomization (days) [‡]	10.1 $\pm$ 7.4	11.2 $\pm$ 7.8	11.6 $\pm$ 7.6	0.004
Infarct Related Coronary Artery				0.06
Left Anterior Descending	205 (32.9%)	448 (36.8%)	123 (38.4%)	
Left Circumflex	113 (18.1%)	169 (13.9%)	48 (15%)	
Right	306 (49%)	599 (49.3%)	149 (46.6%)	
Collateral Circulation [§]	552 (89.2%)	1065 (88.5%)	273 (86.7%)	0.29
Multi-vessel disease	96 (15.5%)	209 (17.3%)	69 (21.6%)	0.03
Left Ventricular Ejection Fraction (%)	48.2 $\pm$ 10	47.9 $\pm$ 11.3	46.2 $\pm$ 12.1	0.02
Mitral Regurgitation Grade				0.002
0	351 (69%)	655 (66%)	145 (56.9%)	
1–3	158 (71%)	337 (34%)	110 (43.1%)	
Successful PCI [¶]	271 (88.6%)	543 (87.7%)	123 (83.1%)	0.24

Variable	eGFR > 90 N = 624 (28.9%)	eGFR 60–90 N = 1216 (56.3%)	eGFR < 60 N = 320 (14.8%)	p-value *
Post-PCI TIMI flow				0.03
0, 1 (closed)	29 (9.6%)	76 (12.4%)	27 (18.4%)	
2, 3 (open)	273 (90.4%)	537 (87.6%)	120 (81.6%)	
Discharge Medications				
Aspirin	605 (97%)	1166 (95.9%)	296 (92.5%)	0.005
Clopidogrel[‡]	319 (51.1%)	591 (48.6%)	154 (48.1%)	0.54
Lipid lowering agent	533 (85.4%)	994 (81.7%)	235 (73.4%)	<0.0001
Insulin	43 (6.9%)	59 (4.9%)	35 (10.9%)	0.0003
Anti-arrhythmic (other than Beta Blocker)	14 (2.2%)	45 (3.7%)	25 (7.8%)	0.0001
Digoxin	12 (1.9%)	28 (2.3%)	19 (5.9%)	0.0006
Diuretic	74 (11.9%)	182 (15%)	107 (33.4%)	<0.0001

* p-value for differences between the three eGFR categories;

[‡]Hyperlipidemia is defined a previous diagnosis of hyperlipidemia, history of treatment with lipid lowering medication, or fasting LDL ≥ 130;

[‡]Time to randomization was interval between MI and randomization;

[§]Angiographically visible collateral vessels;

[¶]Successful PCI was defined as <50% residual stenosis with TIMI grade 2 or 3 flow (note that 65 patients with excellent technical results but poor reflow were categorized as successful PCI).

[#]No significant differences exist between the MED and PCI groups in all eGFR groups, except use of clopidogrel (more likely in PCI group across all 3 eGFR categories (p<0.05)).

Table 2

Outcomes broken down by eGFR stage; Hazard ratios with 99% confidence intervals. Heart failure endpoints are for hospitalizations.

Variable	Estimated Glomerular Filtration Rate (eGFR in mL/min/1.73m ²)								Adjusted p-value*
	90+ (N=624)		60-89 (N=1216)		<60(N=320)		HR per 10 unit decrease in eGFR	p-value	
	No.	Estimated 6yr-Rate	No.	Estimated 6yr-Rate	No.	Estimated 6yr-Rate			
Primary End Point	93	16.9	211	19.2	102	34.9	1.15 (1.07-1.22)	<.0001	0.0001
All cause death	56	10.2	135	12.4	75	26.0	1.21 (1.11-1.31)	<.0001	<.0001
Re-infarction	36	6.7	74	6.9	23	8.9	1.03 (0.92-1.14)	0.52	0.83
Class IV Heart Failure	19	3.3	45	4.1	36	12.4	1.29 (1.12-1.48)	<.0001	0.0008
Class III or IV Heart Failure	33	5.9	68	6.1	42	14.5	1.17 (1.05-1.31)	0.0003	0.02
Any Class Heart Failure	41	7.4	85	7.8	52	17.9	1.20 (1.09-1.33)	<.0001	0.0019
Cardiovascular death	36	6.5	75	6.7	36	12.6	1.14 (1.03-1.27)	0.002	0.09
Non-cardiovascular death [†]	15	2.9	46	4.5	34	13.1	1.30 (1.13-1.50)	<.0001	<.0001
Death from cancer	5	1.1	19	1.9	14	5.8	1.34 (1.06-1.67)	0.001	0.004

* Adjusted p-value – with covariates of left ventricular ejection fraction, time to randomization, rates on exam, and history of diabetes, peripheral vascular disease or heart failure.

[†] A small number of deaths were unclassified

Table 3

Outcomes by estimated glomerular filtration rate (eGFR) and treatment group.

Outcome	eGFR 90+ N=624					eGFR 60-89 N=1216					eGFR <60 N=320				
	PCI*(N=308)		MED*(N=316)			PCI (N = 625)		MED (N = 591)			PCI (N=151)		MED (N=169)		
	No.	Estimated 6yr-Rate (%)	No.	Estimated 6yr-Rate (%)	Hazard Ratio (99% CI)	No.	Estimated 6yr-Rate (%)	No.	Estimated 6yr-Rate (%)	Hazard Ratio (99% CI)	No.	Estimated 6yr-Rate (%)	No.	Estimated 6yr-Rate (%)	Hazard Ratio (99% CI)
Primary End Point	49	18.2	44	15.6	1.19 (0.70-2.03)	116	20.2	95	18.0	1.18 (0.83-1.69)	44	31.7	58	37.7	0.84 (0.50-1.41)
Death	32	12.0	24	8.6	1.40 (0.70-2.82)	70	12.2	65	12.6	1.03 (0.66-1.60)	31	22.9	44	28.8	0.74 (0.42-1.41)
Re-infarction	18	7.0	18	6.3	1.06 (0.45-2.50)	42	7.6	32	6.2	1.27 (0.70-2.33)	11	8.4	12	9.3	0.94 (0.35-2.98)
Class IV Heart Failure	8	2.8	11	3.7	0.77 (0.23-2.53)	26	4.6	19	3.5	1.31 (0.60-2.84)	15	10.5	21	14.2	0.81 (0.34-1.93)
Class III/IV Heart Failure	15	5.7	18	6.1	0.87 (0.35-2.14)	37	6.4	31	5.7	1.14 (0.61-2.13)	19	13.2	23	15.7	0.94 (0.42-2.09)
Any Class Heart Failure	20	7.6	21	7.3	0.99 (0.44-2.22)	47	8.5	38	7.1	1.19 (0.68-2.08)					
Cardiovascular death	16	6.1	20	7.0	0.84 (0.35-1.98)	43	7.3	32	6.2	1.28 (0.70-2.34)					
					0.41					0.22					0.40
					0.21					0.87					0.26
					0.86					0.30					0.97
					0.57					0.38					0.52
					0.69					0.60					0.84
					0.98					0.44					
					0.59					0.29					

Outcome	eGFR <60 N=320		PCI (N=151)		MED (N=169)		PCI vs MED	
	No.	Estimated 6yr-Rate (%)	No.	Estimated 6yr-Rate (%)	No.	Estimated 6yr-Rate (%)	Hazard Ratio (99% CI)	p-value
Any Class Heart Failure	23	16.3	29	19.4			0.89 (0.44–1.83)	0.69
Cardiovascular death	13	9.1	23	15.6			0.63 (0.26–1.53)	0.18

* PCI denoted randomization to PCI in addition to optimal medical therapy; MED denotes randomization to optimal medical therapy alone.
CI-Confidence Interval; eGFR are displayed in(mL/min/1.73m²); Heart failure endpoints are for hospitalization