Contrast-Induced Nephropathy and Long-Term Clinical Outcomes Following Percutaneous Coronary Intervention in Patients With Advanced Renal Dysfunction (Estimated Glomerular Filtration Rate <30 ml/min/1.73 m^2)

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The incidence of contrast-induced nephropathy (CIN) increases with the progression of renal dysfunction. Recent reports have shown that percutaneous coronary intervention (PCI) can be safely performed even in patients with advanced renal dysfunction by appropriate CIN-prevention strategies. However, data are limited regarding the occurrence and prognostic influence of CIN in patients with advanced renal dysfunction. We examined the data obtained from 323 consecutive patients with advanced renal dysfunction (eGFR <30 ml/min/1.73 m^2) who underwent PCI at 5 hospitals. CIN was defined as a ≥25% increase in baseline serum creatinine levels and/or a ≥0.5 mg/dl increase in absolute serum creatinine levels within 72 hours after PCI. Incidence of all-cause death and the initiation of permanent dialysis were examined during follow-up. The prevalence of emergency/urgent PCI was 53.3%. Intravascular ultrasound was used in 266 patients (82.4%), and the volume of contrast used was 71.7 ± 57.2 ml. CIN was observed in 31 patients (9.7%). The median follow-up duration was 656 days (interquartile range 257−1143 days). The cumulative rates of all-cause death or the initiation of permanent dialysis, all-cause death, and the initiation of permanent dialysis were 38.1%, 25.9%, and 18.2%, respectively, at 2 years. A comparison between patients with and without CIN showed no significant intergroup differences in the occurrence of the aforementioned events. In conclusion, the incidence of CIN was not high in Japanese patients with advanced renal dysfunction in routine clinical practice. Whereas, the long-term prognosis following PCI is observed to be poor in this studied population, and CIN did not show a significant prognostic influence. **(Am J Cardiol 2019;123:361−367)**

Contrast-induced nephropathy (CIN), a common and serious complication of percutaneous coronary intervention (PCI), is associated with poor clinical outcomes.[1,2] Moreover, it has been reported that the incidence of CIN increases with the progression of renal dysfunction. Notably, renal dysfunction itself is also associated with increased cardiac morbidity and mortality, particularly in patients presenting with coronary artery disease (CAD).[3−7] Therefore, in patients with advanced renal dysfunction, it is important to consider both, appropriate renal protection and coronary revascularization simultaneously. However, data remain limited regarding considering this balance in clinical practice. This study clarifies the long-term clinical outcomes and prognostic influence of CIN in Japanese patients with advanced renal dysfunction who undergo PCI.

Methods

Data were obtained from 323 consecutive patients with advanced renal dysfunction (estimated glomerular filtration rate [eGFR] <30 ml/min/1.73 m^2 before undergoing PCI), who underwent PCI across 5 hospitals in 2011 and 2016, and we enrolled at the first procedure during the period. Exclusion criteria were: patients receiving dialysis, patients who had been scheduled to initiate dialysis, and patients receiving veno-arterial extracorporeal membrane oxygenation. Data pertaining to baseline clinical, laboratory, angiographic, and procedural characteristics as well as clinical follow-up were obtained from hospital records or databases at each center. This study was performed based on the guidelines of the Declaration of Helsinki, and the

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See page 366 for disclosure information.

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research protocol was approved by the Ethics Committees at all 5 centers.

PCI procedures were performed using standard interventional techniques. Selection of the approach site, factors associated with stent use and its type, mechanical support, and other interventional devices were left to the discretion of the operator. Nonionic contrast agents with low osmolality (iohexol, iomeprol, and iopamidol) were used for all angiography procedures.

Serum creatinine levels were measured before performing PCI and also multiple times over 3 days post-PCI, and the occurrence of CIN was recorded. CIN was defined as either a 25% increase in baseline serum creatinine levels or a 0.5 mg/dl (44 μmol/l) increase in absolute serum creatinine levels within 72 hours after the contrast agent had been administered during the PCI procedure.[8]

The primary composite endpoint was the incidence of all-cause death or the initiation of permanent dialysis. Other endpoints included myocardial infarction, stroke or transient ischemic attack, and target vessel revascularization.

The eGFR was calculated using the revised Japanese equation: eGFR (ml/min/1.73 m^2) = 194 × serum creatinine-1.094 × age-0.287 × 0.739 (in women).[9] All-cause death was defined as any death occurring after the PCI procedure. Cardiovascular death was defined as any death secondary to a cardiovascular cause. Deaths related to an unknown cause were considered cardiac death. Shock was defined as systolic blood pressure <80 mm Hg and/or patients requiring treatment with inotropes at the time the PCI was performed. Anemia was defined as a baseline hemoglobin level <11.0 g/dl.[10]

All patient data were pooled in a single prespecified structured dataset for analysis. Continuous variables have been expressed as means ± standard deviations or as medians (interquartile range). Categorical variables have been expressed as percentages. The Student's *t* test or the Mann−Whitney *U* test was used to compare continuous variables, and the chi-square or the Fisher exact test was used to compare categorical variables. Cumulative event rates were estimated using the Kaplan−Meier method, and differences in event rate were evaluated using the log-rank test. Multivariate Cox proportional hazard regression analysis was used to determine independent predictors of primary endpoint, all-cause death, and the initiation of permanent dialysis. Variables showing a p value <0.1 using univariate analysis and judged to be of clinical significance were included in the model. The results have been presented as hazard ratios (HR) with 95% confidence intervals (CI), and p values. A two-sided p value <0.05 was considered statistically significant. All statistical analyses were performed using the SPSS software version 18.0 (IBM, Armonk, NY).

Results

Baseline clinical, angiographic and procedural characteristics have been presented in Table 1. Among the overall number of patients studied (n = 323), 17% showed an eGFR <15 ml/min/1.73 m^2, and majority of the patients presented with acute coronary syndrome (acute myocardial infarction or unstable angina). The prevalence of emergency/urgent PCI was 53%. The volume of contrast used in this study was 72 ± 57 ml, and preoperative fluid replacement was performed in 185 patients (57.3%).

CIN occurred in 31 patients (9.7%). A comparison of the baseline characteristics between patients who developed CIN and those who did not (Table 1) showed that patients with CIN more frequently presented with shock, pulmonary congestion, and acute myocardial infarction. No statistically significant intergroup differences were observed with regard to age, the presence of coronary risk factors, and renal function. Among patients who developed CIN, the rate of emergency/urgent PCI was higher, and the use of intra-aortic balloon pumping was more common (Table 1). Additionally, the volume of contrast agent used was higher, and the rate of intentional preoperative fluid replacement was lower.

The median patient follow-up was 656 days (interquartile range 257−1143 days). Kaplan−Meier curves for the primary endpoint of all-cause death or initiation of permanent dialysis, all-cause death, and the initiation of permanent dialysis are presented in Figure 1, and the estimated rates of clinical events at 2 years are summarized in Figure 2. The cumulative rates of the primary endpoint, death, and the initiation of dialysis were 38.1%, 25.9%, and 18.2%, respectively, at 2 years. The number of clinical events during follow-up cumulatively counted at the time of the latest clinical follow-up, and the details of the causes of death are presented in Table 2. Among all 95 deaths, 63 (66.3%) were related to cardiovascular causes, primarily to cardiac death. Noncardiovascular deaths included those related to infection, cancer, and renal failure.

Cumulative event rates estimated for patients with and without CIN are shown in Figure 3. There were no statistically significant intergroup differences in the occurrence of the primary endpoint, all-cause death, and the initiation of permanent dialysis.

Details pertaining to multivariate Cox regression analyses performed for the assessment of the primary endpoint, all-cause death, and the initiation of permanent dialysis are shown in Tables 3, respectively. Body mass index (BMI), eGFR <15 ml/min/1.73 m^2, shock, and pulmonary congestion were independent predictors of death or the initiation of permanent dialysis (Table 3A). Age, BMI, left ventricular ejection fraction, and pulmonary congestion were observed to be independent predictors of death (Table 3B). Anemia and eGFR <15 ml/min/1.73 m^2 were independent predictors of the initiation of permanent dialysis (Table 3C). The development of CIN was not observed to be associated with the incidence of the aforementioned endpoints (Table 3A-C).

Discussion

The primary findings of the present study are: (1) The incidence of CIN following PCI was 9.7% among Japanese patients with advanced renal dysfunction in clinical practice; (2) The patients who developed CIN were more frequently emergency/urgent cases, presented with poor circulatory dynamics at PCI, had a higher volume of contrast agent, and less frequently received preoperative fluid replacement, (3) The cumulative rates of all-cause death or

Table 1
Patient, angiographic and procedural characteristics

Variable	Overall n = 323	Contrast-Induced Nephropathy		p Value*
		Yes (n = 31)	No (n = 289)	
Age (years)	76.6±9.4	77.9±8.2	.5±9.4	0.52
Men	211 (65%)	19 (61%)	191 (66%)	0.59
Body mass index (kg/m^2)	23.0±4.0	23.1±3.4	22.9±4.1	0.53
Hypertension	270 (84%)	28 (90%)	240 (83%)	0.30
Diabetes mellitus	181 (56%)	21 (68%)	160 (55%)	0.19
Dyslipidemia	260 (81%)	25 (81%)	233 (81%)	1.00
Current smoker	63 (20%)	6 (20%)	57 (20%)	0.96
Anemia	176 (55%)	18 (58%)	157 (54%)	0.69
eGFR<15 mL/min/1.73 m^2	54 (17%)	5 (16%)	49 (17%)	0.91
Prior myocardial infarction	86 (27%)	8 (26%)	78 (27%)	0.89
Prior PCI	104 (32%)	8 (26%)	96 (33%)	0.4
Prior coronary artery bypass grafting	59 (18%)	4 (13%)	55 (19%)	0.4
Prior stroke or transient ischemic attack	53 (17%)	6 (19%)	46 (16%)	0.63
Peripheral artery disease	64 (20%)	5 (17%)	58 (20%)	0.66
Prior heart failure	102 (32%)	6 (19%)	96 (33%)	0.11
Left ventricular ejection fraction (%)	53±15	55±14	53±15	0.55
Serum creatinine (mg/dL)	2.46±1.16	2.35±0.98	2.48±1.18	0.77
eGFR (mL/min/1.73 m^2)	21.5±6.0	21.7±5.8	21.5±6.0	1.00
Status at PCI				
Shock	40 (12%)	8 (26%)	31 (11%)	0.04
Pulmonary congestion	79 (25%)	15 (48%)	62 (22%)	0.001
Clinical presentation				
STEMI or NSTEMI	111 (34%)	17 (55%)	91 (32%)	0.045
Unstable angina pectoris	83 (26%)	7 (23%)	76 (26%)	0.65
Stable or silent myocardial ischemia	129 (40%)	7 (23%)	122 (42%)	0.03
Emergency or urgent	172 (53%)	24 (77%)	145 (50%)	0.004
Multivessel coronary disease	221 (68%)	23 (74%)	197 (68%)	0.49
PCI of coronary artery				
Right coronary artery	141 (44%)	14 (45%)	127 (44%)	0.90
Left main coronary artery	23 (7%)	7 (23%)	16 (6%)	0.003
Left anterior descending coronary artery	130 (40%)	14 (45%)	113 (39%)	0.51
Left circumflex coronary artery	57 18%)	4 (13%)	53 (18%)	0.45
Saphenous vein graft	6 (2%)	0 (0%)	6 (2%)	0.54
Multivessel PCI	21 (7%)	3 (10%)	18 (6%)	0.33
Bare metal stent use	52 (16%)	3 (10%)	49 (17%)	0.30
Drug-eluting stent use	223 (69%)	21 (68%)	200 (69%)	0.87
Use of stent <3.0 mm	112 (35%)	8 (26%)	103 (36%)	0.27
Intravascular ultrasound	266 (82%)	22 (71%)	242 (84%)	0.08
Intra-aortic balloon pumping	59 (18%)	13 (42%)	44 (15%)	<0.001
Contrast volume (mL)	72 ± 57	88 ± 54	70 ± 57	0.02
Preoperative fluid replacement[+]	185 (57%)	8 (26%)	177 (61%)	<0.001
Hydrocarbonate	63 (20%)	6 (19%)	57 (20%)	0.96

Data have been presented as means ± SD, or as numbers (percentages).

* Comparison between patients with and without contrast-induced nephropathy.

[+] Preoperative fluid replacement introduced from the day of operation or previous day. Hypertension was defined as systolic/diastolic blood pressure ≥140/90 mm Hg, or as having received antihypertensive drugs. Dyslipidemia was defined as low-density lipoprotein level ≥140 mg/dL, triglycerides level ≥150 mg/dL, or high-density lipoprotein level <40 mg/dL, or as having received treatment. Anemia was defined as a baseline hemoglobin level <11.0 g/dL. eGFR = estimated glomerular filtration rate; NSTEMI = non−ST-elevation myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation; STEM = ST-elevation myocardial infarction.

initiation of dialysis, all-cause death, and the initiation of dialysis were high, and majority of deaths were attributable to cardiac death, (4) Low BMI, baseline eGFR (<15 ml/min/1.73 m^2), shock, and pulmonary congestion served as independent predictors of death or the initiation of permanent dialysis, (5) In patients with advanced renal insufficiency, CIN did not affect the long-term prognosis (death or initiation of permanent dialysis).

Renal dysfunction has been shown to be an independent prognostic factor for morbidity and mortality in the general population, as well as in patients with CAD, and progressive renal dysfunction is associated with worsening prognosis.[5,11] Most previous studies have reported a poor natural prognosis in patients with advanced renal dysfunction,[12−14] and cardiac death is the primary cause of death. Mortality rates are reportedly higher in patients with advanced renal

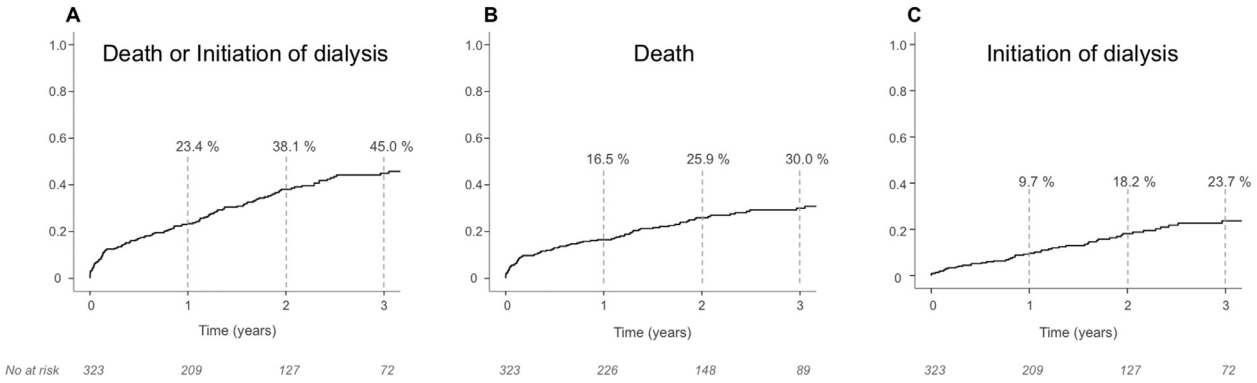

Figure 1. Kaplan-Meier curves in the overall population: All-cause death or the initiation of dialysis; all-cause death; the initiation of dialysis.

dysfunction concomitant with CAD: 15% to 30% at 1 year and 25% to 45% at 2 years.[15–17] Our present study included patients with advanced renal dysfunction who underwent PCI and demonstrated high cumulative rates of all-cause death or the initiation of dialysis. Although data remain limited, the prognosis of patients with advanced renal dysfunction concomitant with CAD was demonstrated to be still poor in Japanese patients presenting to routine clinical practice.

The incidence of CIN after PCI is higher in patients with renal dysfunction than in those without renal dysfunction, and this figure becomes higher with a decline in eGFR.[18,19] Reportedly, the incidence rate was 10% to 30% among patients with eGFR <30 ml/min/1.73 m^2.[18,19] In this study, the incidence rate of CIN was 9.7%, which was lower than that observed in previous reports. In this study, although approximately 50% of the patients underwent emergency/urgent procedures, the amount of contrast agent used was lower than that described by previous reports. Moreover, intravascular imaging was used in most cases, and appropriate preoperative fluid replacement was performed as possible. Such optimized strategies utilized in routine Japanese clinical practice might help to reduce the occurrence of CIN.[20] Furthermore, patients who developed CIN were observed to have received a larger volume of contrast agent and also showed the presence of various factors related to a poor hemodynamic status, as previously described.[21]

Several studies have reported that the development of CIN following a PCI procedure in patients with renal dysfunction is associated with poor prognosis;[22,23] however, only few studies have described this condition in patients with advanced renal dysfunction. In this study, the occurrence of CIN did not affect long-term outcomes. Possible causes that could explain this result are: (1) Background fluctuations in serum creatinine levels were reported and such fluctuations were greater in those with advanced renal dysfunction, which can more frequently result in fulfilling the definition of CIN.[24,25] Therefore, current criteria that have been established to assess CIN could not accurately assess the extent of renal damage in patients with advanced renal dysfunction, thereby leading to a difficulty in evaluating prognosis. (2) A few studies have reported that the prognosis was worse in patients with a severe degree of CIN, and a significant change in serum creatinine levels may reflect the prognosis in patients with advanced renal dysfunction as well.[26,27] However, the incidence rate of

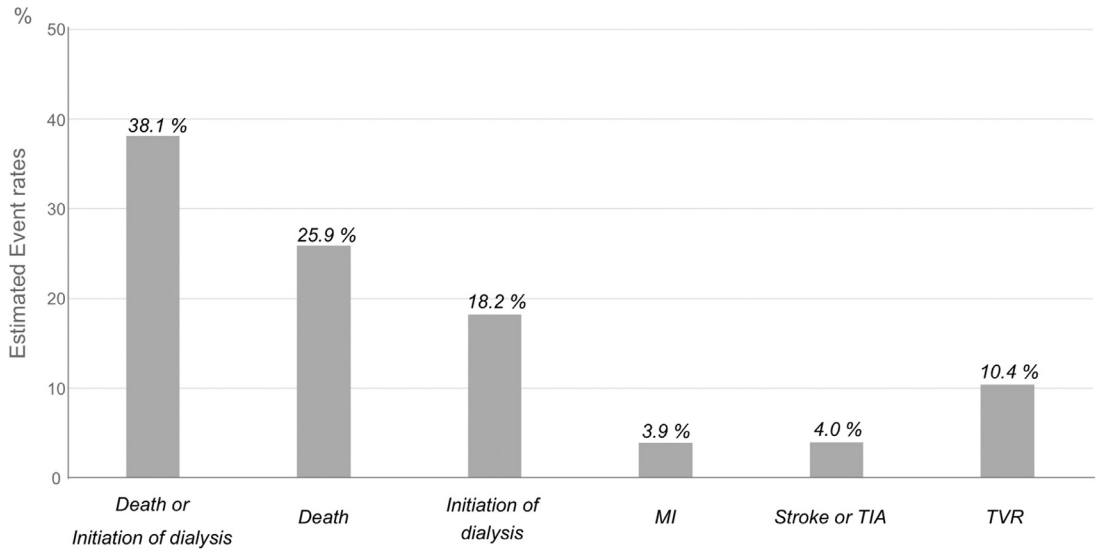

Figure 2. The cumulative rates of adverse events in the overall population at 2 years. MI = myocardial infarction; TIA = transient ischemic attack; TVR = target vessel revascularization.

Table 2
Outcomes during the entire observation period and details regarding the cause of death

Variable	Overall n = 323	Contrast-Induced Nephropathy	
		Yes (n = 31)	No (n = 289)
Outcomes			
Death or initiation of permanent dialysis	135	15	118
Death	95	11	82
Initiation of permanent dialysis	54	5	49
Myocardial infarction	9	2	7
Stroke or transient ischemic attack	13	0	13
Target vessel revascularization	32	2	30
Details of the cause of death	n = 95	n = 11	n = 82
Cardiovascular death	63 (66%)	7 (64%)	54 (66%)
Cardiac	59 (62%)	7 (64%)	50 (61%)
Vascular	4 (4%)	0	4 (5%)
Noncardiovascular death	32 (34%)	4 (36%)	28 (34%)
Infection	9 (10%)	1 (9%)	8 (10%)
Cancer	7 (7%)	0	7 (9%)
Renal failure	5 (5%)	3 (27%)	2 (2%)
Bleeding	3 (3%)	0	3 (4%)
Others	8 (8%)	0	8 (10%)

Values have been presented as a number, or number (%).

CIN itself was low in this study; therefore, it might be difficult to examine the influence of CIN on long-term outcomes. (3) Although clinically, CIN is observed to significantly affect patients with normal-to-mild renal dysfunction, the influence of CIN might become less significant in patients with advanced renal dysfunction in whom the overall prognosis is very poor. Thus, the definition and clinical significance of CIN in patients with advanced renal dysfunction may need to be re-evaluated.

Multivariate analysis performed in this study showed that the initiation of dialysis in patients with advanced renal dysfunction was determined in baseline renal function, and CIN was not associated with the initiation of dialysis. Moreover, in this group of patients, the occurrence of cardiac death was more common than the need for the initiation of dialysis. Of note, reportedly coronary angiography/interventions are frequently avoided in patients with advanced renal dysfunction because clinicians divert their attention to and prioritize the avoidance of the administration of the contrast agent, which may result in poor outcomes.[28,29] Our findings however suggest that if necessary, clinicians should not hesitate to proceed with an angiography/intervention in patients with advanced renal dysfunction.

There are several limitations in this study. First, despite of a multicenter study, this was a retrospective observational study, and our findings may have excluded causal inferences. Second, some important data such as presence of proteinuria were lacking. In addition, differences in CIN prevention strategies used across different centers including PCI strategies and timing of initiation of dialysis cannot be ignored. Third, patients in this study were limited to those who underwent PCI. Therefore, we could not compare the outcomes with patients who did not undergo PCI. Fourth, the study population was relatively small, especially in CIN group.

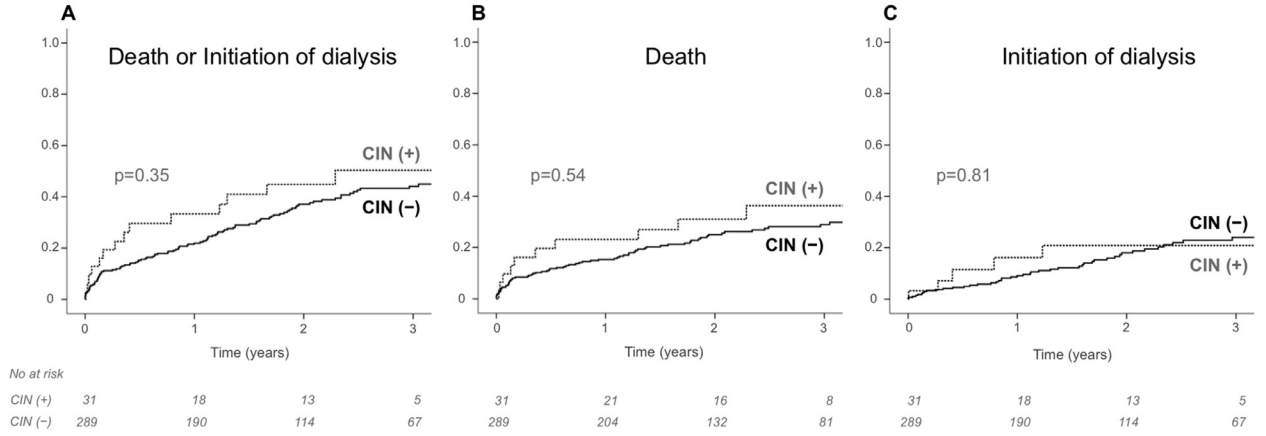

Figure 3. Kaplan-Meier curves in the patients with and without CIN: All-cause death or the initiation of dialysis; all-cause death; the initiation of dialysis. CIN = contrast-induced nephropathy.

Table 3
Cox regression analysis to assess the predictors

A. Death or the initiation of permanent dialysis Variable	Multivariate analysis		
	HR	95% CI	p Value
Age (years)	1.01	0.99−1.03	0.36
Men	1.36	0.89−2.09	0.16
Body mass index	0.92	0.87−0.97	0.003
Dyslipidemia	0.91	0.58−1.44	0.69
Anemia	1.39	0.94−2.05	0.10
eGFR<15 mL/min/1.73 m^2 (vs. 15≤eGFR<30)	3.02	1.97−4.63	<0.001
Left ventricular ejection fraction	1.00	0.98−1.01	0.50
Shock	1.97	1.04−3.71	0.04
Pulmonary congestion	1.93	1.26−2.97	0.003
Acute myocardial infarction	1.03	0.67−1.57	0.91
Intra-aortic balloon pumping	0.80	0.46−1.38	0.43
Contrast-induced nephropathy	0.79	0.41−1.55	0.50
B. Death Variable	Multivariate analysis		
	HR	95% CI	p Value
Age	1.05	1.02−1.08	0.003
Body mass index	0.90	0.84−0.96	0.002
Hypertension	0.84	0.49−1.43	0.51
Dyslipidemia	0.99	0.58−1.67	0.96
Anemia	1.20	0.75−1.92	0.44
Left ventricular ejection fraction	0.98	0.97−0.996	0.01
Shock	1.25	0.61−2.56	0.54
Pulmonary congestion	1.94	1.15−3.28	0.01
Acute myocardial infarction	1.54	0.94−2.53	0.09
Intra-aortic balloon pumping	1.26	0.69−2.29	0.46
Contrast-induced nephropathy	0.50	0.21−1.18	0.11
C. Initiation of permanent dialysis Variable	Multivariate analysis		
	HR	95% CI	p Value
Age	0.98	0.96−1.01	0.26
Men	1.99	0.99−4.02	0.05
Diabetes	1.53	0.82−2.85	0.18
Anemia	2.13	1.14−3.98	0.02
eGFR <15 mL/min/1.73 m^2 (vs. 15≤ eGFR<30)	7.20	4.03−12.87	<0.001
Peripheral artery disease	1.41	0.77−2.59	0.27
Contrast-induced nephropathy	1.38	0.53−3.63	0.51

The multivariate model includes variables showing a p value <0.1 using univariate analysis and judged to be of clinical significance.
Acute myocardial infarction = ST-segment elevation myocardial infarction or non-ST-segment elevation myocardial infarction.
CI = confidence interval; eGFR = estimated glomerular filtration rate; HR = hazard ratio.

Disclosures

Hideki Ishii received lecture fees from Astellas Pharma Inc., Astrazeneca Inc., Daiichi-Sankyo Pharma Inc., and MSD K. K. Yusuke Uemura received lecture fees from Otsuka Pharma Ltd. Itsuro Morishima received lecture fees from Daiichi-Sankyo Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Abbott Japan. Toyoaki Murohara received lecture fees from Bayel Pharmaceutical Co., Ltd., Daiichi-Sankyo Co., Ltd., Dainippon Sumitomo Pharma Co., Ltd., Kowa Co., Ltd., MSD K. K., Mitsubishi Tanabe Pharma Co., Nippon Boehringer Ingelheim Co., Ltd., Novartis Pharma K. K., Pfizer Japan Inc., Sanofi-aventis K. K., and Takeda Pharmaceutical Co., Ltd. Toyoaki Murohara received unrestricted research grant for Department of Cardiology, Nagoya University Graduate School of Medicine from Astellas Pharma Inc., Daiichi-Sankyo Co., Ltd., Dainippon Sumitomo Pharma Co., Ltd., Kowa Co., Ltd., MSD K. K., Mitsubishi Tanabe Pharma Co., Nippon Boehringer Ingelheim Co., Ltd., Novartis Pharma K. K., Otsuka Pharma Ltd., Pfizer Japan Inc., Sanofi-aventis K. K., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

1. Giacoppo D, Madhavan MV, Baber U, Warren J, Bansilal S, Witzenbichler B, Dangas GD, Kirtane AJ, Xu K, Kornowski R, Brener SJ, Genereux P, Stone GW, Mehran R. Impact of contrast-induced acute kidney injury after percutaneous coronary intervention on short- and

long-term outcomes pooled analysis from the HORIZONS-AMI and ACUITY trials. *Circ Cardiovasc Interv* 2015;8:e002475.
2. Watabe H, Sato A, Hoshi T, Takeyasu N, Abe D, Akiyama D, Kakefuda Y, Nishina H, Noguchi Y, Aonuma K. Association of contrast-induced acute kidney injury with long-term cardiovascular events in acute coronary syndrome patients with chronic kidney disease undergoing emergent percutaneous coronary intervention. *Int J Cardiol* 2014;174:57–63.
3. Yazaki Y, Iijima R, Nakamura M, Sugi K. Relationship between renal function stage and clinical outcomes after paclitaxel-eluting stent implantation. *J Cardiol* 2011;57:61–68.
4. Sadeghi HM, Stone GW, Grines CL, Mehran R, Dixon SR, Lansky AJ, Fahy M, Cox DA, Garcia E, Tcheng JE, Griffin JJ, Stuckey TD, Turco M, Carroll JD. Impact of renal insufficiency in patients undergoing primary angioplasty for acute myocardial infarction. *Circulation* 2003;108:2769–2775.
5. Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, de Jong PE, Coresh J, Gansevoort RT, Chronic Kidney Disease Prognosis. Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010;375:2073–2081.
6. Go AS, Chertow GM, Fan DJ, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004;351:1296–1305.
7. Zhang Q, Ma CS, Nie SP, Du X, Lv Q, Kang JP, Zhang Y, Hu R, Jia CQ, Liu XM, Liu XH, Dong JZ, Chen F, Zhou YJ, Lv SZ, Huang FJ, Gu CX, Wu XS. Prevalence and impact of renal insufficiency on clinical outcomes of patients undergoing coronary revascularization. *Circ J* 2007;71:1299–1304.
8. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012;120:C179–C184.
9. Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, Yamagata K, Tomino Y, Yokoyama H, Hishida A. Collaborators developing the Japanese equation for estimated GFR Collaborators developing the Japanese equation for estimated GFR. Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis* 2009;53:982–992.
10. Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, Reddan D, Investigators C. Correction of anemia with epoetin alfa in chronic kidney disease. *N Engl J Med* 2006;355:2085–2098.
11. Best PJM, Lennon R, Ting HH, Bell MR, Rihal CS, Holmes DR, Berger PB. The impact of renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary interventions. *J Am Coll Cardiol* 2002;39:1113–1119.
12. Bansal N, McCulloch CE, Rahman M, Kusek JW, Anderson AH, Xie D, Townsend RR, Lora CM, Wright J, Go AS, Ojo A, Alper A, Lustigova E, Cuevas M, Kallem R, Hsu CY, Investigators CS. Blood pressure and risk of all-cause mortality in advanced chronic kidney disease and hemodialysis the chronic renal insufficiency cohort study. *Hypertension* 2015;65:93–100.
13. Nakayama M, Sato T, Sato H, Yamaguchi Y, Obara K, Kurihara I, Sato K, Hotta O, Seino J, Miyata M, Takeuchi K, Nakayama K, Matsushima M, Otaka T, Kinoshita Y, Taguma Y, Ito S. Different clinical outcomes for cardiovascular events and mortality in chronic kidney disease according to underlying renal disease: the Gonryo study. *Clin Exp Nephrol* 2010;14:333–339.
14. Landray MJ, Emberson JR, Blackwell L, Dasgupta T, Zakeri R, Morgan MD, Ferro CJ, Vickery S, Ayrton P, Nair D, Dalton RN, Lamb EJ, Baigent C, Townend JN, Wheeler DC. Prediction of ESRD and death among people with CKD: the chronic renal impairment in Birmingham (CRIB) prospective cohort study. *Am J Kidney Dis* 2010;56:1082–1094.
15. Reddan DN, Szczech LA, Tuttle RH, Shaw LK, Jones RH, Schwab SJ, Smith MS, Califf RM, Mark DB, Owen WF. Chronic kidney disease, mortality, and treatment strategies among patients with clinically significant coronary artery disease. *J Am Soc Nephrol* 2003;14:2373–2380.
16. Komiya T, Ueno G, Kadota K, Mitsudo K, Okabayashi H, Nishiwaki N, Hanyu M, Kimura T, Tanaka S, Marui A, Sakata R. Investigators CR-K. An optimal strategy for coronary revascularization in patients with severe renal dysfunction. *Eur J Cardiothorac Surg* 2015;48:293–300.
17. Charytan DM, Varma MR, Silbaugh TS, Lovett AF, Normand SLT, Mauri L. Long-term clinical outcomes following drug-eluting or bare-metal stent placement in patients with severely reduced GFR: results of the Massachusetts Data Analysis Center (Mass-DAC) state registry. *Am J Kidney Dis* 2011;57:202–211.
18. Tsai TT, Patel UD, Chang TI, Kennedy KF, Masoudi FA, Matheny ME, Kosiborod M, Amin AP, Messenger JC, Rumsfeld JS, Spertus JA. Contemporary incidence, predictors, and outcomes of acute kidney injury in patients undergoing percutaneous coronary interventions. *JACC-Cardiovasc Interv* 2014;7:1–9.
19. McCullough PA. Contrast-induced acute kidney injury. *J Am Coll Cardiol* 2008;51:1419–1428.
20. Ogata N, Ikari Y, Nanasato M, Okutsu M, Kametani R, Abe M, Uehara Y, Sumitsuji S. Safety margin of minimized contrast volume during percutaneous coronary intervention in patients with chronic kidney disease. *Cardiovasc Interv Ther* 2014;29:209–215.
21. Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, Mintz GS, Lansky AJ, Moses JW, Stone GW, Leon MB, Dangas G. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention – development and initial validation. *J Am Coll Cardiol* 2004;44:1393–1399.
22. Kim JH, Yang JH, Choi SH, Bin Song Y, Hahn JY, Choi JH, Lee SH, Gwon HC. Predictors of outcomes of contrast-induced acute kidney injury after percutaneous coronary intervention in patients with chronic kidney disease. *Am J Cardiol* 2014;114:1830–1835.
23. Abe M, Morimoto T, Akao M, Furukawa Y, Nakagawa Y, Shizuta S, Ehara N, Taniguchi R, Doi T, Nishiyama K, Ozasa N, Saito N, Hoshino K, Mitsuoka H, Toma M, Tamura T, Haruna Y, Kita T, Kimura T. Relation of contrast-induced nephropathy to long-term mortality after percutaneous coronary intervention. *Am J Cardiol* 2014;114:362–368.
24. Newhouse JH, Kho D, Rao QA, Starren J. Frequency of serum creatinine changes in the absence of iodinated contrast material: implications for studies of contrast nephrotoxicity. *Am J Roentgenol* 2008;191:376–382.
25. Bruce RJ, Djamali A, Shinki K, Michel SJ, Fine JP, Pozniak MA. Background fluctuation of kidney function versus contrast-induced nephrotoxicity. *Am J Roentgenol* 2009;192:711–718.
26. Weisbord SD, Chen HY, Stone RA, Kip KE, Fine MJ, Saul MI, Palevsky PM. Associations of increases in serum creatinine with mortality and length of hospital stay after coronary angiography. *J Am Soc Nephrol* 2006;17:2871–2877.
27. Valle JA, McCoy LA, Maddox TM, Rumsfeld JS, Ho PM, Casserly IP, Nallamothu BK, Roe MT, Tsai TT, Messenger JC. Longitudinal risk of adverse events in patients with acute kidney injury after percutaneous coronary intervention insights from the National Cardiovascular Data Registry. *Circ Cardiovasc Interv* 2017;10:e004439.
28. Chertow GM, Normand SLT, McNeil BJ. "Renalism": inappropriately low rates of coronary angiography in elderly individuals with renal insufficiency. *J Am Soc Nephrol* 2004;15:2462–2468.
29. Charytan DM, Setoguchi S, Solomon DH, Avorn J, Winkelmayer WC. Clinical presentation of myocardial infarction contributes to lower use of coronary angiography in patients with chronic kidney disease. *Kidney Int* 2007;71:938–945.