# POST-CONTRAST ACUTE KIDNEY INJURY AFTER CATHETER ANGIOGRAPHY AND EVALUATION OF RISK FACTORS

Makoto Koga, Koichi Ishiyama, Tomoki Tozawa, Motoko Sasajima, Kento Hatakeyama and Manabu Hashimoto

Department of Radiology, Akita University School of Medicine,

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#### Abstract

**Purpose :** The present study aimed to determine the rate of post-contrast acute kidney injury (PC-AKI) after catheter angiography other than cardiac angiography (CAG), and identify relevant risk factors.

**Materials and methods :** This retrospective study analyzed data from 314 patients who underwent angiography between October 2013 and September 2018. We investigated the incidence of PC-AKI, defined as a  $\geq$ 50% increase or  $\geq$ 0.3 mg/dL increase in serum creatinine (SCr) values 1-3 days after angiography according to the European Society of Urogenital Radiology guidelines on contrast media, version 10.0. The effects of patient- and procedure-related factors on the incidence of PC-AKI were evaluated. Data were analyzed using chi-squared and Mann-Whitney *U* tests, and multivariate logistic regression analysis.

**Results :** PC-AKI developed in 16/314 patients (5.1%). Multivariate logistic regression analysis revealed a correlation of incidence of PC-AKI with advanced age, decreased estimated glomerular filtration rate (eGFR), shock symptoms, and high-dose contrast media within 24 hours. In all patients with PC-AKI, SCr values returned to baseline within 2 weeks.

**Conclusions :** PC-AKI after angiographic examinations developed in 5.1% of patients, and the increase in SCr was reversible. Advanced age, decreased eGFR, shock symptoms, and high-dose contrast media within 24 hours are possible risk factors.

Key words: PC-AKI, post-contrast acute kidney injury, CIN, contrast-induced nephropathy

# INTRODUCTION

Iodinated contrast medium is an essential component of diagnostic imaging procedures such as fluoroscopy, computed tomography (CT), and catheter angiography. The side effects of its intravascular use in these procedures are the third most critical cause of hospital-acquired renal insufficiency, after decreased renal blood flow and drug-related causes<sup>1)</sup>. Acute kidney injury (AKI) caused by iodinated contrast medium is generally reversible and resolves within a few weeks; however, a small number of patients who develop AKI after contrast administration subsequently undergo dialysis treatment<sup>2)</sup>.

Contrast-induced nephropathy (CIN) has been widely used as diagnostic criterion for AKI caused by iodinated contrast medium, and several previous studies have demonstrated the incidence, risk factors, and prevention of CIN<sup>3-18)</sup>. Most of these studies targeted patients who underwent contrast-enhanced CT or cardiac angiography

Corresponding author: Makoto Koga, MD

Department of Radiology, Akita University School of Medicine, 44-2 Hasunuma Hiroomote, Akita 010-8543, Japan Tel: +81-18-834-1111

Fax: +81-18-836-2623

E-mail: makoto@doc.med.akita-u.ac.jp

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(CAG), and few have targeted angiographic examinations other than CAG. The incidence of CIN after catheter treatment may be affected by patients' baseline characteristics. In our department, we perform catheter angiography mainly on peripheral blood vessels. In contrast to patients who undergo CAG, fewer of the patients who undergo angiography on peripheral blood vessels have heart disease, and embolization is performed for treatment of bleeding, aneurysms, and tumors. The present study was conducted to evaluate the incidence of CIN in our catheter angiography department, and focused on peripheral vascular procedures. The European Society of Urogenital Radiology (ESUR) guidelines on contrast media, version 10.0, published in 201819, newly defined post-contrast acute kidney injury (PC-AKI) as a >50% increase or >0.3 mg/dL increase in serum creatinine (SCr) values at 48-72 hours, consistent with the Kidney Disease Improving Global Outcomes (KDIGO) AKI guidelines<sup>20)</sup>. The frequency of AKI following iodinated contrast medium administration depends on which diagnostic criteria are used ; in particular, SCr values before iodinated contrast medium administration are thought to have a significant impact on its frequency.

The present retrospective study aimed to determine the incidence of PC-AKI according to the new diagnostic criteria and identify the risk factors for PC-AKI in patients who underwent catheter angiography other than CAG.

#### MATERIAL AND METHODS

### Patient selection

Of a cumulative total of 1,458 patients who underwent catheter angiography by radiologists at our institution between October 2013 and September 2018, we excluded patients who had received anticancer treatment in the 3 days prior to angiography ; those who were undergoing maintenance hemodialysis ; and those who had incomplete data regarding the following : baseline SCr and hemoglobin values before catheter angiography, SCr values within three days after angiography for a diagnosis of PC-AKI, type and dose of contrast medium injected, weight, medical history, vital signs, and contents of intravenous drip infusion. The data of a final total of 314 patients were included for analysis [Figure 1].

This retrospective study was approved by the Ethics Committee of our institution, and the requirement for informed consent was waived. All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of our institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients were informed about the disclosure of information on our institutional home page and were able to opt out of this study.

#### Definitions and analysis of data

The baseline laboratory values were those obtained at the last blood examination before angiography. PC-AKI was defined as a >50% increase or >0.3 mg/dL increase in serum creatinine (SCr) values 1-3 days after angiography, according to the European Society of Urogenital Radiology (ESUR) guidelines on contrast media, version 10.0; and contrast-induced nephropathy (CIN) was defined as a >25% increase or >0.5 mg/dL increase in SCr values within 3 days of angiography.

The incidence of PC-AKI in the 314 patients was obtained from their medical records. Also recorded and investigated with respect to their effect on the incidence of PC-AKI were patients' age; sex; history of diabetes mellitus, heart disease (e.g., chronic heart failure, ischemic heart disease), hypertension, dyslipidemia and hyperuricemia; values of serum creatinine, estimated glomerular filtration rate (eGFR), and serum hemoglobin; bodyweight; the incidence of bleeding and shock symptoms; iodine dose per bodyweight (during angiography, and the total within 24 hours of angiography); first-pass renal exposure to contrast media; intra-renal arterial injection of contrast media; and saline hydration before angiography. We recorded the dose of iodine dose per bodyweight during angiography and also the total dose within 24 hours of angiography to investigate the effect of repeated contrast medium injection over a short time interval. First-pass renal exposure to contrast medium was defined as contrast injection into the renal artery or suprarenal aorta. Shock was defined clinically as a rapid decrease in blood pressure and impaired consciousness. We considered patients to have a diagnosis



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Fig. 1. Patients selection flow

After applying exclusion criteria, the data of a final total of 314 patients were included for analysis.

of shock if these symptoms had been recorded in the medical record by the attending physician. Intravenous saline infusion was defined as infusion of 500 ml or more of physiological saline for the purpose of preventing decreased renal function. In all cases, saline infusion was within 24 hours prior to angiography. The definitions of advanced age, decreased eGFR, low and high bodyweight, and high iodine dose are provided in Tables 1 and 2. Anemia was defined as the standard lower limit of hemoglobin (<13.7 g/dL in males, <11.6 g/dL in females).

These factors were compared among patients with PC-AKI using Pearson's Chi-squared test with Yates' continuity correction, Mann-Whitney U test, and multivariate logistic regression analysis. The data were analyzed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan)<sup>21)</sup>. P values <0.05 were considered to indicate statistical significance. Among the candidate risk factors mentioned above, factors with a p value <0.15 in the univariate analysis were included in multivariate logistic regression analysis, including first-pass renal exposure to contrast media, according to the ESUR guidelines on contrast media, version 10.0.

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#### RESULTS

# Baseline characteristics and procedure-related parameters

The baseline characteristics and procedure-related parameters of all 314 patients are shown in Tables 1 and 2. Mean age was  $61.2 \pm 15.6$  years, and 148 (47.1%) were female. We show the mean of bodyweight, the numbers of advanced age, lower bodyweight, diabetes mellitus, previous history of heart failure, hypertension, dyslipidemia, hyperuricemia, decreased eGFR, anemia, bleeding and shock symptoms in Table 1. And we show type of contrast medium used for angiography, the mean of contrast medium dose, the number of high dose of contrast medium, intra-arterial injection, first-pass renal exposure, intra-renal arterial injection, interventional therapeutic procedure, urgent catheter angiography and contrast-enhanced computed tomography (CT) obtained within 24 hours of angiography in Table 2. Additionally, we show details of interventional therapeutic procedure in 211 cases in Table 3. Renal arteriography procedures were performed in 29 cases, the breakdown is that only angiography is 2, TAE for renal artery true aneurysm is 5, TAE for renal hemorrhage, pseudo-aneurysm, ruptured AML is 8, TAE for arteriovenous fistula is 4, TAE for unruptured renal AML is 9 and PTA for renal artery stenosis is 1. In regard to renal arterial embolization, in the case of aneurysms, packing was performed and parental patency was well maintained, and renal infarction could be minimized by superselective treatment of AML, AVF, and bleeding. Therefore, we determined that embolization had a limited effect on renal function, and included these patients in the study.

## Incidence of PC-AKI and related risk factors

Table 4 shows the incidence and severity of PC-AKI in

	All patients $(n = 314)$
Age (years)	$61.2 \pm 15.6 (20-90)$
Advanced age ( $\geq$ 70 years)	110 (35.0%)
Sex	
Female	148 (47.1%)
Male	166 (52.9%)
Bodyweight (kg)	$58.9 \pm 11.6  (35.6  107)$
Lower bodyweight (<50 kg)	76 (24.2%)
Diabetes mellitus	42 (13.4%)
Previous history of heart failure	17 (5.4%)
Hypertension	110 (35.0%)
Dyslipidemia	37 (11.2%)
Hyperuricemia	20 (6.4%)
Serum creatinine (mg/dL)	$0.75 \pm 0.35  (0.26  2.71)$
>1.0 mg/dL	46 (14.6%)
eGFR (mL/min/1.73 m <sup>2</sup> )	$84.5 \pm 30.5  (19.3  222.2)$
Decreased eGFR (<45 mL/min/1.73 m <sup>2</sup> )	29 (9.2%)
Serum hemoglobin (g/dL)	$11.6 \pm 2.5 (4.6 - 17.3)$
Anemia	187 (59.6%)
Bleeding	113 (36.0%)
Shock symptoms	30 (9.6%)

Table 1. Patients' baseline characteristics

Data are presented as the mean  $\pm$  standard deviation (range) or number of patients (percentage).

PC-AKI : post-contrast acute kidney injury, eGFR : estimated glomerular filtration rate

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	All parients $(n=314)$
Type of CM used for angiography	
Non-ionic, monomeric iodinated CM	308 (98.1%)
Ionic monoacidic dimeric CM	6 (1.9%)
CM dose used for angiography (mg I/kg)	$816 \pm 392 \ (89-2,667)$
High dose during angiography ( $\geq$ 1,000 mg I/kg)	82 (26.1%)
CECT obtained within 24 hours of angiography	104 (33.1%)
Total CM dose within 24 hours of angiography (mg I/kg)	$951 \pm 442 \ (89 - 3,048)$
High dose within 24 hours of angiography ( $\geq$ 1,000 mg I/kg)	120 (38.2%)
Intravenous saline infusion before angiography	22 (7.0%)
Urgent catheter angiography	99 (31.5%)
Intra-arterial CM injection	283 (90.1%)
First-pass renal exposure of CM	35 (11.1%)
Intra-renal arterial CM injection	29 (9.2%)
Interventional therapeutic procedure	211 (67.2%)

#### Table 2. Procedure-related parameters

Data are presented as the mean  $\pm$  standard deviation (range) or number of patients (percentage).

PC-AKI: post-contrast acute kidney injury, CM: contrast media, CECT: contrast-enhanced computed tomography

Table 3.	Details of interventional therapeutic proce-
	dures in 211 patients

	All parients ( $n=211$ )
TAE (not for hemorrhage)	83
head and neck	21
spine	8
chest	5
abdomen and pelvis	48
lower extremities	1
TAE (for hemorrhage)	72
chest	14
abdomen and pelvis	58
Placement of port-catheter system	12
TVE for cranial dural AVF	15
PTPE	12
BRTO	7
PTA or stent implantation	10

Data are presented as number of patients.

TAE : transcatheter arterial embolization, PTA : percutaneous transluminal angioplasty, TVE : transvenous embolization, AVF : arteriovenous fistula, PTPE : Percutaneous Transhepatic Portal vein Embolization, BRTO : balloom occluded retrograde transvenous obliteration

Table 4. Incluence of r C-AKI and Chy	Table 4.	Incidence	of PC-AKI	and CIN
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	All patients $(n = 314)$
PC-AKI	16 (5.1%)
>50% increase in SCr value	9 (2.9%)
>0.3 mg/dL increase in SCr value	14 (4.5%)
both >50% and 0.3 mg/dL increase in SCr value	7 (2.2%)
CIN	25 (8.0%)
>25% increase in SCr value	25 (8.0%)
>0.5 mg/dL increase in SCr value	9 (2.9%)
both >25% and 0.5 mg/dL increase in SCr value	9 (2.9%)

Data are presented as the number of patients (percentage).

PC-AKI: post-contrast acute kidney injury, SCr: serum creatinine, CIN: contrast-induced nephropathy

the 314 patients. PC-AKI occurred in 16/314 (5.1%) patients, all of whom subsequently improved and showed a return to baseline of SCr values within 2 weeks (mean time to baseline, 2.9 days) [Table 5]. Comparisons of patient- and procedure-related factors in patients with and without PC-AKI are shown in Table 6. PC-AKI developed in 6 (20.7%) of the 29 patients with decreased PC-AKI after catheter angiography

	Patients with PC-AKI ( $n = 16$ )
Baseline eGFR (mL/min/1.73 m <sup>2</sup> )	$57.1 \pm 27.9 (22.7 - 132.0)$
Baseline SCr (mg/dL)	$1.12 \pm 0.53 \ (0.45 - 2.62)$
Peak SCr value at 2-3 days (mg/dL)	$1.76 \pm 0.80 \ (0.71  3.35)$
Increase of SCr (mg/dL)	$0.64 \pm 0.45 \ (0.26  1.83)$
Increase rate of SCr (%)	$61.4 \pm 34.6 \ (19.2  130.0)$
Time for SCr to return to baseline value (days)	$2.9 \pm 3.1 (1-14)$

Table 5. SCr value over time in patients with PC-AKI

Data are presented as the mean  $\pm$  standard deviation (range).

PC-AKI: Post-contrast acute kidney injury, eGFR: estimated glomerular filtration rate, SCr: serum creatinine

	With PC-AKI $(n = 16)$	Without PC-AKI $(n = 298)$	Incidence of PC-AKI (%)	<i>p</i> value
Advanced age	10 ( 62.5%)	100 (33.6%)	9.1	0.036*
Female	7 (43.8%)	141 (47.3%)	4.7	0.983
Lower bodyweight (<50 kg)	2 ( 12.5%)	74 (24.8%)	2.6	0.411
Diabetes mellitus	3 ( 18.8%)	39 (13.1%)	7.1	0.786
Previous history of heart failure	1 ( 6.2%)	16 ( 5.4%)	5.9	1.000
Hypertension	6 ( 37.5%)	104 (34.9%)	5.5	1.000
Dyslipidemia	2 ( 12.5%)	35 (11.7%)	5.4	1.000
Hyperuricemia	2 ( 12.5%)	18 ( 6.0%)	10.0	0.613
Decreased eGFR (<45 ml/min/1.73 m <sup>2</sup> )	6 ( 37.5%)	23 ( 7.7%)	20.7	< 0.001*
Anemia	15 ( 93.8%)	172 (57.7%)	8.0	0.009*
Bleeding	13 ( 81.2%)	100 (33.6%)	11.5	0.087
Shock symptoms	9 ( 56.2%)	21 ( 7.0%)	30.0	< 0.001*
High dose during angiography ( $\geq$ 1,000 mg I/kg)	6 ( 37.5%)	76 (25.5%)	7.3	0.440
High dose within 24 hours (≥1,000 mg I/kg)	12 ( 75.0%)	108 (36.2%)	10.0	0.004*
Intravenous saline infusion before angiography	1 ( 6.2%)	21 ( 7%)	4.5	1.000
Intra-arterial CM injection	16 (100.0%)	267 (89.6%)	5.7	0.353
First-pass renal exposure of CM	3 ( 18.8%)	32 (10.7%)	8.6	0.559
Intra-renal arterial CM injection	2 ( 12.5%)	27 ( 9.1%)	6.9	0.984
Interventional therapeutic procedure	12 ( 75.0%)	199 (66.8%)	5.7	0.683

Table 6. Comparison of patient- and procedure-related factors with and without PC-AKI

Data are presented as the number of patients (percentage).

Statistical analyses were performed using chi-squared and Mann-Whitney U tests. P values <0.05 are considered to indicate significance.

PC-AKI: post-contrast acute kidney injury, eGFR: estimated glomerular filtration rate, CM: contrast media \*Statistically significant

eGFR ; thus, decreased eGFR was correlated with PC-AKI ( $\phi < 0.001$ ). PC-AKI was also correlated with advanced age ( $\phi = 0.036$ ), anemia ( $\phi = 0.009$ ), bleeding ( $\phi < 0.001$ ), shock symptoms ( $\phi < 0.001$ ), and high iodine dose within 24 hours of angiography ( $\phi = 0.004$ ). Multivariate logistic regression analysis performed for advanced age, decreased eGFR, anemia, bleeding, shock symptoms, high dose within 24 hours and first-pass renal exposure revealed a correlation of PC-AKI with advanced age (p = 0.025), decreased eGFR (p = 0.040), shock

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	odd ratio	95% confidence interval	<i>p</i> value
Advanced age ( $\geq$ 70 years)	4.47	1.20-16.60	0.025*
Decreased eGFR (<45 mL/min/1.73 m <sup>2</sup> )	4.41	1.07-18.10	0.040*
Anemia	4.66	0.51 - 42.50	0.172
Bleeding	1.56	0.29- 8.41	0.602
Shock symptoms	13.6	2.87-64.50	0.001*
High dose CM within 24 hours ( $\geq$ 1,000 mg I/kg)	7.28	1.70-31.20	0.007*
First-pass renal exposure of CM	4.51	0.74-27.30	0.101

Table 7. Multivariate analysis of risk factors for PC-AKI

Data are presented as the mean  $\pm$  standard deviation (range) or number of patients (percentage). Statistical analyses were performed using chi-squared and Mann-Whitney *U* tests. *P* values <0.05 are considered to indicate significance.

PC-AKI: post-contrast acute kidney injury, eGFR: estimated glomerular filtration rate, CM: contrast media

\*Statistically significant

symptoms (p = 0.001) and high dose within 24 hours (p = 0.007) [Table 7]. The flow of data analysis is shown in Figure 2.

#### DISCUSSION

The most widely used diagnostic criterion for AKI due to iodinated contrast medium is contrast-induced nephropathy (CIN), defined as a >25% increase or >0.5mg/dL increase in SCr values within 72 hours<sup>22)</sup>. The European Society of Urogenital Radiology (ESUR) guidelines on contrast media, version 10.0, published in 2018<sup>19)</sup>, newly defined post-contrast acute kidney injury (PC-AKI) as a >50% increase or >0.3 mg/dL increase in serum creatinine (SCr) values at 48-72 hours, consistent with the Kidney Disease Improving Global Outcomes (KDIGO) AKI guidelines<sup>20)</sup>. The frequency of AKI following administration of iodinated contrast medium depends on which diagnostic criteria are used. In patients with baseline SCr values <1.2 mg/dL, the SCr values for PC-AKI are higher than those for CIN. On the other hand, in patients with baseline SCr values >1.2 mg/dL, the SCr values for PC-AKI are lower than those for CIN [Figure 3]. Therefore, in patients with original renal dysfunction, the diagnostic criteria for PC-AKI might be more sensitive than those for CIN. In addition, the diagnostic criteria for PC-AKI are limited to 48-72 hours, which might also have the decreased the frequency.

The reported incidence of nephropathy after injection of contrast medium varies among studies, possibly due to differences in the selected patients and the diagnostic criteria. For example, the incidence of nephropathy has been reported as 2.1%-11.5% in patients who underwent CT with intravenous iodinated medium<sup>3-6)</sup>, 1.4%-16.5% in those who underwent  $CAG^{7-11}$ ; and as <5% in patients with intact renal function, 20%-30% in patients with renal failure, and >30% in patients with diabetic nephropathy<sup>12)</sup>. In the present study, the incidence of PC-AKI in all 314 patients was 5.1%, and that of CIN, which is the traditional diagnostic criterion, was 8.0%; thus, the incidence of PC-AKI was less than that of CIN. We consider that the reason for the lower incidence of PC-AKI compared with CIN might be because the present study included few patients with SCr values >1.2 mg/dL (28, 8.9%) and the period for diagnosis was limited to 1-3 davs.

Several studies have reported an association of CIN with chronic renal failure, diabetes mellitus, advanced age, shock symptoms, congestive heart failure, dehydration, anemia, dose of contrast medium, and type of contrast medium<sup>12-15</sup>. Another study found that diabetes mellitus alone is not necessarily a risk factor for CIN, but it becomes such when combined with renal dysfunction<sup>16</sup>. In addition, performing contrast CT at short intervals<sup>17,18</sup> and first-pass renal exposure to contrast media<sup>19</sup> have been reported as risk factors. Mehran *et al.* 

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#### PC-AKI after catheter angiography



#### Fig. 2. Data analysis flow

PC-AKI was correlated with decreased eGFR, advanced age, anemia, bleeding, shock symptoms, and high iodine dose within 24 hours of angiography. Multivariate logistic regression analysis performed for advanced age, decreased eGFR, anemia, bleeding, shock symptoms, high dose within 24 hours and first-pass renal exposure revealed a correlation of PC-AKI with advanced age, decreased eGFR, shock symptoms and high dose within 24 hours.

devised a method for evaluating the risk for CIN, including factors such as dehydration, cardiac insufficiency, advanced age, anemia, diabetes mellitus, renal function degeneration, and high dose of injected contrast medium<sup>13)</sup>. Several studies have reported that intravenous infusion of saline solution is effective for preventing CIN<sup>23-26)</sup>. Tsushima *et al.* reported that chronic and acute kidney disease were identified as risk factors for CIN at almost all institutions, and intravenous drip infusion of saline and reduction of contrast media volume were generally performed to prevent CIN in these patients. They also reported that at almost all institutions in Japan, patients with risk factors for CIN receive intravenous drip infusion of saline and reduction of contrast media volume to



Fig. 3. SCr levels for diagnosis of CIN and PC-AKI The line graph shows SCr levels after contrast administration, for diagnosis of CIN or PC-AKI corresponding to the baseline SCr levels. For baseline SCr values <1.2 mg/dL, the SCr values diagnosed as PC-AKI after contrast administration are higher than those diagnosed as CIN. For baseline SCr values >1.2 mg/dL, however, the SCr values diagnosed as PC-AKI are lower than those diagnosed as CIN.

CIN: contrast-induced nephropathy, PC-AKI: post-contrast acute kidney injury, SCr: serum creatinine

prevent CIN when undergoing examinations with iodinated contrast media<sup>27)</sup>.

In the present study, the incidence of PC-AKI was correlated with advanced age ( $\geq 70$  years) (p = 0.020), decreased eGFR (p < 0.040), shock symptoms (p = 0.001), and injection of high-dose contrast medium within 24 hours of angiography (p = 0.007). However, PC-AKI was not significantly correlated with first-pass renal exposure to contrast media, which is indicated as a risk factor for PC-AKI in the ESUR guidelines on contrast media, version 10.0<sup>19</sup>. In 35 patients with first-pass renal exposure to contrast media, transcatheter arterial embolization (TAE) was performed for renal hemorrhage, pseudo-aneurysm and arteriovenous fistula in 12 patients (34.3%), and percutaneous transluminal angioplasty was performed in 1 patient (2.9%) [Table 1]. Accordingly, we thought that the interventional procedure could possibly have improved renal function in some of these cas-In addition, in the present study, there was no staes.

tistically significant association of PC-AKI with any of diabetes mellitus, iodine dose during angiography, or intravenous saline infusion, which did show an association with CIN in several previous studies<sup>12-15)</sup>. Because the number of cases in the present study was small, further studies with more cases are needed in the future to confirm the present results.

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Although it is known that AKI after contrast medium administration is generally transient and usually improves within a few weeks<sup>28)</sup>, some studies have reported a significant relationship between CIN and short- or long-term mortality<sup>29-31)</sup>. Therefore, we consider that we should always attempt to prevent AKI after contrast medium administration. Among the risk factors for AKI, it is relatively easy to control factors related to iodinated contrast medium administration; therefore, we should reduce the volume of contrast medium administered and avoid repeated contrast injections within a short interval as much as possible. For example, pa(30)

## PC-AKI after catheter angiography

	With advanced age $(n = 110)$	Without advanced age $(n = 204)$	<i>p</i> value
Sex			
Female	56 (50.9%)	92 (45.1%)	0.387
Male	54 (49.1%)	112 (54.9%)	
Bodyweight (kg)	$55.3 \pm 9.5$ (35.6-80.5)	$60.8 \pm 12.2$ (37.5-107)	< 0.001*
Lower bodyweight (<50 kg)	36 (32.7%)	40 (19.6)	0.142
Diabetes mellitus	19 (17.3%)	23 (11.3%)	0.188
Previous history of heart failure	7 ( 6.4%)	0 (0%)	< 0.001*
Hypertension	48 (43.6%)	62 (30.4%)	0.026
Dyslipidemia	17 (15.5%)	20 ( 9.8%)	0.194
Hyperuricemia	3 ( 2.7%)	17 ( 8.3%)	0.089
Serum creatinine (mg/dL)	$0.77 \pm 0.31$ (0.33-1.67)	$0.73 \pm 0.37$ (0.26-2.71)	0.138
>1.0 mg/dL	18 (16.4%)	28 (13.7%)	0.643
eGFR (mL/min/1.73 m <sup>2</sup> )	$75.1 \pm 26.6$ (23.9-139.7)	$89.5 \pm 31.3$ (19.3-222.2)	< 0.001*
Decreased eGFR (<45 mL/min/1.73 m <sup>2</sup> )	13 (11.8%)	16 ( 7.8%)	0.339
Serum hemoglobin (g/dL)	$11.1 \pm 2.4$ (5.8-15.8)	$\begin{array}{c} 11.8 \pm 2.5 \\ (4.6017.6) \end{array}$	0.021*
Anemia	72 (65.5%)	115 (56.4%)	0.149
Bleeding	45 (40.9%)	68 ( 3.3%)	0.226
Shock symptoms	12 (10.9%)	18 ( 8.8%)	0.69

Table 8.	Comparison of patien	ts' baseline characteristics	s with and without advanced age

Data are presented as the mean  $\pm$  standard deviation (range) or number of patients (percentage). Statistical analyses were performed using chi-squared and Mann-Whitney *U* tests. *P* values <0.05 are considered to indicate significance.

eGFR: estimated glomerular filtration rate

\*Statistically significant

tients with acute trauma or hemorrhagic shock occasionally undergo TAE after contrast-enhanced CT. In such cases, we consider that the volume of contrast medium should be reduced in both TAE and CT. In addition, intravenous saline infusion can be given to prevent PC-AKI, especially in patients with risk factors.

This study has some limitations. First, the number of patients included in this study was relatively small. Therefore, the statistical analysis was limited. Second, the study design was retrospective. Because the exact time of blood collection was uncertain in some patients, we defined the period of PC-AKI as 1-3 days rather than 48-72. In addition, the number of days from blood sampling at baseline to catheter angiography was not fixed, and there was variation in the number of samples ob-

tained and the timings used to determine PC-AKI at 1-3 days after angiography. Therefore, the baseline parameter values and the determination of PC-AKI might be uncertain. Some of the present patients with decreased eGFR underwent intravenous infusion of saline to prevent renal dysfunction, but the volume of saline and the infusion rate varied by patient. It is known that advanced age had correlation of anemia, renal dysfunction. In this study, advanced age was not correlated with decreased eGFR (p = 0.039) or anemia (p = 0.149), but correlated with eGFR (p < 0.001) and serum hemoglobin (p = 0.021) [Table 8]. Therefore we thought that these factors might have confounding effects.

#### Conclusion

In this study, PC-AKI developed in 5.1% of patients after angiographic examinations other than CAG. All patients with PC-AKI showed improvement and SCr values returned to baseline within a few weeks. Advanced age. decreased eGFR, shock symptoms, and high-dose contrast media within 24 hours of angiography are possible risk factors for PC-AKI after angiography. Among these, the volume of contrast medium administered is the easiest to control and should therefore also be reduced in other examinations that are repeated within a short interval, as well as in angiographic examinations other than CAG. In recent years, the use of low-energy CT images created with dual-energy CT has improved the detectability of contrast medium in CT examinations, which will enable use of a reduced volume of iodinated contrast medium in patients with renal dysfunction<sup>32-34</sup>. We consider that the volume could also be reduced by evaluating the CT images in detail prior to the angiographic examination, to carefully select the blood vessels to be imaged.

# Conflicts of interest : COI

The authors declare no conflicts of interest associated with this manuscript.

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#### REFERENCES

- Nash, K., Hafeez, A. and Hou, S. (2002) Hospitalacquired renal insufficiency. *Am. J. Kidney Dis.*, 39, 930–936.
- Morcos, S.K. (1998) Contrast media-induced nephrotoxicity — questions and answers. *Br. J. Radiol.*, 71, 357-365.
- Hipp, A., Desai, S., Lopez, C. and Sinert, R. (2008) The incidence of contrast-induced nephropathy in

trauma patients. Eur. J. Emerg. Med., 15, 134-139.

- Rashid, A.H., Brieva, J.L. and Stokes, B. (2009) Incidence of contrast-induced nephropathy in intensive care patients undergoing computerised tomography and prevalence of risk factors. *Anaesth. Intensive Care*, 37, 968-975.
- Weisbord, S.D., Mor, M.K., Resnick, A.L., Hartwig, K.C., Palevsky, P.M. and Fine, M.J. (2008) Incidence and outcomes of contrast-induced AKI following computed tomography. *Clin. J. Am. Soc. Nephrol.*, 3, 1274-1281.
- McGillicuddy, E.A., Schuster, K.M., Kaplan, L.J., Maung, A.A., Lui, F.Y., Maerz, L.L. and Davis, K.A. (2010) Contrast-induced nephropathy in elderly trauma patients. *J. Trauma*, 68, 294-297.
- Rihal, C.S., Textor, S.C., Grill, D.E., *et al.* (2002) Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation*, 105, 2259–2264.
- Weisbord, S.D., Hartwig, K.C., Sonel, A.F., Fine, M.J. and Palevsky, P. (2008) The incidence of clinically significant contrast-induced nephropathy following non-emergent coronary angiography. *Catheter. Cardiovasc. Interv.*, **71**, 879-885.
- McCullough, P.A., Wolyn, R., Rocher, L.L., Levin, R.N. and O'Neill, W.W. (1997) Acute renal failure after coronary intervention : incidence, risk factors, and relationship to mortality. *Am. J. Med.*, **103**, 368–375.
- Iakovou, I., Dangas, G., Mehran, R., *et al.* (2003) Impact of gender on the incidence and outcome of contrast-induced nephropathy after percutaneous coronary intervention. *J. Invasive Cardiol.*, 15, 18-22.
- Jabara, R., Gadesam, R.R., Pendyala, L.K., Knopf, W.D., Chronos, N., Chen, J.P., Viel, K., King, S.B. 3rd and Manoukian, S.V. (2009) Impact of the definition utilized on the rate of contrast-induced nephropathy in percutaneous coronary intervention. *Am. J. Cardiol.*, 103, 1657-1662.
- Morcos, S.K. (1999) Contrast-media-induced nephrotoxicity : a consensus report. Contrast Media Safety Committee, European Society of Urogenital Radiology (ESUR). *Eur. Radiol.*, 9, 1602– 1613.
- 13) Mehran, R., Aymong, E.D., Nikolsky, E., et al. (2004)

(32)

A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention : development and initial validation. *J. Am. Coll. Cardiol.*, **44**, 1393–1399.

- 14) Cigarroa, R.G., Lange, R.A., Williams, R.H. and Hillis, L.D. (1989) Dosing of contrast material to prevent contrast nephropathy in patients with renal disease. *Am. J. Med.*, 86, 649-652.
- 15) Abe, M., Kimura, T., Morimoto, T., Furukawa, Y. and Kita, T. (2009) Incidence of and risk factors for contrast-induced nephropathy after cardiac catheterization in Japanese patients. *Circ. J.*, 73, 1518-1522.
- McCullough, P.A. (2008) Contrast-induced acute kidney injury. J. Am. Coll. Cardiol., 51, 1419-1428.
- Trivedi, H. and Foley, W.D. (2010) Contrast-induced nephropathy after a second contrast exposure. *Ren. Fail.*, 32, 796-801.
- 18) Hong, S.I., Ahn, S., Lee, Y.S., Kim, W.Y., Lim, K.S., Lee, J.H. and Lee, J.L. (2016) Contrast-induced nephropathy in patients with active cancer undergoing contrast-enhanced computed tomography. *Support. Care Cancer*, 24, 1011–1017.
- ESUR Contrast Media Safety Committee. ESUR guidelines on contrast media, version 10.0. European Society of Urogenital Radiology. http://www. esur-cm.org/index.php/en/ Accessed November 28, 2018.
- Kidney disease : improving global outcomes (KDIGO) acute kidney injury work group (2012) KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl*, 2, 1-138.
- Kanda, Y. (2013) Investigation of the freely available easy-to-use software 'EZR' for medical statistics. *Bone Marrow Transpl.*, 48, 452-458.
- 22) Stacul, F, van der Molen, A.J., Reimer, P, *et al.* (2011) Contrast induced nephropathy : updated ESUR Contrast Media Safety Committee guidelines. *Eur. Radiol.*, 21, 2527-2541.
- Eisenberg, R.L., Bank, W.O. and Hedgcock, M.W. (1980) Renal failure after major angiography. *Am. J. Med.*, 68, 43-46.
- 24) Eisenberg, R.L., Bank, W.O. and Hedgock, M.W. (1980) Renal failure after major angiography can be avoided with hydration. *AJR. Am. J. Roentgenol.*, 136, 859–861.
- 25) Trivedi, H.S., Moore, H., Nasr, S., Aggarwal, K.,

Agrawal, A., Goel, P. and Hewett, J. (2003) A randomized prospective trial to assess the role of saline hydration on the development of contrast nephrotoxicity. *Nephron Clin. Pract.*, **93**, C29-34.

- 26) Mueller, C., Buerkle, G., Buettner, H.J., Petersen, J., Perruchoud, A.P., Eriksson, U., Marsch, S. and Roskamm, H. (2002) Prevention of contrast mediaassociated nephropathy : randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty. *Arch. Intern. Med.*, 162, 329– 336.
- 27) Tsushima, Y., Ishiguchi, T., Murakami, T., *et al.* (2016) Safe use of iodinated and gadolinium-based contrast media in current practice in Japan : a questionnaire survey. *Jpn. J. Radiol.*, 34, 130-139.
- Barrett, B.J. and Parfrey, P.S. (2006) Clinical practice. Preventing nephropathy induced by contrast medium. *N. Engl. J. Med.*, **354**, 379–386.
- 29) From, A.M., Bartholmai, B.J., Williams, A.W., Cha, S.S. and McDonald, F.S. (2008) Mortality associated with nephropathy after radiographic contrast exposure. *Mayo Clin. Proc.*, 83, 1095–1100.
- 30) Gruberg, L., Mintz, G.S., Mehran, R., Gangas, G., Lansky, A.J., Kent, K.M., Pichard, A.D., Satler, L.F. and Leon, M.B. (2000) The prognostic implications of further renal function deterioration within 48 h of interventional coronary procedures in patients with pre-existent chronic renal insufficiency. *J. Am. Coll. Cardiol.*, 36, 1542-1548.
- 31) Senoo, T., Motohiro, M., Kamihata, H., Yamamoto, S., Isono, T., Manabe, K., Sakuma, T., Yoshida, S., Sutani, Y. and Iwasaka, T. (2010) Contrast-induced nephropathy in patients undergoing emergency percutaneous coronary intervention for acute coronary syndrome. *Am. J. Cardiol.*, **105**, 624-628.
- 32) Patino, M., Parakh, A., Lo, G.C., Agrawal, M., Kambadakone, A.R., Oliveira, G.R. and Sahani, D.V. (2019) Virtual Monochromatic Dual-Energy Aortoiliac CT Angiography With Reduced Iodine Dose : A Prospective Randomized Study. Am. J. Roentgenol,, 212, 467-474.
- 33) Shuman, W.P., Mileto, A., Busey, J.M., Desai, N. and Koprowicz, K.M. (2019) Dual-Energy CT Urography With 50% Reduced Iodine Dose Versus Single-Energy CT Urography With Standard Iodine Dose. *Am. J. Roentgenol.*, **212**, 117-123.

34) Shuman, W.P., Chan, K.T., Busey, J.M., Mitsumori, L.M. and Koprowicz, K.M. (2016) Dual-energy CT Aortography with 50% Reduced Iodine Dose Versus Single-energy CT Aortography with Standard Iodine Dose. *Acad. Radiol.*, **23**, 611-618.