

**ORIGINAL****The ratio of contrast medium volume to estimated glomerular filtration rate as a predictor of contrast-induced nephropathy after endovascular aortic repair**Yohei Kawatani<sup>1,2</sup>, Hirotsugu Kurobe<sup>1</sup>, Yoshitsugu Nakamura<sup>2</sup>, Takaki Hori<sup>2</sup>, and Tetsuya Kitagawa<sup>1</sup><sup>1</sup>Department of Cardiovascular Surgery, Institute of Biomedical Sciences, Tokushima University Graduate School, <sup>2</sup>Department of Cardiovascular Surgery, Chiba-Nishi General Hospital

**Abstract : Objective :** This study aimed to determine the perioperative predictors of contrast medium-induced nephropathy (CIN) after endovascular aortic repair (EVAR). **Materials and Methods :** The data of 203 consecutive patients who underwent elective EVAR for thoracic and abdominal aortic aneurysm between January 2014 and September 2014 were retrospectively analyzed. CIN was defined according to the diagnostic criteria of the European Society of Urogenital Radiology. **Results :** Fourteen patients (6.9%) developed CIN after EVAR. Contrast medium volume (CV), preoperative serum creatinine, estimated glomerular filtration rate (eGFR), and the CV/eGFR ratio were significantly related with CIN development after EVAR. The CV/eGFR ratio was significantly higher in patients with CIN than those without CIN. Receiver operator characteristic curve analysis showed that the area under the curve of the CV/eGFR ratio was 0.782, indicating that it was the most important predictor. The appropriate CV/eGFR ratio cutoff was >1.62. Sensitivity and specificity were 85.7% and 65.6%, respectively. **Conclusions :** The CV/eGFR ratio was a useful predictor of contrast medium-induced nephropathy after EVAR. It is possible that the score can be used in patients when managing the EVAR techniques and contrast medium volume. *J. Med. Invest.* 65 : 116-121, February, 2018

**Keywords :** endovascular aortic repair, contrast medium volume, estimated estimated glomerular filtration rate, contrast induced nephropathy

**INTRODUCTION**

Endovascular aortic repair (EVAR) for thoracic and abdominal aortic aneurysm has been accepted as a minimally invasive surgery for aortic aneurysm and dissection in recent history and has been performed in more patients. The contrast medium used is an inevitable cause of acute kidney injury (1, 2), with the resulting condition referred to as “contrast medium-induced nephropathy (CIN)”. CIN is a major cause of acute kidney injury in the hospital (3) and a common associated complication of EVAR (4, 5). It is associated with a longer hospital stay, renal impairment, and higher mortality (5, 6). Zarkowsky *et al* (7). reported that postoperative renal dysfunction after EVAR was associated with decreased estimated long-term survival. Additionally, CIN is reported to be a risk factor of cardiac event after percutaneous coronary intervention (PCI) (8).

Preprocedural renal impairment has been reported to be a risk factor for developing CIN (9). Additionally, the contrast medium volume (CV) used in the procedure is also reported to be a risk factor of CIN (8, 10). The CV/estimated glomerular filtration rate (CV/eGFR) ratio is reported to be a useful predictor of CIN after PCI (11, 12).

Prevention of CIN is crucial, and thus, the main objective of this study was to determine the perioperative predictors of CIN after EVAR, particularly the CV/eGFR ratio, as well as to evaluate the relationship between CIN after EVAR, determine clinical outcomes, and recommend useful approaches for CIN prevention

after EVAR.

**MATERIALS AND METHODS***Patient selection*

We performed EVAR on 217 consecutive patients at Chiba-Nishi General Hospital from January 2014 to September 2014. Among the 217 patients, 14 patients who underwent emergent EVAR for ruptured aortic aneurysm or EVAR using median thoracotomy procedure were excluded from this study. We included patients with aneurysm with and without dissection. The renal arteries of all patients were patent on preoperative and postoperative CT and intraoperative aortography. Based on the definition given by the European Society of Urogenital Radiology (13), obvious renal artery occlusion or stenosis during the operation due to device manipulation or thrombus migration was set as an exclusion criterion. However, no patient was excluded for this reason. Finally, 203 patients who underwent elective EVAR were enrolled in this study (mean age, 71.4 ± 10.3 years ; 80.7% men). One hundred patients underwent EVAR for abdominal aortic aneurysm and 103 patients underwent EVAR for thoracic aortic aneurysm.

*Definition of contrast-induced nephropathy*

Iopamidol, a non-ionic high-osmolality contrast agent, was used as an intraoperative contrast medium. CIN was defined according to the diagnostic criteria of the European Society of Urogenital Radiology as “a condition in which a decrease in renal function within 3 days of the intravascular administration of a CM in the absence of an alternative etiology. An increase in serum creatinine by more than 25% or 44 μmol/L (0.5 mg/dL) indicates CIN (13).”

Received for publication January 17, 2018 ; accepted January 24, 2018.

Address correspondence and reprint requests to Yohei Kawatani, MD, Department of Cardiovascular Surgery, Tokushima University Graduate School, 3-18-15, Kuramoto, Tokushima, Tokushima 770-8503, Japan and Fax : +81-88-633-7408.

### Data collection and evaluation

All clinical data were retrospectively collected from the patients' medical records. Data related to the patients' demographics and preoperative status were also collected, including age, sex, and medical history, such as hypertension (patients receiving medication or remaining untreated), diabetes (patients receiving insulin), and impaired left ventricular function (ejection fraction < 30%). The serum creatinine value obtained from the last blood test before the day EVAR was performed was used as the preoperative serum creatinine level, and postoperative serum creatinine level was defined as the highest serum creatinine value obtained during the first to third postoperative days. We predicted the eGFR using the calculation method recommended by the Japanese Society of Nephrology (14) :  $194 \times \text{serum creatinine level}^{-1.094} \times \text{age}^{-0.287}$  (for men) and  $194 \times \text{serum creatinine level}^{-1.094} \times \text{age}^{-0.287} \times 0.739$  (for women).

The surgery-related factors were type of procedure (EVAR for thoracic or abdominal aortic aneurysm), operation time, and quantity of contrast medium used.

The treatment outcomes were hospital death, 1-year survival, renal replacement therapy, length of ICU stay, and length of postoperative hospitalization.

### Perioperative and intraoperative management

Patients with a preoperative serum creatinine level > 1.3 mg/dL were hospitalized before EVAR and received Ringer's lactate solution (60 mL/h) intravenously for more than 12 hours. Postoperative initiation of food intake was accompanied by termination of reinfusion fluid ; in cases where serum creatinine levels remained elevated, hydration was continued until an improvement in serum creatinine levels was observed. No patient underwent preoperative enhanced CT 3 days before the operation.

An anesthesiologist performed intraoperative fluid management, including fluid control and hemodynamic monitoring, using an arterial line.

### Endovascular aortic repair

All surgeries were performed under general anesthesia. The access route for stent graft insertion was via the femoral artery through an inguinal incision ; a sheath was placed in the artery and the stent graft was inserted. If the landing zone was short, embolization of the left subclavian artery or internal iliac artery was performed during EVAR for the thoracic or abdominal aorta, respectively, to lengthen the landing zone sufficiently. Embolization was accomplished with coils and/or vascular plugs. All patients awoke in the operating room and were subsequently transferred to the ICU.

We used endografts such as Conformable GORE TAG (W.L. Gore & Associates ; Flagstaff, AZ, USA), Relay Plus (Bolton Medical, Barcelona, Spain), TX2 TAA Endovascular Graft (Cook, Bloomington, IN, USA) and Valiant Captivia Thoracic Stent Graft (Medtronic, Santa Rosa, CA, USA) for thoracic aneurysms, and the Aorfix stent graft (Lombard Medical, Didcot, UK), Endurant II (Medtronic), GORE EXCLUDER AAA Endoprosthesis (W.L. Gore & Associates), Powerlink stentgraft (Endologix, Irvine, CA, USA), and Zenith flex (Cook) for abdominal aneurysms. The endograft was chosen based on the anatomical features of each patient and graft availability.

### Statistical analysis

Continuous variables are presented as the mean  $\pm$  standard deviation, and categorical variables are presented as the number and percentage of the total. Continuous variables were analyzed using Student's t-tests, whereas categorical variables were compared using chi-squared tests. Differences were considered statistically significant if  $P < 0.05$ .

We performed a multiple logistic regression analysis on appropriate items with  $P < 0.05$  in the univariate analyses to examine the factors with the greatest influence on CIN development. An evaluation of an additional cutoff point of different variables was performed using receiver operator characteristic curve analysis. All statistical analyses were performed on a personal computer using the statistical software package SPSS for Mac, version 23 (IBM® Corp., Armonk, NY, USA).

### Consent for publication

All patients undergoing surgery at our facility were informed of the significance of publishing their clinical data at academic meetings or in scientific literature, and they all provided informed consent to participate in studies conducted at our facility. Before using the patients' treatment data, we obtained consent from the patients themselves or from proxies with permission to make decisions on behalf of the patients.

## RESULTS

### Patient characteristics and CIN

Fourteen patients (6.9%) developed CIN. Table 1 shows patient characteristics in the CIN and non-CIN groups. Only low left ventricular function was a significant risk factor of CIN ; other patient characteristics were not significantly different (Table 1).

### CIN and risk factors

The volume of contrast medium used during surgery was greater in the CIN group than the non-CIN group. There were no significant differences among surgery types (EVAR for the thoracic or abdominal aorta), aortic etiology (true aneurysm or aortic dissection), operation time, and radiation time between the CIN and non-CIN groups. Preoperative serum creatinine level and eGFR were significantly higher and lower, respectively, in the CIN group, compared with those of the non-CIN group. Simultaneous embolization of the left subclavian artery or internal iliac artery was performed during EVAR for the thoracic or abdominal aorta, respectively, was performed in 65 cases, which was associated with CIN. The CV/eGFR ratio was significantly higher in the CIN group (Table 1).

We performed logistic regression analysis for preoperative serum creatinine level, low left ventricular function, simultaneous embolization, and contrast medium volume. We excluded preoperative the eGFR and the CV/eGFR ratio in this analysis because these are scores which were derived from and were strongly associated with other variables. The results of the analysis revealed that the preoperative serum creatinine level had the greatest impact on the development of CIN (Table 2).

In this study, we also evaluated simultaneous arterial embolization and CIN. The patients' characteristics and preoperative renal function were not significantly different between patients undergoing EVAR with simultaneous arterial embolization (E group) and those undergoing EVAR without simultaneous arterial embolization (N group). However, the volume of the contrast medium was significantly greater, and fluoroscopy time and operation time were significantly longer in the E group ; moreover, simultaneous arterial embolization was associated with CIN (Table 3).

### ROC analysis for predictors of CIN

ROC analysis was performed on the amount of contrast medium volume used, preoperative serum creatinine, preoperative eGFR, and CV/eGFR ratio, which were significant predictors of CIN.

The area under the curve (AUC) of CV/eGFR ratio was 0.782, which was the greatest among the aforementioned predictors. CV/eGFR ratio > 1.62 was considered the most appropriate cutoff

**Table 1.** Preoperative patient characteristics, comorbidities, pathophysiological and technical features related to perioperative renal function and CIN or non-CIN

	CIN (n=14)	Non-CIN (n=189)	Total (n=203)	P-value (n=189)
Age, years	76.4 ± 10.9	71.1 ± 10.2	71.5 ± 10.3	0.056
Sex, male/female	14/0	150/39	164/39	0.076
BSA, m <sup>2</sup>	1.60 ± 0.169	1.64 ± 0.188	1.64 ± 0.180	0.443
BMI, kg/m <sup>2</sup>	21.6 ± 4.16	22.8 ± 3.79	22.7 ± 3.82	0.316
Hypertension, n (%)	11 (78.6)	142 (75.1)	153 (75.3)	1
Diabetes mellitus, n (%)	0 (0)	5 (2.6)	5 (2.5)	1
Low left ventricular function, n (%)	2 (14.3)	3 (1.6)	5 (2.5)	0.039*
Stroke, n (%)	0 (0)	10 (5.3)	10 (4.9)	0.481
Dyslipidemia, n (%)	5 (35.7)	95 (50.3)	100 (49.3)	0.22
Thoracic/abdominal, n	9/5	91/98	100/103	0.279
Aortic dissection, n (%)	6 (42.9)	52 (27.5)	58	0.230
Simultaneous arterial embolization, n (%)	8 (57.1)	57 (30.2)	65	0.04*
Operation time, min	126 ± 58.4	117 ± 55.8	117 ± 56.4	0.583
Fluoroscopy time, min	24.6 ± 13.6	21.8 ± 15.3	22.0 ± 15.2	0.471
Contrast volume, mL	104.4 ± 43.0	85.5 ± 27.8	86.8 ± 29.4	0.019*
Preoperative creatinine, mg/dL	1.37 ± 0.58	0.942 ± 0.32	0.971 ± 0.34	< 0.001*
Preoperative eGFR, mL/min/1.73 m <sup>2</sup>	46.7 ± 19.8	62.9 ± 18.7	61.8 ± 19.2	0.013*
CV/eGFR ratio	2.39 ± 0.98	1.51 ± 0.74	1.56 ± 0.79	< 0.001*
CV/eGFR ratio > 1.62, n (%)	11 (78.6)	61 (32.3)	72	0.001*

Values are presented as mean ± standard deviation or n (%).

Abbreviations : BSA, body surface area ; BMI, body mass index ; TEVAR, thoracic endovascular aortic repair ; eGFR, estimated glomerular filtration rates ; CV, amount of contrast medium ; CIN, contrast medium-induced nephropathy.

Low left ventricular function was defined as left ventricular ejection fraction of 30% or below.

\*Statistically significant.

**Table 2.** Factors associated with the development of CIN.

	Odds ratio	P-value	95% CI
Contrast medium volume	1.07	0.020	1.01-1.13
Low left ventricular function	19.53	0.008	2.19-173.80
Preoperative serum creatinine level	64.75	0.006	3.30-1270.86
Simultaneous arterial embolization	2.54	0.202	0.607-10.63

Abbreviations : CIN, contrast-induced nephropathy ; CI, confidence interval.

Low left ventricular function was defined as left ventricular ejection fraction of 30% or lower.

value (Figure 1), with 85.7% sensitivity and 65.6% specificity for detecting CIN. More patients with CV/eGFR ratio > 1.62 were observed in the CIN group (group odds ratio, 7.694 ; 95% confidence interval, 2.071-28.587, P = 0.001) (Table 1). Serum creatinine was also adequately high AUC. The cut off value was 1.135. The sensitivity was 71.4% and the specificity was 88.4%.

#### *Relationship between CIN after EVAR and clinical outcomes*

Hospital deaths and 1-year mortality were worse in the CIN group than in the non-CIN group. The lengths of ICU hospital stay were longer in the CIN group than in the non-CIN group. Only one patient received renal replacement therapy in the CIN group, but the difference was not statistically significant (Table 4).

#### *Relationship between CV/eGFR ratio and the development of CIN and clinical outcomes*

We evaluated the relationship between the development of CIN and CV/eGFR ratio using the cutoff value obtained in the ROC analysis (CV/eGFR ratio > 1.62).

Seventy-two patients had a CV/eGFR ratio > 1.62, which was seen in 35% of the enrolled patients. CIN was observed more frequently in patients in the group with CV/eGFR ratio > 1.62. Additionally, hospital death and 1-year mortality rate were significantly higher in patients with CV/eGFR ratio > 1.62. The length of hospital stay was significantly longer in patients with CV/eGFR ratio > 1.62 (Table 4).

## DISCUSSION

CIN has been studied extensively in PCI and reported to have an adverse effect on treatment outcomes after PCI. Developing CIN results in worse treatment outcomes related to mortality, serious morbidity, and myocardial infarction after PCI (15). Postoperative renal dysfunction after EVAR has been reported to be associated with decreased estimated long-term survival (7). Additionally, this study demonstrated that CIN immediately after EVAR was associated with more hospital deaths and worsened 1-year mortality. Therefore, efforts should be undergone to prevent CIN after EVAR.

Developing CIN after endovascular treatment is associated with several etiologies and causes including renal vasoconstriction (16), ischemic and hypoxic damage to the renal medulla (17, 18), and direct toxic effects to the tubular epithelium (19). Maintaining preoperative and postoperative blood perfusion in the kidney and urine flow is very important to protect kidney function.

Selistre *et al* (20). reported that heart failure was a risk factor for CIN after intravenous injection of contrast medium following enhanced computed tomography, which is not an invasive procedure involving hemodynamic change. A few reports on CIN after EVAR indicated that low left ventricular function (5) and heart failure were also risk factors for CIN (10). Furthermore, the present study

Table 3. Relationship between pathophysiological and technical features related to perioperative renal function and simultaneous arterial embolization

	E group (n=65)	N group (n=138)	Total (n=203)	P-value
Age, years	73.6 ± 9.9	71.3 ± 10.4	71.5 ± 10.3	0.426
Sex, male/female	56/9	108/30	164/39	0.183
BSA, m <sup>2</sup>	1.6 ± 0.19	1.6 ± 0.12	1.64 ± 0.18	0.280
BMI, kg/m <sup>2</sup>	22.6 ± 3.5	22.8 ± 4.0	22.7 ± 3.8	0.398
Operation time, min	141.9 ± 51.0	106.3 ± 54.2	117.0 ± 56.4	< 0.001*
Fluoroscopy time, min	32.7 ± 18.6	16.9 ± 9.7	22.0 ± 15.2	< 0.001*
Contrast volume, mL	105.4 ± 25.6	78.0 ± 16.7	86.8 ± 29.4	< 0.001*
Preoperative creatinine, mg/dL	0.98 ± 0.34	0.97 ± 0.36	0.971 ± 0.36	0.428
Preoperative eGFR, mL/min/1.73 m <sup>2</sup>	61.8 ± 19.7	61.8 ± 18.8	61.8 ± 19.2	0.500
CV/eGFR ratio	1.93 ± 0.89	1.36 ± 0.65	1.56 ± 0.79	< 0.001*
CIN, n (%)	8 (12.3)	6 (4.3)	14 (6.9)	0.040*

Values are presented as mean ± standard deviation, n (%), or n/n.

E group, patients undergoing EVAR with arterial embolization ; N group, patients undergoing EVAR without arterial embolization.

Abbreviations : BSA, body surface area ; BMI, body mass index ; eGFR, estimated glomerular filtration rates ; CV/eGFR ratio, contrast medium volume/estimated glomerular filtration rate ; CIN, contrast medium-induced nephropathy ; EVAR, endovascular aortic repair.

\*Statistically significant.

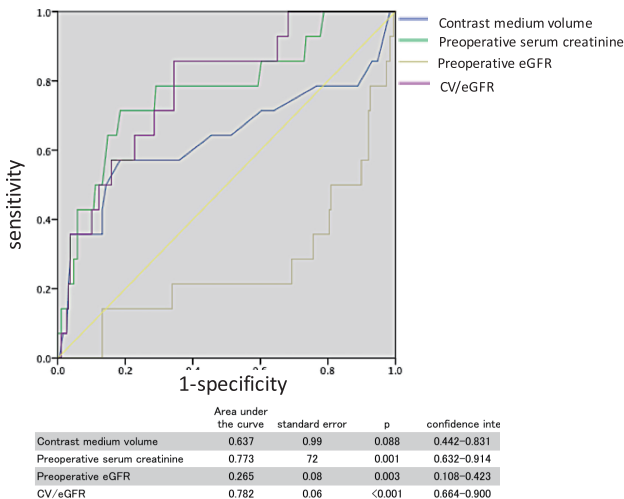


Fig 1. ROC analysis about the amount of used contrast medium, preoperative serum creatinine, preoperative eGFR and CV/eGFR ratio. The area under the curve of the CV/eGFR ratio was the greatest of the above four factors.

also demonstrated that low left ventricular function was a risk factor for CIN. These results suggest that lower renal perfusion due to low left ventricular function is suspected in CIN pathophysiology.

As Li H *et al* (21). demonstrated that lower systolic arterial pressure was associated with developing CIN, unstable hemodynamics during surgery may contribute to the development of CIN. It is very important to preserve renal perfusion and urinary flow before and during EVAR to protect the kidney. It is believed that increasing renal blood flow and urinary flow through hydration can reduce the renal exposure to contrast media (13, 22). We assumed that patients with a preoperative serum creatinine level > 1.3 mg/dL were at great risk for CIN. According to the Canadian Association of Radiologists consensus guidelines for prevention, we administered Ringer’s lactate solution (60 mL/h) intravenously for more than 12 hours to these patients (23). Although it was expected that the fluid infusion contributed to the prevention of CIN, 14 patients

developed CIN.

Diabetes mellitus is a well-known risk factor for CIN, but it was not a significant risk factor in this study. One of the reasons might be the definition of diabetes in this study. We set diabetes mellitus as insulin dependent diabetes, which made the prevalence of diabetes very low. If we had used another definition such as “patients who took oral hypoglycemic agents or patients receiving insulin”, the prevalence might have been higher and the results of statistical analysis might have been different.

Although further analysis of long-term results is required, we anticipate that maintaining stable hemodynamics by fluid infusion and administrating inotropes particularly in patients with low left ventricular function will lead to better outcomes with less incidence of CIN.

In this study, the amount of contrast medium used during surgery was larger in the CIN group than in the non-CIN group. Additionally, we revealed that performing simultaneous embolization of the left subclavian or internal iliac artery during EVAR for thoracic or abdominal aortic aneurysm, respectively, was associated with the development of CIN. The amount of contrast medium used during surgery, operation time, and fluoroscopy time were greater in patients who underwent arterial embolization during EVAR than in those who underwent EVAR only. We strongly suspect that the increased amount of contrast medium administered in the embolization procedure was a cause of CIN development because, although the patients’ characteristics and preoperative renal function did not differ significantly between the two groups, the contrast medium volume and CV/eGFR ratio were greater in patients undergoing simultaneous arterial embolization. Tran *et al* (24). reported that in patients who underwent fenestrated EVAR for juxtarenal or paravisceral aortic aneurysm, fluoroscopy time, operative time, and contrast volume were associated with the development of CIN. In addition, they concluded that increased surgical complexity was a risk factor for CIN. They suggested that minimizing surrogate markers for operative complexity is important (24). We also suggest that additional endovascular procedures should be performed in patients who have preoperative risk factors for CIN, including embolization of arteries separately from EVAR to minimize the complexity of the operation. This involves reducing the amount of contrast medium used in each procedure to prevent CIN.

In many fields including EVAR, preoperative renal impairment



**Table 4.** Relationship between clinical outcomes and development of CIN and CV/eGFR > 1.62.

	CIN (n=14)	Non-CIN (n=189)	Total (n=203)	P-value
Hospital death, n (%)	2 (14.3)	1 (0.5)	3 (1.5)	0.013*
Renal replacement therapy, n (%)	1 (7.1)	0 (0)	1 (0.49)	0.335
ICU stay, days	4.07 ± 3.26	2.44 ± 2.62	2.73 ± 1.69	0.029*
Hospital stay, days	17.2 ± 11.0	10.9 ± 7.5	11.4 ± 7.9	0.004*
One-year mortality, n (%)	3 (21.4)	3 (1.6)	6 (3.0)	0.005*

	CV/eGFR > 1.62 (n=72)	CV/eGFR ≤ 1.62 (n=131)	Total (n=203)	P-value
CIN, n (%)	11 (15)	3 (2.3)	14 (6.9)	0.001*
Hospital death, n (%)	3 (4.2)	0 (0)	3 (1.5)	0.043*
Renal replacement therapy, n (%)	1 (1.4)	0 (0)	1 (0.49)	0.335
ICU stay, days	2.94 ± 4.43	2.33 ± 0.63	2.73 ± 1.69	0.127
Hospital stay, days	13.2 ± 10.8	10.3 ± 5.5	11.4 ± 7.9	0.014*
One-year mortality, n (%)	5 (6.9)	1 (0.8)	6 (3.0)	0.022*

Values are presented as mean ± standard deviation or n (%).

Abbreviations : ICU, intensive care unit ; CIN, contrast medium-induced nephropathy.

\*Statistically significant.

was reported to be a risk factor for CIN (25). Serum creatinine level is a widely used indicator of renal function. Moreover, a high preoperative creatinine level has been reported to be a risk factor for CIN (26). However, serum creatinine level does not increase until the eGFR has decreased by 50% or more (27). We used eGFR to consider the predictive value of the CV/eGFR ratio.

The CV/eGFR ratio represents a comparison between the patient's preoperative risk factors and the potential harm of the contrast medium volume used in EVAR. On ROC analysis, CV/eGFR ratio was the most appropriate predictive value, and the optimal cutoff value was 1.62.

The CV/eGFR ratio could predict CIN appropriately. In addition, interestingly, patients with a CV/eGFR ratio > 1.62 required a longer hospital stay and had increased likelihood of hospital death and worsened 1-year mortality. The present results suggest that a CV/eGFR ratio > 1.62 was a useful predictor for developing CIN and worsened outcomes after EVAR. Our study results imply that consideration of both the contrast medium volume and the preoperative renal impairment are more useful predictors of CIN in EVAR than those of CIN in PCI.

We performed EVAR under general anesthesia. Generally, the general anesthesia has more negative chronotropic and inotropic effects than the local anesthesia commonly used for PCI. Therefore, hemodynamic status during EVAR affects not only the preservation of renal function, but it also the development of CIN more than those during PCI. It is not appropriate to use the cutoff value based on another endovascular method such as PCI. Some studies on the usefulness of the CV/eGFR ratio in PCI have calculated these cutoff values. One study (14) focused on CIN after PCI proposed a cutoff value of CV/eGFR ratio > 3.1, which was greater than the cutoff value of 1.62 obtained in this study. This difference in optimal cutoff values among endovascular procedures must be clarified. This study is valuable because there are very few reports on the cutoff value for preventing CIN after EVAR.

Using the CV/eGFR ratio of 1.62 in each patient, we can calculate the amount of contrast medium necessary and determine the risk of developing CIN before surgery. Thus, we can decide on the amount of contrast medium needed for each surgery and balance the amount with the technical requirement and risk of CIN in each patient objectively, and not based on the surgeon's experience. Using the CV/eGFR ratio cutoff value (1.62) appropriately can improve the safety of EVAR in terms of preventing CIN.

In addition to CV/eGFR, serum creatinine also had adequately high AUC. We assume that serum creatinine is also important predictor for CIN after EVAR. Serum creatinine is a preoperative value, which does not include intraoperative factor such as CV. Therefore, using serum creatinine, we can predict CIN before operations based on patients' background. The results about serum creatinine can be useful for prevention of CIN. We performed intravenous hydration in the patients with serum creatinine level above 1.3. But according to the result in this study (appropriate cut off value of serum creatinine was 1.135), we have to set more strict criteria for intravenous hydration. It may be appropriate to perform intravenous hydration in patients with serum creatinine level above 1.135. Serum creatinine and CV/eGFR are both useful for predicting CIN after EVAR. But, CV/eGFR is useful not only for predicting CIN but also planning operation procedure including the amount of contrast medium volume use.

This study has some limitations. First, it included a small number of cases and followed a retrospective design. Second, the study participants had small differences in characteristics such as lower BMI and BSA than those in Western patients. In addition, we used only one contrast medium (iopamidol). The subjects of this study were elderly patients. Therefore, it was possible that we underestimated eGFR. Using cystatin C could have enabled us to estimate GFR more precisely, and could have made CV/eGFR more accurate. Further prospective studies with a large number of patients including many races and more than one contrast agent are needed to confirm the efficacy of the CV/eGFR ratio for preventing CIN.

## CONCLUSION

This study demonstrated that the CV/eGFR ratio was an appropriate predictor of CIN development after EVAR. We can calculate the safe maximum amount of contrast medium in each patient using the CV/eGFR ratio cutoff value of 1.62. We recommend taking the preoperative predictive value of an individual patient into account and managing the EVAR techniques and CV. Consequently, we will be able to reduce the incidence of CIN and improve the quality of life in patients after EVAR.

## DISCLOSURE STATEMENT (COI)

The authors declare that there is no conflict of interests regarding the publication of this paper.

## AUTHOR CONTRIBUTIONS

Study conception : YK, HK, YN, TH and TK

Data collection : YK

Analysis : YK

Investigation : YK, YN, HK, TK

Writing : YK, TK

Critical review and revision : all authors

Final approval of the article : all authors

Accountability for all aspects of the work : all authors

## ACKNOWLEDGEMENT

This study was presented in the Japanese College of Angiology Award session at the 58th annual meeting of Japanese Collage of Angiology, Nagoya, Japan, November 19-21, 2017

## REFERENCES

- Parfrey PS, Griffiths SM, Barrett BJ, *et al* : Contrast material-induced renal failure in patients with diabetes mellitus, renal insufficiency, or both. A prospective controlled study. *N Engl J Med* 320 : 143-9, 1989
- Solomon R : Contrast-medium-induced acute renal failure. *Kidney Int* 53 : 230-42, 1998
- Nash K, Hafeez A, Hou S : Hospital-acquired renal insufficiency. *Am J Kidney Dis* 39 : 930-6, 2002
- Guneyli S, Bozkaya H, Cinar C, *et al* : The incidence of contrast medium-induced nephropathy following endovascular aortic aneurysm repair : assessment of risk factors. *Jpn J Radiol* 33 : 253-9, 2015
- Kawatani Y, Nakamura Y, Mochida Y, *et al* : Contrast medium induced nephropathy after endovascular stent graft placement : an examination of its prevalence and risk factors. *Radiol Res Pract* 2016 : 5950986, 2016
- Abe M, Morimoto T, Akao M, *et al* : Relation of contrast-induced nephropathy to long-term mortality after percutaneous coronary intervention. *Am J Cardiol* 114 : 362-8, 2014
- Zarkowsky DS, Hicks CW, Bostock IC, *et al* : Renal dysfunction and the associated decrease in survival after elective endovascular aneurysm repair. *J Vasc Surg* 64 : 1278-85, 2016
- Dangas G, Iakovou I, Nikolsky E, *et al* : Contrast-induced nephropathy after percutaneous coronary interventions in relation to chronic kidney disease and hemodynamic variables. *Am J Cardiol* 95 : 13-9, 2005
- Lautin EM, Freeman NJ, Schoenfeld AH, *et al* : Radiocontrast-associated renal dysfunction : incidence and risk factors. *AJR Am J Roentgenol* 157 : 49-58, 1991
- Mehran R, Aymong ED, Nikolsky E, *et al* : A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention : development and initial validation. *J Am Coll Cardiol* 44 : 1393-9, 2004
- Liu Y, Tan N, Zhou YL, *et al* : The contrast medium volume to estimated glomerular filtration rate ratio as a predictor of contrast-induced nephropathy after primary percutaneous coronary intervention. *Int Urol Nephrol* 44 : 221-9, 2012
- Wang XC, Fu XH, Wang YB, *et al* : Prediction of contrast-induced nephropathy in diabetics undergoing elective percutaneous coronary intervention : role of the ratio of contrast medium volume to estimated glomerular filtration rate. *Chin Med J (Engl)* 124 : 892-6, 2011
- Barrett BJ, Parfrey PS : Clinical practice. Preventing nephropathy induced by contrast medium. *N Engl J Med* 354 : 379-86, 2006
- Matsuo S, Imai E, Horio M, *et al* : Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis* 53 : 982-92, 2009
- Rihal CS, Textor SC, Grill DE, *et al* : Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* 105 : 2259-64, 2002
- Cantley LG, Spokes K, Clark B, *et al* : Role of endothelin and prostaglandins in radiocontrast-induced renal artery constriction. *Kidney Int* 44 : 1217-23, 1993
- Russo D, Minutolo R, Cianciaruso B, *et al* : Early effects of contrast media on renal hemodynamics and tubular function in chronic renal failure. *J Am Soc Nephrol* 6 : 1451-8, 1995
- Liss P, Nygren A, Olsson U, *et al* : Effects of contrast media and mannitol on renal medullary blood flow and red cell aggregation in the rat kidney. *Kidney Int* 49 : 1268-75, 1996
- Humes HD, Hunt DA, White MD : Direct toxic effect of the radiocontrast agent diatrizoate on renal proximal tubule cells. *Am J Physiol* 252 : F246-55, 1987
- Selistre L da S, Souza VC, Dubourg L, *et al* : Contrast-induced nephropathy after computed tomography. *J Bras Nefrol* 37 : 27-31, 2015
- Li H, Huang S, He Y, *et al* : Impact of an early decrease in systolic blood pressure on the risk of contrast-induced nephropathy after percutaneous coronary intervention. *Heart Lung Circ* 25 : 118-23, 2016
- Trivedi H, Nadella R, Szabo A : Hydration with sodium bicarbonate for the prevention of contrast-induced nephropathy : a meta-analysis of randomized controlled trials. *Clin Nephrol* 74 : 288-96, 2010
- Owen RJ, Hiremath S, Myers A, *et al* : Canadian Association of Radiologists consensus guidelines for the prevention of contrast-induced nephropathy : update 2012. *Can Assoc Radiol J* 65 : 96-105, 2014
- Tran K, Fajardo A, Ullery BW, *et al* : Renal function changes after fenestrated endovascular aneurysm repair. *J Vasc Surg* 64 : 273-80, 2016
- Stacul F, van der Molen AJ, Reimer P, *et al* : Contrast induced nephropathy : updated ESUR Contrast Media Safety Committee guidelines. *Eur Radiol* 21 : 2527-41, 2011
- Stadius van Eps RG, Leurs LJ, Hobo R, Harris PL, Buth J : Impact of renal dysfunction on operative mortality following endovascular abdominal aortic aneurysm surgery. *Br J Surg* 94 : 174-8, 2007
- Perrone RD, Madias NE, Levey AS : Serum creatinine as an index of renal function : new insights into old concepts. *Clin Chem* 38 : 1933-53, 1992