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## Prediction of contrast-induced nephropathy after percutaneous coronary intervention: Role of contrast volume/body weight ratio

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**Chaemchoi T, Punyawudho B, Srimahachota S. Prediction of contrast-induced nephropathy after percutaneous coronary intervention: Role of contrast volume/body weight ratio. Chula Med J 2011 Jul - Aug; 55(4): 341 - 54**

**Background** : *The use of contrast media has been closely related to contrast-induced nephropathy (CIN) in several studies. However, there is no firm description of the association. The volume of contrast media and patient characteristics may be important risk factors for CIN. Identifying and quantifying these risk factors may be useful in predicting risk of CIN.*

**Objective** : *To identify important risk factors of CIN after percutaneous coronary intervention (PCI).*

**Design** : *Prospective analytical study*

**Setting** : *King Chulalongkorn Memorial Hospital*

**Method** : *A total of 181 consecutive patients who underwent PCI were enrolled. Patient- and procedure-related factors including calculated volume/body weight (V/BW) ratio were recorded. CIN was defined as an increase in serum creatinine > 25% or > 0.5 mg/dl from pre-PCI value within 72 hours after PCI or diagnosed with CIN. Receiver-operator characteristics (ROC) methods were used to determine the optimal cutoff point of V/BW ratio. The V/BW ratio and other factors were tested for an association with CIN by multivariate logistic regression analysis.*

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**Results** : The incidence of CIN after PCI was 6.1%. The mean of V/BW ratio in patients developing CIN was  $3.2 \pm 2.0$  ml/kg, and those who did not develop CIN was  $2.0 \pm 1.0$  ml/kg ( $p$ -value = 0.001). The ROC curve analysis indicated that V/BW ratio of 2.6 ml/kg was a good discriminator for CIN with concordance statistic (C-statistic) of 0.73. Multivariate logistic regression analysis showed that V/BW ratio  $\geq 2.6$  ml/kg (OR = 8.184;  $p$ -value = 0.003), congestive heart failure (CHF) (OR = 6.465,  $p$ -value = 0.010) and creatinine clearance (CrCl)  $< 30$  ml/min (OR = 6.141,  $p$ -value = 0.019) were associated with CIN after PCI.

**Conclusions** : The risk of CIN after PCI was associated with V/BW ratio  $\geq 2.6$  ml/kg, CrCl  $< 30$  ml/min and CHF. The V/BW ratio  $\geq 2.6$  ml/kg may be a useful predictor in estimating optimal volume of contrast media for individual patient.

**Keywords** : Contrast-induced nephropathy, acute kidney injury, percutaneous coronary intervention.

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ธศิกานต์ เข้มช้อย, บราลี ปัญญาวุธ, สุพจน์ ศรีมหาโชตะ. การทำนายการเกิดภาวะไตทำงานบกพร่องจากสารที่บ่งชี้ภายหลังการทำหัตถการรักษาหลอดเลือดโคโรนารีผ่านสายสวน: บทบาทของอัตราส่วนระหว่างปริมาณสารที่บ่งชี้น้ำหนักตัวของผู้ป่วย. *จุฬาลงกรณ์เวชสาร* 2554 ก.ค. - ส.ค.; 55(4): 341 - 54

- ภูมิหลัง** : การได้รับสารที่บ่งชี้ขณะทำหัตถการรักษาหลอดเลือดโคโรนารีผ่านสายสวน (PCI) มีความสัมพันธ์กับการเกิดภาวะไตทำงานบกพร่องจากสารที่บ่งชี้ (CIN) ปริมาณสารที่บ่งชี้ที่ใช้ สภาวะ และคุณลักษณะของผู้ป่วยอาจเป็นปัจจัยเสี่ยงต่อการเกิด CIN การหาปริมาณสารที่บ่งชี้ และปัจจัยที่มีความสัมพันธ์กับการเกิด CIN อาจช่วยลดความเสี่ยงต่อการเกิด CIN
- วัตถุประสงค์** : เพื่อวิเคราะห์หาปัจจัยเสี่ยงที่มีความสัมพันธ์กับการเกิด CIN ในผู้ป่วยที่ทำ PCI
- รูปแบบการวิจัย** : การศึกษาเชิงวิเคราะห์แบบไปข้างหน้า
- สถานที่ทำการศึกษา** : โรงพยาบาลจุฬาลงกรณ์
- วิธีการศึกษา** : ทำการศึกษาในผู้ป่วยที่ทำ PCI จำนวนทั้งสิ้น 181 ราย โดยการบันทึกข้อมูลเกี่ยวกับคุณลักษณะของผู้ป่วย รายละเอียดกระบวนการทำหัตถการรวมทั้งคำนวณอัตราส่วนระหว่างปริมาณสารที่บ่งชี้ที่ได้รับต่อน้ำหนักตัวของผู้ป่วยแต่ละราย กำหนดให้ภาวะไตทำงานบกพร่องจากสารที่บ่งชี้หมายถึงการตรวจพบการเพิ่มขึ้นของค่าครีเอตินินในซีรัมมากกว่าร้อยละ 25 หรือ 0.5 มิลลิกรัม/เดซิลิตรจากค่าเดิมของผู้ป่วย ภายในระยะเวลา 72 ชั่วโมงภายหลังการทำ PCI หรือได้รับการวินิจฉัยว่าเกิด CIN จากนั้นวิเคราะห์หาจุดตัดอัตราส่วนระหว่างปริมาณสารที่บ่งชี้น้ำหนักตัวที่เป็นปัจจัยเสี่ยงต่อการเกิด CIN โดยใช้วิธีวิเคราะห์ Receiver-operator characteristics (ROC) ตรวจสอบจุดตัดที่ได้จากการวิเคราะห์ ROC method และปัจจัยเสี่ยงอื่น ๆ ต่อความสัมพันธ์กับการเกิด CIN โดยใช้สถิติ multivariate logistic regression analysis

- ผลการศึกษา** : พบอุบัติการณ์การเกิด CIN ในผู้ป่วยที่ทำ PCI 6.1% ค่าเฉลี่ยอัตราส่วนระหว่างปริมาณสารทึบรังสีที่ได้รับต่อน้ำหนักตัว (V/BW) เท่ากับ  $3.2 \pm 2.0$  มิลลิลิตร/กิโลกรัมในผู้ป่วยที่เกิด CIN เปรียบเทียบกับ  $2.0 \pm 1.0$  มิลลิลิตร/กิโลกรัมในผู้ป่วยที่ไม่เกิด CIN ( $p$ -value = 0.001) จากการวิเคราะห์ ROC curve analysis พบว่าที่ V/BW เท่ากับ 2.6 มิลลิลิตร/กิโลกรัม เป็นจุดตัดที่สามารถทำนายแยกระหว่างกลุ่มผู้ป่วยที่เกิดและไม่เกิด CIN ได้ดี โดยมีค่า concordance statistic (C-statistic) = 0.73 จากการวิเคราะห์ multivariate logistic regression พบว่า V/BW มากกว่าหรือเท่ากับ 2.6 มิลลิลิตร/กิโลกรัม (OR 8.184;  $p$ -value = 0.003), ภาวะหัวใจล้มเหลว (OR 6.465;  $p$ -value = 0.010), และอัตราการกรองของไตน้อยกว่า 30 มิลลิลิตร/นาที (OR 6.141;  $p$ -value = 0.019) เป็นปัจจัยที่มีความสัมพันธ์กับการเกิด CIN อย่างมีนัยสำคัญทางสถิติ multivariate model ที่สร้างขึ้นนี้สามารถทำนายแยกกลุ่มผู้ป่วยที่เกิดและไม่เกิด CIN ได้ดี (C-statistic = 0.849)
- สรุป** : การได้รับสารทึบรังสีในปริมาณตั้งแต่ 2.6 เท่าของน้ำหนักตัวขึ้นไป, ภาวะหัวใจล้มเหลวและอัตราการกรองของไตน้อยกว่า 30 มิลลิลิตร/นาที มีความสัมพันธ์กับการเกิด CIN การให้สารทึบรังสีในปริมาณไม่เกิน 2.6 เท่าของน้ำหนักตัวจึงอาจช่วยลดความเสี่ยงต่อการเกิด CIN ในผู้ป่วยที่ทำ PCI
- คำสำคัญ** : Contrast-induced nephropathy, acute kidney injury, percutaneous coronary intervention.

An increasing number of radiological procedures utilizing contrast media have led to a rise in the incidence of acute kidney injury caused by exposure to contrast media, known as contrast-induced nephropathy (CIN).<sup>(1, 2)</sup> So far, the exact mechanism of CIN is unclear; however, an evidence suggests that a combination of direct toxic effects on the tubular epithelial cells and renal ischemia may play a pathogenic role.<sup>(3)</sup> CIN is traditionally defined as an increase in serum creatinine of either 0.5 mg/dl or 25% from baseline within 72 hours after exposure.<sup>(4, 5)</sup> Although, the incidence of CIN is low in general population (0.6 - 2.3%), it is significantly higher in some groups of patients, especially in patients with cardiovascular pathology undergoing coronary angiography and percutaneous coronary intervention (PCI).<sup>(1)</sup> The reported incidence of CIN after PCI was 3.3 - 20%.<sup>(1, 6, 7)</sup> Patients who developed CIN after receiving contrast media have higher complication rates, longer hospital stay, and higher mortality rate compared with patients who did not develop CIN.<sup>(8)</sup> As the majority of patients undergoing cardiac procedures are likely to be discharged within 24 hours after the procedure,<sup>(9)</sup> an assessment of CIN development beyond 24 hours is limited. Therefore, an ability to predict CIN after the procedure would be clinically benefiting. The volume of contrast media administered has been closely related to CIN development in several studies, but the precise role of the volume of contrast media for predicting the risk of CIN is still unknown.<sup>(6, 10-13)</sup> The relationship between contrast volume/body surface area (V/BSA) and the risk of CIN development has been reported. Thus, contrast media dose adjustment based on patient size

is recommended.<sup>(14)</sup> In this study we used a more practical index, i.e., volume of contrast media/body weight (V/BW) for predicting risk of CIN. This index would be practically useful for prediction of CIN after PCI than consideration of volume of contrast media alone.

## Methods

**Study population.** This study was a prospective analytical study. All patients who underwent elective or emergency PCI at King Chulalongkorn Memorial Hospital between November 10<sup>th</sup> 2009 and March 31<sup>st</sup> 2010 were enrolled. Patients were excluded under the following conditions: (1) there was no record of serum creatinine before and/or after the procedure; (2) they had pre-existing end-stage renal disease requiring dialysis; (3) they were using other nephrotoxic drugs, i.e., cisplatin, aminoglycosides, amphotericin B and cyclosporine A. Patient demographics, procedural characteristics and serum creatinine before and within 72 hours after the procedure were recorded. The study has been approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University, and informed consent was obtained from all subjects.

**Definitions.** CIN was defined as an increase in serum creatinine > 25% or > 0.5 mg/dl from pre-PCI value within 72 hours after PCI or diagnosed with CIN. The creatinine clearance (CrCl) was estimated, using the Cockcroft-Gault method as presented in Table 1. Congestive heart failure (CHF) was defined as patients presented with at least one of these signs: (1) dyspnea, (2) edema, (3) lung crepitation, and (4) chest X-ray with pulmonary congestion.

**Table 1.** Creatinine clearance calculation by using the Cockcroft-Gault method.

$$\text{CrCl (ml/min)} = [(140 - \text{age}) \times \text{weight (kg)}] / 72 \times \text{serum creatinine (mg/dl)} \{ \times 0.85 \text{ for female subjects} \}$$

**Statistical analysis.** Continuous data were summarized as the mean value  $\pm$  standard deviation (SD). Categorical data were presented as absolute values and percentages. Comparison of continuous variables was performed by Student *t* test and Wilcoxon rank sum test. Chi-square or Fisher exact tests were used to compare categorical variables as appropriate. Statistical significance for all comparisons was defined when *p*-value  $< 0.05$ . Receiver-operator characteristics (ROC) analysis was used to determine the optimal cutoff point of the total volume of contrast media (V) and V/BW ratio. SPSS (version 17.0, SPSS Inc., Chicago, Illinois) was used to analyze all the data.

All risk factors were initially screened for association with CIN by univariate logistic regression analysis at *p*-value  $< 0.20$ . The selected variables from univariate analysis were then tested by multivariate logistic regression in a forward stepwise manner using *p*-value  $< 0.05$  as cutoff criteria. The goodness of fit of multivariate logistic regression model was assessed by using the Hosmer-Lemeshow method and satisfied when *p*-value  $> 0.05$ . The ability to distinguish CIN patients from non-CIN patients (discriminative ability) was evaluated by using concordance statistic (C-statistic) and satisfied when C-statistic  $> 0.5$ .

## Results

A total of 181 consecutive patients were included in this study. Patients' demographics and

procedural characteristics are presented in Table 2 and Table 3, respectively. The mean age was  $64.7 \pm 11.6$  years, and there was 27.1% female patients. The mean pre-PCI serum creatinine was  $1.1 \pm 0.4$  mg/dl. When CrCl was estimated, 75 patients (41.4%) had CrCl lower than 60 ml/min. The volume of contrast media administered ranges from 30 to 430 ml. The mean volume of contrast media administered was  $128.2 \pm 62.1$  ml. From 181 patients enrolled in this study, 11 patients (6.1%) developed CIN. The mean difference of serum creatinine between post- and pre-PCI in patients developing CIN and those who did not develop CIN were 0.677 mg/dl and -0.098 mg/dl, respectively (*p*-value = 0.013).

Table 4 demonstrates the univariate factors associated with CIN. Patients developing CIN were older, had lower body weight, higher pre-PCI serum creatinine and lower CrCl compared with those who did not develop the complication. The means of V/BW ratio were  $3.2 \pm 2.0$  ml/kg and  $2.0 \pm 1.0$  ml/kg in patients with and without CIN, respectively. The relationship between V/BW ratio and CIN development after PCI is shown in Figure 1. In the univariate analysis, factors significantly associated with CIN were age, age  $\geq 70$  years old, female gender, weight, CHF, need for transfusion of PRBC, pre-PCI serum creatinine, pre-PCI serum creatinine  $\geq 1.5$  mg/dl, CrCl, CrCl  $< 60$  ml/min, CrCl  $< 30$  ml/min, volume of contrast media administered  $\geq 240$  ml, V/BW ratio and volume of contrast media/body surface area (V/BSA) ratio.

**Table 2.** Patient demographics.

Variable	Patients (n=181)
Age (years)	64.7 ± 11.6
Age ≥ 70 years	66 (36.5%)
Female	49 (27.1%)
Weight (kg)	65.1 ± 12.1
Body mass index (kg/m <sup>2</sup> )	24.8 ± 3.9
Body surface area (m <sup>2</sup> )	1.61 ± 0.41
Diabetes mellitus (DM)	71 (39.2%)
DM with CrCl < 60 ml/min	35 (19.3%)
Hypertension	123 (68%)
Congestive heart failure	23 (12.7%)
Dyslipidemia	104 (57.5%)
Sepsis	2 (1.1%)
Transfusion of packed red blood cell (PRBC) <sup>‡</sup>	14 (7.7%)
ACEI/ARB*	94 (52.5%)
Pre-PCI serum creatinine (mg/dl)	1.1 ± 0.4
Pre-PCI serum creatinine ≥ 1.5 mg/dl	19 (10.5%)
CrCl (ml/min)	61.9 ± 22.3
CrCl ≥ 60	106 (58.6%)
30-59	56 (30.9%)
15-29	16 (8.8%)
< 15	3 (1.7%)
CrCl < 60 ml/min without DM	40 (22.1%)
Baseline hematocrit (%)	39.4 ± 5.2

Transfusion of packed red blood cell (PRBC)<sup>‡</sup> = Patients who had hematocrit drop and need for transfusion of PRBC before PCI (percutaneous coronary intervention)

ACEI/ARB\* = Patients receiving angiotensin-converting enzyme inhibitors or angiotensin receptor blockers



**Table 3.** Procedural characteristics.

Variable	Patients (n=181)
Emergency PCI	26 (14.4%)
Duration of procedure (min)	72.9 ± 40.0
Volume of contrast media administered (ml)	128.2 ± 62.1
Contrast volume ≥ 240 ml	12 (6.6%)
Type of contrast media	
Iopromide	161 (89%)
Iodixanol	18 (9.9%)
Iopromide + Iodixanol	1 (0.55%)
Iopamidol	1 (0.55%)
N-Acetylcysteine (NAC) †	41 (22.7%)
Single vessel PCI	120 (66.3%)
Multivessel PCI	61 (33.7%)

N-Acetylcysteine (NAC) † = Patients receiving NAC pre and/or post procedure for prevention of contrast induced nephropathy

**Table 4.** Univariate analysis of patient demographics and procedural characteristics with CIN after PCI.

Variable	CIN (n = 11)	No CIN (n = 170)	p-value
Age (years)	74.9 ± 12.1	64.1 ± 11.3	0.004*
Age ≥ 70 years	8 (72.7%)	58 (34.1%)	0.019*
Female	6 (54.5%)	43 (25.3%)	0.045*
Weight (kg)	54.8 ± 14.9	65.8 ± 11.7	0.005*
Body surface area (m <sup>2</sup> )	1.54 ± 0.24	1.62 ± 0.42	0.538
Diabetes mellitus	3 (27.3%)	68 (40%)	0.408
DM with CrCl < 60 ml/min	2 (18.2%)	33 (19.4%)	0.920
Hypertension	8 (72.7%)	115 (67.6%)	0.727
Congestive heart failure	5 (45.5%)	18 (10.6%)	0.003*
Sepsis	2 (18.2%)	0	0.999
Transfusion of PRBC <sup>‡</sup>	3 (27.3%)	11 (6.5%)	0.023*
ACEI/ARB**	5 (45.5%)	89 (53%)	0.629
pre-PCI SCr <sup>□</sup> (mg/dl)	1.45 ± 0.8	1.04 ± 0.4	0.004*
pre-PCI SCr ≥ 1.5 mg/dl	4 (36.4%)	15 (8.8%)	0.009*
CrCl (ml/min)	40.7 ± 24.5	63.3 ± 21.5	0.002*

**Table 4.** Univariate analysis of patient demographics and procedural characteristics with CIN after PCI. (Continued)

Variable	CIN (n = 11)	No CIN(n = 170)	p-value
CrCl < 60 ml/min	8 (72.7%)	67 (39.4%)	0.042*
CrCl < 60 ml/min without DM	6 (54.5%)	34 (20%)	0.014*
CrCl < 30 ml/min	4 (36.4%)	15 (8.8%)	0.009*
Emergency PCI	3 (27.3%)	23 (13.5%)	0.220
Multivessel PCI	2 (18.2%)	59 (34.7%)	0.275
Iopromide	10 (90.9%)	151 (88.8%)	1.000
Volume of contrast media (ml)	160.9 ± 79.3	126.1 ± 60.6	0.081
Volume of contrast ≥ 240 ml	3 (27.3%)	9 (5.3%)	0.017*
V/BW ratio (ml/kg)	3.2 ± 2.0	2.0 ± 1.0	0.001*
V/BSA ratio (ml/m <sup>2</sup> )	109.0 ± 60.1	74.6 ± 34.8	0.007*
N-Acetylcysteine (NAC) <sup>□</sup>	5 (45.5%)	36 (21.2%)	0.074

\*significance at p-value < 0.05, SCr<sup>□</sup> = serum creatinine, CrCl = creatinine clearance, V/BW = volume of contrast/body weight, V/BSA = volume of contrast/body surface area

ACEI/ARB\*\* = Patients receiving angiotensin-converting enzyme inhibitors or angiotensin receptor blockers

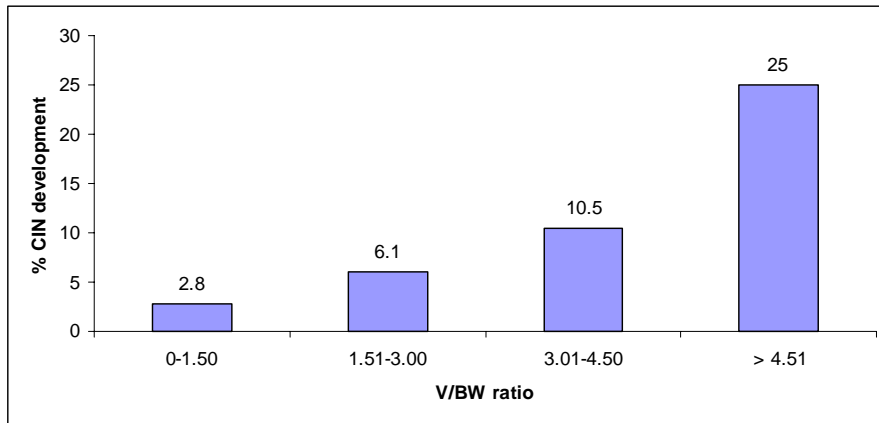
Transfusion of PRBC<sup>‡</sup> = Patients who had hematocrit drop and need for transfusion of PRBC before PCI

N-Acetylcysteine (NAC)<sup>□</sup> = Patients receiving NAC pre and/or post procedure for prevention of CIN

**Table 5.** Multivariate predictors of CIN after PCI.

Variable	Model coefficient	OR	95% CI	p-value
CHF	1.866	6.465	1.566 - 26.686	0.010
CrCl < 30 ml/min	1.815	6.141	1.349 - 27.957	0.019
V/BW ratio ≥ 2.6 ml/kg	2.102	8.184	2.015 - 33.245	0.003

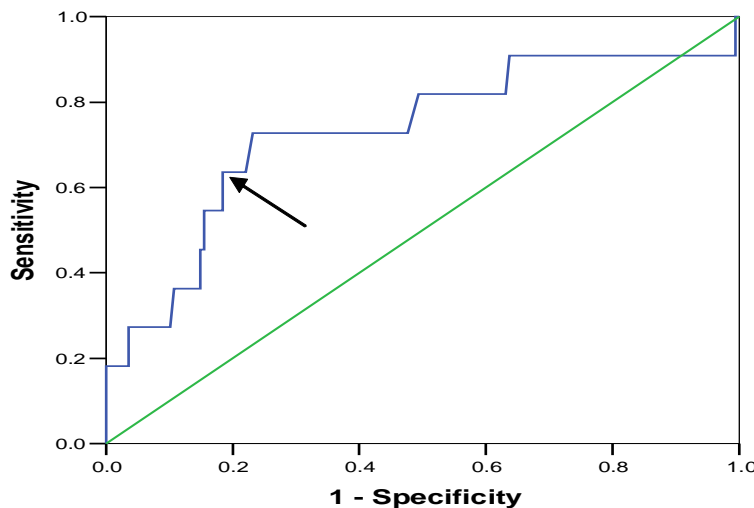
CHF = congestive heart failure, CrCl = creatinine clearance, V/BW = volume of contrast/body weight



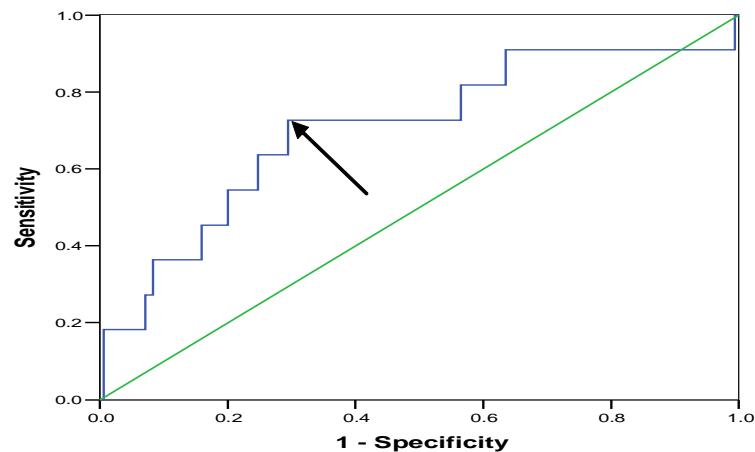
**Figure 1.** Relationship between V/BW ratio and CIN development after PCI.

Receiver-operator characteristics (ROC) curve analysis demonstrated good discriminative ability (C-statistic = 0.73) at V/BW ratio of 2.6 ml/kg (Figure 2). At this value, the sensitivity and specificity for detection of CIN were 64% and 82%, respectively. When V/BW ratio  $\geq 2.6$  ml/kg was tested in the univariate analysis, it was a significant predictor of CIN ( $p$ -value = 0.002). ROC curve analysis also

showed that V/BSA ratio  $\geq 80$  ml/m<sup>2</sup> was a good discriminator for CIN with C-statistic of 0.70. The sensitivity and specificity for detection of CIN at this value were 73% and 70%, respectively (Figure 3). Furthermore, the univariate analysis indicated that V/BSA ratio  $\geq 80$  ml/m<sup>2</sup> was associated with CIN with  $p$ -value of 0.009.



**Figure 2.** ROC analysis indicated an optimum cutoff point value for V/BW ratio is 2.6 ml/kg.



**Figure 3.** ROC analysis showed that V/BSA of 80 ml/m<sup>2</sup> is a good discriminator for CIN.

Multivariate analysis showed that CHF, CrCl < 30 ml/min and V/BW ratio  $\geq$  2.6 ml/kg were significant predictors of CIN (Table 5). The multivariate logistic regression model demonstrated good discriminative ability with C-statistic of 0.849. The *p*-value of the Hosmer-Lemeshow statistics was 0.807 (chi-square = 0.43) indicating that the model was appropriate. The Nagelkerke R<sup>2</sup> was 0.308, indicating that approximately 31% of the variation in CIN development after PCI could be explained by this multivariate model.

### Discussion

Contrast-induced nephropathy is a recognized complication after PCI.<sup>(1,4)</sup> The volume of contrast media administered has been closely correlated with CIN development in several studies, but the precise role of contrast volume for predicting risk of CIN has not been established.<sup>(6, 10, 11, 13)</sup> In this study, we proposed the use of V/BW ratio in assessing the risk of CIN after PCI. Because the dose of contrast media is usually adjusted on a basis of patient body weight,<sup>(15)</sup> we also believed that using V/BW as a

predictor of CIN should be more precisely predict safety profile of contrast media than the use of volume of contrast media.

Several studies have sought to determine the relationship between volume of contrast media administered and the risk of CIN after PCI.<sup>(6, 12, 13, 15, 16)</sup> The reported safety cutoff point of contrast volume varies from 70 ml to 220 ml.<sup>(10)</sup> Cigarroa and colleagues proposed a formula to calculate a safe weight- and creatinine- adjusted maximum contrast dose (MCD) (MCD = 5 x body weight (kg)/ serum creatinine).<sup>(15)</sup> The exceeding use of MCD was associated with a higher risk of CIN in patients with chronic kidney disease (creatinine concentration > 1.8 mg/dl).<sup>(15)</sup> In a registry of more than 16,000 PCIs, an exceeding use of MCD was the strongest predictor of nephropathy requiring dialysis in patients undergoing elective coronary interventions.<sup>(12)</sup> On the contrary, total contrast volume as a continuous variable was not a significant predictor of nephropathy requiring dialysis.<sup>(12)</sup> Moreover, a 3-fold higher incidence of CIN after primary PCI in both normal renal function and renal insufficiency patients was found to be associated

with an exceeding use of MCD.<sup>(6)</sup> In addition, an association between contrast volume/body surface area (V/BSA) and the risk of CIN was reported, suggesting an adjustment of contrast volume to the patient size, regardless of a presence or absence of chronic kidney disease.<sup>(14)</sup>

In our study of 181 patients who were undergoing PCI, the incidence of CIN after PCI was 6.1%. In contrast to a previous study, we used a more practical index, V/BW ratio, for prediction of CIN after PCI. Multivariable analysis showed that CHF, CrCl < 30 ml/min, and V/BW ratio  $\geq$  2.6 ml/kg were significant covariates. The V/BW ratio  $\geq$  2.6 ml/kg was found to be the strongest predictor of CIN after PCI. Patients who received contrast volume higher than this cutoff value were 8 times more likely to develop CIN. The total contrast volume as a continuous variable was not associated with CIN in the univariate analysis. Although, a high volume of contrast media ( $\geq$  240 ml) was associated with CIN in the univariate analysis, this index was not retained in the final model in the multivariate analysis. Moreover, from the multivariate analysis, we did not find that V/BSA was a significant predictor of CIN.

N-acetylcysteine (NAC) has been shown to be effective for the prevention of CIN in some studies.<sup>(17-19)</sup> NAC administration was added into the univariate model as a binary variable and was not found to be a significant variable ( $p$ -value = 0.074). Subgroup analysis in patients with CrCl < 60 ml/min was performed. However, we did not find any preventive effect of NAC. (OR = 2.469, 95% CI = 0.544 – 11.203).

Several risk factors associated with CIN after PCI have been identified.<sup>(10,11)</sup> Chronic kidney disease

is a major risk factor of CIN.<sup>(10, 11, 20)</sup> Our study found that CrCl < 30 ml/min was a significant predictor of CIN after PCI. Patients with CrCl < 30 ml/min were 6 times more likely to develop the complication. Our results show that there is an association between CHF and CIN after PCI (OR = 6.465, 95% CI = 1.566 - 26.686,  $p$ -value = 0.010) which is consistent with previous studies.<sup>(10, 11, 14, 21)</sup> Given that an association between V/BW ratio and CIN remained after an adjustment for other important factors, these results support our original hypothesis. The cut point of 2.6 may be a useful predictor in estimating volume of contrast media that is likely to increase risk of CIN.

### Study limitations

Although, 80% of the patients who were developing CIN started to have a rise in serum creatinine within the first 24 hours after exposure to the contrast media,<sup>(1)</sup> the limited data on serum creatinine beyond 24 hours after PCI in the present study could result in a slight underestimation of CIN. However, the delay in serum creatinine elevation beyond 24 hours after PCI may not be clinically significant.<sup>(1, 22)</sup> Moreover, we cannot exclude the possibility that other factors, apart from variables identified in our study, such as hemodynamic instability may also contribute to the risk of renal impairment. Finally, some variables such as pre- and post-PCI intravenous hydration were not assessed their effects on CIN in this study.

### Conclusion

Risk predictors of CIN after PCI included V/BW ratio  $\geq$  2.6 ml/kg, CrCl < 30 ml/min and CHF. The V/BW ratio  $\geq$  2.6 ml/kg can be used in clinical practice

as cutoff criteria for estimating an optimal volume of contrast to prevent the risk of CIN development.

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