Contrast induced nephropathy in hypertensive patients after elective percutaneous coronary intervention

Cut Aryfa Andra¹*, Andi Khairul¹, Cut Aria Arina², Zulfikri Mukhtar¹, Isfanuddin Nyak Kaoy¹

¹Department of Cardiology, University of Sumatera Utara, Jl. dr. Mansur Kampus USU Medan 20155
²Department of Neurology, University of Sumatera Utara, Jl. dr. Mansur Kampus USU Medan 20155

*Email: andra1711@gmail.com

Abstract. Contrast induced nephropathy (CIN) is the third lead cause of hospital acquired renal failure and was associated with significant morbidity and mortality. We hypothesized that hypertension is an independent risk factor for the development of CIN in patients undergoing elective percutaneous coronary intervention (PCI). The case-control method was used, 138 patients scheduled for elective PCI. We measured serum creatinine at baseline and after 24 hours of the procedure. CIN was defined as arising in serum creatinine of at least 44 µmol/l (0.5 mg/dl) or 25% rise from baseline. All patients received low osmolality nonionic contrast during PCI. Hypertension was defined as self-reported a history of treated or untreated diagnosed high blood pressure. One hundred thirty-eight patients (74.6%) were male, and 35 patients (25.4%) were female. Among the 138 patients, 86 (62.3%) were hypertensive patients whereas 52 (37.7%) were nonhypertensive patients. There was no difference in baseline serum creatinine levels and the amount of contrast media in patient with and without CIN. CIN developed in 42 patients, 39 patients (92.9%) were hypertensive compared to 3 patients (7.1%) without hypertension with p value < 0.05. (Odds ratio 16.8, 95% CI 4.542 - 62.412). This study showed that hypertension was a risk factor for the development of CIN

Keywords: complications, contrast media, coronary angiography, risk factors, nephropathy

1. Introduction
Contrast media (CM) was used increasingly in diagnostic and interventional procedure. This result in the rising incidence of iatrogenic renal function impairment caused by exposure to CM, a condition known as CIN. Radiographic CM is responsible for 11% of cases of hospital-acquired renal insufficiency, the third most common cause of renal failure after impaired renal perfusion and the use of nephrotoxic medications. Among all procedures utilizing CM for diagnostic or therapeutic purposes, coronary angiography and percutaneous coronary interventions (PCI) was associated with the highest rates of CIN [1]. CIN is a serious clinical problem associated with increased morbidity and mortality [2,3]. It is the third most common cause of hospital-acquired acute renal failure, after surgery and hypotension [4].
The definition of CIN includes three necessary components: an absolute or relative increase in serum creatinine compared to the baseline values, a temporal relationship between the rise in serum creatinine and exposure to a contrast agent, and the exclusion of alternative explanations for renal impairment [1]. CIN is typically defined in the recent literature as an increase in serum creatinine (SCr) occurring within the first 24 h after contrast exposure and peaking up to 5 days afterwards and is usually defined as an increase in SCr concentration of ≥ 0.5 or 1.0 mg/dl or relative increase of ≥ 25 or 50% over baseline [5,6]. Development of CIN has important effects on patient outcome and may contribute to other post-PCI complication including death, myocardial infarction and stroke [5]. The consequences of CIN are prolonged hospital stay, increased nonrenal morbidity and increased cardiovascular risk and mortality [7].

Arterial hypertension is a major cardiovascular risk factor and an important cause of chronic renal dysfunction. Early studies documented the presence of arteriolosclerosis and tubulointerstitial changes in nearly 100% of kidneys from patients with hypertension. Patients with hypertension would constitute a large and important risk group because of the high prevalence of the disorder in the general population as well as among patients undergoing coronary angiography [8]. The aim of the present report is to evaluate the impact of hypertension on the incidence of contrast nephropathy in patients undergoing percutaneous coronary intervention.

2. Methods
This study is case control study, the sample was taken consecutively. The written informed consent was obtained from all subjects who were admitted to Haji Adam Malik Hospital in North Sumatera, Medan, Indonesia during the study. Inclusion criteria were patients with documented SCr taken within one week before elective PCI and age >18 years old. We excluded patients who had end stage renal disease and required dialysis, patients who had recent contrast exposure before elective PCI. Patients underwent elective PCI according to the current guidelines. All patients received low osmolality nonionic contrast during PCI. CIN in our study was defined as an increase in serum creatinine of at least 44 µmol/l (0.5 mg/dl) or 25% rise from baseline recorded 24 hours before and after elective PCI. Hypertension was defined as self-reported a history of treated or untreated diagnosed high blood pressure.

Patients were assigned to received hydration with 0.9% saline (isotonic) with an infusion rate of 1 ml/kg body weight/hour. After the procedure, hydration was continued until 12 hours.

All sample matched with inclusion and exclusion criteria, demography data and others data were taken. Demography data were expressed as mean ± standard deviation or median and range. We used Chi-Square test (nominal data) and Students t-test (numerical data) to univariate analysis. Logistic regression analysis was used to multivariate analysis to test the hypothesis that hypertension is an independent risk factor for development CIN. P value < 0.05 was significant.

3. Results and Discussion
Total 138 patients included in this study. One hundred thirty-eight patients (74.6%) were male, and 35 patients (25.4%) were female. Among the 138 patients, 86 (62.3%) were hypertensive patients whereas 52 (37.7%) were nonhypertensive patients. Table 1 showed the differences in the baseline clinical characteristic between patients with CIN and without CIN. There was no difference in gender, age, history of smoking, hyperlipidemia and family history, whereas there were differences in body mass index, hypertension and diabetes mellitus with the p value <0.05.
Table 1. Baseline Clinical Characteristic

| Variable           | Total            | CIN (-) N=96 | CIN (+) N=42 | p value |
|--------------------|------------------|--------------|--------------|---------|
| 1 Men (%)          | 103 (74.6%)      | 71 (74.0%)   | 32 (76.2%)   | 0.782   |
| 2 Age (years)      | 56.7 ± 8.9       | 56.2 ± 9.6   | 58.5 ± 7.1   | 0.120   |
| 3 Body Mass Index  | 25.7 ± 3.3       | 25.3 ± 3.1   | 28.6 ± 2.8   | <0.001* |
| 4 Hypertension (%) | 86 (62.3%)       | 47 (49.0%)   | 39 (92.9%)   | <0.001* |
| 5 Diabetes Mellitus| 31 (22.5%)       | 16 (16.7%)   | 15 (35.7%)   | 0.014*  |
| 6 Smoker           | 87 (63.0%)       | 61 (63.5%)   | 26 (61.9%)   | 0.855   |
| 7 Hyperlipidemia   | 33 (23.9%)       | 25 (26.0%)   | 8 (19.0%)    | 0.375   |
| 8 Family History   | 13 (9.5%)        | 12 (12.6%)   | 1 (2.4%)     | 0.065   |

Table 2 showed the differences in the baseline laboratory values. There was no difference in baseline serum creatinine levels and the amount of contrast media in patient with and without CIN, whereas there were differences in GFR<60 and leucocyte level (p value<0.05).

Table 2. Baseline Laboratory Values

| Variable       | Total            | CIN (-) N=96 | CIN (+) N=42 | P value |
|----------------|------------------|--------------|--------------|---------|
| GFR ≤60        | 51 (37.0%)       | 41 (42.7%)   | 10 (23.8%)   | 0.034*  |
| Hemoglobin     | 13.0 ± 1.7       | 13.0 ± 1.6   | 13.1 ± 1.7   | 0.703   |
| Leucocyte      | 8000 (3080 – 19600) | 8505 (3080 – 19600) | 7570 (4400 – 17490) | 0.003  |
| Hematocrit     | 40.0 ± 5.1       | 40.1 ± 5.2   | 39.7 ± 4.9   | 0.685   |
| Ureum          | 30.0 (14.0 – 105.0) | 30 (14 – 105) | 29 (16 – 76.3) | 0.749  |
| Creatinin      | 1.1 (0.6 – 2.8)  | 1.1 (0.6 – 2.8) | 1.0 (0.6 – 2.3) | 0.232  |
| Blood glucose  | 112 (63.0 – 364.0) | 110 (63 – 364) | 116.5 (81 – 364) | 0.103  |
| SGOT           | 26 (12 – 292)    | 26 (12 – 292) | 27.5 (12 – 90) | 0.976  |
| SGPT           | 24 (6 – 128)     | 25 (6 – 128)  | 21 (6 – 71)   | 0.676   |
| Contrast volume | 200 (50 – 400)   | 200 (50 – 400) | 200 (75 – 300) | 0.080  |

Table 3 showed the prevalence of CIN in hypertension and non-hypertension patients. CIN was developed in 42 patients, 39 patients (92.9%) were hypertensive compared to 3 patients (7.1%) without hypertension with p value < 0.05. Logistic regression analysis was used to multivariate analysis to test the hypothesis that hypertension is an independent risk factor for development CIN and the result showed that hypertension was a risk factor for the development of CIN with p value <0.001, Odds ratio 16.836 and 95% CI 4.542-62.412.

Table 3. CIN in patients with and without hypertension

|                  | CIN (+)       | CIN (-)       |
|------------------|---------------|---------------|
| Hypertension     | 39 (92.9%)    | 47 (49.0%)    |
| Non Hypertension | 3 (7.1%)      | 49 (51%)      |
### Tabel 4. Multivariate analysis

| Variable            | P value | OR    | 95% CI       |
|---------------------|---------|-------|--------------|
| Hypertension        | <0.001  | 16.836| 4.542 – 62.412 |
| Diabetes Mellitus   | 0.024   | 3.186 | 1.168 – 8.695 |

The main result of the present study is that hypertension is an independent risk factor for the development of contrast nephropathy. A recently published analysis reported an incidence of contrast nephropathy of 13% among patients with glomerular filtration rate above 60 ml/min/1.73 m². Nevertheless, hypertension was also an independent predictor of contrast nephropathy in this study [9].

The subtle renal injury could be a reason for increased risk of contrast nephropathy in hypertensive patients. Nearly all patients with hypertension have pathological changes on renal biopsy [8]. Cowley et al. proposed reduced renal medullary flow with local tissue ischemia as a cause of hypertension. The same mechanism could be responsible for increased incidence of contrast nephropathy [10].

Previous studies raised the debate whether or not only patients with preexisting renal dysfunction should receive hydration before exposure to radiographic contrast agents [11]. Our result indicates that hydration should not be restricted to patients with established kidney disease. Especially patients with hypertension should be carefully prepared before being exposed to radiographic contrast media.

### 4. Conclusions

Hypertension is an independent risk factor for the development of CIN. Care must be taken before radiographic contrast agents are used in hypertensive patients.

### Acknowledgments

The authors gratefully acknowledge that the present research is supported by Ministry of Research and Technology and Higher Education Republic of Indonesia. The support is under the research grant BP-PTN USU of Year 2017.

### References

[1] Mehran R, Nikolsky E (2006) Contrast induced nephropathy: definition, epidemiology, and patients at risk. *Kidney International*. 69:S11-S15.

[2] Toprak O, Cirit M (2006) Risk factor for contrast induced nephropathy. *Kidney Blood Press Res*. 29:84-93.

[3] Marenzi G, Assanelli E, Campodonico J, Lauri G, Marana I, Demetrio M, et al. (2009) Contrast volume during primary percutaneous coronary intervention and subsequent contrast induced nephropathy and mortality. *Ann Intern Med*. 150:170-7.

[4] Gleeson TG, Bulugahapitiya S (2004) Contast induced nephropathy. *AJR*.183:1673-89.

[5] Brinker JA, Davidson CJ, Laskey W. (2005) Preventing in hospital cardiac and renal complications in high risk PCI patients. *Eur Heart J Supp*.7(Suppl G):G13-G24.

[6] McCullough PA (2008) Contast induced acute kidney injury. *J Am Coll Cardiol*. 51:1419-28.

[7] Stermn G, Nyman U. Contrast medium induced nephropathy: aspects on incidence, consequences, risk factors and prevention. *Libyan J Med*. Downloaded from: www.ljm.org.ly

[8] Conen D, Buerkle G, Perruchoud AP, Buettner HJ, Mueller C (2006) Hypertension is an independent risk factor for contrast nephropathy after percutaneous coronary intervention. *International Journal Of Cardiology*.110:237241.

[9] Dangas G, Iakovou I, Nikolsky E, et al. (2005) Contrast induced nephropathy after percutaneous coronary intervention in relation to chronic kidney disease and hemodynamic variables. *Am J Cardiol*. 95:13-9.
[10] Cowley Jr AW, Mattson DL, Lu S, Roman RJ (1995) The renal medulla and hypertension. Hypertension. 25:663-73.

[11] Barrett BJ, Parfrey PS (2006) Preventing nephropathy induced by contrast medium. *N Eng J Med*. 354:379-86.