

# The Achievability of Minimum Contrast Procedures for the Prevention of Contrast Induced Nephropathy in Patients with Chronic Kidney Disease: A Prospective, Multicentre Trial

Yoshiaki Kawase<sup>1\*</sup>, Hitoshi Matsuo<sup>1</sup>, Tomohiko Teramoto<sup>2</sup>, Osamu Matsuda<sup>3</sup>, Yoriyasu Suzuki<sup>3</sup>, Etsuo Tsuchikane<sup>2</sup> and Takahiko Suzuki<sup>2</sup>

<sup>1</sup>Department of Cardiovascular Medicine, Gifu Heart Center, Gifu City, Gifu, Japan

<sup>2</sup>Department of Cardiovascular Medicine, Toyohashi Heart Center, Toyohashi City, Aichi, Japan

<sup>3</sup>Department of Cardiovascular Medicine, Nagoya Heart Center, Nagoya, Aichi, Japan

\*Corresponding author: Yoshiaki Kawase, Department of Cardiovascular Medicine, Gifu Heart Center, 4-14-4 Yabutaminami Gifu City, Gifu, Japan 500-8384, Tel: +81-58-277-2277; E-mail: [ykawase@heart-center.or.jp](mailto:ykawase@heart-center.or.jp)

Received date: November 10, 2014; Accepted date: November 28, 2014; Published date: November 29, 2014

Copyright: © 2014 Kawase Y, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited

## Abstract

### Background

The practical utility of minimum contrast procedures in a real world setting is unclear. In this trial, the reality of this strategy was investigated.

### Methods

Patients with an estimated glomerular filtration rate (eGFR) of  $\leq 45$  ml/min/1.73m<sup>2</sup> were included in this study with dates ranging from Jan 17th 2012 to Oct 8th 2013. Various methods to minimize the amount of contrast media were applied. An achievement rate of contrast volume/eGFR $<2.0$  was calculated and the characteristics of the patients and catheter procedures were investigated.

### Results

A total of 88 patients were enrolled. There were 34 patients who underwent a diagnostic coronary angiogram (CAG group) and 54 patients who underwent an interventional procedure (PCI group). The PCI group tended to use a larger amount of contrast media compared to the CAG group ( $39 \pm 49$  ml vs  $25 \pm 14$  ml,  $p=0.06$ ). A ratio of contrast volume to eGFR of less than 2.0 was achieved in 100% of the CAG group but in only 82% of the PCI group. The patients with complex procedures (complex PCI) such as use of a rotablator and treatment of chronic total occlusion used significantly more contrast media than patients with other procedures (simple PCI). ( $87 \pm 69$  ml vs  $23 \pm 27$  ml,  $p=0.006$ ) Surprisingly, when simple PCI group was compared to the CAG group, there was no difference in the contrast volume used. ( $23 \pm 27$  vs  $25 \pm 14$  ml,  $p=0.708$ )

### Conclusions

Simple PCI can be done as safely as in CAG patients with chronic kidney dysfunction. Complex PCI should be done with careful assessment of the balance between risk and benefit.

**Keywords:** Chronic kidney disease; Minimum contrast procedures; Contrast induced nephropathy; Percutaneous coronary intervention

## Introduction

Contrast induced nephropathy (CIN) is an important complication following exposure to iodinated contrast media. It is defined as an absolute creatinine level increase of 0.5 mg/dl and/or as a relative creatinine increase of 25% 48-72 hours after the usage of contrast media [1-5].

The occurrence of CIN is associated with increased mortality and morbidity [3,6,7]. There have been various attempts to reduce the incidence of this complication with pharmaceutical approaches.

However, none have resulted without controversy, in the establishment of key drugs that can effectively prevent CIN [1,8,9]. As of today, the established and widely accepted regimen to prevent the occurrence of CIN has only been hydration with intravenous infusion of isotonic saline (NaCl 0.9%). Minimizing the amount of contrast media to be used is a more intuitive way to prevent this complication but the amount of the contrast media needs to be extremely low in order to see a meaningful preventive effect [10-13]. There have been sporadic case reports about the possibility of minimum contrast procedures utilizing various imaging modalities and techniques [14-16]. However, the practical utility of these procedures in a real world setting is not clear. In this trial, the reality of this strategy in real world practice was investigated prospectively.

## Materials and Methods

### Patients

The study population consisted of patients who underwent either a coronary angiogram (CAG) or percutaneous coronary intervention (PCI) from Jan 17th, 2012 to Oct 8th, 2013 in three medical hospitals. Patients were screened at outpatient department with a blood test and echocardiogram. The patients whose estimated glomerular filtration rate (eGFR) of >45 ml/min/1.73 m<sup>2</sup> or who were not suitable for receiving hydration with intravenous infusion of isotonic saline were excluded from the study (i.e. acute coronary syndrome, hemodialysis, cardiogenic shock, severe chronic heart failure, refusal of staying in the hospital for hydration, etc). Patients were admitted to the hospital the day before the procedure and were administered body weight (kg)×1 ml of isotonic saline at least 12 hours before and after the catheter procedures.

The ethics committee at all three hospitals approved the protocol, and a written informed consent was obtained from all patients.

### Clinical demographics

The hospital records of all patients were reviewed to obtain clinical demographics, laboratory results, and drug information. Risk factors for coronary artery disease were defined as diabetes mellitus, hypertension, hypercholesterolemia (medication dependent), smoking (active smoking or having stopped smoking <6 months before the study), and family history. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) study group equation for Japanese people as follows:  $eGFR = 0.881 \times 186 \times [\text{serum creatinine (mg/dL)}]^{-1.154} \times (\text{age})^{-0.203} (\times 0.742 \text{ for women})$  [17].

### Minimum contrast procedures

1	Use small diameter catheters (i.e, 4-5 French for diagnostic and 5-6 French for interventional procedure if it is possible) without side-holes.
2	Use biplane angiography machine
3	Remove contrast from the catheter by aspiration prior to insertion of another device (wire, balloon, IVUS, etc).
4	Use a pressure wire rather than taking multiple coronary angiogram to evaluate the severity of coronary stenosis
5	Do not do ad hoc PCI unless there is an unavoidable reason
6	Use IVUS for pre-PCI lesion assessment, selection of the size of therapeutic devices, and post-PCI result assessment.
7	During PCI, especially in the treatment of CTO, use a microcatheter for the selected regional imaging with extremely minimum amount of contrast.
8	During the treatment of CTO, use IVUS guide wire manipulation whenever it is applicable.
9	Start with the target CV/eGFR<1 and consider if the procedures can be done with the target CV/eGFR<2 when the volume of contrast exceeded CV/eGFR=1.
	Make CV/eGFR<2 as a final target dose of contrast volume.

**Table 1:** Modified Ultra-low Contrast technique; IVUS: intravascular ultrasound, PCI: percutaneous coronary intervention; CTO: chronic total occlusion; CV/eGFR: the ratio of contrast volume to the estimated glomerular filtration rate

Modified Ultra-Low Contrast techniques from previous reports were applied. The details about the techniques are shown in Table 1.

It is reported that the ratio of the volume of contrast media to the creatinine clearance>3.7 is an independent predictor of CIN [18]. Although eGFR is a brief version of creatinine clearance, we made the ratio of contrast volume to the eGFR (CV/eGFR)<2.0 as a final target dose of contrast media to be used. We set up a safety margin for the final target contrast media volume assuming an abnormal coronary anatomy, complications during the procedure, and an ad hoc procedure in a case in which it is unavoidable. All procedures were performed using low-osmolarity contrast media (Iohexol, Iopaidol).

### The definition of procedures

We defined procedures with the use of a rotablator<sup>TM</sup> (Boston Scientific, MA, USA) and the treatment of chronic total occlusion (CTO) as complex PCI. The procedures without complex PCI were defined as simple PCI.

### The definition of CIN

The blood examinations were performed pre hydration, 48 hours after the procedure, and at 1 week after the procedure. The occurrence of CIN was defined as an absolute creatinine level increase of 0.5 mg/dl and/or as a relative creatinine increase of 25% [4,5]. The percent change of creatinine between pre and 48 hours after procedures was calculated as; % change of creatinine = (Post creatinine - Pre creatinine)\*100 / Pre creatinine.

### Statistical analysis

The results are presented as mean ± standard deviation. An unpaired t test for continuous and normally distributed variables and Mann-Whitney's U test for continuous and non-normally distributed variables were used. A chi-squared test was used for categorical variables. Two-sided p-values of less than 0.05 were considered statistically significant. All statistical tests were performed using SPSS version 21 (SPSS Inc., Chicago, IL, USA).

### Results

A total of 3878 patients were admitted to three hospitals for either an elective CAG or PCI during the study period. Of the patients who agreed to stay in the hospital for three days to do a peri-procedural hydration, and blood examination 48 hours and 1 week after the procedures, 104 patients met the inclusion criteria of eGFR≤45 (out of 465 eligible patients in entire cohort) and were considered to enter the study. Six patients were excluded from the study due to heart failure. Ten patients were excluded due to various reasons (entry to the other studies, etc). As a result, a total of 88 patients (34 patients with CAG and 54 patients with PCI) were enrolled and analyzed.

### CAG and PCI

There were 34 patients who underwent a cardiac angiogram (CAG group) and 54 patients who underwent a percutaneous coronary intervention (PCI group). The PCI group tended to use a larger amount of contrast media (39 ± 49ml vs 25 ± 14 ml, p=0.06) and underwent a significantly longer procedure (90 ± 60 min vs 28 ± 13 min, p<0.001) compared to the CAG group. However, there was no significant difference in the % change of creatinine between the two groups (-9.1 ± 10.5 vs -7.2 ± 10.4, p=0.404) (Table 2).

	CAG group (n=34)	PCI group (n=54)	p value
Age (years)	79 ± 7	75 ± 7	0.004
Male (%)	19 (56)	41 (76)	0.049
Height (cm)	153 ± 11	159 ± 8	0.018
Body weight (kg)	57 ± 13	62 ± 11	0.032
Body Mass Index	24 ± 4	25 ± 3	0.396
Body Surface Area (m <sup>2</sup> )	1.5 ± 0.2	1.6 ± 0.2	0.013
Diabetes mellitus (%)	13 (38)	25 (47)	0.412
Hypertension (%)	32 (94)	47 (87)	0.286
Hypercholesterolemia (%)	15 (44)	34 (63)	0.083
Ejection fraction (%)	60 ± 13	61 ± 11	0.671
Baseline creatinine (mg/dl)	1.3 ± 0.3	1.5 ± 0.4	0.008
Baseline eGFR (ml/min/1.73m <sup>2</sup> )	38 ± 9	35 ± 8	0.193
Baseline eGFR<30 (%)	9 (27)	12 (22)	0.649
Day 2 after procedure creatinine (mg/dl)	1.2 ± 0.3	1.4 ± 0.4	0.036
Day 2 after procedure eGFR (ml/min/1.73 m <sup>2</sup> )	37 ± 13	38 ± 11	0.642
% change of creatinine (%)	-7.2 ± 10.4	-9.1 ± 10.5	0.404
1 week after procedure creatinine (mg/dl)	1.3 ± 0.4	1.5 ± 0.5	0.009
1 week after procedure eGFR (ml/min/1.73 m <sup>2</sup> )	37 ± 11	36 ± 11	0.563
Radial approach (%)	32 (94)	37 (69)	0.004
Contrast volume (ml)	25 ± 14	39 ± 49	0.06
Contrast volume/eGFR	0.7 ± 0.3	1.1 ± 1.4	0.644
Contrast volume/eGFR<1.0 (%)	29 (85)	36 (67)	0.053
Contrast volume/eGFR<2.0 (%)	34 (100)	44 (82)	0.08
Contrast volume/eGFR<3.0 (%)	34 (100)	46 (85)	0.019
Previous PCI (%)	20 (59)	28 (52)	0.522
Previous CABG (%)	3 (9)	9 (17)	0.297
Procedure time (min)	28 ± 13	90 ± 60	<0.001

**Table 2:** Characteristics of patients between CAG and PCI group; CAG: coronary artery angiography, PCI: percutaneous coronary intervention; eGFR: estimated glomerular filtration rate, CABG: coronary artery bypass graft, % change of creatinine = (Post creatinine – Pre creatinine)\*100 / Pre creatinine

All procedures were without serious complication and all of the interventional procedures were successful. None of the studied patients suffered from CIN or nephropathy requiring dialysis.

### Factors associated with CV/eGFR>=2

A ratio of contrast volume to eGFR (CV/eGFR)<2.0 was achieved in the entire CAG group but in only 82% of the PCI group (Table 2). When comparing patients with CV/eGFR<2 and >=2, the latter group had less radial approaches (40% vs 83%, p=0.002), longer procedure times (123 ± 62 min vs 59 ± 51 min, p<0.001), more PCIs (100% vs 56%, p=0.008), the use of a rotator (40% vs 4%, p<0.001), and the treatment of CTO (30% vs 4%, p=0.002) (Table 3).

	CV/eGFR<2 (n=78)	CV/eGFR>=2 (n=10)	p value
Age (years)	77 ± 7	73 ± 8	0.155
Male (%)	54 (69)	6 (60)	0.555
Height (cm)	157 ± 10	155 ± 10	0.551
Body weight (kg)	61 ± 12	55 ± 11	0.198
Body Mass Index	24.5 ± 3.4	23.1 ± 4.0	0.305
Body Surface Area (m <sup>2</sup> )	1.6 ± 0.2	1.5 ± 0.2	0.243
Diabetes mellitus (%)	34 (44)	4 (40)	0.803
Hypertension (%)	71 (91)	8 (80)	0.279
Hypercholesterolemia (%)	46 (59)	3 (30)	0.082
Ejection fraction (%)	61 ± 11	59 ± 15	0.738
Baseline creatinine (mg/dl)	1.4 ± 0.4	1.5 ± 0.2	0.134
Baseline eGFR (ml/min/1.73m <sup>2</sup> )	38 ± 12	36 ± 8	0.093
Baseline eGFR<30 (%)	18 (23)	3 (30)	0.629
Day 2 after procedure creatinine (mg/dl)	1.3 ± 0.4	1.4 ± 0.3	0.318
Day 2 after procedure eGFR (ml/min/1.73m <sup>2</sup> )	38 ± 12	36 ± 8	0.628
% change of creatinine (%)	-8. ± 9.5	-7.5 ± 16.6	0.873
1 week after procedure creatinine (mg/dl)	1.4 ± 0.5	1.4 ± 0.4	0.86
1 week after procedure eGFR (ml/min/1.73m <sup>2</sup> )	37 ± 11	32 ± 6	0.239
Radial approach (%)	65 (83)	4 (40)	0.002
PCI (%)	44 (56)	10 (100)	0.008
Previous PCI (%)	41 (53)	7 (70)	0.297
Previous CABG (%)	9 (12)	3 (30)	0.109
Ad hoc procedure (%)	6 (8)	3 (30)	0.007
Minimum lumen diameter (mm)	0.9 ± 0.4	0.8 ± 0.7	0.767
Reference vessel diameter (mm)	2.6 ± 0.5	2.8 ± 0.3	0.307
Lesion Length (mm)	18 ± 12	30 ± 22	0.059
Severe calcification (%)	1 (2)	3 (30)	0.003

Severe bending (%)	2 (5)	0 (0)	0.492
Bifurcation lesion (%)	4 (9)	3 (30)	0.076
Rotablator (%)	3 (4)	4 (40)	<0.001
Chronic total occlusion (%)	3 (4)	3 (30)	0.002
Contrast volume (ml)	22 ± 17	124 ± 52	<0.001
Procedure time (min)	59 ± 51	123 ± 62	<0.001

**Table 3:** Characteristics of patients with or without CV/eGFR $\geq$ 2; CV/eGFR: the ratio of contrast volume to the estimated glomerular filtration rate; PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, % change of creatinine = (Post creatinine - Pre creatinine)\*100 / Pre creatinine

### CAG and simple PCI

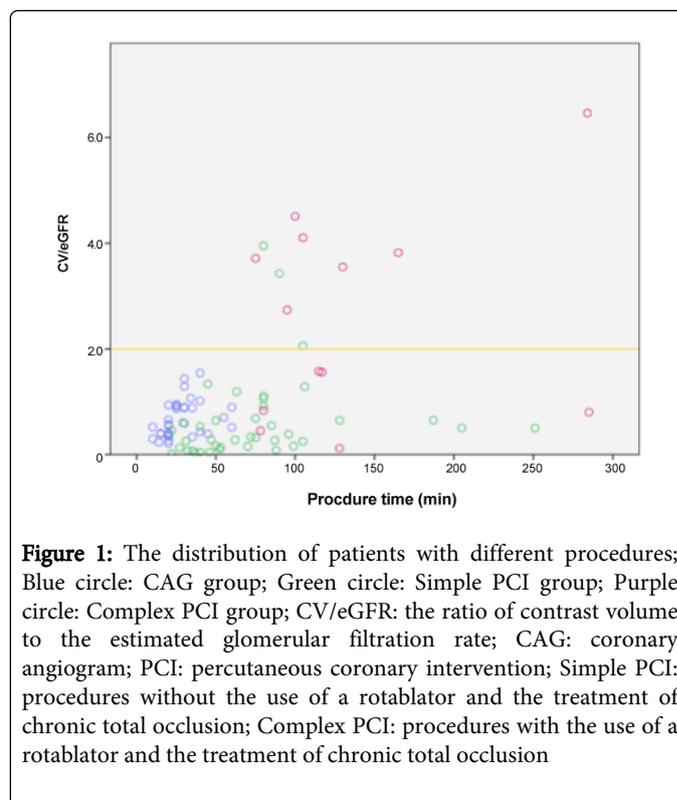
Surprisingly, when the simple PCI group was compared to the CAG group, there was no significant difference in the contrast volume used (23 ± 27 vs 25 ± 14 ml, p=0.708) despite the simple PCI group requiring a significantly longer procedure time (77 ± 49 min vs 28 ± 13 min, p<0.001). Moreover, the simple PCI group showed more negative % change of creatinine compared to the CAG group (-11 ± 9 vs -7 ± 10, p=0.014).

### Simple PCI and complex PCI

Compared to the simple PCI group, the complex PCI group had more severe lesion characteristics such as severe calcification (23% vs 2%; p=0.013) or smaller minimum lumen diameter (0.6 ± 0.6 mm vs 1.0 ± 0.4 mm; p=0.022). These differences led to longer procedure times (135 ± 71 min vs 76 ± 49 min; p=0.012), larger contrast volumes (87 ± 69 ml vs 23 ± 27 ml; p=0.006), less achievement of CV/eGFR<2 (46% vs 93%; p<0.001), and less negative % change of creatinine (-4.1 ± 14.4% vs -10.6 ± 8.5%; p=0.049) in the complex PCI group compared to those of the simple PCI group.

### The distribution of the patients with each procedure in the dimensions of procedure time and CV/eGFR

Figure 1 shows a scattergram of patients with each procedure in the dimensions of procedure time and CV/eGFR. The CAG group was concentrated in a limited area both in procedure time and contrast volume. The complex PCI group showed widest dispersion both in procedure time and CV/eGFR. The simple PCI group seemed to be able to limit the amount of contrast media regardless of the length of the procedure time. Only three cases in the simple PCI group could not achieve CV/eGFR<2.0. All three of these patients had an ad hoc PCI performed due to various reasons (patient seemed not to be able to tolerate a second procedure, the operator was confident to finish the treatment with extremely small addition of contrast media, etc).



**Figure 1:** The distribution of patients with different procedures; Blue circle: CAG group; Green circle: Simple PCI group; Purple circle: Complex PCI group; CV/eGFR: the ratio of contrast volume to the estimated glomerular filtration rate; CAG: coronary angiogram; PCI: percutaneous coronary intervention; Simple PCI: procedures without the use of a rotablator and the treatment of chronic total occlusion; Complex PCI: procedures with the use of a rotablator and the treatment of chronic total occlusion

### Discussion

The findings in this study are (1) a CAG is predictable both in procedure time and CV/eGFR. All patients undergoing a CAG could achieve CV/eGFR<2.0. (2) Patients with PCI are less predictable both in procedure time and CV/eGFR. However, the patients who could not achieve CV/eGFR<2 have certain characteristics of their procedures and situations.

After various reports have shown the relationship between contrast volume and the occurrence of CIN, there have been several case reports about the possibility of minimum contrast procedures utilizing various imaging modalities and techniques not only in CAG, but also in the most challenging case of PCI, in other words, in the treatment of CTO [11,12,14-16]. Seeking the way to perform complicated procedures with minimum contrast volume is of paramount importance since it is implied that these patients have a more predicted CIN risk factors and tend to use more contrast media due to the complicated nature of their lesions [13].

However, the practical utility of this procedure in a real world setting is not clear and these reports may lead to the reckless application of PCI in patients with chronic kidney dysfunction.

### The achievability of CV/eGFR $\geq$ 2

In this trial, even with vigorous procedures in high volume centers, the amount of contrast media was not perfectly under control in certain situations. However, if we excluded several procedures and situations such as ad hoc PCI and complex PCI, all procedures could be performed with CV/eGFR<2.0 in patients with chronic kidney dysfunction. This is surprising considering the fact that each group has around 20-30% of patients with eGFR<30 ml/min/1.73 m<sup>2</sup>.

Furthermore, when we exclude the complex PCI group, the amount of contrast media is almost equivalent between the CAG and the simple PCI group. The % change of creatinine showed an even better result in the simple PCI group.

From a different viewpoint, the present study proved that even in complex PCI, there are cases that can be performed with CV/eGFR<2.0. A study with a larger cohort is warranted to verify the findings of this report.

### Minimum contrast procedures in complex PCI

Although there is a report that even a treatment of a chronic total occlusion can be performed with only 10 ml of contrast media, the average amount of contrast media used in complex PCI was  $87 \pm 69$  ml in the present study [15]. One of the reasons for this discrepancy is a procedure using a rotablator. A rotablator is a device that consists of a brass burr coated with diamond chips measuring 30-120  $\mu$ m in diameter. This burr rotates at certain speed and selectively removes hard tissue. Soft tissue is supposed to be deflected by the elastic recoil of normal segments of the vessel. However, compared to other angioplasty, those using a rotablator are associated with four times the risk of perforation [19]. To detect this serious and lifethreatening complication as soon as possible, frequent administration of contrast media during the procedure is mandatory. This limits the possibility to do this procedure without the administration of the appropriate amount of contrast media.

The other reason for this discrepancy is diverseness in the anatomical type of CTO. Without a good collateral channel to be used for retrograde angiography or retrograde approach, the possibility of a minimum contrast procedure is slim in the treatment of CTO. This diversity makes it difficult to predict the amount of contrast media to be used in these most challenging types of PCI [20,21].

### Limitation

First, the patients who are not suitable for the pre procedural hydration were excluded from the study as in the other previous studies that tested the applicability of these techniques in elective and stable patients [14-16]. Therefore, the result of this study is not applicable for the patient with acute coronary syndrome and heart failure who are intolerable to hydration. However, these are actually the patients who are known to be at a high risk for CIN and would receive most benefit from minimum contrast procedures.

Second, it is likely that acute kidney injury after PCI is multifactorial. Even if we performed the procedures with absolutely zero contrast, there is still a risk of acute kidney injury after PCI, e.g. by cholesterol embolization [22].

Third, the sample size was limited in this study. Therefore, the results from this study should be considered as hypothesis generating. Furthermore, we fortunately did not encounter patients with CIN. Again, the number of patients with CV/eGFR $\geq$ 2.0 was too small in this study. It should be considered that patients with CV/eGFR $\geq$ 2.0 due to the unexpected contrast media overuse have the same higher possibility to have CIN [12].

Fourth, the amount of contrast media to be used in this study in complex PCI was extremely low considering the nature of the complexity of these lesions [13]. It should be noted that this level of procedures can be achieved only in the hospitals that are focusing on developing the level of techniques in procedures.

Fifth and lastly, for patients who are not eligible for hydration and minimum contrast procedures, the quest to seek a pharmaceutical approach to prevent the occurrence of CIN should be continued.

### Conclusion

Both the CAG and the simple PCI group without ad hoc PCI were performed with CV/eGFR<2.0. However, complex PCI were risk factors for the overuse of contrast media and should be paid an extreme caution for their application in patients with chronic kidney disease.

### Acknowledgments

Special thanks go to Yumiko Hasegawa for her work to collect and analyze all study related data and Hidemaro Sato for his support in statistics.

### References

- Owen RJ, Hiremath S, Myers A, Fraser-Hill M, Barrett BJ (2014) Canadian Association of Radiologists consensus guidelines for the prevention of contrast-induced nephropathy: update 2012. *Can Assoc Radiol J* 65: 96-105.
- Golshahi J, Nasri H, Gharipour M (2014) Contrast-induced nephropathy; A literature review. *J Nephrothol* 3: 51-56.
- Ohno I, Hayashi H, Aonuma K, Horio M, Kashihara N, et al. (2013) Guidelines on the use of iodinated contrast media in patients with kidney disease 2012: digest version : JSN, JRS, and JCS Joint Working Group. *Clin Exp Nephrol* 17: 441-479.
- Aurelio A, Durante A (2014) Contrast-induced nephropathy in percutaneous coronary interventions: pathogenesis, risk factors, outcome, prevention and treatment. *Cardiology* 128: 62-72.
- Aspelin P, Aubry P, Fransson SG, Strasser R, Willenbrock R, et al. (2003) Nephrotoxic effects in high-risk patients undergoing angiography. *N Engl J Med* 348: 491-499.
- McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW (1997) Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. *Am J Med* 103: 368-375.
- Weisbord SD, Chen H, Stone RA, Kip KE, Fine MJ, et al. (2006) Associations of increases in serum creatinine with mortality and length of hospital stay after coronary angiography. *J Am Soc Nephrol* 17: 2871-2877.
- Schweiger MJ, Chambers CE, Davidson CJ, Blankenship J, Bhalla NP, et al. (2007) Prevention of contrast induced nephropathy: recommendations for the high risk patient undergoing cardiovascular procedures. *Catheter Cardiovasc Interv* 69: 135-140.
- Carbonell N, Blasco M, Sanjuán R, Pérez-Sancho E, Sanchis J, et al. (2007) Intravenous N-acetylcysteine for preventing contrast-induced nephropathy: a randomised trial. *Int J Cardiol* 115: 57-62.
- Madsen TE, Pearson RR, Muhlestein JB, Lappé DL, Bair TL, et al. (2009) Risk of nephropathy is not increased by the administration of larger volume of contrast during coronary angiography. *Crit Pathw Cardiol* 8: 167-171.
- Kane GC, Doyle BJ, Lerman A, Barsness GW, Best PJ, et al. (2008) Ultra-low contrast volumes reduce rates of contrast-induced nephropathy in patients with chronic kidney disease undergoing coronary angiography. *J Am Coll Cardiol* 51: 89-90.
- Ogata N, Ikari Y, Nanasato M, Okutsu M, Kametani R, et al. (2014) Safety margin of minimized contrast volume during percutaneous coronary intervention in patients with chronic kidney disease. *Cardiovasc Interv Ther* 29: 209-215.
- Kooiman J, Seth M, Share D, Dixon S, Gurm HS (2014) The association between contrast dose and renal complications post PCI across the continuum of procedural estimated risk. *PLoS One* 9: e90233.

14. Nayak KR, Mehta HS, Price MJ, Russo RJ, Stinis CT, et al. (2010) A novel technique for ultra-low contrast administration during angiography or intervention. *Catheter Cardiovasc Interv* 75: 1076-1083.
15. Uehara Y, Shimizu M, Yoshimura M (2013) A case of CTO treated with minimum use of contrast media. *Catheter Cardiovasc Interv* 82: E884-887.
16. Ogata N, Matsukage T, Toda E, Tamiya S, Fujii T, et al. (2011) Intravascular ultrasound-guided percutaneous coronary interventions with minimum contrast volume for prevention of the radiocontrast-induced nephropathy: report of two cases. *Cardiovasc Interv Ther* 26: 83-88.
17. Imai E, Horio M, Nitta K, Yamagata K, Iseki K, et al. (2007) Estimation of glomerular filtration rate by the MDRD study equation modified for Japanese patients with chronic kidney disease. *Clin Exp Nephrol* 11: 41-50
18. Laskey WK, Jenkins C, Selzer F, Marroquin OC, Wilensky RL, et al. (2007) Volume-to-creatinine clearance ratio: a pharmacokinetically based risk factor for prediction of early creatinine increase after percutaneous coronary intervention. *J Am Coll Cardiol* 50: 584-590.
19. Wasiak J, Law J, Watson P, Spinks A (2012) Percutaneous transluminal rotational atherectomy for coronary artery disease. *Cochrane Database Syst Rev* 12: CD003334.
20. Sumitsuji S, Inoue K, Ochiai M, Tsuchikane E, Ikeno F (2011) Fundamental wire technique and current standard strategy of percutaneous intervention for chronic total occlusion with histopathological insights. *JACC Cardiovasc Interv* 4: 941-951.
21. Rathore S, Katoh O, Matsuo H, Terashima M, Tanaka N, et al. (2009) Retrograde percutaneous recanalization of chronic total occlusion of the coronary arteries: procedural outcomes and predictors of success in contemporary practice. *Circ Cardiovasc Interv* 2: 124-132.
22. Cuddy E, Robertson S, Cross S, Isles C (2005) Risks of coronary angiography. *Lancet* 366: 1825.