

Letter to the Editor

A simple pre-procedural risk score for contrast-induced nephropathy among patients with chronic total occlusion undergoing percutaneous coronary intervention



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Contrast-induced nephropathy (CIN) had been demonstrated to be associated with short- and long-term adverse outcomes in patients after percutaneous coronary intervention (PCI) [1–3]. Complex PCI procedure for coronary chronic total occlusion (CTO) lesions with high risk of CIN may adversely affect the benefit of the revascularization success, because of patients with CTO–PCI administered large contrast medium (CM), and are generally older and more likely to have reduced ventricular ejection function, and worse renal function than patients without CTO, which were risk factors of CIN [4].

Identifying patients at high risk of CIN before PCI is of utmost clinical importance to make timely pre-procedural decisions regarding the therapeutic intervention to minimizing the risk. Therefore, we aimed to derive a simple pre-procedural risk score to predict CIN risk in patients with CTO before PCI.

All consecutive patients with CTO who underwent our institution's basic PCI protocol between January 2010 and September 2012 were enrolled prospectively. The study conformed to the ethical principles laid down in the declaration of Helsinki and the protocol was approved by our hospital's ethics committee. Written informed consent was obtained from all patients before the procedure.

Serum creatinine (SCr) was measured upon admission, and within 48–72 h after CM exposure. Left ventricular function was evaluated in patients with echocardiography within 24 h before the procedure. PCI was performed by interventional cardiologists according to standard clinical practice. Nonionic, low-osmolality CM was used in all patients. 0.9% Normal saline at a rate of 1 mL/kg/h was administered intravenously 3–12 h before and 6–12 h after exposure to CM.

The primary end-point was CIN, which was defined as an absolute increase in SCr of ≥ 0.5 mg/dL over baseline values within 48–72 h after CM exposure [5]. The secondary end-points were major adverse clinical events (MACEs), including all-cause mortality renal replacement therapy, acute heart failure, or cerebrovascular events in hospital.

Continuous variables are expressed as mean $\pm$ SD and compared with *t*-test. Categorical variables are reported as absolute values and/or percentages and compared by χ^2 test or Fisher's exact test. Predictors of CIN were derived from demographic, clinical, and procedural variables in the training cohort. Variables with $p < 0.20$ in the univariate analysis, together with other known CIN risk factors were entered into the multivariate logistic regression analysis by forward stepwise selection to identify independent predictors of CIN. The adjusted odds ratio (OR) and 95% confidence interval (CI) were calculated. The model's predictive performance (discrimination) and calibration were assessed using receiver operating characteristic (ROC) curves and the calibration slope respectively. All data analyses were performed using SAS version 9.3. A two-tailed $p < 0.05$ was always requested for statistical significance.

The total eligible patients ($n = 728$) were randomized in a 3:2 ratio to create a training ($n = 495$) and a validation cohort ($n = 233$) for risk score development. Overall, 15 (3.0%) patients developed CIN in training dataset. Compared to patients without CIN, age ≥ 75 years, LVEF $< 40\%$ and baseline SCr levels of > 1.5 mg/dL were more common among CIN patients. However, there were no significant differences between the two groups in other demographic, clinical, baseline laboratory, and PCI procedure data (Table 1).

Those variables that were significant in the univariate analysis, together with other known risk CIN factors, were included in the multivariate analysis. The results of the latter analysis showed that age ≥ 75 years (OR: 4.43, $p = 0.011$), LVEF $< 40\%$ (OR: 3.58, $p = 0.038$) and SCr > 1.5 mg/

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Table 1
Baseline clinical features in patients with and without CIN of the training dataset.

Variable	CIN (n = 15)	Non-CIN (n = 480)	P value
Demographics			
Age, (years)	72.0 ± 9.4	62.0 ± 10.7	<0.001
Age ≥ 75 years, (%)	6 (40.0)	61 (12.7)	0.002
Women (%)	3 (20.0)	80 (16.7)	0.108
SBP (mm Hg)	129.4 ± 26.1	128.6 ± 18.6	0.909
DBP (mm Hg)	72.5 ± 10.6	75.8 ± 11.5	0.268
Medical history, n (%)			
Smokers	5 (33.3)	211 (44.0)	0.414
Hypertension	10 (66.7)	285 (59.4)	0.571
Diabetes	5 (33.3)	125 (26.0)	0.527
Hypercholesterolemia	2 (13.3)	73 (15.2)	0.842
Prior MI	1 (6.7)	74 (15.4)	0.352
Prior CABG	0 (0.0)	14 (2.9)	0.502
Laboratory findings			
Baseline SCr (μmol/L)	128.0 ± 46.7	88.3 ± 24.9	0.005
Baseline SCr > 1.5 mg/dL, n (%)	6 (40.0)	27 (5.6)	<0.001
LVEF%	46.7 ± 14.9	56.1 ± 13.1	0.007
LVEF < 40%	5 (33.3)	53 (12.3)	0.018
HCT	0.38 ± 0.06	0.39 ± 0.05	0.132
Anemia, n (%)	7 (46.7)	166 (34.6)	0.334
Hypoalbuminemia, n (%)	2 (13.3)	73 (15.2)	0.842
Medication, n (%)			
Statin	15 (100.0)	469 (97.7)	0.553
ACEI/ARB	13 (86.7)	435 (90.6)	0.607
Calcium channel blocker	4 (26.7)	76 (15.8)	0.262
Procedural characteristic			
Contrast volume (mL)	158.7 ± 66.6	155.0 ± 68.7	0.838
Contrast exposure time (min)	108.2 ± 34.7	91.6 ± 47.3	0.178
Number of diseased vessels (n)	3.0 ± 0.9	2.6 ± 0.9	0.050
Number of stents	1.9 ± 1.2	1.9 ± 1.4	0.907
Mehran risk score	10.6 ± 5.2	5.2 ± 3.8	<0.001

Abbreviations: BP: blood pressure; CABG: coronary artery bypass grafting; MI: myocardial infarction; SCr: serum creatinine; LVEF: left ventricular ejection fraction; HCT: hematocrit; ACEI/ARB: angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; Mehran risk score: model to define contrast-induced nephropathy (CIN) by Mehran et al. Anemia was defined using World Health Organization criteria: baseline hematocrit value of <39% for men and <36% for women. Hypoalbuminemia was defined as the serum albumin of <35 g/L.

dL (OR: 8.99, $p < 0.001$) were significantly and independently related to CIN. The multivariate model ($\chi^2 = 22.72$, $p < 0.001$; $-2LL = 108.40$) had a C-statistic of 0.8. The Hosmer–Lemeshow statistic did not suggest a lack of fit (degrees of freedom 8, $\chi^2 = 0.195$, $p = 0.907$).

Using these three variables as risk indicators for CIN, we developed a risk scoring system. For this purpose, the beta values from the logistic model were used, assigning an integer value of 1 for each 1.0 increment in beta (age ≥ 75 years: 1, LVEF < 40%: 1 and SCr > 1.5 mg/dL: 2). For each patient, the score was calculated as the sum of the weighted integer coefficients (range 0–4).

ROC curve analysis showed that the present risk score model had good predictive value for CIN (C-statistic = 0.789) in the training dataset. An adequate discriminative power was also demonstrated in the validation dataset (C-statistic = 0.864). Furthermore, the predictive accuracy of our risk score for CIN was similar to Mehran score in both the training (0.789 vs. 0.799, $p = 0.866$) (Fig. 1A) and total cohort (0.812 vs. 0.843, $p = 0.430$) (Fig. 1B).

We further divided the present risk score model into the following three groups: low risk (score 0, CIN incidence 0), moderate risk (score = 1, CIN incidence 5.10%), and high risk (score ≥ 2, CIN incidence 19.44%) in training group. Based on this classification, the incidence of CIN in the validation group was 0.97%, 9.76%, 10% in patients with a low, moderate, and high risk score, respectively. Both the rate of in-hospital death and MACEs were significantly associated with the low, moderate, and high risk score, respectively ($p < 0.001$).

The present study developed a simple pre-procedural risk score, including only 3 key risk factors, with a good ability for predicting CIN and in-hospital complications in patients with CTO before PCI.

Several risk scores have been established to predict the risk of CIN [6–9]. The Mehran risk score was the most widely used and classic model for CIN. However, it was established for complete risk assessment only after CM exposure, which is rather inconvenient in clinical practice. In addition, precautionary measures could not be adopted and less individually tailored procedures used in those patients at high risk of CIN. However, although the present risk score did not include peri-procedural factors (e.g. CM volume), its predictive value was similar to Mehran risk score. Apart from its simplicity, the present risk score is also characterized by a good discriminative ability (C-statistic = 0.789). The use of only three easily calculated variables and the quick applicability of our CIN risk scores before the procedure, might render it more clinically attractive, rather than a more elaborate combination that needs to be calculated by a computer from eight or more factors [7].

The present study has several limitations. First, it was a prospective, observational study in a single center, so the inherent weakness cannot be avoided. Second, the statistical power of the present study might not

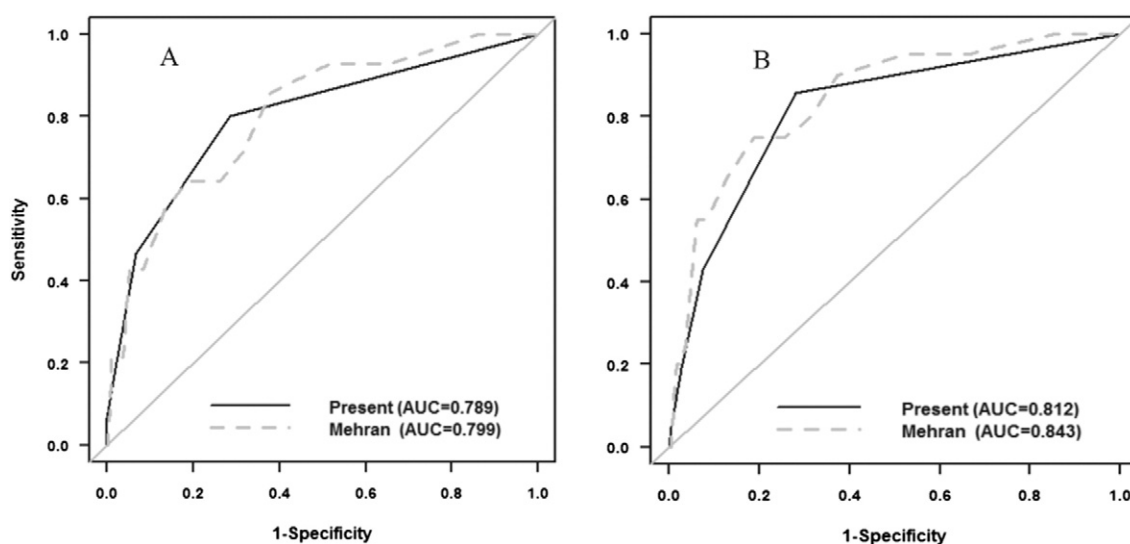


Fig. 1. Area under the receiver operating characteristic curve of the present risk score and the Mehran risk score for predicting contrast-induced nephropathy in training (A) and entire cohort (B).

be very strong because our risk score was derived from and validated by a single center. The score needs to be confirmed and validated in a large multicenter trial.

The simple pre-procedural risk score based upon readily available information including age ≥ 75 years, LVEF $< 40\%$ and SCr > 1.5 mg/dL, but without peri-procedural variables showed excellent predictive ability for identifying patients with CTO-PCI who are at high risk of CIN. We anticipated that this scoring system may be useful for assisting interventional teams in decision making regarding therapeutic strategies.

Conflict of interest

None.

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