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Comparison Between Two Risk Models for Predicting Contrast-Induced Acute Kidney Injury in Patients with Reduced Glomerular Filtration Rate Undergoing Percutaneous Coronary Intervention

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ABSTRACT

Background*:* Contrast-induced acute kidney injury (CI-AKI) is a frequent complication after percutaneous coronary intervention (PCI) and severely affects morbidity and mortality. Multiple prediction models for the development of contrast-induced nephropathy (CIN) have been published using heterogeneous characteristics of study populations.

Objectives*:* We sought to compare two contrast-induced acute kidney injury-risk prediction models in patients with reduced glomerular filtration rates undergoing percutaneous coronary interventions.

Methods: A cross-sectional study.

Results*:* We evaluated 135 patients who underwent percutaneous coronary intervention from January to May 2017 at Cho Ray Hospital, Ho Chi Minh City, Vietnam. The mean age of the study participants was 68.9±9.9 years and 71.9% were male. The mean baseline creatinine was 1.35±0.35 mg/dl. Contrast-induced acute kidney injury occurred in 18 patients (13.3%). Univariate regression analysis showed that a history of myocardial infarction (OR 0.34), left ventricular ejection fraction (OR 0.94), left ventricular ejection fraction <40% (OR 3.5), hemoglobin (OR 0.98), and Mehran scores (OR 1.16), as well as ACEF-MDRD scores (OR 1.8), were the independent predictors of contrast-induced acute kidney injury. Multivariate regression analysis showed that no single factor was able to predict the incidence of contrast-induced acute kidney injury. Area under curves of Mehran risk scores and ACEF-MDRD risk scores in predicting the incidence of contrast induced acute kidney injury were 0.64 and 0.68, respectively (p=0.61).

Conclusions: The study showed that the ACEF-MDRD risk model and Mehran risk model were of similar value in predicting the incidence of contrast-induced acute kidney injury in patients with reduced glomerular rate undergoing percutaneous coronary intervention.

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INTRODUCTION

The elective or emergency percutaneous coronary intervention has been proposed as a crucial strategy for coronary revascularization and contributes to reducing morbidity and mortality rates of ischemic heart disease. Contrast-induced acute kidney injury (CI-AKI) is a frequent complication after percutaneous coronary intervention (PCI). The contrast media that is used in the PCI is one of three main common causes of induced acute kidney injury in hospital patients, aside from hypotension and surgery [1]. CI-AKI is strongly associated with poor outcomes such as increased morbidity and mortality rates, prolonged length of hospital stay, and long-term kidney deterioration [2], [3].

Apart from the effect on clinical outcomes, following kidney disease due to CI-AKI causes negative impact on treatment cost and quality of life (QoL) of the patients. Evidence from southern Vietnam showed that direct medical costs were approximately 957 US dollars (US$) per patient with chronic kidney disease (CKD) and about US$ 2,800 per year [4, 5]. Kidney disease obviously poses a huge economic burden on patients, their families, as well as society. Moreover, worsening stages of CKD were proven to be significantly associated with most of the health-related QoL indicators [6]. The mean HRQoL scores of CKD patients were below average (42.9±9.7) [6].

Currently, the main therapy to avoid CI-AKI is in its prevention because pharmacologic prophylaxis still remains controversial [7]. Acknowledging and adjusting the risk factors increasing the incidence of CI-AKI and grading the individual risk stratification of patients have been the pivotal strategies [8]. Patients who underwent PCI were at a high risk for CI-AKI when considering factors such as hypotension, severe congestive heart failure, history of chronic kidney disease, advanced age, anemia, and high contrast volume [9]. In order to determine high-risk patients, many risk models for predicting CI-AKI were developed [10], [11-13].

In terms of application, the Mehran risk score published by Mehran et al. has been the most popular risk model, well validated in patients who underwent percutaneous coronary intervention [14]. Further, ACEF-MDRD was developed according to basic clinical characteristics, including age, left ventricular ejection fraction by echocardiography, and estimated glomerular filtration rate according to the Modification of Diet in Renal Disease formula [15], [16]. This risk score was well validated in patients who underwent PCI for both chronic and acute coronary syndrome. A risk model was considered to be a potential model when it was not only highly predictable but also was applied widely in different study populations [17].

Therefore, we sought to compare the predictive value of two clinical scores for predicting CI-AKI in patients with reduced glomerular filtration rates (GFR) who are undergoing PCI.

METHODS

Study population

A cross-sectional study was performed at Cho Ray Hospital (Ho Chi Minh City, Vietnam). The study population consisted of all consecutive patients who underwent the elective or emergency PCI for the indication of coronary revascularization between January 2017 and May 2017. Inclusion criteria were as follows: (1) aged 18 years or older; (2) patients underwent emergency, urgent, or elective coronary angiogram with evidence of ischemic heart disease during their hospital stay; (3) baseline estimated glomerular filtration rates (eGFR) below 60 mL/min/1.73 m^2; and (4) written informed consent was obtained before enrolment in the study. Exclusion criteria were as follows: (1) patients with a history of using intravascular contrast media within a week before procedures or history of adverse reactions to contrast agents; (2) patients with end-stage renal disease or requiring renal replacement therapy; (3) patients experiencing pregnancy or lactation; (4) patients who experienced PCI related complications or who died within 24 hours post procedure; and (5) patients with a lack of available laboratory data.

Protocol study

Laboratory tests were recorded before PCI according to the standard protocol of procedures. Serum creatinine was measured on admission, 12 hours, 24 hours, 48 hours, and 72 hours after contrast media exposure, as well as at hospital discharge. In all patients, the echocardiogram was performed by

cardiologists within 12 hours from admission or before the PCI procedure. PCI procedure was performed at the catheterization lab according to the protocol approved by standard guidelines. Contrast media for coronary angiogram was Xeretic 300mg/mL.

Clinical definitions

Creatinine clearance was measured by applying the Modification of Diet in Renal Disease (MDRD) formula [18]. CI-AKI by AKIN criteria was defined as an increase ≥ 0.3 mg/dL or ≥ 50% in serum creatinine levels from baseline values within the first 24–72 hours after contrast media exposure [19]. Hypotension was defined as a systolic blood pressure ≤ 90 mmHg for at least one hour and requiring therapeutic support with inotropic medicines [14]. Anemia was defined based on World Health Organization criteria: baseline hematocrit value < 39% for men and < 36% for women [20]. Prior chronic kidney disease was defined as baseline serum creatinine > 1.5 mg/dl. The left ventricular ejection fraction (LVEF) was estimated by Simpson's method on two planes and then described as the average value [21].

Risk score calculation

Mehran scores [14] included eight clinical and procedural variables and their weighted integers: hypotension (5 points), intra-aortic balloon pump (IABP) (5 points), congestive heart failure (5 points), estimated glomerular filtration rate (2 points for an eGFR between 60 and 40 mL/min/1.73 m^2, 4 points for an eGFR between 40 and 20 mL/min/1.73 m^2, and 4 points for an eGFR <20 mL/min/1.73 m^2), age [75 years (4 points), diabetes (3 points), anemia (3 points) and volume of contrast (1 point for each 100 mL)].

ACEF-MDRD scores [22] were calculated using the formula of age/LVEF, and one point was added for every 10 mL/min/1.73 m^2 reduction in eGFR < 60 mL/min/1.73 m^2 (up to a maximum of 6 points). Therefore, an eGFR of between 50–59, 40–49, and 30–39 mL/min/1.73 m^2 would have received 1, 2 and 3 points, respectively.

STATISTICAL ANALYSIS

Continuous variables were expressed as mean (± standard deviation) or median (interquartile range). Categorical variables were represented by relative and absolute frequencies. We divided our patients into two groups based on the presence of CI-AKI. Two groups were compared using the Student's t-test (for normally distributed variables) or the Wilcoxon rank-sum test (for other variables) for continuous variables, the chi-squared test or Fisher's exact tests for categorical variables. The receiver operating characteristic (ROC) curve was computed, and the area under the curve (AUC) and its 95% confidence interval (CI) were used to predict CI-AKI. Comparison of ROC curves was performed by DeLong test using the software MedCalc (version 12.5.0.0, bvba, Belgium). Youden index analysis was performed to determine the best cutoff value of ACEF-MDRD scores (considering sensibility and specificity) and Mehran scores to predict CI-AKI. Data were analyzed using Stata statistics software, version 13, for Windows (Stata Statistical Software: Release 13, Collage-Station, TX, StataCorp LP, 2013). Statistical significance was defined when the p-value was less than 0.05.

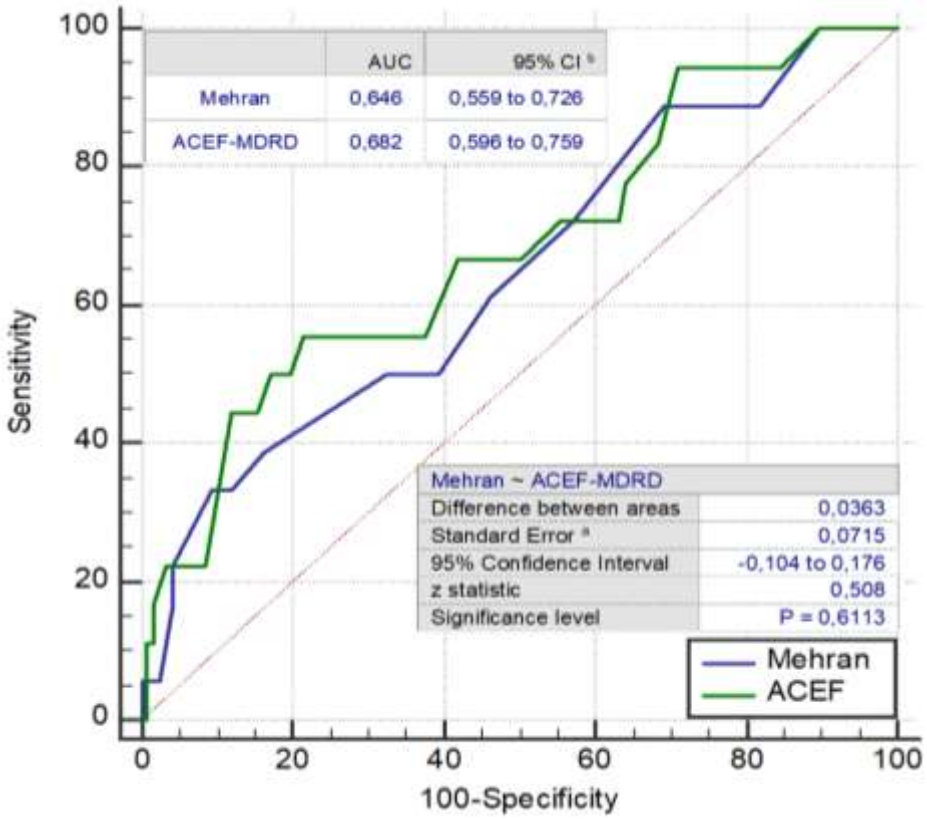

Fig. 1: Receiver operator characteristic (ROC) showing areas under the curve (AUC) of Mehran and ACEF-MDRD scores for CI-AKI

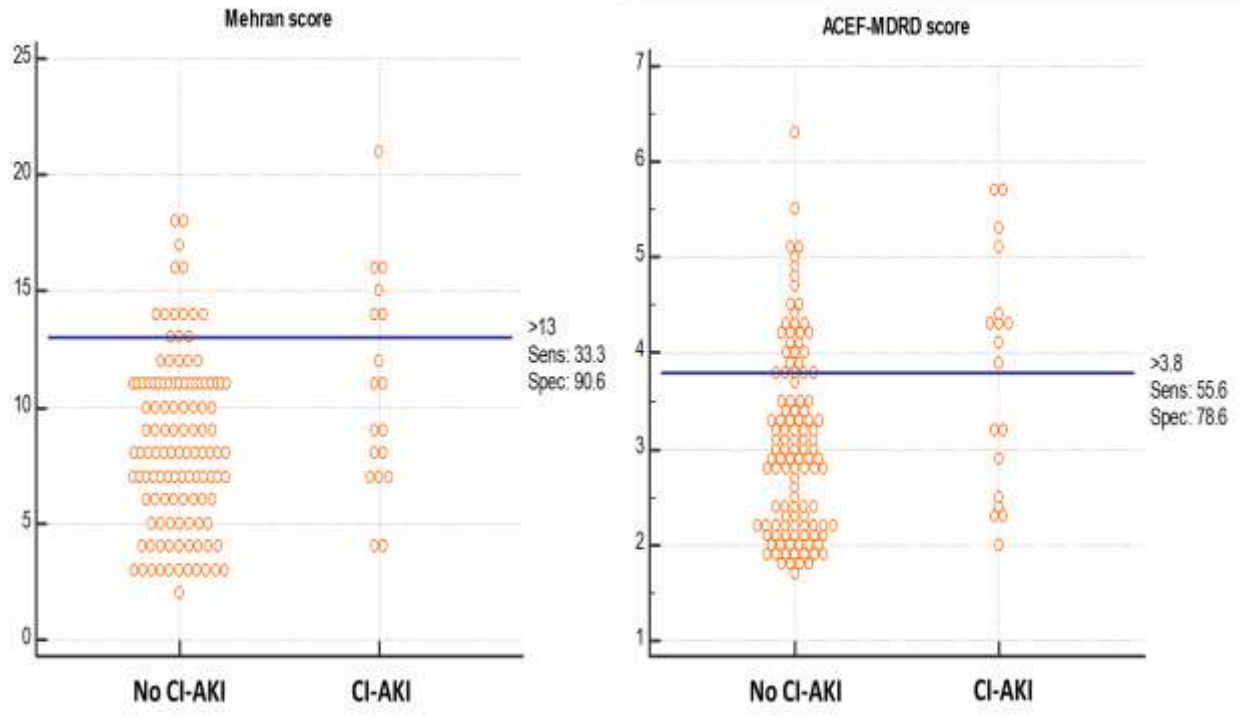

Fig. 2. The cut-off value of Mehran and ACEF-MDRD scores for CI-AKI

RESULTS

The study population consisted of 135 patients with reduced GFR < 60 mL/minute/1.73 m^2 who underwent coronary angiogram. Of these 135 patients, 71 (52.6%) were male. The mean age of the study population was 68.0±9.9 years, and 27.7% of the patients were of advanced age (> 75 years). Nineteen patients were undergoing emergency PCI, and 116 patients were undergoing elective PCI. At the time of admission, 5.9% of the patients had hypotension, 45.9% of the patients had anemia, and a history of previous myocardial infarction was observed in 20.7% of the study population. The mean creatinine clearance of the study population was 47.2±8.0 mL/minute/1.73 m^2. CI-AKI occurred in 13.3% of the patients. Clinical characteristics of patients according to the presence of CI-AKI are shown in Table 1. In this study, we did not record any cases to be taken IABP. CI-AKI occurred more frequently in patients with history of previous myocardial infarction (MI), LVEF < 50%, and anemia. In univariate analysis, previous myocardial infarction, LVEF, LVEF < 50%, hemoglobin levels, Mehran, and ACEF-MDRD were predictors of CI-AKI. After multivariate analysis, there was no factor in predicting CI-AKI (shown in Table 2).

ROC curves are presented in Figure 2. Areas under the ROC curve (95% CI) of Mehran and ACEF-MDRD scores were 0.646 (0.559-0.626) and 0.682 (0.59–0.70), respectively. Comparing both scores with DeLong test results, the ACEF-MDRD score's AUC was not significantly different from the Mehran score's one (P=0.61). A Mehran score cutoff point of 13 yielded a sensitivity of 33.3% and specificity of 90.6%. An ACEF-MDRD score cutoff point of 3.8 yielded a sensitivity of 55.6% and specificity of 78.6% (shown in Figure 2). CI-AKI was developed by 10.2% of the patients with Mehran scores below 13 and by 35.3% of patients when Mehran scores were above the cutoff. Low-risk scores had an excellent negative predictive value of 64.7% (46.3–81.3%), while high-risk scores had positive predictive value of 10.2% (7.5–13.6%). CI-AKI was developed by 8% of the patients with ACEF-MDRD scores below 3.8 and by 28.6% of patients when ACEF-MDRD scores were above the cutoff. Low-risk scores had excellent negative predictive value of 71.4% (59.3–81.1%), while high-risk scores had positive predictive value of 8% (4.9– 12.8%) (Shown in Table 3).

DISCUSSION

Through comparing the values among two risk scores for predicting the CI-AKI in patients with reduced creatinine clearance undergoing PCI, we found that Mehran and ACEF-MDRD scores were the most valuable tools to identify patients at high risk for developing CI-AKI. ACEF-MDRD scores' AUC were higher than Mehran scores' AUC, but this difference was not significant. Aside from being friendly scores, ACEF-MDRD scores were good predictors of CI-AKI [14].

Table 1: Baseline characteristics of study population

Variable	Overall n=135	CI-AKI n=18	No CI-AKI n=117	*p* value
Demographic				
Age, years	68.9±9.9	69.0±10.9	68.9±9.7	0.96
Age > 75, (%)	36 (27.7)	5 (27.8)	31 (26.5)	0.90
Male gender, *n* (%)	71 (52.6)	13 (72.2)	58 (49.6)	0.07
Hypertension, *n* (%)	115 (85.2)	14 (77.8)	101 (86.3)	0.34
CHF, *n* (%)	68 (50.4)	11 (61.1)	57 (48.7)	0.32
Diabetes mellitus, *n* (%)	39 (28.9)	4 (22.2)	35 (29.9)	0.50

Current smoking, *n* (%)	53 (39.3)	10 (55.6)	43 (36.8)	0.13
History of MI, *n* (%)	28 (20.7)	7 (38.9)	21 (18.0)	0.04
History of PCI, *n* (%)	25 (18.5)	4 (22.2)	21 (18.0)	0.66
History of CKD, n (%)	11 (8.2)	3 (16.7)	8 (6.8)	0.16
Clinical and laboratory test				
Systolic blood pressure, mm/Hg	121.1±23.2	122.2±21.6	120.9±23.5	0.41
Diastolic blood pressure, mm/Hg	72.2±12.3	74.4±10.4	71.2±12.4	0.41
Hypotension, *n* (%)	8 (5.9)	1 (5.6)	7 (6.0)	1.00
Heart rate, per minute	78.6±16.2	78.4±16.5	78.7±16.7	0.93
BMI, kg/m^2	23.9±2.9	23.6±2.6	23.9±2.9	0.62
LVEF, %	52.8±14.3	43.3±14.7	54.8±13.7	0.002
LVEF < 40%, *n* (%)	25 (18.5)	7 (38.9)	18 (15.4)	0.017
Hemoglobin, G/L	125.8±22.6	115.0±29.2	127.4±21.1	0.03
Glycemia, mg/dL	145.8±72.8	147.2±74.5	137.7±61.9	0.61
Serum uric acid, mg/dL	7.3±2.1	7.8±2.5	7.2±2.0	0.32
LDL-C, mg/dL	114.1±52.1	118.1±34.7	113.5±54.3	0.72
HDL-C, mg/dL	35.5±12.7	36.2±12.6	31.2±10.3	0.10
Triglyceride, mg/dL	160.0±127.5	154.3±67.1	160.9±134.6	0.84
Baseline creatinine, mg/dL	1.35±0.35	1.42±0.18	1.34±0.37	0.39
Baseline eGFR, mL/minute/1,72 m^2	47.5±7.5	46.4±7.2	47.7±7.6	0.51
Volume contrast, mL	217.1±41.1	204.5±20.9	219.3±43.1	0.16
ACEF-MDRD score	3.16±1.02	3.78±1.21	3.06±1.22	0.005
Mehran score	8.73±3.84	10.72±4.57	8.42±3.64	0.017

Notes: CI-AKI, contrast-induced acute kidney injury; CHF, congestive heart failure; MI, myocardial infraction; PCI, percutaneous coronary intervention; CKD, chronic kidney disease; BMI, body mass index; LVEF, left ventricular ejection fraction; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate.

Table 2: Predictors of CI-AKI in univariate and multivariate analysis

Characteristic	OR	Cl 95%	*p*-value
Univariate analysis			
Prior myocardial infarction	0.34	0.12-0.99	0.04
LVEF	0.94	0.91-0.92	0.004

LVEF < 40%	3.5	1.20-10.2	0.022
Hemoglobin	0.98	0.95-0.99	0.034
ACEF-MDRD score	1.88	1.18-3.02	0.008
Mehran score	1.16	1.02-1.32	0.021
Multivariate analysis			
Prior myocardial infarction	0.62	0.19-2.05	0.434
Ejection fraction	0.95	0.88-1.01	0.11
Ejection fraction < 40%	0.59	0.09-3.74	0.576
Hemoglobin	0.98	0.95-1.00	0.059
ACEF-MDRD score	1.25	0.65-2.40	0.508
Mehran score	1.01	0.86-1.20	0.867

Notes: CI-AKI, contrast-induced acute kidney injury; OR, odds ratio; CI, confidence interval; LVEF, left ventricular ejection fraction.

Table 3. Frequencies and percentages of CI-AKI in patients with the cut-off point of Mehran and ACEF-MDRD scores

	Total	CI-AKI	No CI-AKI	Predictive value
Mehran score				
Mehran < 13	118 (100)	12 (10.2)	106 (89.8)	Negative: 64.7% (43.6-81.3)
Mehran > 13	17 (100)	6 (35.3)	11 (64.7)	Positive: 10.2% (7.5-13.6)
ACEF-MDRD score				
ACEF < 3.8	100 (100)	8 (8.0)	92 (92.0)	Negative: 71.4% (59.3-81.1)
ACEF > 3.8	35 (100)	10 (28.6)	25 (72.4)	Positive: 8% (4.9-12.8%)

Notes: CI-AKI, contrast-induced acute kidney injury

CI-AKI is a common complication in invasive procedures using contrast media, especially in patients who present several risk factors for acute kidney injury, such as advanced age, anemia, hypotension, and chronic kidney disease (eGFR < 60 ml/minute/1.73 m^2). In our study, mean creatinine clearance was estimated according to the MRDR formula at 47.2±8.0 mL/minute/1.73 m^2, so this cohort study was among the patient group at high risk for developing CI-AKI. Various risk models have been developed to identify optimally high-risk patients occurring CI-AKI. CI-AKI in patients at high risk may be prevented by adjusting risk factors such as anemia, effective volume depletion, or delaying the PCI procedure. Each study population has different characteristics, so it is not available to apply only one model for assessing the risk of patients among many different populations [9], [10], [13], [15], [23]. For example, Brown et al. validated a risk score after a National Veterans Health Administration population, with all its specifications and features [12]. Further, the study has been conducted to compare two risk scores in a cohort from Vietnam undergoing emergency or elective PCI.

Many risk scores have been created to fit different cohorts, such as stable patients or unstable patients undergoing emergency/urgent or elective PCI. Kul et al. found that the Zwolle risk score was a predictor of CI-AKI in patients with acute ST elevation myocardial infraction who underwent PCI, and its AUC was similar to the Mehran score (0.85 versus 0.79) [11]. However, Zwolle risk scores are only completely calculated after coronary angiography results are available, which means that the patient must be

exposed to contrast before the stratifying risks of CI-AKI. Liu et al. [22] have noted that the GRACE score is an independent predictor of CI-AKI in patients undergoing primary PCI, with a similar AUC compared to ACEF-MDRD scores in our study (0.723 and 0.682, respectively) [24]. Further, SYNTAX and PRECISE-DAPT scores have also been documented for CI-AKI prediction and well validated. It is known that these risk scores, such as GRACE, PRECISE-DAPT, and SYNTAX scores, have many variables and high complexity, so there is a disadvantage in using these scores in clinical practice application [25], [26].

In fact, assessing the predictive role of a risk score is not only based on the ability to predict by the AUC, but also on convenience, simplicity, and clinical applicability of that risk score. The present research results showed that the Mehran and ACEF-MDRD scores both had a high ability to predict CI-AKI with the AUC area of 0.66 and 0.682, respectively (shown in Figure 1). Other authors have tested the predictive value of these scores in different population studies. Araujo et al. found that the predictive ability of Mehran and ACEF-MDRD scores for developing CI-AKI were 0.649 and 0.733, respectively [15]. Zeng et al. reported that the predictive ability of these two scores was higher for patients with diabetes, the AUC of the Mehran score was 0.843, and that the AUC of ACEF-MDRD score was 0.796 for predicting CI-AKI [27].

According to the European Society of Cardiology guidelines on myocardial revascularization in 2018 [8], the main strategy for patients at high identified risk for CI-AKI includes fluid management and avoiding extravagant use in terms of the volume of contrast media. In this study, the negative predictive values for developing CI-AKI in patients at low risk according to Mehran scores (< 13 points) and ACEF-MDRD scores (< 3.8 points) were 64.7% and 71.4%, respectively (shown in Table 3). This means, for example, that a physician could acquire a higher volume of contrast media to warrant a high-quality angiographic result in patients with low Mehran scores or low ACEF-MDRD scores. In addition, patients with a low Mehran or ACEF-MDRD score could avoid excessive hydration to reduce the development of pulmonary congestion or edema, a condition that usually occurs in patients with acute coronary syndrome.

LIMITATIONS

The present study has some limitations. First, this was a single-center study with a small sample size, and no follow-up. In a multicenter study, our results should be assessed and the application of risk model validated in a larger population. Second, the obstructive severity of coronary branches was not revealed. It is known that in the case of multiple significantly obstructed branches of coronary arteries, physicians must use larger contrast volumes, thus increasing the risk of CI-AKI. Third, although all protocol procedures were performed according to the standard guidelines in the world, this study was derived from a third-world country registry such as Vietnam, meaning that medications and devices used during procedures may have changed the outcomes; event prediction may consequently differ.

CONCLUSION

The study revealed that Mehran risk scores and ACEF-MDRD risk scores were independent predictors for CI-AKI in patients undergoing elective of emergency PCI. ACEF-MDRD scores were simple, user-friendly tools with high predictive value that are easy to apply in clinical practice. Moreover, due to the limitations in the present study, other investigations of larger populations and multi-center studies need to be conducted to ensure ideal results.

STATEMENT OF ETHICS

The study was carried out in accordance with the Declaration of Helsinki and was approved by the ethics committee in biomedical research at the University of Medicine and Pharmacy in Ho Chi Minh City, Vietnam.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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None declared.

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