ORIGINAL ARTICLE

Validation of Four Clinical Risk Scores for Predicting Contrast-Induced Nephropathy in Patients Undergoing Percutaneous Coronary Intervention

Validación de cuatro reglas de predicción clínica de la nefropatía inducida por contraste en pacientes llevados a intervención coronaria percutánea

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ABSTRACT

Background: Contrast-induced nephropathy (CIN) is the acute deterioration of kidney function after the administration of intravenous contrast media and is associated with significant morbidity and mortality. Several clinical risk scores to predict CIN are currently available. The aim of the present study is to validate four risk scores for predicting CIN in patients undergoing percutaneous coronary intervention (PCI).
Methods: We conducted a retrospective single-center cohort study including adult patients undergoing PCI between January 2014 and December 2018. Patients on dialysis, those who died during the procedure or lack of necessary data for the analysis were excluded. The four risk scores were estimated for each patient and the area under the ROC curve for the development of CIN was calculated.
Results: The four risk scores were calculated in 785 patients; 109 (13.8%) developed CIN and 14 (1.7%) required dialysis. Mean age was 65 years and 36.1% were women. Mean glomerular filtration rate was 69.1 mL/min. The areas under the curve for each risk score to predict CIN and dialysis were: Mehran 0.574 and 0.881, respectively; Gao, 0.487 and 0.831; Lin, 0.572 and 0.854; and Bartholomew, 0.506 and 0.754.
Conclusions: The use of the Mehran, Gao, Lin, and Bartholomew risk scores in patients undergoing PCI showed poor discriminatory ability for CIN, although their performance was excellent for predicting the need for dialysis.

Keywords: Percutaneous coronary intervention - Myocardial infarction - Acute kidney injury - Contrast Media - Risk factors - Prognosis

RESUMEN

Introducción: La nefropatía inducida por contraste (NIC) es el empeoramiento agudo de la función renal tras administrarse medio de contraste endovenoso, y conlleva una importante carga de morbilidad y mortalidad. Actualmente se cuenta con múltiples reglas clínicas para predecir su desarrollo. El objetivo del presente trabajo es validar cuatro reglas para la predicción de la nefropatía inducida por contraste en pacientes llevados a procedimiento intervencionista coronario percutáneo (ICP) .
Material y métodos: Estudio de cohorte retrospectiva unicéntrico, que incluyó adultos llevados a ICP entre enero de 2014 y diciembre de 2018. Se excluyeron pacientes en diálisis, los que murieron durante el procedimiento o aquellos de los que no se dispusiera de los datos necesarios para el análisis. Se aplicaron las cuatro reglas de predicción, se obtuvo la puntuación de cada una para cada uno de los pacientes y se calculó el área bajo la curva ROC para el desarrollo de NIC.
Resultados: En 785 pacientes se pudo calcular las cuatro reglas; 109 (13,8%) desarrollaron NIC y 14 (1,7%) requirieron diálisis. La media de edad fue 65 años y el 36,1% fueron mujeres. La media de tasa de filtración glomerular fue 69,1 mL/min. La regla de Mehran obtuvo un área bajo la curva de 0,574 para NIC y 0,881 para diálisis; Gao, 0,487 para NIC y 0,831 para diálisis; Lin, 0,572 para NIC y 0,854 para diálisis; y Bartholomew, 0,506 para NIC y 0,754 para diálisis.
Conclusiones: La aplicación de las reglas de predicción clínica de Mehran, Gao, Lin y Bartholomew en pacientes llevados a ICP mostró una pobre capacidad de discriminación para la NIC aunque su desempeño fue excelente para predecir la necesidad de diálisis.

Palabras clave: Intervención coronaria percutánea - Infarto del miocardio - Lesión renal aguda - Medios de contraste - Factores de riesgo - Pronóstico

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Abbreviations

AUC	Area under the curve	**LR**	Likelihood ratio
CI	Confidence interval	**MRS**	Mehran Risk Score
PCI	Percutaneous coronary intervention	**CIN**	Contrast-induced nephropathy
LOESS	Locally estimated scatterplot smoothing	**ACS**	Acute coronary syndrome
AKI	Acute kidney injury		

INTRODUCTION

Contrast-induced nephropathy (CIN) is defined as an increase in baseline creatinine levels > 0.5 mg/dL or increase from baseline level > 25% within 24-72 hours after contrast-media administration (1, 2) and is considered the third leading cause of hospital-acquired acute kidney injury (AKI). It is the major complication related to the administration of contrast media in patients undergoing interventional cardiology procedures. (3)

The incidence of CIN is variable and depends on the definition used, population of reference and presence of risk factors in the population. It accounts for 30% of all hospital-acquired AKI (4,5) and up to 10% in patients undergoing percutaneous coronary interventions (PCIs) for acute coronary syndromes (ACS). (3, 6-9) In a study performed in Colombia, Fuentes et al. documented and incidence of 13.1% and found that creatinine levels > 1.5 mg/dL, diabetes and chronic kidney failure were associated with CIN development; in this group, mortality was 9.5%, and 2.5% required hemodialysis. (10)

Several clinical risk scores have been developed to identify patients at risk of CIN and implement management strategies. The Mehran Risk Score (MRS), developed in 2004 from a cohort of 5571 patients undergoing PCI, is one of the clinical prediction rules most widely used. This score evaluates 8 variables: sex, age, hematocrit, contrast media volume, diabetes, hypotension, use of intra-aortic balloon pump (IABP), heart failure and glomerular filtration rate. (11) Other risk scores have also been developed, as the one published by Gao et al., which considered age > 60 years, hypertension, acute myocardial infarction, heart failure, use of IABP, reduced glomerular filtration rate and contrast media volume > 100 mL as risk factors for CIN. (12) The risk score by Lin considered age > 75 years, serum baseline creatinine > 1.5 mg/dL, hypotension and use of IABP, (13) while Bartholomew included estimated glomerular filtration rate < 60 mL/min, urgent PCI, use of IABP, diabetes, heart failure, hypertension, peripheral vascular disease and contrast volume >260 mL. (14)

The aim of the present study was to identify the performance of these risk scores in patients undergoing PCI to identify strategies for the prediction and management of this condition.

METHODS

We conducted an observational, retrospective cohort study in patients > 18 years undergoing PCI in the catheterization laboratory of Hospital San José de Bogotá between January 1, 2014, and December 31, 2018. Patients with end-stage kidney disease on chronic dialysis, exposure to media contrast within ≤ 1 week of the index procedure, absence of report of the medical record or creatinine levels after the procedure were excluded from the study.

The records of the procedures performed in the catheterization laboratory were reviewed, including those of patients with creatinine levels measured 48-72 h after the procedure. The outcome variables evaluated were the development of CIN (increase in creatinine level ≥ 0.5 mg/dL or > 25% in mg/dL within 48-72 h) and dialysis requirement after the procedure. The date collected were used to calculate the scores obtained with the MRS, Gao, Lin and Bartholomew prediction rules.

Statistical analysis

Categorical variables are expressed as absolute and relative frequencies. Quantitative variables are reported as measures of central tendency and dispersion according to their distribution. ROC curves were constructed according to the different values obtained by the prediction rules, considering the sensitivity and specificity for the development of the outcomes, and the respective areas under the curve (AUC) with their 95% confidence intervals (CI) were calculated. The Youden's index was used to calculate the cutoff point of the score for each outcome with the best discriminating ability, which was used to construct contingency tables and calculate the operating characteristics (sensitivity, specificity, accuracy, positive and negative predictive values, positive and negative likelihood ratios [LR]).

Each score was calibrated, and the points obtained (x-axis) were plotted against the proportion of events observed (y-axis) using LOESS (locally estimated scatterplot smoothing) curves and by calculating the Brier score. All the statistical calculations were performed with R statistical software, version 4.0.2 (R Foundation, Vienna, Austria) using the pROC, ROCit and Cutpointr packages. This study was approved by the institutional review board of Hospital San José de Bogotá. An informed consent form was not required due to the retrospective nature of the study. This research received no specific grant from any funding agency.

RESULTS

Of the 1758 patients undergoing PCI during the study period, data from 785 patients were available to calculate the risk scores. The characteristics of the patients are summarized in Table 1. Mean age was 65 +-11 years and 36.1% were women. Contrast-induced nephropathy occurred in 109 (13.9%) patients; 14 (1.7%) required dialysis and 18 (2.3%) died. Advanced heart failure was present in 216 patients (27.5%), 135 (17.1%) had a history of myocardial infarction (MI), 194 (24.7%) of diabetes and 155 (19.7%) of chronic kidney disease. Mean media contrast volume required

for the procedure was 87 ± 58 mL.

Table 2 and Figure 1 show the ROC curves and their respective areas under the curve; none of the risk scores adequately predicted the development of CIN (AUC between 0.49 and 0.57); however, their ability to predict the need for dialysis (AUC between 0.75 and 0.88) was excellent. The MRS obtained the best performance for dialysis requirement, with an AUC of 0.881 (95% CI, 0.796-0.967), although the CIs widely overlapped.

When considering the MRS, after using the Youden's index, the best discrimination cutoff point for CIN was 7.67 and for dialysis requirement 9.14. The operating characteristics of the different cutoff points for both outcomes are shown in Table 3. A cutoff point ≥ 9 presented the best accuracy (71.5%) to predict CIN, with specificity of 77.5% and sensitivity of only 33.9%. A cutoff point ≥ 10 presented the best accuracy (81.8%) to predict dialysis requirement, with specificity of 88.7% and sensitivity of 81.7%; the positive predictive value was only 7.8%.

The calibration curves show an adequate result for the MRS and Lin score for both outcomes and the results improve as the score increases. Gao and Bartholomew scores presented poor calibration to predict the development of CIN. The Brier scores for the MRS to predict CIN and dialysis requirement were 0.285 and 0.225, respectively, confirming good calibration.

DISCUSSION

Contrast-induced nephropathy is an iatrogenic disease with high morbidity and mortality due to a significant rate of adverse renal and cardiovascular events, (15,16) and mortality. (17) Peri-procedural hydration regimes and the use low-osmolar contrast agents are the only effective measures to prevent CIN; (18) therefore, identifying high risk patients will allow closer monitoring and rapid intervention. (19) The results of the present study do not support the use of any of the risk scores evaluated to predict the development of CIN; the highest AUC obtained was 0.57 for the MRS. The situation was very different for dialysis requirement, since the AUC ranged between 0.75 and 0.88, and the obtained for the MRS was the highest; yet the confidence intervals overlapped.

A systematic review conducted in 2017 found 74 models for predicting the risk of CIN with 10 also predicting the development of dialysis. One article reported only a model that predicted the risk of CIN requiring dialysis. The weighted mean AUC of these models was 0.89 (95 % CI, 0.87-0.90). (20) Despite this large number of studies, we could not to identify if any of these models were applied in a Latin American population.

Table 1. Patients' characteristics

Characteristics	June/July (n=610)	Patients with CIN	Patients requirinng dialysis
Age, mean (SD)	65 (11)	64 (14)	66 (11.4)
Female sex, n (%)	284 (36.1)	43 (39.4)	3 (21.4)
Comorbidities			
Heart failure	216 (27.5)	37 (33.9)	4 (28.5)
Myocardial infarction	135 (17.1)	15 (13.7)	3 (21.4)
Diabetes mellitus	194 (24.7)	33 (30.2)	10 (71.4)
Chronic kidney disease	155 (19.7)	22 (20.1)	10 (71.4)
Laboratory tests, mean (SD)			
Glomerular filtration rate (mL/min)	69.21 (25.1)	71 (32.1)	28.6 (30.6)
Creatinine levels (mg/dL)	1.07 (0.7)	1.32 (1.4)	3.35 (2.2)
Hemoglobin (mg/dL)	13.8 (2.6)	13.4 (3.7)	9.94 (2.5)
Use of protective measures, n (%)	208 (26.4)	31 (28.4)	5 (35.7)
Contrast media volume (mL), mean (SD)	87 (58)	81.3 (50)	96.4 (55)
Shock, n (%)	34 (4.3)	7 (6.4)	4 (28.5)
Use of IABP, n (%)	3 (0.38)	0 (0)	0 (0)
Mortality, n (%)	18 (2.2)	9 (8.2)	3 (21.4)

CIN: contrast-induced nephropathy. SD: standard deviation
IABP: intra-aortic balloon pump

Table 2. Results of the areas under the ROC curves with their corresponding 95% confidence intervals for each risk score to predict each outcome evaluated

Clinical risk score	Contrast-induced nephropathy AUC	Contrast-induced nephropathy 95% CI	Dialysis requirement AUC	Dialysis requirement 95% CI
Mehran (11)	0.5744	0.515-0.6338	0.8812	0.7957-0.9667
Gao (12)	0.4873	0.4258-0.5489	0.8316	0.7022-0.961
Lin (13)	0.5720	0.5214-0.6225	0.8537	0.7689-0.9384
Bartholomew (14)	0.5064	0.451-0.5619	0.7536	0.6505-0.8567

AUC: area under the curve

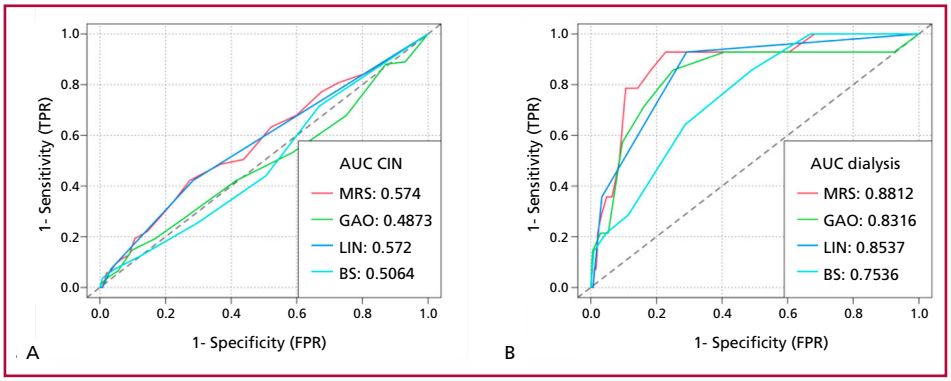

Fig. 1. ROC curves for each risk score to predict each outcome evaluated; a) contrast-induced nephropathy (CIN); b) dialysis requirement.

	Contrast-induced nephropathy			Dialysis requirement		
Cutoff point	**≥ 7**	**≥ 8**	**≥ 9**	**≥ 8**	**≥ 9**	**≥ 10**
True positive results	53	46	37	13	13	12
True negative results	427	491	524	553	595	630
False positive results	249	185	152	218	176	141
False negative results	56	63	72	1	1	2
Total	785	785	785	785	785	785
Accuracy (%):	61.1	68.4	71.5	72.1	77.5	81.8
Sensitivity (%):	48.6	42.2	33.9	92.9	92.9	85.7
Specificity (%):	63.2	72.6	77.5	71.7	77.2	81.7
PPV (%):	17.5	19.9	19.6	5.6	6.9	7.8
NPV (%):	88.4	88.6	87.9	99.8	99.8	99.7
LR +:	1.320	1.542	1.510	3.284	4.068	4.687
LR –:	0.813	0.796	0.852	0.100	0.093	0.175

PPV: positive predictive value. NPV: negative predictive value.
LR: likelihood ratio

Table 3. Operating characteristics for the cutoff points evaluated with the Mehran Risk Score

The MRS developed in a cohort of 5571 patients undergoing PCI reached in this population an AUC of 0.67 for predicting CIN. (11) So far, it has been the risk score most frequently validated. We could identify eight risk scores evaluated in patients undergoing PCI: four scores in ST-elevation myocardial infarction (STEMI) patients (19,21-23), one in elective PCI (24) and three in combined populations. (25-27) In 2013, Andò et al. reported an incidence of CIN of 5.2% in series of 507 STEMI patients in Messina (Italy) with an AUC of 0.80 (95% CI, 0.77-0.84). (21) Liu et al. reported an AUC of 0.84 among 251 STEMI patients in Guangdong (China) in 2014. (19) Ivanes et al. found an AUC of 0.590 among 322 STEMI patients in Tours (France) in 2014. (22) The same group of Liu evaluated 422 STEMI patients in 2016 and found an AUC of 0.643 (95 % CI, 0.57-0.71). (23)

They also validated the score in 2248 patients referred to elective PCI, reporting and AUC of 0.773. (24) In 2016, the group of Abellás-Sequeiros analyzed 1520 patients from Santiago de Compostela (Spain) with acute coronary syndromes referred to PCI and reported an AUC of 0.82 (0.78-0.86). (25) In Boston (USA), Araujo et al. included 5540 patients undergoing PCI in 2016; 68% were urgent procedures with an AUC of 0.80. (26) Chatterjee et al. reported an AUC of 0.78 among 11 454 patients from the Nationwide Inpatient Sample of the United States referred to multivessel PCI. (27)

Only one validation was identified for the Gao risk score with an AUC of 0.617 (95% CI, 0.54-0.69) in 422 STEMI patients in Guangdong (China) in 2016. (23) The original paper documented and AUC of 0.76 and 0.71 in the derivation cohort and validation cohort, respectively, in 3945 patients. (12) The Lin risk score obtained an AUC of 0.853 for predicting CIN in 692 patients in the derivation cohort, (13) and of 0.555 (95% CI 0.48-0.63) in the validation cohort described by Liu. The AUC for predicting CIN was not reported in the original study of the Bartholomew risk score; (14) it was validated in the study by Tziakas et al. in 2013 in 488 patients referred for elective or urgent PCI in Alexandroupolis (Greece), who reported an AUC of 0.584 (95 % CI 0.54-0.63). (28)

From what has been described above, most risk scores validated showed a good or at least moderate performance for predicting CIN. Nevertheless, there were exceptions, as in our case.

The retrospective nature of the present study is one limitation, which may induce selection or misclassification biases, although the factors evaluated are in general objective; in addition, the single-center nature

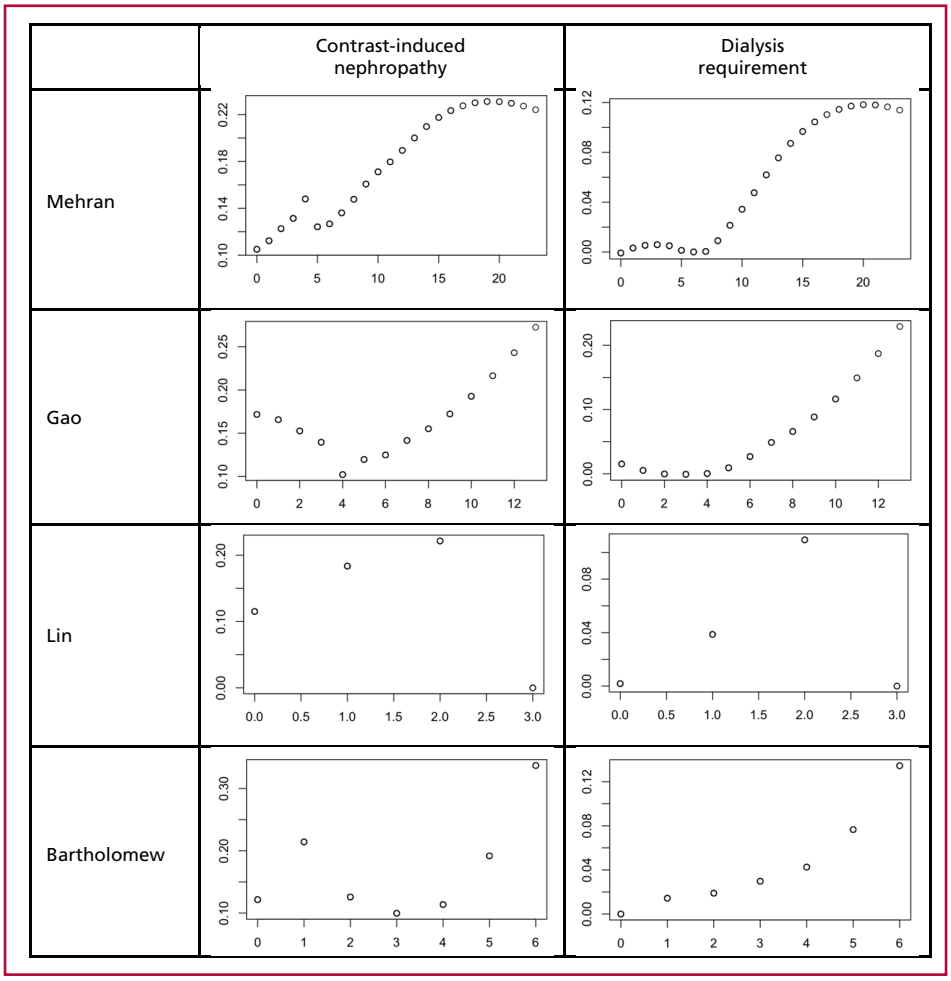

Fig. 2. Calibration curve using LOESS

of the study prevents from extrapolating the results to other populations. The fact that we have included a large sample of patients and outcomes is a strength of our study that allowed us to validate the risk scores included. Furthermore, we did not find any studies in the literature considering dialysis requirement, a key outcome in the progression of CIN, as an endpoint.

CONCLUSIONS

The use of the Mehran, Gao, Lin, and Bartholomew risk scores in patients undergoing percutaneous coronary intervention showed poor discriminatory ability for CIN, although their performance was excellent for predicting the need for dialysis.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

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