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ORIGINAL ARTICLE

External Multicenter Validation of the Mehran Risk Score for Contrast Induced Acute Kidney Injury

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Abstract

Background: Contrast induced acute kidney injury (CIAKI) is a known complication of percutaneous coronary intervention (PCI). Mehran Risk Score (MR score) has been previously shown to predict CIAKI, renal replacement therapy (RRT), and one-year mortality in patients undergoing PCI. The purpose of our study was to externally validate the MR score.

Methods: To examine the utility of the MR score we reviewed records of 931 adult patients who underwent PCI in 2005 at 3 academic medical centers. Patients with acute myocardial infarction, end stage renal disease and contrast exposure within one week of PCI were excluded. MR score was calculated for each patient and stratified into 4 groups: MR score 0-5 (group 1), 6-10 (group 2), 11-15 (group 3), ≥ 16 (group 4). CIAKI was defined as an increase in serum creatinine of 25% or 0.5 mg/dl over baseline 48 hours post PCI. Need for hemodialysis was assessed within 1 month after PCI. All-cause mortality was assessed 1 year after PCI. Likelihood ratio was calculated to assess the MR score discrimination for our data as well as Mehran, et al.

Results: The overall incidence of CIAKI, hemodialysis and mortality were 12.2%, 0.4%, and 9.0% respectively. A higher MR score was strongly associated with development of CIAKI and mortality ($p < 0.01$ for trend). There was no difference in the rate of CIAKI overall or in each MR score group when the 2 populations were compared, however, the risk of death was higher in our population (RR 1.58, CI 1.37-1.89, $p < 0.001$).

Conclusion: In conclusion, we were able to externally validate the MR score as a useful tool to predict CIAKI and one-year all-cause mortality post PCI.

Keywords

Contrast induced acute kidney injury, Percutaneous coronary intervention, Mehran risk score

Introduction

Contrast-induced acute kidney injury (CIAKI) occurs in approximately 7% of patients undergoing percutaneous coronary intervention (PCI) [1]. Its incidence varies depending on the definition used and the cohort studied. CIAKI is associated with increased length [2,3] and cost of in-hospital stay [4], and increased mortality [5,6]. Despite identifying several risk factors and instituting preventive measures, PCI still remains a common cause of hospital-acquired acute kidney injury (AKI) [7]. Several clinical trials have aimed to reduce CIAKI by use of agents such as normal saline, 0.45% saline, N-acetylcysteine, theophylline, fenoldopam, dopamine, and furosemide [8]. However, to date no agent has proven to be effective in the prevention of CIAKI [8,9]. A risk predicting score that helps in identifying patients at increased risk of developing CIAKI may aid in targeted application of these therapies to better test their effectiveness.

Mehran, et al. derived a risk score (MR score) for predicting CIAKI post PCI from a prospective interventional cardiology database. MR score is simple, accounts for the cumulative nature of risk assessments based on weighted integers and had a robust development dataset (N = 5,571) that predicted risk for developing CIAKI, need for renal replacement therapy (RRT) and one-year mortality [10] (Table 1). Risk predicting scores developed in other contexts such as acute kidney injury following cardiac surgery have failed to show similar accuracy in external cohorts than when they were initially developed [11]. Thus, externally validating the Mehran risk score (MRS)

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Table 1: The mehran risk score.

Risk Factor	Points
Hypotension*	5
Intra-aortic balloon pump	5
Congestive heart failure†	5
Age > 75 years	4
Anemia‡	3
Diabetes	3
Contrast volume	1 for each 100 cc
Chronic kidney disease Serum creatinine > 1.5 mg/dL or GFR < 60 ml/min/1.73 m^2	 4 2 for GFR 40-59 4 for GFR 20-39 6 for GFR < 20

*Systolic blood pressure < 80 mmHg for at least one hour requiring inotropic support with medications or IABP within 24 hours periprocedurally; †NYHA functional class III or IV and/or history of pulmonary edema; ‡Hematocrit < 39% for men or < 36% for women.

serves as an important tool for clinicians and patients to make informed decisions and further generalize it applicability. We undertook a multi-center validation of this score among patients undergoing non-emergent PCI from across three different academic institutions.

Methods

We reviewed all records of patients ages > 18 years who underwent PCI in 2005 at three hospitals, Strong Memorial Hospital/University of Rochester, Rochester, NY; Rochester General Hospital, Rochester, NY; and Memorial Medical Center/Southern Illinois University, Springfield, Illinois. The study was approved by the respective institutional review boards. Patients with baseline serum creatinine and a serum creatinine at 48 hours post-PCI were included. Patients were excluded if they presented with an acute myocardial infarction, had end stage renal disease on dialysis, were exposed to intravenous contrast within one week of PCI, or did not have data available regarding pre- and post-PCI serum creatinine. Data were collected regarding demographics, clinical characteristics, co-morbidities, laboratory data and PCI data. The MR score was calculated for each patient who were then stratified into four groups: MR score 0-5 (group 1), 6-10 (group 2), 11-15 (group 3), and ≥ 16 (group 4). Patients could have slightly different MR score based on whether the serum creatinine or estimated glomerular filtration rate was used.

Clinical definitions and follow-up

CIAKI was defined as an increase in serum creatinine of ≥ 25% or ≥ 0.5 mg/dl over baseline at 48 hours post-PCI. Chronic kidney disease was defined as baseline serum creatinine > 1.5 mg/dl or an estimated glomerular filtration rate < 60 ml/min/1.73 m^2 (Levey modified `Modification of Diet in Renal Disease formula). Anemia

Table 2: Baseline demographics, comorbidities, and procedural characteristics.

Variable	Value or Frequency (n = 931)
Age (yrs) (median, IQR)	65 (56-75)
Age > 75	23.6%
Caucasian	92.5%
Male	68.1%
Diabetes mellitus	37.9%
Hypertension	83.7%
Hyperlipidemia	77.7%
Smoking history	52.2%
Congestive heart failure	11.1%
Hypotension	1.3%
Previous myocardial infarction	30.8%
Previous CABG	24.4%
Peripheral vascular disease	13.1%
Previous angioplasty	37.6%
Hematocrit (%) (median, IQR)	40 (37-43)
Anemia	26.9%
Baseline serum Cr (mg/dl) (median, IQR) < 1.5 1.5-2.0 > 2.0	 1.0 (0.9-1.2) 85.5% 11.7% 2.8%
Baseline eGFR (ml/min 1.73 m^2) (median, IQR) > 60 40-60 20-40 < 20	73 (57-89) 69.8% 20.8% 9.1% 0.2%
Multivessel coronary artery disease	60.6%
Multivessel PCI	23.7%
Treated saphenous vein graft	7.0%
Intra-aortic balloon pump	1.3%
Contrast volume (ml) (median, IQR)	193 (135-258)
Contrast volume > 150 ml	67.1%
Pre-treated with intravenous sodium bicarbonate	3.4%
Pre-treated with N-acetycysteine	15.2%

was defined using World Health Organization criteria: baseline hematocrit value < 39% for men and < 36% for women. Hypotension was defined as systolic blood pressure < 80 mmHg for at least one hour requiring inotropic support with medications or intra-aortic balloon pump within 24 hours following PCI. Renal replacement therapy (RRT) initiation was assessed within one month after PCI. All-cause mortality was assessed within one year after PCI and was ascertained using hospital medical records or the Social Security Death Index at http://ssdi.rootsweb.ancestry.com

Statistical analysis

Summary statistics for the demographic, clinical, laboratory, and procedural characteristics of the population were computed. The proportions of patients who had each of the outcomes (CIAKI, renal replacement therapy and death) were calculated for the entire population and for each MR score subgroup. Continuous variables were compared between patients with and without outcomes using ANOVA or Kruskal-Wallis as appropriate. Discrete variables were compared using Chi Square and Fisher's Exact as appropriate. In order to assess MR score discrimination, likelihood ratios (LR) were calculated for each MR score group within our dataset and also for the dataset reported in Mehran, et al. [10]. A Chi Square for trend was used to compare the occurrence of CIAKI, RRT and death by MR score group. All calculations were performed using Stata, Release 11, College Station, TX.

Results

After applying inclusion and exclusion criteria a total of 931 consecutive patients from the three different hospitals were included in the study. Table 2 details baseline demographics, clinical characteristics, laboratory and PCI data. Overall, the mean age was 65 (mean ± SD) years and the population was 68.1% male and 92.5% Caucasian. Compared to Mehran, et al. our population had a higher rate of most co-morbidities including hypertension (83.7% *vs.* 62.1%), diabetes mellitus (37.9% *vs.* 30.7%), and congestive heart failure (11.1% *vs.* 6.0%). However, our population had lower rates of prior myocardial infarction (30.8% *vs.* 53.4%), previous revascularization with angioplasty (37.6% *vs.* 49.4%) or coronary artery bypass graft (24.4% *vs.* 39.9%), hypotension (1.3% *vs.* 8.3%), and use of intra-aortic balloon pump (1.3% *vs.* 7.1%). Our population had a higher rate of multi-vessel coronary artery disease (60.6% *vs.* 26.9%). Our population had lower amounts of intravenous contrast used (median 193 ± 123 ml *vs.* 261±122 ml). The baseline serum creatinine of our cohort was similar to that of Mehran, et al. 1.0 ± 0.3 mg/dl, eGFR 73 ± 16 and 30.2% had CKD *vs.* eGFR was 72.7 ± 21.1 and 26.4% had CKD, respectively.

The overall incidence of CIAKI was 12.2%, similar to the 13.1% event rate in the development dataset of Mehran, et al. The overall rate of RRT within one month of PCI was 0.4% in our population compared to 0.6% in Mehran, et al. report. The overall rate of death at one year was 9.0% compared to 6.0% in Mehran, et al. report.

As detailed previously, patients were stratified into a low-risk group (Group 1, MR score 0-5, n = 508, 54.6%), moderate risk group (Group 2, MR score 6-10, n = 283, 30.4%), high risk group (Group 3, MR score 11-15, n = 114, 12.2%), and very high-risk group (Group 4, MR score ≥ 16, n = 26, 2.8%). Overall, our population skewed towards a higher MR score than the original derivation dataset from Mehran, et al. (59.2% in MR score group 1, 31.7% in MR score group 2, 7.9% in MR score group 3, and 1.1% in MR score group 4).

Table 3 details the event rates and respective likelihood ratios stratified by MR score group. A higher MR score was strongly associated with development of CIAKI and mortality ($p < 0.01$). The LR ratios for MR score group 4 were most predictive of CIAKI, RRT, and one- year all-cause mortality, with LR of 7.2, 19.3, and 6.3, respectively. Conversely, the LR for MR score group 1 were moderately predictive against those outcomes, with LR of 0.4, 0, and 0.3, respectively. The LR for MR score group 2 were not predictive of CIAKI, RRT, and one-year all-cause mortality, with LR between 0.8 and 1.1. The LR for MR score group 3 were mildly predictive of the outcomes, with LR between 2.1 and 4.3.

Table 3 also compares our results with those previously reported by Mehran, et al. There was no difference in the rate of CIAKI overall or in each MR score group when the two populations were compared. However, the risk of death was higher in our population (RR 1.58, 95% CI: 1.37 to 1.89, $p < 0.001$). The likelihood ratios between the two populations were quite similar overall.

Discussion

Angiography remains the gold standard for the diagnosis and management of CAD. Chronic kidney disease is prevalent in patients with CAD. The co-existence of these conditions puts patents at higher risk for CIAKI related to nephrotoxic contrast exposure [1]. The MR score was proposed to help identify patients undergoing non-emergent PCI at highest risk for CIAKI and death related to contrast exposure.

Table 3: Outcomes and likelihood ratios.

	MRS Group 1		MRS Group 2		MRS Group 3		MRS Group 4	
	Reuter	Mehran	Reuter	Mehran	Reuter	Mehran	Reuter	Mehran
Patients (n)	508	2486	283	1633	114	599	26	154
CIN (%)	5.7	7.5	13.1	14	30.7	26.1	50	57.3
HD (%)	0	0.04	0.4	0.12	0.9	1.09	7.7	12.6
LR CIN	0.4	0.5	1.1	1.0	3.2	2.3	7.2	8.5
LR HD	0	0.07	0.8	0.2	2.1	2.0	19.3	23.5
LR Mortality	0.3	0.3	0.9	1.0	4.3	3.0	6.3	7.5

Our study, designed to externally validate MR score, was conducted at 3 centers (2 university teaching hospitals in geographically different areas of the country and 1 community-based teaching hospital). When compared to the patient characteristics in Mehran study, our cohort had a higher prevalence of several co-morbidities. Despite these differences, MR score accurately predicted the risk of CIAKI and one-year all-cause mortality. Patients with high MR score (group 4) were found to have > 10-fold increase incidence of CIAKI and one-year all-cause mortality when compared to those with low MR score (group 1). Although fewer of our patients required RRT than in the Mehran study, we did find that there was a greater likelihood of RRT in patients with higher MR scores. The lower need for RRT in our cohort might be explained by different thresholds for initiation of renal replacement therapy at different institutions. The higher mortality rates in our cohort compared to the Mehran, may reflect the higher prevalence of co-morbidities such as diabetes mellitus and congestive heart failure in our cohort. Moreover, because our study was retrospective, serum creatinine values 48-72 hours post PCI were only available in hospitalized patients who tend to have more risk factors than patients undergoing elective PCI. Prospective collection of data in Mehran's study may have captured more post-PCI serum creatinine values in patients undergoing elective outpatient procedures.

We found that MR score is a valid tool that can be used by clinicians to identify patient populations that are at risk for CIAKI following non-emergent PCI. There have been other validation studies published previously. Sgura and coworkers applied the MR score to predict the risk of CIAKI in patients undergoing PCI for acute ST elevation myocardial infarction (STEMI) [12,13]. Patients with a low-risk score had a slightly higher incidence of CIAKI (14.4%) compared to those with a high-risk score (14.2%), and a there was a 10-fold increase in one-year all cause mortality in the very high-risk patients as compared to a 6-fold increase in patients with a low-risk score. This study only included patients with STEMI, which may explain the higher morbidity and mortality rates that were reported. Recently R.A. Abella's-Sequeiros, et al. reported a validation study [14] that showed an overall incidence of CIAKI of 7.8% which was significantly lower than our study. The rate of CIAKI increased with increased risk category 2.4%, 7.2%, 18.6%, 40% for low, moderate, high and very high-risk groups. Compared to our cohort, their population was older but had lower prevalence of diabetes mellitus, peripheral vascular disease and prior MI, which could explain the lower incidence of CIAKI. Moreover, their study included patients from one center in Europe whereas our study included patients from three different centers. Our study is the first multicenter validation of the MR score in heterogeneous population undergoing non-emergent PCI.

CIAKI is an important complication of coronary angiography and PCI. In order to give informed consent for the procedure, patients and families need to understand its risks. Merely mentioning the development of CIAKI, along with the impact of hemodialysis on the quality of life, might make patients reluctant to undergo a potentially lifesaving procedure. Accordingly, accurate risk stratification with hard end points provides patients with a valid and accurate means for making decisions. Hopefully, we can reduce the risk of CIAKI by identifying the patients at high risk and implementing preventive measures. [7,15,16]. As such, predictive scores such as MR score can be of substantial benefit for both clinical decision-making and research.

Our study has several limitations. Variables which may impact CIAKI such as peri-procedural hydration volume, proteinuria, and nephrotoxic medications [17,18] were not included in our analysis since our goal was to validate MR score and these variables were not considered in the Mehran study. Similarly, although we collected information regarding N-acetyl cysteine and sodium bicarbonate administration, we did not include them in risk prediction since they were not considered in Mehran's study and the role of these interventions in preventing CIAKI has not been clearly defined [19,20]. Approximately 60% of patients in our cohort had multivessel coronary disease, however less than 25% of cohort patients underwent multivessel PCI, which suggests that coronary artery bypass rates may be higher in our population than in Mehran's cohort. Our study, like other studies evaluating prognostic impact of CIAKI, fails to confirm whether CIAKI is a causative factor in post PCI mortality or whether it is simply a marker of patients with multiple co-morbidities [21]. A prospective randomized trial would conclusively answer that question. Although ours was a retrospective study which introduced variability in the timing of post-PCI follow up serum creatinine measurements, our results were comparable to those of Mehran, et al.

In conclusion, we were able to externally validate MR score as a useful tool in predicting the risk of CIAKI and death following non-emergent PCI in a heterogeneous population at three different hospitals. The MR score can help clinicians identify and stratify patients according to risk for CIAKI. Because interventions may be variably effective in different risk groups, the MR score may also aid researchers stratify patients into different risk groups for future CIAKI prevention studies.

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