ORIGINAL ARTICLE

SIGNIFICANCE OF CANADA ACUTE CORONARY SYNDROME RISK SCORE IN EMERGENCY PERCUTANEOUS REVASCULARIZATION FOR THE PREDICTION OF CONTRAST INDUCED NEPHROPATHY

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Objectives: This study was conducted to compare the accuracy of Canada Acute Coronary Syndrome (C-ACS) score against Mehran risk score (MRS) in primary percutaneous coronary intervention (PCI) patients for risk stratification of contrast induced nephropathy (CIN) at a tertiary care cardiac hospital.

Methodology: In this study we included adult patients presented with chief presenting complaint of typical chest pain to emergency department within 12 hours of onset of symptoms, diagnosed with ST-segment elevation myocardial infarction (STEMI) and taken to the catheterization laboratory for primary PCI. Two scores MRS and C-ACS were computed and CIN was defined based on the variations in creatinine level, absolute 0.5 mg/dL or relative 25% increase at 48-72 hours.

Results: Study included a total of 593 patients with mean age of 52.22±11.1 years and 488(82.3%) were male patients. A total of 53(8.9%) patients developed CIN after primary PCI. The area under the curve (AUC) was 0.745 [0.675-0.815] and 0. 647 [0.560-0.733] for MRS and C-ACS score respectively. The threshold value C-ACS ≥ 1 has sensitivity of 47.2% [33.3%-61.4%] and specificity of 80.2% [76.6%-83.5%]. Similarly, MRS ≥6.5 has sensitivity of 64.2% [49.8%-76.9%] and specificity of 75% [71.1%-78.6%].

Conclusion: C-ACS score is found to be less sensitive but more specific in identifying patients at high risk of CIN. Predictive value of C-ACS was observed to be lower than that of MRS. In the tradeoff of simplicity and accuracy, clinicians may consider accuracy and prefer MRS over C-ACS for the risk stratification of CIN.

Keywords: primary PCI, STEMI, CIN, Mehran risk score, Canada Acute Coronary Syndrome

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INTRODUCTION

Both American and European clinical practice guidelines recommend primary percutaneous coronary intervention (PCI) as preferred strategy for the early revascularization of patients within 12 hours of diagnosis of ST-segment elevation myocardial infarction (STEMI).[1,2] A significant improvement has been witnessed in the outcomes of STEMI patients in recent years with the adoption of primary PCI, however, among various other complications associated with percutaneous procedures, risk of incidence of contrast induced nephropathy (CIN) also remains substential.[3] A significantly higher mortality and morbidity rates have been reported to be associated the incidence of CIN and consequently, increase healthcare expenditures, extended hospital stay than usual, and increased utilization of resources.[4] It still remains the 3rd commonest hospital acquired kidney injury with the incidence rate ranging from 10.4% to 23.2% despite improved understanding of the phenomenon and related risk factors and advancements in the formulation of contrast medium.[5-8]

The pathophysiology behind the incidence of acute kidney injury in following few hour of contrast exposure is not very clear. Among various possible causes of CIN, tubular necrosis, chemokine damage, oxidative strain, and imbalance between vasodilator and vasoconstrictor all are known to be potential mechanisms behind CIN.[5] Similarly, literature regarding optimal treatment options for the patients with CIN are also not conclusive, hence, the best available clinical strategy is prevention and pre-procedure identification of patients at higher risk of development of CIN. There is also low concordance in literature regarding the preventive pharmacologic and

non-pharmacological strategies.[9,10] Therefore, due to its prognostic and pathophysiological implications it has become more essential in recent years.[11] Hence, with appropriate non-pharmacological and pharmacological preventive strategies, it is also important to identify patients with high risk features for the development of CIN. A number of system related, procedure related and patients related high risk features have been identified in various past studies, such factors consisted of volume depletion and hemodynamic alterations as a result of heart failure or cardiogenic shock, co-morbidities such as diabetes and chronic kidney diseases, and complex procedures requiring increased amount of contrast.[5,12]

Although, a number of scoring systems have been introduced but the most established one is the Mehran risk score (MRS).[13] It has been also recently validated by the Kumar R et al.[14] in the STEMI patients. The Canada Acute Coronary Syndrome (C-ACS) score is among other most commonly used scoring system, simplicity of its computation makes it a potential candidate for the CIN risk stratification in the context of primary PCI.[14,15] It has been reported to have significant role in CIN risk assessment due to the fact that all of its components, age, congestive heart failure, and hemodynamic variations, are by on their own are the important predictors of CIN.[16] Therefore, aim of this study was to evaluate and compare the predictive value of C-ACS score against MRS for the prediction of the development of CIN in STEMI patients after primary PCI at a tertiary care cardiac hospital.

METHODOLOGY

This descriptive study was conducted at a tertiary care hospital for cardiovascular diseases located in Karachi Pakistan between September 2020 and March 2021. Prior to the initiation of study, institutional ethical review board approval was obtained (ERC-56/2021). Consent for the participation was obtained from all the included patients. In this study we included adult patients with chief presenting complaint of typical chest pain who presented to the emergency department within 12 hours of onset of symptoms, diagnosed with STEMI and taken to the catheterization laboratory for primary PCI. Patients with cardiogenic shock, Killip class IV, chronic kidney disease (CKD), or had history of contrast exposure within past 7 days were excluded.

Data for the study were collected using a structured proforma consisted of clinical characteristics, demographic details, baseline hemodynamics, diagnosis, angiographic characteristics, post procedure in-hospital outcomes and complications. Diagnosis of STEMI was made as per the 4th universal definition of MI based on electrocardiography (ECG) and history at presentation. All primary PCI procedures were performed free of cost as per the institutional policy. All procedures were performed as per the clinical practice guidelines by consultant cardiologists. CIN was defined base on the serum creatinine level recorded at the arrival and after 48 to 72 hour of primary PCI procedure. We adopted the most commonly used definition of CIN in literature in the context of percutaneous coronary interventions. Patients with increase of 0.5 mg/dL or 25% relative to baseline level at 48 to 72 hour of procedure were categorized to have CIN. Two scores MRS and C-ACS were computed and recorded for all the patients.

Collected data were entered and analysis using IBM SPSS version 19. Mean ±, standard deviation (SD)/median [interquartile range (IQR)] or frequency and percentage were computed to summarize the collected variables. The receiver operating characteristic (ROC) curve analysis was performed to compare the MRS and C-ACS score for the prediction of CIN. Area under the curve (AUC) and its 95% confidence interval for both the scores were computed. Sensitivity and specificity analysis were performed against the optimal threshold value of the scores computed using Youden Index (J statistic). Collected clinical data were compared for the patients with and without CIN by conducting independent sample t-test/Mann-Whitney U test or Chi-square/Fisher's exact test. P-value ≤ 0.05 was considered statistically.

RESULTS

Study included a total of 593 with mean age of 52.22 ± 11.1 years and 488 (82.3%) were male patients. A total of 53 (8.9%) patients developed CIN after primary PCI. Incidence of CIN was found to be associated with older age (59.68 ± 10.2 vs. 51.49 ± 10.92 years; p<0.001), delay in hospital arrival from the time of symptom onset (360 [265 - 500] vs. 320 [230 - 420] minutes; p=0.039), elevated arrival creatinine level (1.1 ± 0.3 vs. 0.9 ± 0.2 mg/dL; p<0.001), higher killip class (III: 13.2% vs. 3.3%), intubation (20.8% vs. 5.4%; p<0.001), presence of arrhythmias on arrival (18.9% vs. 7%; p=0.006), diabetes (43.4% vs. 23.9%; p=0.002), history of cerebrovascular accident (5.7% vs. 0.6%; p=0.011), elevated left ventricular end-diastolic pressure (19.8 ± 6.8 vs. 16.6 ± 4.9 mmHg; p<0.001), reduced ejection fraction (37.3 ± 10.2 vs. 42.3 ± 8.4%; p<0.001), triple vessel disease (35.8% vs. 19.1%) (Table 1).

CIN was also found to be associated with increased in-hospital mortality rate (7.5% (4/53) vs. 1.7% (9/540); p=0.022) and other complications such as re-infarction (3.8% (2/53) vs. 0.2% (1/540); p=0.022) and

arrhythmias (9.4% (5/53) vs. 0.9% (5/540); p=0.001) (Table 1).

Table 1: Demographic, clinical, angiographic, and procedural findings of patients with and without contrast induced nephropathy

	Total	Non-CIN	CIN	P-value
Total (N)	593	540	53	-
Gender				
Male	488 (82.3%)	446 (82.6%)	42 (79.2%)	0.542
Female	105 (17.7%)	94 (17.4%)	11 (20.8%)	
Age (years)	52.22 ± 11.1	51.49 ± 10.92	59.68 ± 10.2	<0.001*
<65 years	492 (83%)	459 (85%)	33 (62.3%)	0.001*
65 to 75 years	88 (14.8%)	71 (13.1%)	17 (32.1%)	
>75 years	13 (2.2%)	10 (1.9%)	3 (5.7%)	
Total ischemic time (minutes)	320 [230 - 430]	320 [230 - 420]	360 [265 - 500]	0.039*
Killip classification				
I	516 (87%)	483 (89.4%)	33 (62.3%)	<0.001*
II	52 (8.8%)	39 (7.2%)	13 (24.5%)	
III	25 (4.2%)	18 (3.3%)	7 (13.2%)	
Type of myocardial infarction				
Anterior	315 (53.1%)	285 (52.8%)	30 (56.6%)	0.071
Inferior	111 (18.7%)	106 (19.6%)	5 (9.4%)	
Inferior with RV	109 (18.4%)	97 (18%)	12 (22.6%)	
Inferior - posterior	36 (6.1%)	30 (5.6%)	6 (11.3%)	
Lateral	11 (1.9%)	11 (2%)	0 (0%)	
Posterior	11 (1.9%)	11 (2%)	0 (0%)	
Intubated	40 (6.7%)	29 (5.4%)	11 (20.8%)	<0.001*
Arrhythmias on presentation	48 (8.1%)	38 (7%)	10 (18.9%)	0.006*
Co-morbid				
Hypertension	267 (45%)	237 (43.9%)	30 (56.6%)	0.076
Smoking	205 (34.6%)	194 (35.9%)	11 (20.8%)	0.027*
Diabetes mellitus	152 (25.6%)	129 (23.9%)	23 (43.4%)	0.002*
Cerebrovascular accident	6 (1%)	3 (0.6%)	3 (5.7%)	0.011*
Access for procedure				
Radial	466 (78.6%)	434 (80.4%)	32 (60.4%)	<0.001*
Femoral	127 (21.4%)	106 (19.6%)	21 (39.6%)	
LVEDP (mmHg)	16.9 ± 5.2	16.6 ± 4.9	19.8 ± 6.8	<0.001*
LV ejection fraction (%)	41.9 ± 8.7	42.3 ± 8.4	37.3 ± 10.2	<0.001*
IABP used	7 (1.2%)	3 (0.6%)	4 (7.5%)	0.002*
Number of diseased vessels				
1 vessel	266 (44.9%)	252 (46.7%)	14 (26.4%)	0.004*
2 vessel	205 (34.6%)	185 (34.3%)	20 (37.7%)	
3 vessel	122 (20.6%)	103 (19.1%)	19 (35.8%)	
Infarct related artery				
Left main	5 (0.8%)	4 (0.7%)	1 (1.9%)	0.679
Non-Proximal LAD	115 (19.4%)	106 (19.6%)	9 (17%)	
Proximal LAD	200 (33.7%)	180 (33.3%)	20 (37.7%)	
Left circumflex	73 (12.3%)	64 (11.9%)	9 (17%)	
Right coronary artery	193 (32.5%)	179 (33.1%)	14 (26.4%)	
Diagonal	6 (1%)	6 (1.1%)	0 (0%)	
Ramus	1 (0.2%)	1 (0.2%)	0 (0%)	
Fluoroscopy time (minutes)	14.7 ± 7.9	14.6 ± 8	15.2 ± 7	0.629
Contrast volume (ml)	119 ± 36.6	118.4 ± 35.7	125.8 ± 44.6	0.161

CIN=contrast induced nephropathy, RV=right ventricular, LV=left ventricular, LVEDP= left ventricular end-diastolic pressure, LAD=left anterior descending artery, IABP=intra-aortic balloon pump
**significant at 5%*

The AUC was 0.745 [95% CI; 0.675-0.815] and 0. 647 [95% CI; 0.560-0.733] for MRS and C-ACS score respectively (Figure 1). The optimal threshold value for C-ACS was found to be ≥ 1 with sensitivity of 47.2% [95% CI; 33.3% - 61.4%] and specificity of 80.2% [95% CI; 76.6% - 83.5%]. Similarly, ≥6.5 was found to be the optimal threshold value for MRS with sensitivity of 64.2% [95% CI; 49.8% - 76.9%] and specificity of 75% [95% CI; 71.1% - 78.6%] (Table 2).

DISCUSSION

Considering the importance of CIN risk stratification, we have conducted this study to compare the predictive value of C-ACS score, a simple clinical scoring system, against well-established MRS score.

We observed predictive value of C-ACS score is much lower than that of MRS with AUC of 0. 647 vs. 0.745 respectively. C-ACS score of ≥ 1 was found to be more specific (80.2%) than sensitive (47.2%). Various system, operator, patient and procedure related factors were found to be associated with increased incidence of CIN such as older age, delay in hospital arrival from the time of symptom onset, elevated arrival creatinine level, higher killip class at presentation, intubation, presence of arrhythmias at arrival, diabetes, history of cerebrovascular accident, elevated Left ventricular end-diastolic pressure, reduced ejection fraction, and triple vessel disease. Similarly, patients who developed CIN were found to be at an increased risk of re-infarction, arrhythmias, and in-hospital mortality.

Table 2: Accuracy of Canada Acute Coronary Syndrome (C-ACS) and Mehran score for the prediction of contrast induced nephropathy

	Contrast Induced Nephropathy	
	No	**Yes**
Total (N)	**540**	**53**
Canada Acute Coronary Syndrome score		
< 1	80.2% (433)	52.8% (28)
≥ 1	19.8% (107)	47.2% (25)
Accuracy	77.2% [95% CI; 73.6% - 80.6%]	
Sensitivity	47.2% [95% CI; 33.3% - 61.4%]	
Specificity	80.2% [95% CI; 76.6% - 83.5%]	
Positive predictive value (PPV)	18.9% [95% CI; 14.4% - 24.6%]	
Negative predictive value (NPV)	93.9% [95% CI; 92.3% - 95.2%]	
Mehran risk score (MRS)		
< 6.5	75% (405)	35.8% (19)
≥ 6.5	25% (135)	64.2% (34)
Accuracy	74% [95% CI; 70.3% - 77.5%]	
Sensitivity	64.2% [95% CI; 49.8% - 76.9%]	
Specificity	75% [95% CI; 71.1% - 78.6%]	
Positive predictive value (PPV)	20.1% [95% CI; 16.4% - 24.4%]	
Negative predictive value (NPV)	95.5% [95% CI; 93.7% - 96.8%]	

The incidence rate of CIN in our study was 8.9% which was lower than the rate of CIN reported by the studies conducted in our population, the previously reported incidence rates are 10.2% and 12.4% by Ullah I et al.[17] and Batra MK et al.[12] respectively in our population. Relatively lower incidence rate in our study may be due exclusion of cardiogenic shock patients, Killip class IV, chronic kidney disease (CKD), and patients exposed to the contrast medium for any diagnostic or treatment procedure.

Though C-ACS is very simple scoring system comprised of only 4 clinical parameters without including any laboratory, biological, or procedural factor. All four of its parameters are well establish predictors of CIN such as hemodynamic variations, congestive heart failure, and older age.[16] In a study, discriminative power of the C-ACS score was reported to be comparable as that of the MRS with AUC of 0.822 vs. 0.751 respectively.[15] However, results of our study were not as supportive as results of Liu Y-H et al.[15], a recent study by Kumar R et al.[14] had similar observation regarding role C-ACS for the prediction of CIN in primary PCI patients with 0.671 [0.593 - 0.749] AUC for C-ACS.

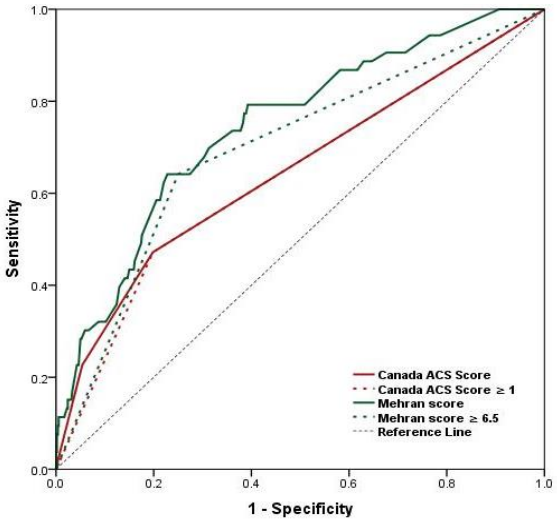

Figure 1: Receiver operating characteristics curve for Mehran score and Canada Acute Coronary Syndrome for the prediction of contrast induced nephropathy

Although, simplicity of the risk model is important but the ultimate criteria for the model selection is the accuracy of prediction and ability of model to identify individuals at increased risk of development of CIN. The C-ACS score showed low sensitivity in CIN prediction and it was observed to fail in reaching the accuracy level of MRS. More research work is need to in order to improve CIN risk stratification of the patients undergoing primary PCI.

Our study has some limitations, first and foremost due to a small number of events, multivariable association analysis could not be performed. Secondly, CIN was defined based on variations in serum creatinine level, more direct assessment of kidney function such as kidney morphology and proteinuria and use of imaging modalities would have increased the accuracy of assessment. Our study had a small sample size and a single center coverage, a large scale studies with more direct assessment of post procedure kidney

function are needed to validate the usefulness of C-ACS.

CONCLUSION

C-ACS score is found to be less sensitive but more specific in identifying patients at high risk of CIN. Predictive value of C-AVS was observed to be lower than that of MRS. In the tradeoff of simplicity (C-ACS) and accuracy (MRS), clinicians may consider accuracy and prefer MRS over C-ACS for the prediction of CIN in primary PCI setting. However, further large scale studies are needed to determine the role of C-ACS for risk stratification with more direct assessment of kidney function.

AUTHORS' CONTRIBUTION

AK, KZN, SK and RK: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. SA, MTF, SK, MM, OK, JAS and TS: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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