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Mehran and AGEF Risk Scores in Contrast-Induced Nephropathy Among Patients Undergoing Primary Percutaneous Coronary Intervention

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Abstract

Background: Primary percutaneous coronary intervention (PCI) is the treatment of choice for ST-segment elevation myocardial infarction (STEMI). Contrast induced nephropathy (CIN) is a serious complication which complicates PCI, resulting in increased morbidity, hospital stay, short and long term adverse outcomes. Prediction of high risk patients for development of CIN is of great importance to conduct preventive measures. Various scoring systems were developed to set up high risk criteria.

Aim of Study: To detect the relation between Mehran and AGEF risk scores and CIN. Also, to report other high risk criteria to predict CIN.

Patients and Methods: The study included 250 patients with acute STEMI treated by primary PCI. Patients with coronary anatomy not suitable for PCI, with pre-existing renal troubles, on chronic dialysis and who need urgent coronary artery by-pass surgery were excluded.

Results: CIN developed among 90 patients (36%). There was no significant association between CIN and patients' age or weight. The independent predictors of the occurrence of CIN were, in order, Mehran score (OR=6.4), Diabetes (OR= 5.8), AGEF score (OR=3.3) creatinine clearance (OR=1.02), non-osmolar contrast volume (OR=0.991). Females, those with low ejection fraction (EF) or previous history of ischemic heart disease (IHD) were susceptible for CIN.

Conclusion: CIN is a challenging health problem among patients undergoing primary PCI. Mehran risk score has a better predictive power that AGEF score in predicting CIN. Several other factors are associated with CIN development like diabetes, female gender, low EF history of IHD and use of non-osmolar contrast.

Key Words: *Primary PCI – Contrast induced nephropathy – Mehran score – AGEF score.*

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Introduction

CONTRAST induced nephropathy (CIN) is one of the complications of primary percuta-neous coronary intervention (PPCI) [1]. CIN is defined as an elevation of serum creatinine (Scr) of more than 25% or ≥0.5mg/dl (44 μmol/l) from baseline within 48h of the angiographic procedure and after excluding other factors that may cause nephropathy such as nephrotoxins. It is self-limited in most instances, with Scr levels peaking in 3-5 days and gradually returning to baseline levels within 7-10 days [2].

(AKI) and represents about 12% of the cases [3]. The reported incidence of CIN after percutaneous coronary intervention (PCI) varies between 0 and 24%, depending on the prevalence of associated risk factors, with the higher incidence being reported after emergency PCI [4].

Prediction of high risk patients for development of CIN is of great importance to conduct preventive measures for them. Various scoring systems were developed to set up high risk criteria. These scores are AGEF, and Mehran scores. Comparison between the different risk scores in the prediction of CIN is deficient [5].

This study aimed to identify the actual prevalence CIN among patients who undergo primary PCI in our cath lab. and to compare different risk factors associated with its development, and to search for some other parameters that could help in the prediction of CIN.

Patients and Methods

Study design:

Cross-sectional, observational hospital based study, conducted in Assiut University Hospital.

Study population: The study included 256 patients who had ST elevation myocardial infarction (STEMI) and underwent PPCI in our hospital (Assiut University Hospital) starting from the beginning of May 2016 till end of May 2017. Of these patients, 6 patients were excluded as 3 of them were on regular dialysis, 2 died during the pro-cedure, and one required urgent Coronary artery bypass grafting (CABG).

Sample size:

Sample size was calculated using Epi-info version 7. Based on previous studies, the prevalence of Contrast-Induced Nephropathy in patients undergoing PPCI for acute myocardial infarction was 5.2% with a power of 80 and worst expected value 2.2%, the sample needed for the study was estimated to be about 210 patients.

Inclusion and exclusion criteria:

Inclusion criteria:

All patients with STEMI who were eligible for primary PCI were enrolled in the study. Diagnosis of STEMI was based on the Third Universal Definition of MI, implemented by a joint task force from the European Society of Cardiology (ESC), American College of Cardiology (ACC) Foundation, American Heart Association (AHA), and the World Heart Federation (WHF), when two criteria are met [6].

Detection of an increase or decrease in cardiac biomarker values (preferably using cardiac troponin [cTn]) with at least one value above the 99 th percentile of the upper reference limit (URL) and with at least one of the following findings:

- Symptoms of ischemia.
- New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB).
- Development of pathologic Q waves on the ECG.
- Imaging evidence of new loss of viable myocardium or a new regional wall motion abnormality.

Exclusion criteria: The patients were excluded if the coronary anatomy was not suitable for PCI, if emergency bypass grafting was required, if patients were on chronic peritoneal or hemodialytic treatment, or is known to have pre-existing renal impairment or underwent previous CABG.

Patients and Methods:

All patients were subjected to: Full history taking; including age, sex, history of diabetes mellitus (DM), hypertension (HTN), smoking, and dyslipidemia. Also,to assess the onset of chest pain and time to reperfusion. Thorough physical examination was done to all patients including assessment of Killip score and detection of signs of heart failure. Twelve-lead ECG was done to all patients to diagnose STEMI. Baseline venous blood samples were collected for assessment of hemoglobin (HB) level, serum creatinine, and electrolytes before the procedure. Also, kidney function assessment using creatinine clearance using Cockcroft-Gault formula was done [7].

CIN was defined as an elevation of serum creatinine (Scr) of more than 25% or ≥0.5mg/dl (44 μmol/l) from baseline within 48 hours of the angiographic proce-dure and after excluding other factors that may cause nephropathy such as nephrotoxins [8].

*Coronary angiography and primary PCI:*Were done by an interventional cardiologist. Coronary anatomy was evaluated and assessed. After the procedure, volume of used contrast material and time of X-ray exposure were obtained. Echocardiography: Was done immediately after transfer of the patient to CCU to assess the ejection fraction of the heart by (m-mode) [9].

Daily follow-up: for serum creatinine was done at 24, 48 hours.

Mehran and AGEF risk scores: Were calculated for each patient.

Mehran risk score includes 8 prognostic variables: Hypotension (5 points, if systolic blood pressure <80mmHg for at least 1h requiring inotropic support), use of intra-aortic balloon pump (5 points), congestive heart failure (5 points, if class III/IV by New York Heart Association classification or history of pulmonary edema), age (4 points, if >75 years), anemia (3 points, if hematocrit <39% for men and <36% for women), diabetes mellitus (3 points), contrast media volume (1 point per 100mL), and estimated glomerular filtration rate 2 points, if GFR 60 to 40 GFR mL/min per $1.73m^2$; 4 points, if GFR 40 to 20; 6 points, if GFR<20), if the score is <5 so, it is low risk, from 6 to 10 it is moderate risk, from 11 to16 it is high risk and more than 16 it is very high risk [10].

AGEF risk score was calculated it as age/EF (%) +1 (if Scr >2.0mg/dL) and age/EF (%) +0 (if Scr <2.0mg/dl) so grading of AGEF score <1, from 12, >2 [11].

Ethical considerations:

*Ethical appr*oval:

An approval for the study is obtained from the ethical committee in our Institution.

Risk-benefit assessment:

All procedures performed in this protocol are following the institution standards of care for the patients, with no special additional maneuvers that could carry a risk to the patient.

Confidentiality:

Any data taken from the patient either from history, examination or investigations dealt with in a confidential manner.

Research statement:

Every patient was informed about the nature and steps of the study.

Informed consent:

Written consent was obtained from each patient participating in the study.

Statistical analysis:

Data collected and analyzed by computer program SPSS" ver. 23" Chicago. USA. Data expressed as mean, standard deviation and number, percentage. *t*-test or Mann-Whitney if necessary was used to determine significant for numeric variable. Chi. Square with Fisher exact correction was used to determine significance for non-numeric variable. Also using paired *t*-test to determine significance between numeric variables pre & post "Creatinine, Cr clearance". Multivariate Binary Logistic Regression was done including significant univariate predictors of CIN. A *p*-value of <0.05 was considered significant.

Results

In this study, 250 patients were included. Among them about 81% were males and 19% females. The mean age was 53.8±11.90 and 16% known to have cardiovascular diseases.

CIN developed among 90 patients (36%). Table (1) shows the comparison between group A (no CIN) and group B (CIN) as regard the demographic characteristics, cardiovascular risk prevalence, scores and contrast details. Female gender showed a significant increase in CIN development compared to males. Other univariate predictors of CIN were previous IHD, diabetes mellitus, lower ejection fraction, creatinine clearance, Mehran and AGEF risk scores, contrast volume and contrast type.

Using Mehran risk score, the prevalence of CIN was (33.88%) in low risk group, and (38.8%) in moderate risk group, versus (100%) of high risk group (p<0.001) as shown in Fig. (1). There was a significant increase in the development of CIN with increase in AGEF score (p<0.001) with (27.35%) in the group of AGEF score <1, (40.31%) in the group with AGEF score 1-2, versus (60.1%) in patients with in AGEF score >2, as shown in Fig. (2).

Infarct related artery had no impact on the incidence of CIN (p<0.275) as shown in Table (2). Multivariate Binary Logistic Regression showed that the independent predictors of the occurrence of CIN were in order of Mehran score (OR 6.4), diabetes (OR 5.8), AGEF score (OR 3.3), IRA as RCA (OR 2.1), Creatinine clearance (OR 1.02), non-osmolar contrast volume (OR 0.991) as shown in Table (3).

Table (1): Relation between risk factors and CIN in the study group.

Item	Group A (no CIN) "n=160"	Group B (CIN) "n= 90"	*p*-value
Age	53.15±11.91	55.21±10.45	0.287
Weight	87.67±17.51	87.95±13.04	0.898
Female gender	28 (59.6%)	19 (40.4%)	0.03
Smoker	80 (50.0%)	41 (45.6%)	0.795
Hypertension	36 (22.5%)	24 (26.7%)	0.277
(IHD)*	21 (13.12%)	21 (23.20%)	0.02
Diabetic			
EF**	29 (11.87%)	50 (55.55%)	0.0001
Dyslipidemia	65.34±2.34	48.23±1.89	0.001
Creatinine	3 (1.9%)		0.260
Creatinine clearance	0.93±0.30	0.93±0.10	0.957
Killip class	139.6±62.5	115.8±37.8	0.0001
Mehran score	1.06±0.30	1.12±0.44	
AGEF score	2.39±1.43	3.46±2.39	0.166
Contrast volume	0.99±0.46	1.86±0.41	0.001
Contrast type	141.06±37.21	152.48±52.06	0.001
• Low–osmolar "226"	151 (66.8%)	75 (33.2%)	0.02
• High–osmolar "24"	9 (41.67%)	15 (58.33%)	0.01

* : Previous ischemic heart disease.
**: Ejection fraction.

Table (2): Infarct related artery and CIN.

Item	NON RCA "n=174"	RCA "n=76"	*p* value
Group A "n=160"	115(66.09%)	45(59.21%)	*p*=0.275n.s
Group B "n=90"	59(33.90%)	31(40.78%)	

Table (3): Multivariate binary logistic regression analysis for the predictors of contrast induced nephropathy.

Variable	Odd Ratio	95% Confidence Interval	*p*-value
Mehran Score	6.4	1.4–29.4	0.017
Diabetes	5.8	3.0–11.3	<0.0001
AGEF Score	3.3	1.8–6.2	<0.0001
Creatinine Clearance	1.02	1.01–1.03	<0.0001
Non-osmolar Contrast volume	0.991	0.984–0.999	0.02

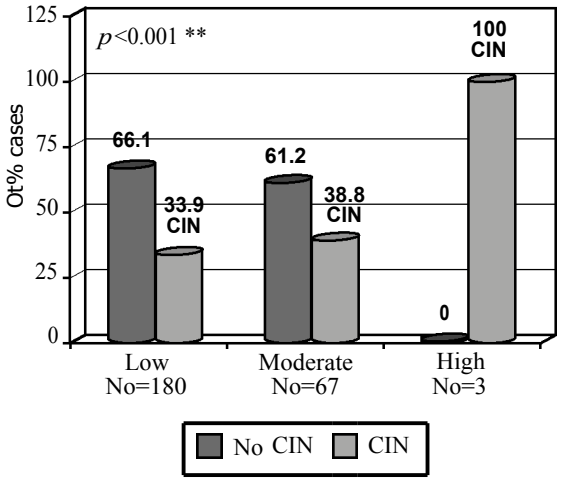

Fig. (1): Relation between Mehran risk score and CIN.

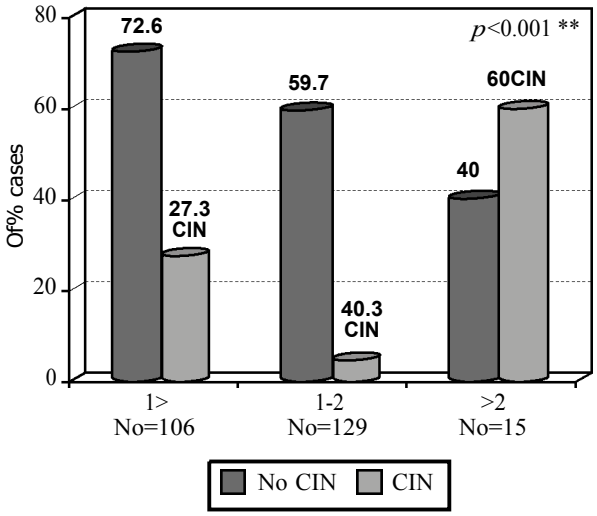

Fig. (2): Relation between AGEF score and CIN.

Discussion

Contrast-induced nephropathy (CIN) is a serious complication of angiographic procedures resulting from administration of iodinated contrast media (CM) [8]. The development of CIN is associated with a longer hospital stay, an increased morbidity and mortality, in addition to a higher financial cost [12].

Accurate risk stratification for contrast-induced nephropathy (CIN) is important for patients with ST-segment elevation myocardial infarction (STE-MI) undergoing primary PCI. Few trials were done to compare different risk scores in prediction CIN incidence.

In our study we used two different risk scores (Mehran and AGEF) to detect the validity and the predictive value of each one in CIN development after PPCI.

The prevalence of CIN development in our study was 36%, which is higher than that reported by Liu and coworkers [11], also higher than in study were 23% developed CIN [13] and in Maioli et al., among 442 patients 23.2% developed CIN [14]. This may be explained by inclusion of only 20 patients that had ejection fraction lower than 40% EF in the study which is one of the major factors that affect the incidence of CIN.

The independent predictors of the occurrence of CIN, using multivariate binary logistic regression were, in order, Mehran score, diabetes, AGEF score, creatinine clearance, non-osmolar contrast volume. Ando et al. used logistic regression analysis, ROC curve analysis and found that both AGEF and Mehran score as predictors of CIN [15]. In the study of Han et al., using logistic regression analysis to independent risk factors, found that, diastolic dysfunction (DD), increased Mehran score, ST-segment-elevation myocardial infarction, higher HbA1c and left anterior descending lesion, as well as the use of diuretics [13].

In our study, Mehran score proved by multivariate logistic regression analysis to be the strongest independent predictor of CIN with an Odd ratio of 6.4. Mehran risk score, in patients who developed CIN was 3.46±2.39, versus 2.39± 1.43 in non CIN groups. This is lower than the study of Liu et al., in which mean ± SD Mehran score was 10.8±3.8. This may be explained by the fact that their study included a large number of patients with age >75 years (16.8%), eGFR (15.4%) and anemic patients in their study were 35.1% [11].

After classifying Mehran risk score: Into low, intermediate and high risk, we found that the prevalence was 33.88%, 38.80% and 100% respectively, which means that patients with high risk Mehran develop CIN more commonly. In high risk sector the incidence was very high because our study included only 3 patients with high risk Mehran risk score so the incidence in not representative of the actual incidence. These results were different from the results of Liu et al., who reported Mehran risk score prevalence to be 13%,

21% and 35% respectively in low, intermediate and high risk [11].

AGEF score was the third most important independent predictor of CIN with an odd ration of 3.3. It was 1.86±0.41 in CIN group versus 0.99± 0.46 in non CIN group which was the same as reported by Lui et al., with a mean AGEF 1.3 ±0.6 [11]. Al-so when we classified patients according to AGEF score <1,1-2, >2 the incidence was 27.35%, 40.31%, and 60.0% respectively. Those results were different from those of Liu et al., who reported the incidence to be 19%, 19% and 32% in the same groups. The differences between our study and that of Liu et al., could be attributed to some extent by the larger number of patients (442 patients) which were enrolled in their study [11].

Also, the study of Giuseppo Ando et al., who reported that AGEF score was a predictor of CIN at logistic regression analysis, with a 5-fold increase in odds for each 1-point increase in AGEF score [15].

Diabetes was the second most important independent predictor of CIN with an odd ratio of 5.8. The percent of diabetes in patient who developed CIN was significantly higher compared to patients who didn't develop (55.55% vs 11.87%). Diabetes is considered to be one of the risk factors of Mehran risk score, also an important predisposing factor for CIN, particularly in patients with renal functional impairment. Renal hypoxia, combined with the generation of reactive oxygen species, plays a central role in the pathogenesis of CIN, and the diabetic kidney is particularly susceptible to intensified hypoxic and oxidative stress following the administration of contrast media [16]. While in Han et al., study the percent of diabetes in patients who develop CIN to those who didn't develop CIN was nearly the same (20.5:21.3) [13].

Creatinine clearance was an independent predictor of CIN. It was significantly lower in patient who developed CIN (p<0.0001). This may be due to the lower glomerular filtration rate resulting in nephropathy, so creatinine clearance is a good indicator for CIN development.

We also searched for a relation between development of CIN and contrast media regarding both volume and contrast type, taking into consideration that contrast volume represents one item in Mehran risk score. We found that there was a statistically significant increase in contrast volume in patients who developed CIN compared to those who didn't't develop. There was increased incidence of CIN with the use of high osmolar, while there was decreased incidence of CIN with the use of lowosmolar. Contrast volume was the last independent predictor of CIN in our study.

The mean age of our study population who developed CIN was 55.2±10.25 years which wasn't different from the group that didn't develop CIN. This was contradictory with Liu et al., who that noticed that the patients in the CIN group were older (72.60±10.11) [17], by the fact that most of our patients were younger than 70 years so age was not significant.

There was no difference in the percent of hypertension between the group who developed CIN and those who did not (26.7% versus 22.5%). This supports the fact that hypertension didn't play an important role in development of CIN [17].

There was statistically significant increased percent of patients with previous IHD in group who developed CIN vs. patients with no CIN (23.20% vs 13.12%). This stresses the importance of taking good history from the patient. This is in contrast to the results of Ando et al., who showed that previous IHD had no significant effect on the development of CIN [15].

The mean EF was significantly lower in the group who developed CIN vs patient who didn't (48.23±1.89 vs 65.34±2.34). This means that as the EF decreases, the prob-ability of development of hypotension increases and the filtrating pressure at the glomeruli decreases. Similar results were reported by Ando et al., who reported that their patients had more severe impairment in both basal EF and global hemodynamic status as expressed by KILIIP score and worse basal serum creatinine and eGFR than patients without CIN [15].

Conclusion: CIN is a challenging health problem among patients undergoing primary PCI. I ts important to calculate the risk scores as Mehran and AGEF scores to predict patients with high risk for CIN development to conduct preventive measures. Mehran risk score has a better predictive power that AGEF score in predicting CIN. Using low osmolar non-ionic contrast media and limiting the amount of contrast media to the least possible volume are important preventive measures. Care should be taken in dealing with patients with female gender, diabetes, previous IHD and reduced ejection fraction as they are more prone to CIN development.

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دراسة أختلال وظائف الكلى الناتج عن الصبغة فى مرضى الجلطة الحديثة بالشريان التاجى للقلب بعد إجراء القسطرة القلبية التداخلية العلاجية عن طريق حساب درجة مهران ودرجة أجيف

خلفية الموضوع: القسطرة التداخلية العاجلة لمرضى الجلطة الحديثة بالشريان التاجى وأختلال وظائف الكلى هى واحدة من أخطر المضاعفات التى يمكن أن تحدث نتيجة للقسطرة التداخلية وتزيد من معدلات البقاء فى المستشفى والمرض والمضاعفات طويلة المدى حتى يمكن أن تحدث الوفاة.

الهدف من العمل:

تهدف الدراسة إلى: حساب نسبة حدوث وأختلاف وظائف الكلى الناتج عن الصبغة فى القسطرة التداخلية العاجلة لشرايين القلب التاجية والتعرف على الأشخاص الذين فى خطر كبير لحدوثه وفقاً لدرجة المخاطر عن طريق حساب درجة مهران ودرجة أجيف.

المرضى وطرق أختيارهم: تم أختيار ٢٥٠حالة من قسم أمراض القلب، مستشفى جامعة أسيوط، قسم قسطرة القلب. تم أستبعاد المرضى الذين يعانون من تشريح الشريان التاجى غير مناسب ومرضى الغسيل الكلوى والمرضى الذين يحتاجون إلى جراحة لتغيير شريان التاجى المستعجلة.

النتائج: حدوث أختلال لوظائف الكلى فى ٣٦٪ من المرضى. لم يكن هناك أرتباط كبير بين أختلال وظائف وسن المريض أو وزنه. كانت التنبؤات المستقلة لحدوث الأختلال بالترتيب، درجة مهران (OR=6.4)، مرض السكر (OR=5.8)، درجة أجيف (OR=3.3)، الشريان التاجى الأيمن (OR=2.1)، تصفية الكرياتنين (OR=1.02) حجمالصبغة المستخدم (الغير أوزمولارى) (OR=0.991) وكانت الأناث اللواتى لديهن نسبة منخفضة فى كفاءة عضلة القلب (EF) أو التاريخ السابق لمرضى القصور فىالشريان التاجى (IHD) عرضة للإصابة بأختلال الوظائف.

الملخص: أختلال وظائف الكلى وهو مشكلة صحية صعبة بين المرضى الذين يخضعون لقسطرة تداخلية درجة مهران لديها قدرة تنبؤية أفضل لدرجة أجيف فى التنبؤ بأختلال الوظائف هناك العديد من العوامل الأخرى المرتبطة بحدوث أختلال الوظائف مثل مرض السكرى، والجنس (الأناث)، وأنخفاض فى كفاءة القلب والتاريخ السابق للمريض الذى يعانى من القصور فى الشريان التاجى وأستخدام الصبغة المستخدم (الغير أوزمولارى).