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The TIMI Risk Index as a Predictor of Contrast-Induced Nephropathy in Patients Undergoing Primary Percutaneous Coronary Intervention at Haji Adam Malik Hospital Medan

Antonius Leonardo Purba [1*], Refli Hasan [2], Abdul Halim Raynaldo [2]

[1] *Resident of Cardiology Department, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*
[2] *Cardiologist of Cardiology Department, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*

***Corresponding Author**: Antonius Leonardo Purba, Email: poerbaanton@gmail.com

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ABSTRACT

Introduction: ST-segment elevation myocardial infarction (STEMI) is a severe cardiovascular condition requiring urgent treatment through Primary Percutaneous Coronary Intervention (PPCI). However, PPCI increases the risk of Contrast-Induced Nephropathy (CIN), a condition characterized by a significant rise in serum creatinine levels. To minimize the risk of CIN, identifying patients at high risk is essential. This study evaluates the TIMI Risk Index (TRI) as a predictor of CIN in STEMI patients undergoing PPCI at Haji Adam Malik Hospital, Medan.

Methods: This observational analytical study employed a cross-sectional design, focusing on STEMI patients with symptoms lasting less than 12 hours who underwent PPCI between January 2023 and December 2024. Participants were selected according to inclusion and exclusion criteria. Bivariate analysis was used, with the chi-square test for normally distributed data and the Fisher exact test for non-normally distributed data, with a significance level of $p < 0.05$.

Results: The results indicated that TRI effectively predicted CIN occurrence, with a p-value of 0.0001, an area under the curve (AUC) of 0.834, and a 95% confidence interval (CI) of 0.752–0.916. A TRI cut-off score of 23.47 demonstrated a sensitivity of 77.3%, specificity of 77%, a positive predictive value (PPV) of 47.05%, and a negative predictive value (NPV) of 91.8%.

Conclusion: In conclusion, the TRI with a cut-off score of 23.47 is a reliable tool for predicting CIN in STEMI patients undergoing PPCI, offering high sensitivity, specificity, and NPV, which can help improve clinical outcomes by identifying at-risk patients.

Keywords

TIMI Risk Index, Contrast-Induced Nephropathy, Primary Percutaneous Coronary Intervention, STEMI.

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INTRODUCTION

Failure to promptly manage acute cardiovascular events can result in fatal complications. ST-segment elevation myocardial infarction (STEMI) is a sudden heart attack that requires immediate medical attention. Every second following STEMI onset results in myocardial tissue death, making rapid intervention crucial for improving the patient prognosis. Historically, thrombolytic therapy has been the gold standard for treating patients with acute STEMI. However, with advancements in medical technology, Primary Percutaneous Coronary Intervention (PPCI) has emerged as a promising treatment for acute myocardial infarction.[1]

Patients with acute coronary syndrome (ACS) are at a high risk of kidney injury due to haemodynamic instability and inadequate hydration before angiography. Acute Kidney Injury (AKI) is a common complication in STEMI patients, leading to poor clinical outcomes, with AKI incidence documented at 13-19%, and up to 50% in STEMI patients with cardiogenic shock.[2,3] Contrast-Induced Nephropathy (CIN) is

a leading cause of AKI, particularly after coronary interventions, with reported incidence rates ranging from 0-24%. CIN is defined by an increase in serum creatinine (⩾0.5 mg/dL or ⩾25%) within 48-72 hours after contrast exposure, and it worsens the prognosis in patients undergoing percutaneous coronary interventions.[3]

Several factors, including advanced age, contrast volume, diabetes, and hypertension contribute to CIN development. Although the exact pathophysiology remains unclear, CIN is associated with oxidative stress, vasoconstriction, and tubular necrosis. Despite being considered temporary, the persistence of CIN after hospital discharge remains unexplored. Risk scores, such as CHA2DS2-VASc and Mehran, have been developed to predict CIN risk based on clinical and laboratory parameters.[2,3]

The TIMI Risk Index (TRI) is a simple risk score that predicts mortality in patients with STEMI using clinical data without laboratory results. The TRI is associated with mortality and morbidity in various cardiovascular conditions, including STEMI. Recently, TRI has been tested for predicting CIN risk in patients undergoing PPCI.[4,5] Therefore, TRI can serve as an effective, non-laboratory-based tool for predicting CIN in STEMI patients undergoing PPCI, guiding preventive measures, and improving clinical outcomes.

METHOD

This analytical observational study employed a cross-sectional design to evaluate the TIMI Risk Index (TRI) as a predictor of contrast-induced nephropathy (CIN) in patients undergoing Primary Percutaneous Coronary Intervention (PPCI) at Haji Adam Malik Hospital in Medan, Indonesia. The research was conducted at Haji Adam Malik General Hospital, with data collection commencing after ethical approval and continuing until the requisite sample size was achieved. The study will be conducted from January 2023 to December 2024.

The primary independent variable in this study was the TIMI Risk Index (TRI), and the dependent variable was contrast-induced nephropathy (CIN). The study population comprised patients diagnosed with STEMI who presented with symptoms within 12 h of onset and underwent Primary Percutaneous Coronary Intervention (PPCI) at Haji Adam Malik Hospital. A subset of this population that met the inclusion and exclusion criteria was selected as the study subjects.

Subjects were chosen through consecutive sampling based on secondary data from medical records, which included variables such as sex, age, vital signs, and creatinine levels. The sample size was estimated using standard formulas, with a significance level of 95% ($Z = 1.96$) and a margin of error of 5%. The proportion of CIN occurrences reported in previous studies was utilised to calculate the sample size, which was determined to be a minimum of 96 participants.

The inclusion criteria for the study were as follows: patients diagnosed with STEMI within 12 h of symptom onset, patients who underwent primary Percutaneous Coronary Intervention (PPCI) at Haji Adam Malik Hospital, patients with complete medical records, and patients who had undergone creatinine testing prior to the PPCI procedure. The exclusion criteria encompassed patients with incomplete medical records, those who did not undergo follow-up creatinine testing 48-72 hours post-PPCI, patients with a history of previous PCI, patients with STEMI complicated by cardiogenic shock, individuals with chronic kidney disease, and patients undergoing routine haemodialysis.

Upon obtaining informed consent and ethical approval from the Faculty of Medicine, University of Sumatera Utara, all eligible subjects were enrolled in the study. Demographic and clinical data, including age, sex, vital signs, and creatinine levels, were documented. The data were then processed and analysed.

Statistical analyses were conducted using SPSS version 22.0 for Windows NY, Armonk, IBM Corp., (USA Categorical variables are presented as frequencies (n) and percentages (%), whereas continuous variables are expressed as the mean ± standard deviation (SD) for normally distributed data and as median (minimum-maximum) for non-normally distributed data. The normality of the variables was assessed using the Kolmogorov-Smirnov test for samples > 50. Univariable analysis was performed to examine the demographic and clinical characteristics of the study population, whereas multivariable analysis was used to evaluate the effect of the TIMI Risk Index (TRI) on CIN occurrence.

To ascertain the optimal cut-off point for the TRI in predicting CIN, Receiver Operating Curve (ROC) analysis was performed. The analysis presented the Area Under the Curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

The primary instrument employed for data collection was the patients' medical records. The operational definitions applied in the study were as follows: the TIMI Risk Index (TRI) is a scoring system used to predict mortality in STEMI patients, calculated using the following formula: TRI = heart rate × (age/10)² / systolic blood pressure. Contrast-induced nephropathy (CIN) refers to acute kidney dysfunction occurring within 48-72 hours after intravenous contrast administration, defined as an increase in serum creatinine of more than 25% or 0.5 mg/dL. Primary Percutaneous Coronary Intervention (PPCI) is a coronary angioplasty procedure performed within 12 h of symptom onset on the culprit lesion without prior fibrinolytic therapy.

RESULTS

Baseline Characteristics

Table 1. Baseline and Clinical Characteristics of Study Samples (Categorical Data)

Parameter	n (108)
Sex	
Male	82 (75.9%)
Female	26 (24.1%)
Smoking History	
Yes	76 (70.4%)
No	32 (29.6%)
Hypertension History	
Yes	46 (42.6%)
No	62 (57.4%)
Type 2 Diabetes Mellitus	
Yes	29 (26.9%)
No	79 (73.1%)
Coronary Lesion Type	
CAD1VD	41 (38%)
CAD2VD	30 (27.8%)
CAD3VD	37 (34.3%)
CIN Occurrence	
Yes	22 (20.4%)
Access Type	
Femoral	96 (88%)
Radial	12 (12%)
GFR	
≤90 ml/min/1.73m²	70 (64.8%)
>90 ml/min/1.73m²	38 (35.2%)
Age (Years)	57.74 ± 10.49
Contrast Volume (mL)	128.43 ± 43.14
Systolic BP (mmHg)	134.02 ± 26.03
Diastolic BP (mmHg)	79.77 ± 15.72
Heart Rate (beats/min)	81 ± 21
Ejection Fraction (%)	45.35 ± 9.62
Laboratory Parameters	
LDL (mg/dL)	122.56 ± 40.97
Initial Creatinine (mg/dL)	1.02 (0.58 – 3.79)
Final Creatinine (mg/dL)	1.02 (0.5 – 4.06)
TIMI Risk Index	21.27 ± 10.37

This study included 108 participants after applying the inclusion and exclusion criteria. Most of the sample consisted of men (75.9%) and individuals with a history of smoking (70.4%). Hypertension and type 2 diabetes mellitus were observed in 42.6% and 26.9% of the participants, respectively. The distribution of coronary artery disease (CAD) lesions was relatively even, with 38% presenting with single-vessel disease, 27.8% with two-vessel disease, and 34.4% with three-vessel disease.

The study found that 20.4% of participants developed contrast-induced nephropathy (CIN). Most patients underwent percutaneous coronary intervention (PPCI) via the femoral approach (88%). Additionally, 64.8% of patients had a glomerular filtration rate (GFR) of ≤90 ml/min/1.73m^2, a key factor in CIN development. The mean age of the participants was 57.74 years, with an average contrast volume of 128.43 mL, highlighting the clinical characteristics relevant to CIN incidence.

These findings suggest the importance of considering patient demographics, comorbidities, and clinical parameters, including age, GFR, and contrast volume, when predicting the risk of CIN during coronary procedures. Further studies are needed to explore the relationship between these factors and the development of CIN.

This study identified significant differences in both categorical and numerical parameters between participants with and without contrast-induced nephropathy (CIN). Participants with CIN were older (62.09 ± 8.6 years) than those without CIN (56.63 ± 10.68 years), and this age difference was statistically significant (P = 0.029). Additionally, participants who developed CIN received a higher mean contrast volume (160.68 ± 43.57 mL) than those without CIN (120.17 ± 39.19 mL), with this difference being highly significant (P = 0.0001).

Other key findings included a significantly higher heart rate in the CIN group (96.91 ± 15.47 bpm) than in the non-CIN group (76.69 ± 20.05 bpm) (P = 0.0001) and a lower ejection fraction in the CIN group (40.5 ± 9.86%) than in the non-CIN group (46.6 ± 9.20%) (P = 0.007). The TIMI Risk Index score was also notably higher in the CIN group (30.52 ± 12.80) than in the non-CIN group (18.9 ± 8.2) (P = 0.0001). Finally, participants with CIN had a significantly higher final creatinine level (1.45 (0.84 – 3.42) mg/dL) than those without CIN (0.98 (0.5 – 4.06) mg/dL) (P = 0.0001).

These findings suggest that older age, higher contrast volume, elevated heart rate, lower ejection fraction, higher TIMI Risk Index score, and higher creatinine levels are significant factors associated with the development of CIN. These parameters should be closely monitored in patients undergoing coronary procedures to mitigate the risk of CIN.

Table 2. Comparison of Baseline Characteristics Based on CIN Occurrence

Parameter	CIN (Yes)	CIN (No)	P-value
Sex			0.694
Male	16 (72.7%)	66 (76.7%)	
Female	6 (27.3%)	20 (23.3%)	
Smoking History			0.194
Yes	13 (59.1%)	63 (73.3%)	
No	9 (40.9%)	23 (26.7%)	
Hypertension History			0.508
Yes	8 (36.4%)	38 (44.2%)	
No	14 (63.6%)	48 (55.8%)	
GFR			0.189
≤90 ml/min/1.73m²	12 (54.5%)	48 (55.8%)	
>90 ml/min/1.73m²	10 (45.5%)	38 (44.2%)	
Age (Years)	62.09 ± 8.6	56.63 ± 10.68	0.029
Contrast Volume (mL)	160.68 ± 43.57	120.17 ± 39.19	0.0001
Heart Rate (bpm)	97 ± 15	77 ± 20	0.0001
Ejection Fraction (%)	40.5 ± 9.86	46.6 ± 9.20	0.007
TIMI Risk Index	30.52 ± 12.80	18.9 ± 8.2	0.0001

ROC curve analysis was conducted to assess the predictive efficacy of the TIMI Risk Index (TRI) score for the incidence of CIN in patients undergoing coronary angiography. The analysis demonstrated a robust discriminatory capacity of the TRI score, with a P-value of 0.0001, an AUC of 0.834, and a 95% confidence interval (CI) of 0.752–0.916. The optimal TRI cutoff value for predicting CIN occurrence was 23.47, with a sensitivity of 77.3%, specificity of 77%, positive predictive value (PPV) of 47.05%, and negative predictive value (NPV) of 91.8%. An AUC value exceeding 0.5 signifies a significant predictive ability, with values approaching 1 indicating an enhanced predictive strength. An AUC of 0.834 suggests that the TRI score is a highly effective predictor of CIN.

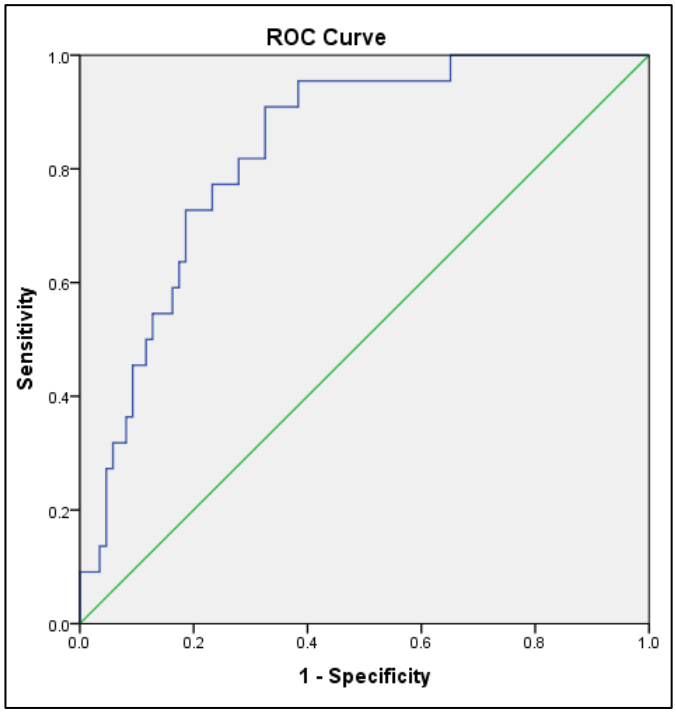

Figure 1. ROC Curve of TRI Score for Detecting CIN

Table 3. AUC, Sensitivity, Specificity, PPV, and NPV of TRI for CIN Detection

Parameter	Cutoff Value	AUC	P-value	Sensitivity	Specificity	95% CI	PPV	NPV
TRI Score	23.47	0.834	0.0001	77.3%	77%	0.752 – 0.916	47.05%	91.8%

DISCUSSION

Contrast-induced nephropathy (CIN) is characterized by kidney dysfunction, defined as a serum creatinine increase of 25% from baseline or an absolute increase of 0.5 mg/dL within 48-72 hours following intravenous contrast administration.[6] This kidney dysfunction is typically acute and manifesting within 2-3 days of post-contrast administration. Some studies suggest that kidney dysfunction persisting up to seven days post-contrast should also be classified as CIN. Serum creatinine levels generally peak between two and five days post-contrast and return to baseline within 14 days.[7] With the rising number of coronary angiography and interventional coronary procedures, coupled with the increased use of contrast media and invasive cardiac procedures in high-risk patients with chronic kidney disease, diabetes mellitus, hypertension, and kidney failure, CIN remains a significant concern.[8-10]

In alignment with existing research, this study successfully demonstrated the prevalence of CIN in patients undergoing coronary angiography. This study also identified several factors contributing to the occurrence of CIN after coronary angiography. Among the 108 samples included in this study, 22 (20.4%) experienced CIN and 86 (79.6%) did not. Previous studies have reported varying prevalence rates of CIN following coronary angiography and PCI. One study indicated that the incidence varies depending on the

procedure, with literature reports ranging from 1.6-2.3% for diagnostic investigations to 14.5% overall in coronary interventions.

In patients older than 60 years, the incidence of contrast-induced nephropathy (CIN) ranges from 8% to 16%. In patients with acute myocardial infarction undergoing coronary intervention, it has been established that being 75 years or older is an independent risk factor for the development of CIN. A study by Kaya et al. demonstrated that an average age of 66.2 ± 12.3 years was associated with a higher incidence of CIN in patients undergoing percutaneous coronary intervention (PCI). Kumar et al. and Cinar et al. also found that patients over 65 years old had an elevated risk of CIN.[5,11]

A study by Khalfallah et al. on patients with CIN after ST-elevation myocardial infarction (STEMI) undergoing PCI found that an average age of 61.4 ± 9.81 years was associated with a higher risk of CIN. Yao et al. similarly demonstrated a higher incidence of CIN in patients undergoing PCI with an average age of 65.70 ± 9.18 years. This study found that the average age of 62.09 ± 8.6 years in patients experiencing CIN is consistent with previous studies.[12]

Regarding risk factors for CIN, this study successfully identified several factors associated with the occurrence of CIN after angiography. The mean age (P = 0.029) and contrast volume (P = 0.0001) were higher in patients with CIN. Meanwhile, the left ventricular ejection fraction (LVEF) was lower (P = 0.007) in patients who developed CIN. Several studies have supported these findings. A study from Taiwan, with conditions similar to those in this study, demonstrated an overall CIN incidence of 7.8% (n=300). Independent predictors of CIN included age (OR 1.03, 95% CI 1.02-1.05, p<0.001), diabetes mellitus (OR 1.87, 95% CI 1.35-2.58, p<0.001), chronic kidney disease (OR 3.65, 95% CI 2.58-5.16, p<0.001), anemia (OR 1.62, 95% CI 1.12-2.34, p=0.01), contrast volume (OR 1.01, 95% CI 1.00-1.02, p=0.02), and LVEF <40% (OR 1.75, 95% CI 1.21-2.53, p=0.003).

Heart rate also plays a role in CIN occurrence. A study by Kaya et al. on patients undergoing PCI showed that a heart rate of 80 ± 20 beats/min was associated with an increased risk of CIN. A study by Kumar et al. demonstrated that a heart rate of 86.36 ± 26.56 beats/min was significantly correlated with CIN occurrence. Additionally, a study by Kumar et al. comparing CIN risk scores in PCI patients found that a heart rate of 88.08 ± 23.28 beats per minute was significantly related to CIN occurrence.[13]

Furthermore, the study conducted by Çınar et al. to assess TRI as a predictor of CIN in STEMI patients demonstrated that a heart rate of 81 ± 16 beats per minute had a significant statistical association with CIN occurrence.[14] Consistent with this finding, the study also revealed that a heart rate of 96 ± 15 beats/min was significantly associated with CIN occurrence (P<0.0001).

A commonly utilised scoring system to predict CIN is the Mehran score, which incorporates several parameters to assess the risk of CIN, including hypotension, IABP use, chronic heart failure, age > 75 years, diabetes mellitus, anaemia, decreased eGFR, and contrast volume. The study indicated that the Mehran score possesses good discriminative power (c-statistic = 0.67); increasing risk scores were strongly associated with CIN (ranging from 8.4% to 55.9% for low and high-risk scores, respectively).[14] In alignment with this, predictors such as age and heart failure events are strongly correlated with CIN after angiography. However, in this study, both systolic and diastolic blood pressures did not exhibit low values, thus not falling into the hypotension category, and consequently, not showing a significant correlation. Diabetes mellitus (DM) did not demonstrate a significant relationship with CIN occurrence in this study, possibly due to the relatively low prevalence of DM in the study participants.

Another study by Firouzi et al. (2020) examined 410 patients (mean age = 61.3 ± 10.8 years) who underwent diagnostic or interventional coronary management: 258 were treated via transfemoral access (TFA) and 152 via transradial access (TRA).[15] A different study reported that the prevalence of CIN after angiography was 49 patients out of a total of 440 cases (12%), comprising both transfemoral and transradial angiography accesses. Patients treated via TFA exhibited a significantly higher incidence of post-procedural CIN (15.1% vs. 6.6%; P=0.01). Multivariate analysis identified TFA as an independent predictor of CIN (OR: 2.37, 95% CI: 1.11-5.10, P=0.027). Moreover, the BARC (Bleeding Academic Research Consortium) and

Mehran scores were independent predictors of CIN.[16] These findings suggest that angiographic access is a predictor of CIN, although this study did not specify the vascular access used.

CONCLUSION

This study underscores that the incidence of contrast-induced nephropathy (CIN) was more prevalent among male patients with a history of smoking, advanced age, and high contrast volume. The significant factors associated with CIN were age, heart rate, contrast volume, and decreased ejection fraction. The TRI score was notably higher in the CIN group than in those without CIN. Furthermore, the TRI score was an effective predictor of CIN occurrence, demonstrating good sensitivity, specificity, and predictive values, suggesting its potential utility in clinical practice for CIN risk assessment.

DECLARATIONS

Ethics approval and consent to participate were obtained. Permission for this study was obtained from the Ethics Committee of the Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to the publication in the Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare no conflicts of interest in this study.

AUTHORS' CONTRIBUTIONS

All authors significantly contributed to the work reported in the execution, acquisition of data, analysis, and interpretation, or in all these areas. Contributed to drafting, revising, or critically reviewing the article. Approved the final version for publication, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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