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Original Article

The association between neutrophil to lymphocyte ratio and contrast induced nephropathy in patients with ST segment elevation myocardial infarction

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Abstract

Aim: The increase in the number of percutaneous coronary interventions(PCI) has also led to an increase in risk associated with intervention-including radiation injury, contrast-induced nephropathy (CIN), risk of stroke, and vascular complications. The development of CIN is an important clinical situation in patients undergoing PCI. In this study we aimed to investigate the association between inflammatory parameters and CIN development in patients with ST segment elevation myocardial infarction (STEMI).

Material and Methods: Patients who underwent coronary angiography with STEMI diagnosis between January 2015 and March 2018 were included in the study. Two groups were formed according to the CIN status and predictors of CIN were investigated.

Results: The average age of the patients is 58±12 years and 78.2% males. In multivariate analysis, NLR (OR: 0.92, 95% CI: 0.86-0.98 and p: 0,022) and Lesion length (OR: 0.88, 95% CI: 0.79-0.98 and p: 0,029)and were associated with CIN development.

Conclusions: In this study, we showed that lesion length and NLR were independent predictors of CIN and we proposed that inflammatory process could play key role in CIN development when compared to traditional risk factors.

Keywords: Neutrophil to lymphocyte ratio; coronary artery disease; contrast-induced nephropathy; propensity score matching.

INTRODUCTION

Percutaneous coronary intervention is a lifesaving approach used increasingly in modern medicine with new techniques and strategies in the diagnosis and treatment of atherosclerotic cardiovascular diseases and it is recommended to be a first line treatment option in current guidelines (1,2). The increase in the number of percutaneous coronary interventions has also led to an increase in risk associated with intervention. Including radiation injury, contrast-induced nephropathy, risk of stroke, and vascular complications (1,3,4).

CIN is a clinical condition that results in impaired renal function after exposure to ionizing contrast agents, resulting in increased in-hospital mortality and CIN development also increases the duration of hospitalization and the cost of treatment. In many studies, CIN development has been associated with increased mortality and morbidity (5,6).

The propensity score matching (PSM) method was described by Rosenbaum and Rubin in 1983 (7). The effects of parameters on treatment response or clinical status can be determined more accurately and This method is more effective than traditional regression models and applied to various clinical researches (8-10). In this study, we aimed to evaluate the association between CIN development and NLR in STEMI patients underwent coronary angiography using PSM analysis.

MATERIAL and METHODS

The study was performed retrospectively in patients admitted to our clinic with STEMI diagnosis and approval of the ethics committee. The records of all patients who underwent coronary angiography at our clinic, between January 2012 and December 2015 were searched. Of the 1518 searched patients, those who underwent CABG (n=36) or whose records were not available due to technical reasons (n=50) were excluded from the study. A final cohort of 1432 patients was included in the present study (Figure 1). The patients were divided into two groups according to the CIN development status and

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the predictors of CIN before and after PSM analysis were investigated.

Definitions

CIN was defined a 25% relative increase, or a 0.5 mg/dL (44 µmol/L) absolute increase, in serum creatinine (Cr) within 72 hours of contrast exposure, in the absence of an alternative explanation (11). Hypertension was defined as having at least two blood pressure measurements >140/90 mmHg or using antihypertensive drugs, whereas diabetes mellitus was defined as having at least two fasting blood glucose measurements >126 mg/dl or using antidiabetic drugs. Estimated glomerular filtration rate (GFR) was calculated by the Cockcroft-Gault formula ([140-age] x [Weight as kg] x [0.85, if female] / [72 x Creatinine]). We collected information regarding the baseline demographic, clinical and angiographic characteristics and laboratory data from the computerized patient record system at our institution. The NLR was calculated as the ratio of the number of neutrophils to the number of lymphocytes.

Coronary angiography

STEMI was evaluated in the current ACC / AHA guidelines as previously defined (3) and appropriate patients underwent coronary angiography (Toshiba Infinix, Toshiba Japan) on the femoral or radial approach with Judkins technique according to operator preference. BMS or DES implantation was performed according to the clinician's choice during angiography and most of the cases were post dilatated with non-compliant balloon. Syntax score were calculated for each patient using the Syntax score calculator in line with the segment and localization criteria defined in the SYNTAX study (12).

Statistics:

Continuous variables were expressed as mean ± standard deviation or median (interquartile range) values, whereas categorical variables were presented in percentages. For comparison of continuous variables, the Independent Student T test or the Mann-Whitney U test was used. Moreover, the Chi-square test was used to compare categorical. We generated a regression model to estimate PS and match the study population. Unmatched patients were excluded from the study. The variables found to be significant in the univariate analysis ($p<0.05$) were subjected to multivariate logistic regression. The receiver operating curve (ROC) was performed to determine the cutoff value of NLR in prediction of CIN.Data was analyzed using the SPSS 22 for Mac (IBM, Armonk, NY, USA).

RESULTS

A total of 1432 patients with STEMI was included in the study (58±12 years and 78.2% males). Patient characteristics before and after propensity score matching are shown in Table 1-2.

Table 1. Baseline clinical, laboratory and anatomical characteristics according to CIN groups

Variables	Before propensity score matching			After propensity score matching		
	CIN (+) Group (n=151)	CIN (-) Group (n=1281)	P Value	CIN (+) Group (n=101)	CIN (-) Group (n=101)	P Value
Age (years)	61±13	55±11.5	<0.001	58.47±13.2	60.9±11.3	0.121
Sex (Male %)	75.5	83.2	0.019	76.2	80.2	0.496
DM (%)	29.8	19	0.002	29.7	25.7	0.53
HT (%)	53	37.6	<0.001	47.5	50.5	0.67
COPD (%)	4.6	4.8	0.945	4	5.9	0.518
Smoking (%)	46.4	59.8	0.002	50	45.5	0.482
Dyslipidemia (%)	37.1	40.9	0.366	42.6	35.5	0.314
Family History (%)	24.5	22.7	0.621	21.7	12.9	0.095
TIMI risk score	3 (1-5)	2.5 (1-4)	<0.001	3 (1-4)	3.1 (1-4)	0.373
Death (%)	7.3	3	0.006	6.9	3	0.196
Stroke (%)	1.3	0.5	0.18	1	0	0.317
CHF (%)	17.2	5.8	<0.001	14.9	9.9	0.28
Re-hospitalization (%)	11.3	4.7	0.001	7.9	5.9	0.58
Hospital Stay (day)	6(4-8)	4(3-6)	<0.001	6.3(4-7)	6.1 (4-7)	0.902
EF (%)	48±8.2	50±7.3	<0.001	46.2±7.8	45.46±7.3	0.63
Contrast media volume (ml)	320 (260-390)	260 (210-295)	<0.001	300 (240-340)	295 (280-320)	0.520
SS	18±5.5	16.7±4.9	0.003	17.5±5	18.4±5	0.06
Lesion Localization (proximal) %	66.9	50.9	<0.001	68.3	63.4	0.459
Lesion Length (mm)	15.4±6.6	14.4±5.1	0.06	16.7±6.7	14.3±4.8	0.008
Number of Stent	1.2 (1-2)	1.3 (1-2)	0.005	1.5 (1-3)	1.3 (1-2)	0.014
No reflow (%)	11.9	6.9	0.025	15.8	9.9	0.209
Medication	Aspirin	82.1	87.4	0.07	80.2	83.2
	Clopidogrel	51.7	49.3	0.59	50.5	55.4
	Beta blocker	67.5	69.4	0.64	63	63.4
	Statin	70.2	69.9	0.94	71.3	73.3
	ACEI/ARB	47	43.6		43.6	36.6

Abbreviations: DM, diabetes mellitus; HT, hypertension; SS, COPD, Chronic obstructive pulmonary disease; TIMI, thrombolysis in myocardial infarction; CHF, congestive heart failure; EF, ejection fraction; SS, Syntax score

Table 2. Baseline laboratory results of the study population according to CIN groups						
GFR (ml/sec/1.73 m2)	85.66±33	91±23	0.003	87.6±26	86±25	0.92
CK (ng/mL)	400 (222-588)	298 (170-477)	<0.001	432 (215-633)	513 (313-671)	0.218
CK-MB (ng/mL)	39 (29-46)	32 (23-43.5)	<0.001	38 (29-46)	39 (32-51)	0.408
Troponin (ng/mL)	2.3 (1.2-5.4)	1.6 (0.5-4)	<0.001	2.8 (1.1-5.6)	6.1 (1.1-8.9)	0.55
Glucose (mg/dl)	133 (106-183)	123 (103-153)	0.008	126 (102-178)	125 (106-173)	0.92
TC (mg/dl)	179±49	179±42	0.812	185±48	177±43	0.29
HDL (mg/dl)	38±12	39±11	0.16	40±12	41.3±13	0.99
LDL (mg/dl)	115±41	114±38	0.791	120±41	113±40	0.203
TG (mg/dl)	104 (77-148)	12 (85-170)	0.022	105 (77-168)	122 (75-159)	0.82
WBC (10^3 /µL)	12.3±4.1	12±3.2	0.592	12.3±3.9	12.3±3.9	0.98
Hemoglobin(g/dl)	13.1±2.09	13.8±1.7	<0.001	13.4±1.9	13.7±1.6	0.23
Neutrophil (10^3 /µL)	9.1±3.7	9.1±3.2	0.07	9.9±3.6	10.1±3.8	0.511
Lymphocyte (10^3 /µL)	1.6 (1.2-2.1)	1.8 (1.3-2.5)	0.004	1.6 (1.2-2.1)	1.4 (0.9-1.8)	0.006
NLR	5.3 (4.1-8.3)	4.7 (3-7.39	0.001	6.7 (4.2-8.4)	8.3(4.9-10.9)	0.019
Platelet (10^3 /µL)	247±61	257±64	0.119	247±59	238±64	0.311

Abbreviations: TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride; WBC, white blood cell; RDW, Red cell distribution width;

After matching procedure, 202 patients were included in the analysis: 101 CIN (+) and 101 CIN (-) patients. All variables were well balanced with the matching procedure (Figure 1). In univariate analysis NLR (OR: 0.92, 95% CI: 0.86-0.98 and p: 0.019), Lesion length (OR: 0.93, 95% CI: 0.88-0.97 and p:0.008) and Number of stent (OR: 0.58, 95% CI: 0.38-0.88 and p: 0.014) were associated with CIN. NLR values according to CIN status were shown in Figure 2. In the multivariate analysis, NLR (OR: 0.92, 95% CI: 0.86-0.98 and p: 0,022) and Lesion length (OR: 0.88, 95% CI: 0.79-0.98 and p: 0.029) were independently associated with CIN (Table 3).

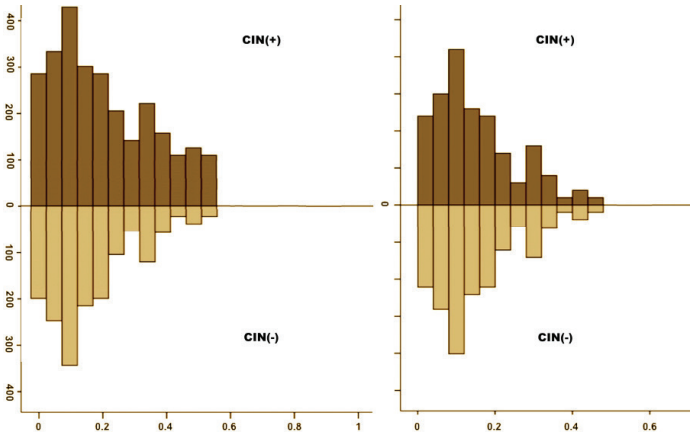

Figure 1. Distribution of propensity scores before and after matching

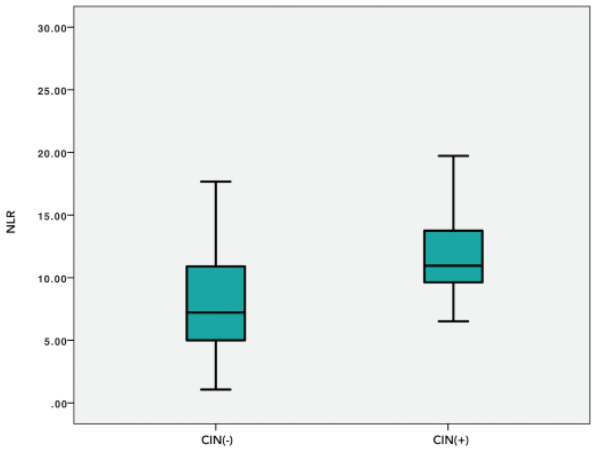

Figure 2. NLR levels according to CIN status

Table 3. Independent Predictors of CIN in logistic regression analysis				
Variables	Univariate OR, 95%CI	Univariate P value	Multivariate OR, 95%CI	Multivariate P value
NLR	0.92 (0.86-0.98)	0.019	0.92 (0.86-0.98)	0.022
Lesion length (mm)	0.93 (0.88-0.97)	0.008	0.88 (0.79-0.98)	0.029
Number of stent	0.58 (0.38-0.88)	0.014	0.36 (0.11-1.21)	0.36

Abbreviations: NLR, neutrophil/lymphocyte ratio; CI, confidence interval; OR, odds ratio

The ROC analysis demonstrated that the best cutoff value of the NLR to predict CIN was equal to or greater than 5.25, with 73% sensitivity and 55% specificity (area under the curve: 0.59, 95%CI: 0.55–0.64, and P=0.04)

DISCUSSION

In this study, we showed that lesion length and NLR were independent predictors of CIN and this is the first study in the literature evaluating the predictors of CIN by PSM analysis.

CIN is a complication that can be diagnosed with a 25% increase in baseline Cr level within 48 hours and is fairly common after contrast media exposure and it could lead to the need for dialysis or kidney dysfunction (13). Although a variety of biomediators in the etiology have been proposed, the exact cause is not definite. However, the development of CIN leads to an increase in duration of hospitalization and increase in mortality and treatment costs. Age, HT, DM, Dyslipidemia, renal insufficiency and nephrotoxic drug use are the traditional risk factors (6,14,15). In the development of CIN, mechanisms such as direct toxic effect of contrast agent, damage of free oxygen radicals, inflammatory reactions, renal tubular blockade and cell death have been shown in various studies. Recent guidelines recommend the use of hypoosmolar contrast agents with intravenous hydration to prevent the development of CIN, but their effect is limited. The use of N-acetyl Cysteine has also been used in various studies and conflicting results have been obtained. With angiography as the first choice for diagnosis and treatment of coronary artery disease, this group of patients has experienced an increased exposure to contrast media, which has led to increased complications (14,16,17).

PSM analysis has been shown to be more accurate than traditional regression models, as it is an increasingly popular method to reduce the bias rate in studies and to calculate the effect of that variable on outcome (10,18). Despite the fact that PSM has been shown to be a good analytical method, there is no study related to the development of CIN evaluated by PSM analysis. This is the first study to show this relation, using PSM analysis, between development of CIN and conventional risk factors, including the lesion length, the number of stents and NLR ratio.

As shown in previous studies, lesion length is associated with increased contrast agent volume and prolongation of the procedure. This is consistent with the literature (19-21). Moreover, After PSM analysis, the relationship between the lesion length and CIN is the important valuable finding of our study. However, since our study population is composed of STEMI patients and most of the lesions are thrombosed and there are no factors that increase the contrast media volume, such as bifurcation stenting techniques, chronic total occlusion or multi-vessel disease, the relationship between CIN development and contrast media volume may not be established. Further studies may be needed to demonstrate this association.

The most important finding of our study was that the NLR ratio was associated with the development of CIN both in univariate and multivariate analysis. The relationship between NLR ratio and CIN development has been shown in previous studies (22-24). In one study, the NLR was found a significant independent predictor of CIN in patients with STEMI treated via primary PCI (25). But demonstration of association between NLR and CIN after PSM analysis has not been shown in the literature before and we speculated that the inflammatory process is more prominent than other traditional risk factors in the development of CIN.

CONCLUSION

NLR as an important diagnostic tool for CIN development when compared to demographic and clinical parameters. The fact that the inflammatory process is more influential than the demographic and clinical features in the development of CIN.

Limitations

Our study has some limitations. First, its retrospective design can be considered as the main limitation. The exclusion of patients undergoing CABG surgery or PCI previously can also be considered as a limitation. On the other hand, decreasing the bias with the PSM analysis contributed to the strength of our study.

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