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Effects of platelet-to-lymphocyte ratio on renal function following acute myocardial infarction

A retrospective observational study

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Abstract

Increased platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) in acute myocardial infarction (AMI), which indicate accelerated thrombus formation and inflammatory response, potentially have prognostic implications. Given that cardiovascular disease and renal function exacerbate each other, an elevated PLR and NLR at admission for AMI may worsen renal function after AMI. However, only a few clinical studies have addressed this issue. Therefore, this study aimed to examine the effects of PLR and NLR at AMI onset on renal function. This retrospective study analyzed data from 234 patients hospitalized for AMI. First, correlations between various parameters (age; sex; body mass index; hemoglobin level, albumin level, B-type natriuretic peptide level, C-reactive protein level, creatinine (Cr) level, blood urea nitrogen (BUN) level, PLR, and NLR at admission; contrast medium usage; and maximum creatine kinase) and Cr and BUN levels at discharge were examined using single and multiple regression analyses. Then, correlations between these parameters and the change in Cr (ΔCr) and BUN levels (ΔBUN) were investigated using single and multiple regression analysis, followed by structural equation modeling (SEM). Multiple regression analysis revealed significant positive correlations between PLR at admission and Cr level at discharge ($\beta = 0.135$, $P = .021$), PLR at admission and BUN level at discharge ($\beta = 0.218$, $P = .006$), PLR at admission and ΔCr ($\beta = 0.244$, $P = .019$), and PLR at admission and ΔBUN ($\beta = 0.312$, $P = .003$). SEM results revealed significant positive correlations between PLR at admission and ΔCr ($\beta = 0.260$, $P = .008$) and PLR at admission and ΔBUN ($\beta = 0.292$, $P = .003$). Conversely, NLR demonstrated a minimal association with renal function at discharge compared to PLR. This study suggests that increased PLR at admission in AMI significantly affects and exacerbates renal function but does not increase NLR at admission. PLR is one of the predictors of renal dysfunction after AMI.

Abbreviations: ACS = acute coronary syndrome, ACT = activated coagulation time, Alb = albumin, AMI = acute myocardial infarction, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CIN = contrast-induced nephropathy, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, NLR = neutrophil-to-lymphocyte ratio, NSTEMI = non ST elevation myocardial infarction, PLR = platelet-to-lymphocyte ratio, RPR = residual platelet reactivity, SEM = structural equation modeling, STEMI = ST elevation myocardial infarction.

Keywords: acute myocardial infarction, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, renal function, structural equation modeling

1. Introduction

The platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) serve as inexpensive markers that can be easily and promptly obtained in clinical settings, and their importance has been reported in diverse medical conditions, such as cancer,[1] cerebrovascular disease,[2] cardiovascular disease,[3–6] and renal disease.[7,8]

Cardiovascular and renal diseases mutually influence each other, and this interaction is known as cardiorenal syndrome.[9,10] Diverse mechanisms are involved in this syndrome, but inflammation is considered to play a major role as it may

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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exacerbate cardiovascular and renal diseases by acting as a mediator. Inflammation also promotes thrombus formation, which further increases inflammation.[11,12] Therefore, thrombus formation may be considered as an influencing factor in both cardiovascular and renal diseases.

Acute myocardial infarction (AMI) is a cardiovascular disease characterized by acute thrombus formation that is central to its pathogenesis. Thrombus formation resulting from plaque disruption in coronary arteries induces myocardial ischemia and is associated with significant systemic consequences.[13] AMI has also been associated with impaired renal function, and the impact of thrombus formation on renal dysfunction following AMI may be substantial.

Consequently, PLR and NLR measurements may be of great significance when examining the impact of AMI on renal function decline. Specifically, PLR and NLR at AMI onset may adversely affect renal function after AMI. However, to the best of our knowledge, few clinical studies have examined this possibility.

Therefore, this study aimed to assess the impact of PLR and NLR at admission on renal function after AMI using various statistical methods.

2. Materials and methods

2.1. Patient population

This study included patients with AMI who required emergency admission to the Jikei University Hospital between September 2014 and March 2023. AMI was diagnosed based on the following criteria: chest pain lasting > 30 minutes, typical electrocardiographic changes, and elevated serum creatine kinase (CK) levels. Of the 285 patients treated for AMI during the study, the following were excluded: death during hospitalization (4 cases), cardiogenic shock (7 cases), coronary spasmodic angina (4 cases), patients undergoing coronary artery bypass grafting (16 cases), hemodialysis (16 cases), and patients who received blood transfusion (4 cases). Finally, 234 patients were included in this study.

This study was approved by the Ethics Committee of the Jikei University School of Medicine (Approval No. 24-355 [7121]), and all procedures complied with the ethical standards of our institution. Given the retrospective nature of the study, informed consent was not obtained from all patients. Instead, notice regarding the study design and contact information was displayed in the public areas of our institution.

2.2. Data collection

This retrospective observational study involved the collection of data from medical records. Various parameters, including age; sex; body mass index (BMI); hemoglobin (Hb) level, albumin (Alb) level, B-type natriuretic peptide (BNP) level, and C-reactive protein (CRP) level at admission; contrast medium usage; maximum CK; PLR and NLR at admission; and creatinine (Cr) and blood urea nitrogen (BUN) levels at admission and discharge were examined and analyzed. The change in Cr level after AMI was denoted as ΔCr (Cr at discharge – Cr at admission), and the change in BUN level after AMI was defined as ΔBUN (BUN at discharge – BUN at admission). Upon admission, patients received intravenous heparin (100 U/kg) in the emergency room, along with aspirin (200 mg) and either prasugrel (20 mg) or clopidogrel (300 mg) orally according to the guidelines.[14] Patients were promptly transferred to the catheterization room. Blood samples were collected after sheath insertion, and the activated coagulation time was measured at intervals of 30 minutes to 1 hours, with additional heparin administered to maintain activated coagulation time within 250 to 400 seconds.

2.3. Statistical analysis

Continuous variables are expressed as the mean ± standard deviation. First, the correlations between various parameters (age; sex; BMI; Hb, Alb, BNP, CRP, Cr, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK) and Cr and BUN at discharge were investigated using single and multiple regression analyses. Next, the correlation between various parameters (age; sex; BMI; Hb, Alb, BNP, CRP, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK) and ΔCr, and the correlation between various parameters (age; sex; BMI; Hb, Alb, BNP, CRP, Cr, PLR, and NLR at admission; contrast medium usage, maximum CK) and ΔBUN were investigated using single and multiple regression analysis. Followed by a path model based on structural equation modeling (SEM) was used to investigate the relationships between various parameters (age; sex; BMI; Hb, Alb, BNP, CRP, PLR, and NLR at admission; contrast medium usage, maximum CK) and ΔCr and ΔBUN.

SEM was used to reduce the potential influence of confounding factors with multiple independent variables. SEM allows the incorporation of multiple dependent variables within a single equation, and path diagrams were constructed and investigated. This statistical method is widely used across various fields, including our previous research.[15–19] Statistical analyses were performed using IBM SPSS Version 25 (SPSS Inc., Chicago) and IBM SPSS AMOS Version 25 (Amos Development Corporation, Meadville) for SEM. Statistical significance was set at $P < .05$.

Furthermore, Bayesian estimation methods were employed using IBM SPSS AMOS Version 25. We previously utilized Bayesian estimation methods in our analyses and obtained research results.[16–19] Bayesian estimation serves as a useful tool for reassessing SEM results.

3. Results

3.1. Study participant characteristics

The clinical characteristics of 234 patients are shown in Tables 1 and 2. The mean age of the patients was 63.2 ± 13.1 years, of whom 89.0% were male. The mean PLR and NLR at admission were 147.6 ± 74.2 and 5.1 ± 3.4, respectively. ΔCr was 0.08 ± 0.15 mg/dL and ΔBUN was 0.53 ± 5.0 mg/dL.

3.2. Regression analysis results

The single regression analysis results are shown in Table 3, and the scatter plots in Figures 1 to 4. No correlation was found between PLR at admission and Cr at discharge (β = 0.080, $P = .22$) and PLR at admission and ΔBUN (β = 0.062, $P = .35$), whereas PLR at admission and BUN at discharge (β = 0.144, $P = .028$) and PLR at admission and ΔCr (β = 0.207, $P = .001$) were significantly positively correlated. Conversely, no correlation was found between NLR at admission and Cr at discharge (β = 0.126, $P = .054$) and NLR at admission and ΔBUN (β = –0.017, $P = .79$). NLR at admission and BUN at discharge (β = 0.145, $P = .026$) and NLR at admission and ΔCr (β = 0.153, $P = .019$) showed significant positive correlations.

The results of the multiple regression analysis are presented in Table 4. Multiple regression analysis showed a significant positive correlation between PLR at admission and Cr at discharge (β = 0.135, $P = .021$); PLR at admission and BUN at discharge (β = 0.218, $P = .006$); PLR at admission and ΔCr (β = 0.244, $P = .019$); and PLR at admission and ΔBUN (β = 0.312, $P = .003$). Conversely, no correlation was found between NLR at admission and Cr at discharge (β = –0.069, $P = .24$); NLR at admission and BUN at discharge (β = –0.120, $P = .14$); and between NLR at admission and ΔCr (β = –0.093, $P = .38$). The NLR at admission and ΔBUN (β = –0.227, $P = .030$) showed a weak negative correlation.

Furthermore, positive correlations were identified in the following relationships by multiple regression analysis: between

maximum CK and Cr at discharge (β = 0.115, P = .005), Cr at admission and at discharge (β = 0.734, P < .001), BUN at admission and Cr at discharge (β = 0.108, P = .043), Hb at admission and BUN at discharge (β = 0.190, P = .008), Cr at admission and BUN at discharge (β = 0.300, P < .001), BUN at admission and at discharge (β = 0.420, P < .001), maximum CK and ΔCr (β = 0.172, P = .020), and Hb at admission and ΔBUN (β = 0.325, P < .001).

Table 1

Patient characteristics.

Characteristic (N = 234)	Mean ± SD, Number (%)
Age	63.2 ± 13.1
Male sex (%)	208 (89.0)
Height (cm)	167.4 ± 8.1
Weight (kg)	71.5 ± 14.9
BMI (kg/m^2)	25.3 ± 4.1
Underlying disease	
Hypertension (%)	165 (70.5)
Dyslipidemia (%)	166 (70.9)
Diabetes mellitus (%)	76 (32.4)
Heart failure (%)	9 (3.8)
Atrial fibrillation (%)	8 (3.4)
Prior MI (%)	17 (7.2)
Prior PCI (%)	22 (9.4
Prior CABG (%)	1 (0.4)
Smoking history	
Current smoker (%)	92 (39.3)
Past smoker (%)	79 (33.8)
Never smoker (%)	63 (27.0)
Medication	
Calcium channel blocker (%)	70 (30.0)
Beta blocker (%)	32 (13.7)
ACE inhibitor (%)	7 3(3.0)
ARB (%)	64 (27.3)
Nitrate (%)	6 (2.6)
Nicorandil (%)	4 (1.7)
Statin (%)	53 (22.6)
Oral antidiabetic agent (%)	43 (18.4)
Insulin (%)	4 (1.7)
Furosemide (%)	5 (2.1)
Trichlormethiazide (%)	2 (0.9)
Azosemido (%)	0 (0.0)
Torasemide (%)	0 (0.0)
Tolvaptan (%)	0 (0.0)
Spironolactone (%)	6 (2.6)
Eplerenone (%)	0 (0.0)
Aspirin (%)	33 (14.1)
Clopidogrel (%)	7 (3.0)
Prasugrel (%)	8 (3.4)
Cilostazol (%)	6 (2.6)
Ticlopidine (%)	0 (0.0)
Warfarin (%)	1 (0.4)
Rivaroxaban (%)	3 (1.3)
Apixaban (%)	2 (0.9)
Edoxaban (%)	4 (1.7)
Predonine (%)	5 (2.1)
Diagnosis	
STEMI (%)	200 (85.5)
NSTEMI (%)	34 (14.5)
Therapy	
Received PCI (%)	234 (100.0)
SAPT at discharge (%)	4 (1.7)
DAPT at discharge (%)	230 (98.3)
Length of hospital stay (d)	11.8 ± 5.5
Length of blood sampling interval (d)	9.4 ± 4.0

ACE = angiotensin-converting enzyme, ARB = angiotensin II type I receptor blocker, BMI = body mass index, CABG = coronary artery bypass grafting, DAPT = dual antiplatelet therapy, MI = myocardial infarction, NSTEMI = non-ST elevation myocardial infarction, PCI = percutaneous coronary intervention, SAPT = single antiplatelet therapy, STEMI = ST elevation myocardial infarction.

3.3. Concept of path model based on SEM

To mitigate the influence of confounding factors and clarify causal relationships, a path model based on SEM was created using various parameters (age; sex; BMI; Hb, Alb, BNP, CRP, PLR, and NLR at admission; contrast medium usage, maximum CK) as independent factors, and ΔCr and ΔBUN as dependent factors. Correlations between factors for these data are indicated by two-way arrows. The paths between the variables are indicated by one-way arrows independent of the dependent variable.

3.4. Results of SEM

The SEM results are presented in Table 5 and Figure 5. Significant positive correlations were observed between PLR at admission and ΔCr (β = 0.260, P = .008) and PLR at admission and ΔBUN (β = 0.292, P = .003). On the other hand, there was no correlation between NLR at admission and ΔCr (β = –0.081, P = .42), whereas NLR at admission and ΔBUN (β = –0.205, P = .040) showed a weak negative correlation. Significant positive correlations were observed between maximum CK and ΔCr (β = 0.141, P = .040) and between Hb level at admission and ΔBUN (β = 0.337, P < .001).

3.5. Results of Bayesian estimation in SEM

Bivariate periphyton posterior plots obtained using Bayesian estimation methods are shown in Figure 6. This figure shows the effect of PLR at admission on ΔCr (x-axis) and ΔBUN (y-axis). In the two-dimensional plot, the horizontal and vertical axes did not intersect at zero, indicating a strong effect of the PLR at admission.

4. Discussion

In this study, we demonstrated the effect of PLR on renal function following AMI using various indices and statistical analysis methods. To the best of our knowledge, this is the first study to use SEM to minimize the influence of confounding factors and evaluate the extent of influence between factors on the progression of renal function after AMI.

Table 2

Patient biochemical and hematological values.

Characteristic (N = 234)	Mean ± SD, Number (%)
WBC at admission (×10^3/μL)	10.0 ± 3.6
Neutrophil at admission (×10^3/μL)	7.5 ± 3.3
Lymphocyte at admission (×10^3/μL)	1.9 ± 0.9
Hb at admission (g/dL)	14.1 ± 1.8
PLT at admission (×10^3/μL)	224.9 ± 55.7
Alb at admission (mg/dL)	3.9 ± 0.4
BNP at admission (pg/mL)	84.6 ± 154.9
CRP at admission (mg/dL)	0.5 ± 1.8
Contrast medium usage (mL)	157.0 ± 50.9
Maximum CK (mg/dL)	2296.4 ± 2099.9
Cr at admission (mg/dL)	0.85 ± 0.2
Cr at discharge (mg/dL)	0.93 ± 0.3
BUN at admission (mg/dL)	16.3 ± 5.1
BUN at discharge (mg/dL)	16.8 ± 6.1
ΔCr	0.08 ± 0.15
ΔBUN	0.53 ± 5.0
PLR at admission	147.6 ± 74.2
NLR at admission	5.1 ± 3.4

Alb = albumin, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio, PLT = platelet, WBC = white blood cell.

4.1. Relationship between inflammation and thrombus formation in renal dysfunction associated with AMI

Hemodynamic changes occur during AMI, including a decrease in renal blood flow and blood pressure due to decreased cardiac output and increased renal venous pressure. Consequently, renin-angiotensin-aldosterone and sympathetic nervous systems are activated, inducing hypoxia in the renal medulla and causing renal dysfunction.[9,20] Decreased vascular endothelial function and nitric oxide activity may also be involved in the pathology. In contrast, during AMI, platelets are more likely to aggregate as inflammation progresses.[11,12] Glycoprotein IIb/IIIa and other molecules on the platelet membrane are activated and bind to fibrinogen, resulting in platelet aggregation. Simultaneously,

Table 3

Single regression analysis results.

	Regression coefficient	Standard error	Standard regression coefficient	Test statics	*P* valve	95% confidence interval
Age	0.004	0.001	0.209	3.260	.001	0.002–0.006
Sex	0.144	0.052	0.177	2.745	.007	0.041–0.274
BMI	0.002	0.004	0.033	0.502	.62	–0.006 to 0.010
Hb at admission	–0.011	0.009	–0.077	–1.174	.24	–0.029 to 0.007
Alb at admission	–0.130	0.045	–0.187	–2.892	.004	–0.218 to –0.041
BNP at admission	0.000	0.000	0. 217	3.334	.001	0.000–0.001
CRP at admission	0.005	0.009	0.032	0.493	.62	–0.014 to 0.023
Contrast medium usage	–0.001	0.000	–0.115	–1.756	.080	–0.001 to 0.000
Maximum CK	2.316×10^{-5}	0.000	0.194	3.008	.003	0.000–0.000
Cr at admission	0.851	0.040	0.816	21.488	<.001	0.773–0.929
BUN at admission	0.026	0.003	0.532	9.579	<.001	0.021–0.031
PLR at admission	0.000	0.000	0.080	1.228	.22	0.000–0.001
NLR at admission	0.009	0.005	0.126	1.936	.054	0.000–0.019
Objective variable: Cr at discharge						
Explanatory variable: Age; Sex; BMI; Hb, Alb, BNP, CRP, Cr, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK						
Age	0.143	0.029	0.308	4.934	<.001	0.086 to –0.201
Sex	–1.346	1.285	–0.069	–1.047	.30	–3.879 to 1.186
BMI at admission	–0.103	0.097	–0.070	–1.061	.29	–0.295 to 0.088
Hb at admission	–0.397	0.224	–0.115	–1.769	.078	–0.839 to 0.045
Alb at admission	–2.738	1.093	–0.162	–2.505	.013	–4.891 to 0.585
BNP at admission	0.012	0.003	0. 307	4.819	<.001	0.007–0.017
CRP at admission	0.206	0.226	0.060	0.911	.36	–0.239 to 0.651
Contrast medium usage	–0.008	0.008	–0.070	–1.075	.28	0.024–0.007
Maximum CK	0.000	0.000	0.104	1.597	.11	0.000–0.001
Cr at admission	13.198	1.415	0.522	9.328	<.001	10.410–15.986
BUN at admission	0.723	0.062	0.610	11.726	<.001	0.601–0.844
PLR at admission	0.012	0.005	0.144	2.215	.028	0.001–0.022
NLR at admission	0.258	0.115	0.145	2.234	.026	0.030–0.486
Objective variable: BUN at discharge						
Explanatory variable: Age; Sex; BMI; Hb, Alb, BNP, CRP, Cr, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK						
Age	0.001	0.001	0.077	1.183	.24	–0.001 to –0.002
Sex	0.004	0.032	0.009	0.135	.89	–0.058 to 0.067
BMI	–0.001	0.002	–0.026	–0.401	.69	–0.006 to 0.004
Hb at admission	0.001	0.006	0.016	0.241	.81	–0.010 to 0.012
Alb at admission	–0.020	0.027	–0.047	–0.718	.47	–0.073 to 0.034
BNP at admission	5.399×10^{-5}	0.000	0. 056	0.840	.40	0.000–0.000
CRP at admission	–0.005	0.006	–0.062	–0.951	.34	–0.016 to 0.006
Contrast medium usage	0.000	0.000	0.116	1.778	.077	0.000–0.001
Maximum CK	1.240×10^{-5}	0.000	0.174	2.694	.008	0.000–0.000
BUN at admission	–0.001	0.002	–0.027	–0.411	.68	–0.005 to 0.003
PLR at admission	0.000	0.000	0.207	3.228	.001	0.000–0.001
NLR at admission	0.007	0.003	0.153	2.363	.019	0.001–0.012
Objective variable: ΔCr						
Explanatory variable: Age; Sex; BMI; Hb, Alb, BNP, CRP, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK						
Age	–0.020	0.025	–0.051	–0.778	.44	–0.069 to –0.030
Sex	0.643	1.064	0.040	0.604	.55	–1.453 to 2.739
BMI	0.129	0.080	0.106	1.609	.11	–0.029 to 0.287
Hb at admission	0.602	0.182	0.212	3.300	.001	0.243–0.961
Alb at admission	0.632	0.914	0.045	0.691	.49	–1.169 to 2.433
BNP at admission	0.000	0.002	0. 004	0.054	.96	–0.004 to 0.004
CRP at admission	–0.147	0.187	–0.051	–0.785	.43	–0.514 to 0.221
Contrast medium usage	0.006	0.006	0.058	0.887	.38	–0.007 to 0.018
Maximum CK	7.082×10^{-5}	0.000	0.030	0.451	.65	0.000–0.000
Cr at admission	0.994	1.369	0.048	0.726	.47	–1.703 to 3.692
PLR at admission	0.004	0.004	0.062	0.945	.35	–0.005 to 0.013
NLR at admission	–0.025	0.096	–0.017	–0.261	.79	–0.215 to 0.165
Objective variable: ΔBUN						
Explanatory variable: Age; Sex; BMI; Hb, Alb, BNP, CRP, Cr, PLR, and NLR at admission; contrast medium usage, maximum CK						

Alb = albumin, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio.

the coagulation system is activated by tissue factors, resulting in thrombin production and fibrin formation from fibrinogen, leading to thrombus formation while adversely affecting renal function.

In addition, platelet activation leads to the formation of platelet-leukocyte complexes through the binding of P-selectin on the platelet membrane surface and P-selectin glycoprotein ligand-1 on the leukocyte surface.[21–23] This complex amplifies inflammatory reactions and thrombus formation. Furthermore, while platelets lack migratory ability, their complex with leukocytes migrates and deposits at the inflammation site, making them more likely to be involved in local thrombus formation. We previously reported that platelets and leukocytes stimulate and amplify each other in acute coronary syndrome (ACS).[18]

Previous studies have implicated elevated PLR in inflammation and a higher risk of contrast-induced nephropathy (CIN) in ACS patients.[24–27] Recent findings have suggested that elevated PLR is involved in inflammatory responses and is a prognostic factor for patients with acute kidney injury.[28,29] Additionally, lymphocytes have been implicated in inflammation and acute kidney injury development.[30,31]

In this study, we proposed that AMI induces inflammation and amplifies crosstalk with platelets, leading to elevated PLR and thrombus formation, which have a negative impact on renal function.

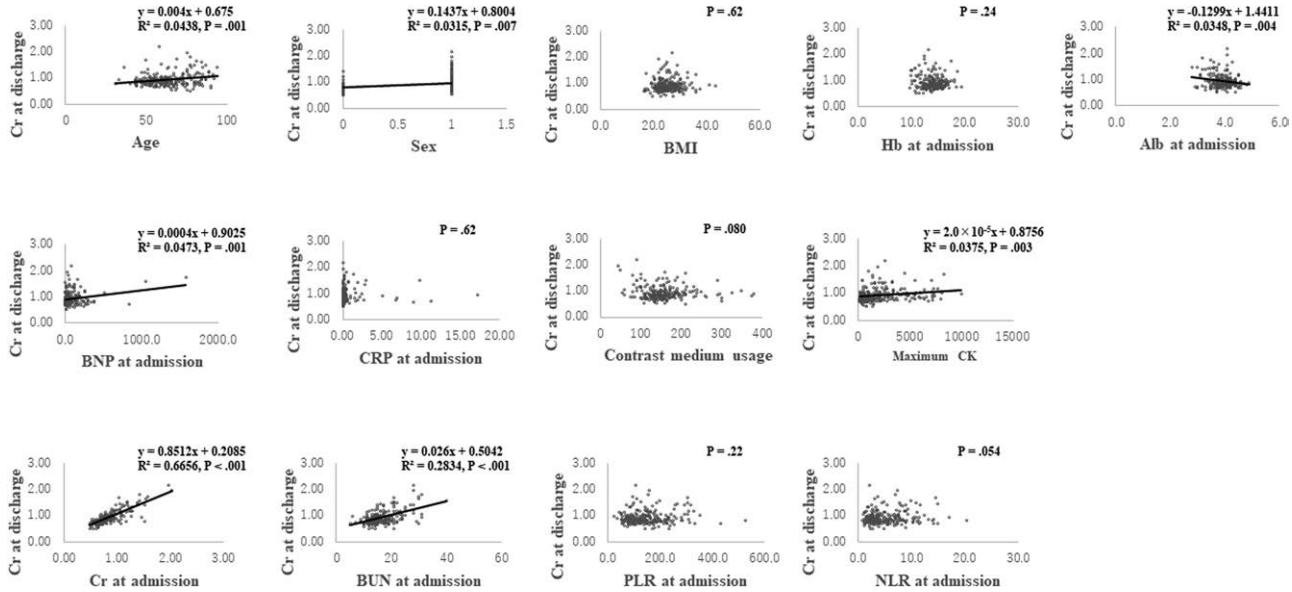

Figure 1. Scatter plots obtained from simple regression analysis The relationship between age; sex; BMI; Hb, Alb, BNP, CRP, Cr, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK and Cr at discharge (13 figures). Alb = albumin, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio.

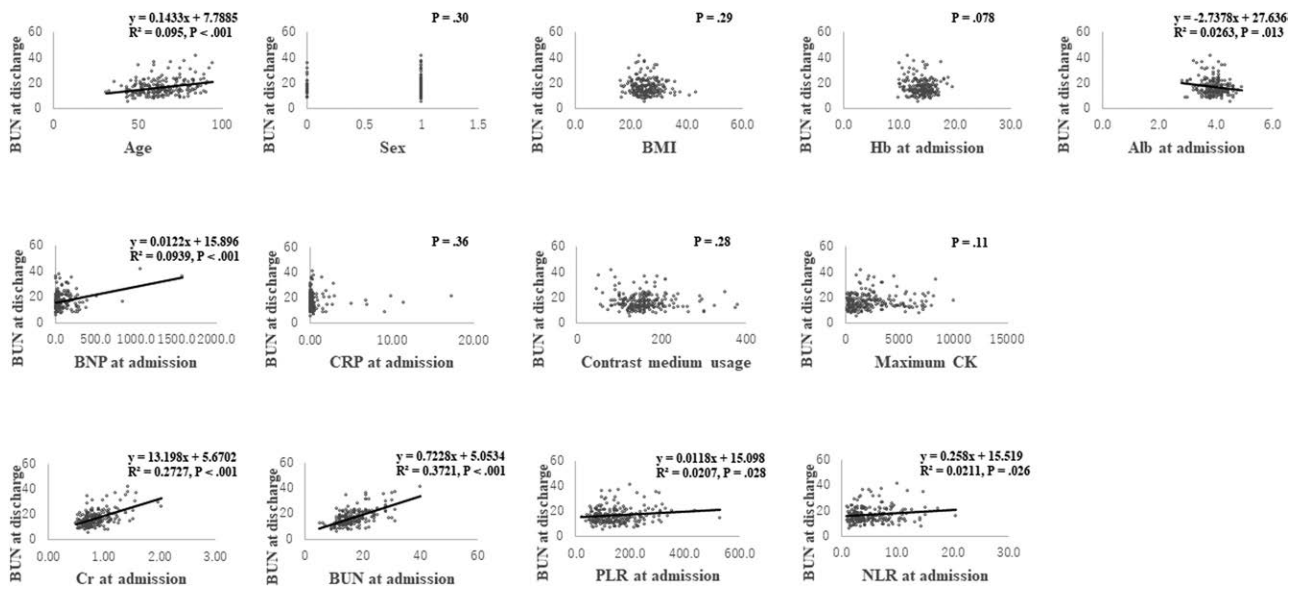

Figure 2. Scatter plots obtained from simple regression analysis. The relationship between age; sex; BMI; Hb, Alb, BNP, CRP, Cr, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK and BUN at discharge (13 figures). Alb = albumin, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio.

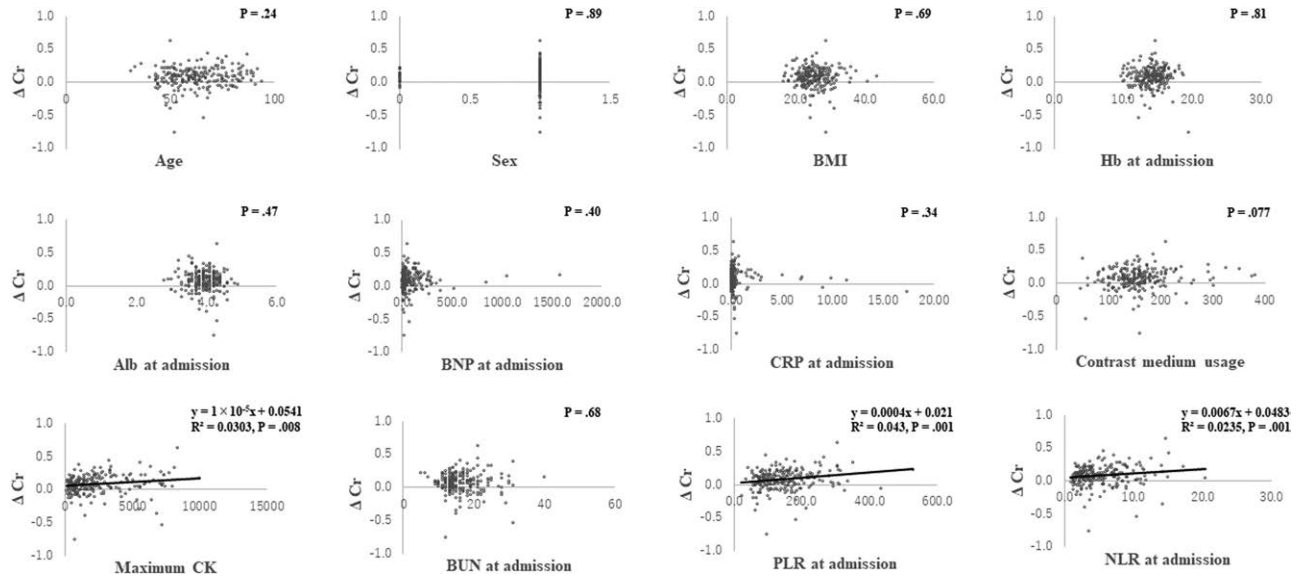

Figure 3. Scatter plots obtained from simple regression analysis. The relationship between age; sex; BMI; Hb, Alb, BNP, CRP, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK and ΔCr (12 figures). Alb = albumin, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio.

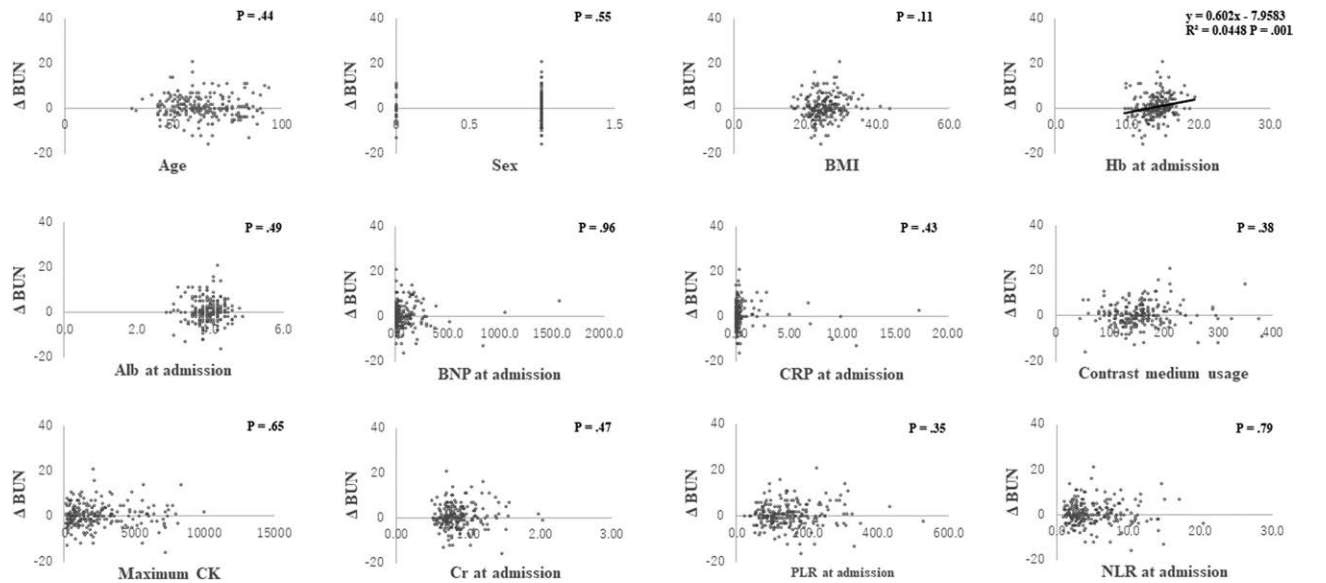

Figure 4. Scatter plots obtained from simple regression analysis. The relationship between age; sex; BMI; Hb, Alb, BNP, CRP, Cr, PLR, and NLR at admission; contrast medium usage, maximum CK and ΔBUN (12 figures). Alb = albumin, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio.

4.2. Effects of antiplatelet agents

All patients in this study underwent percutaneous coronary intervention and received antiplatelet medications during hospitalization. Aspirin exerts its antiplatelet effects by inhibiting cyclooxygenase-1 and suppressing thromboxane A2 production.[32] On the other hand, P2Y12 receptor inhibitors exert their antiplatelet effects by inhibiting binding to adenosine diphosphate receptors.[33] However, it remains unclear whether cyclooxygenase-1 and adenosine diphosphate receptor binding is sufficiently inhibited, necessitating the consideration of residual platelet reactivity (RPR). Elevated RPR during antiplatelet therapy in patients with ischemic heart disease has been reported to be associated with adverse clinical events.[34–38] Moreover, elevated RPR during antiplatelet therapy has been linked to inflammatory conditions,[38,39] potentially reducing the efficacy of antiplatelet therapy.

In this study, we postulate that the increase in RPR during antiplatelet drug therapy associated with inflammation may also trigger thrombus formation, which may have contributed to the negative impact on renal function after AMI.

4.3. NLR and renal dysfunction during ACS treatment

Several studies have shown an association between NLR and an increased incidence of CIN in patients with AMI.[40–42] In this study, increased NLR had minimal association with

Table 4

Multiple regression analysis results.

R^2 = 0.715	Regression coefficient	Standard error	Standard regression coefficient	Test statics	*P* valve	95% confidence interval	VIF
Age	0.001	0.001	0.050	0.927	.36	−0.001 to 0.003	2.168
Sex	0.039	0.034	0.049	1.154	.25	−0.028 to 0.107	1.328
BMI	0.003	0.003	0.048	1.135	.26	−0.002 to 0.008	1.330
Hb at admission	0.006	0.007	0.045	0.860	.39	−0.008 to 0.021	2.019
Alb at admission	−0.031	0.035	−0.045	−0.902	.37	−0.000 to 0.037	1.824
BNP at admission	7.575×10^{-5}	0.000	0.047	1.095	.28	0.000–0.000	1.371
CRP at admission	−0.004	0.006	−0.026	−0.615	.54	−0.015 to 0.008	1.301
Contrast medium usage	0.000	0.000	0.032	0.821	.41	0.000–0.001	1.131
Maximum CK	1.377×10^{-5}	0.000	0.115	2.809	.005	0.000–0.000	1.253
Cr at admission	0.755	0.051	0.734	14.749	<.001	0.654–0.856	1.838
BUN at admission	0.005	0.003	0.108	2.032	.043	0.000–0.010	2.118
PLR at admission	0.000	0.000	0.135	2.332	.021	0.000–0.001	2.481
NLR at admission	−0.005	0.004	−0.069	−1.169	.24	−0.014 to 0.004	2.578

Objective variable: Cr at discharge

Explanatory variable: Age; Sex; BMI; Hb, Alb, BNP, CRP, Cr, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK

R^2 = 0.472	Regression coefficient	Standard error	Standard regression coefficient	Test statics	*P* valve	95% confidence interval	VIF
Age	0.066	0.035	0.138	1.873	.062	−0.003 to 0.135	2.168
Sex	−2.042	1.148	−0.103	−1.779	.077	−4.305 to 0.221	1.328
BMI	0.059	0.089	0.038	0.662	.51	−0.116 to 0.234	1.330
Hb at admission	0.659	0.248	0.190	2.662	.008	0.171–1.147	2.019
Alb at admission	0.405	1.163	0.024	0.348	.73	−1.888 to 2.698	1.824
BNP at admission	0.003	0.002	0.073	1.244	.22	−0.002 to 0.007	1.371
CRP at admission	0.003	0.196	0.001	0.015	.99	−0.383 to 0.389	1.301
Contrast medium usage	0.007	0.006	0.058	1.092	.28	−0.006 to 0.020	1.131
Maximum CK	9.540×10^{-5}	0.000	0.033	0.579	.56	0.000–0.000	1.253
Cr at admission	7.602	1.720	0.300	4.419	<.001	4.211–10.993	1.838
BUN at admission	0.502	0.087	0.420	5.759	<.001	0.330–0.674	2.118
PLR at admission	0.018	0.007	0.218	2.766	.006	0.005–0.031	2.481
NLR at admission	−0.219	0.147	−0.120	−1.487	.14	−0.508 to 0.071	2.578

Objective variable: BUN at discharge

Explanatory variable: Age; Sex; BMI; Hb, Alb, BNP, CRP, Cr, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK

R^2 = 0.103	Regression coefficient	Standard error	Standard regression coefficient	Test statics	P valve	95% confidence interval	VIF
Age	0.001	0.001	0.103	1.074	.28	−0.001 to 0.003	2.164
Sex	−0.005	0.035	−0.010	−0.135	.89	−0.073 to 0.063	1.231
BMI	0.001	0.003	0.034	0.449	.65	−0.004 to 0.007	1.304
Hb at admission	0.006	0.008	0.072	0.777	.44	−0.009 to 0.021	2.018
Alb at admission	−0.008	0.036	−0.020	−0.234	.82	−0.079 to 0.063	1.790
BNP at admission	7.275×10^{-5}	0.000	0.077	1.001	.32	0.000–0.000	1.370
CRP at admission	−0.003	0.006	−0.041	−0.542	.59	−0.015 to 0.009	1.301
Contrast medium usage	0.000	0.000	0.122	1.789	.075	0.000–0.001	1.080
Maximum CK	1.209×10^{-5}	0.000	0.172	2.353	.020	0.000–0.000	1.247
BUN at admission	−0.002	0.002	−0.062	−0.787	.43	−0.006 to 0.003	1.436
PLR at admission	0.000	0.000	0.244	2.367	.019	0.000–0.001	2.478
NLR at admission	−0.004	0.005	−0.093	−0.890	.38	−0.013 to 0.005	2.572

Objective variable: ΔCr

Explanatory variable: Age; Sex; BMI; Hb, Alb, BNP, CRP, BUN, PLR, and NLR at admission; contrast medium usage, maximum CK

R^2 = 0.095	Regression coefficient	Standard error	Standard regression coefficient	Test statics	*P* valve	95% confidence interval	VIF
Age	0.023	0.037	0.058	0.619	.54	−0.050 to 0.095	2.068
Sex	−1.538	1.227	−0.094	−1.253	.21	−3.957 to 0.881	1.320
BMI	0.078	0.095	0.062	0.819	.41	−0.110 to 0.266	1.328
Hb at admission	0.930	0.261	0.325	3.566	<.001	0.416–1.443	1.945
Alb at admission	−0.586	1.233	−0.041	−0.475	.64	−3.017 to 1.845	1.784
BNP at admission	0.000	0.002	0.003	0.044	.97	−0.005 to 0.005	1.310
CRP at admission	−0.062	0.210	−0.022	−0.294	.77	−0.475 to 0.352	1.297
Contrast medium usage	0.005	0.007	0.047	0.671	.50	−0.009 to 0.018	1.126
Maximum CK	3.105×10^{-5}	0.000	0.013	0.176	.86	0.000–0.000	1.247
Cr at admission	2.205	1.519	0.097	1.333	.18	−0.969 to 5.019	1.247
PLR at admission	0.021	0.007	0.312	3.040	.003	0.007–0.035	2.463
NLR at admission	−0.341	0.156	−0.227	−2.187	.030	−0.649 to −0.034	2.523

Objective variable: ΔBUN

Explanatory variable: Age; Sex; BMI; Hb, Alb, BNP, CRP, Cr, PLR, and NLR at admission; contrast medium usage, maximum CK

Alb = albumin, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio.

Table 5

Results of the path model based on structural equation modelling.

Clinical factors			Estimate	Standard error	Test statistic	*P* value	Standard regression coefficient
Age	→	ΔCr	0.001	0.001	1.266	.21	0.112
	→	ΔBUN	0.033	0.034	0.959	.34	0.085
Sex	→	ΔCr	0.002	0.033	0.051	.96	0.004
	→	ΔBUN	−0.804	1.121	−0.717	.47	−0.050
BMI	→	ΔCr	0.001	0.003	0.196	.84	0.014
	→	ΔBUN	0.086	0.087	0.989	.32	0.071
Hb at admission	→	ΔCr	0.011	0.007	1.442	.15	0.124
	→	ΔBUN	0.959	0.245	3.913	<.001	0.337
Alb at admission	→	ΔCr	−0.017	0.035	−0.479	.63	−0.040
	→	ΔBUN	−0.919	1.161	−0.791	.43	−0.066
BNP at admission	→	ΔCr	0.000	0.000	0.600	.55	0.043
	→	ΔBUN	0.000	0.002	0.160	.87	0.011
CRP at admission	→	ΔCr	−0.004	0.006	−0.609	.54	−0.043
	→	ΔBUN	−0.059	0.202	−0.290	.77	−0.021
Contrast medium usage	→	ΔCr	0.000	0.000	1.775	.076	0.114
	→	ΔBUN	0.003	0.006	0.416	.68	0.027
Maximum CK	→	ΔCr	0.000	0.000	2.053	.040	0.141
	→	ΔBUN	0.000	0.000	0.360	.72	0.025
PLR at admission	→	ΔCr	0.001	0.000	2.650	.008	0.260
	→	ΔBUN	0.020	0.007	2.977	.003	0.292
NLR at admission	→	ΔCr	−0.004	0.004	−0.810	.42	−0.081
	→	ΔBUN	−0.301	0.147	−2.050	.040	−0.205

Clinical factors			Estimate	Standard error	Test statistic	*P* value	Correlation coefficient
PLR at admission	⇄	NLR at admission	185.447	20.478	9.056	<.001	0.735
	⇄	Maximum CK	24486.025	10262.630	2.386	.017	0.158
	⇄	Contrast medium usage	−171.712	246.202	−0.697	.47	−0.046
	⇄	CRP at admission	5.522	8.521	0.648	.52	0.042
	⇄	BNP at admission	1153.026	762.397	1.512	.13	0.101
	⇄	Alb at admission	−5362	1.774	−3.022	.003	−0.202
	⇄	Hb at admission	−38.728	8.896	−4.353	<.001	−0.297
	⇄	BMI	−978.781	20.581	−3.828	<.001	−0.259
	⇄	Sex	−3.202	1.510	−2.121	.034	−0.140
	⇄	Age	173.695	64.114	2.709	.007	0.180
NLR at admission	⇄	Maximum CK	2276.183	490.043	4.645	<.001	0.319
	⇄	Contrast medium usage	−3.768	11.331	−0.333	.74	−0.022
	⇄	CRP at admission	0.844	0.396	2.131	.033	0.141
	⇄	BNP at admission	73.440	35.272	2.082	.037	0.139
	⇄	Alb at admission	−0.176	0.081	−2.170	.030	−0.143
	⇄	Hb at admission	−0.794	0.396	−2.003	.045	−0.132
	⇄	BMI	−2.412	0.931	−2.591	.010	−0.172
	⇄	Sex	−0.075	0.069	−1.085	.28	−0.071
	⇄	Age	5.574	2.929	1.903	.057	0.125
Maximum CK	⇄	Contrast medium usage	11196.267	6996.402	1.600	.11	0.105
	⇄	CRP at admission	−588.524	243.897	−2.413	.016	−0.160
	⇄	BNP at admission	−13813.174	21482.112	−0.643	.52	−0.043
	⇄	Alb at admission	90.810	49.561	1.832	.067	0.121
	⇄	Hb at admission	423.521	242.853	1.744	.081	0.115
	⇄	BMI	−40.033	563.743	−0.071	.94	−0.005
	⇄	Sex	65.829	42.516	1.548	.12	0.102
	⇄	Age	−2282.753	1791.372	−1.274	.20	−0.084
Contrast medium usage	⇄	CRP at admission	−5.468	5.854	−0.934	.35	−0.061
	⇄	BNP at admission	−684.768	522.663	−1.310	.19	−0.087
	⇄	Alb at admission	1.576	1.198	1.315	.19	0.086
	⇄	Hb at admission	14.192	5.927	2.395	.017	0.159
	⇄	BMI	37.689	13.898	2.712	.007	0.181
	⇄	Sex	2.237	1.037	2.158	.031	0.143
	⇄	Age	−125.378	44.080	−2.844	.004	−0.189
CRP at admission	⇄	BNP at admission	70.882	18.611	3.809	<.001	0.261
	⇄	Alb at admission	−0.179	0.043	−4.173	<.001	−0.284
	⇄	Hb at admission	−0.289	0.204	−1.422	.16	−0.093
	⇄	BMI	−0.327	0.474	−0.689	.49	−0.045
	⇄	Sex	−0.040	0.036	−1.109	.27	−0.073
	⇄	Age	0.149	1.499	0.100	.92	0.007
BNP at admission	⇄	Alb at admission	−15.443	3.818	−4.044	<.001	−0.278
	⇄	Hb at admission	−32.897	18.184	−1.809	.070	−0.121
	⇄	BMI	−120.760	42.927	−2.813	.005	−0.190
	⇄	Sex	−6.617	3.195	−2.071	.038	−0.139
	⇄	Age	691.797	141.049	4.905	<.001	0.343

(*Continued*)

Table 5

(*Continued*)

Clinical factors			Estimate	Standard error	Test statistic	*P* value	Correlation coefficient
Alb at admission	⇄	Hb at admission	0.326	0.047	7.002	<.001	0.515
	⇄	BMI	0.351	0.099	3.529	<.001	0.238
	⇄	Sex	0.024	0.007	3.279	.001	0.219
	⇄	Age	−2.572	0.349	−7.360	<.001	−0.549
Hb at admission	⇄	BMI	2.747	0.507	5.417	<.001	0.380
	⇄	Sex	0.219	0.038	5.714	<.001	0.403
	⇄	Age	−12.534	1.711	−7.326	<.001	−0.546
BMI	⇄	Sex	0.277	0.085	3.255	.001	0.219
	⇄	Age	−21.135	3.771	−5.604	<.001	−0.395
Sex	⇄	Age	−1.300	0.277	−4.698	<.001	−0.323
e1	⇄	e2	0.264	0.047	5.567	<0.001	0.391

Alb = albumin, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio.

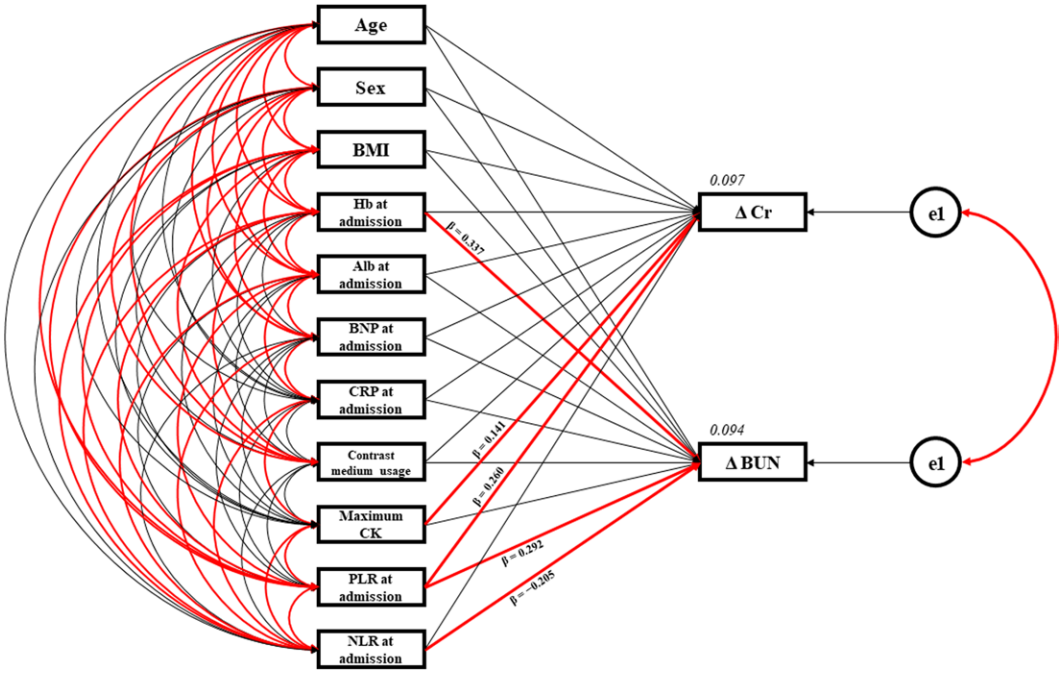

Figure 5. Path model based on structural equation modeling. Path diagram showing the effects of independent variables (age; sex; BMI; Hb, Alb, BNP, CRP, PLR, and NLR at admission; contrast medium usage, maximum CK) on dependent variables (ΔCr and ΔBUN) based on the analysis of covariance structure. Unidirectional arrows drawn from the independent variables to the dependent variables represent positive or negative effects and the relationship between the two variables is drawn as a bidirectional arrow. The dependent variable is accompanied by an error variable. The squared value of the multiple correlation coefficient is presented in the upper right corner of the dependent variable. The estimated standardized coefficient is displayed above the unidirectional arrows, with a value ranging from −1.0 to 1.0, indicating a positive or negative impact. The larger the positive or negative value, the larger the effect. Bidirectional arrows represent the estimates of the correlation coefficients. The bold red typeface indicates the significant values. Alb = albumin, BMI = body mass index, BNP = B-type natriuretic peptide, BUN = blood urea nitrogen, CK = creatine kinase, Cr = creatinine, CRP = C-reactive protein, Hb = hemoglobin, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio.

renal function in the chronic phase, contrary to the results of previous studies. This difference may be attributed to several factors. While previous studies examined the incidence of CIN (defined as a serum creatinine increase of ≥0.5 mg/dL or 25% above the previous value within 72 hours), our study obtained blood samples at hospital discharge of approximately 9.4 ± 4.0 days after treatment. This difference in timing may have contributed to differences in the results. Additionally, in a previous study, NLR in patients with CIN was higher than that in our patient group, and the fact that the previous study population consisted of patients with non-ST-elevation myocardial infarction (NSTEMI) may have contributed to the difference in results.[42] A recent important report has reported that high NLR is a predictor of in-hospital mortality in NSTEMI.[43] In our study, there were 200 ST-elevation myocardial infarction (STEMI) and 34 NSTEMI patients. The lower proportion of NSTEMI patients compared to STEMI patients may have influenced the results of this study. Further verification through prospective studies with larger sample sizes is needed in the future.

5. Discussion of other results

SEM results showed a significant positive correlation between maximum CK and ΔCr, which can be attributed to the metabolic pathway of Cr and the simple hemodynamic effects of infarcted area size. Creatine levels typically increase during myocardial infarction, and CK is necessary for the metabolism of creatine to creatine phosphate and Cr. Therefore, there may be a correlation between the maximum CK and ΔCr.

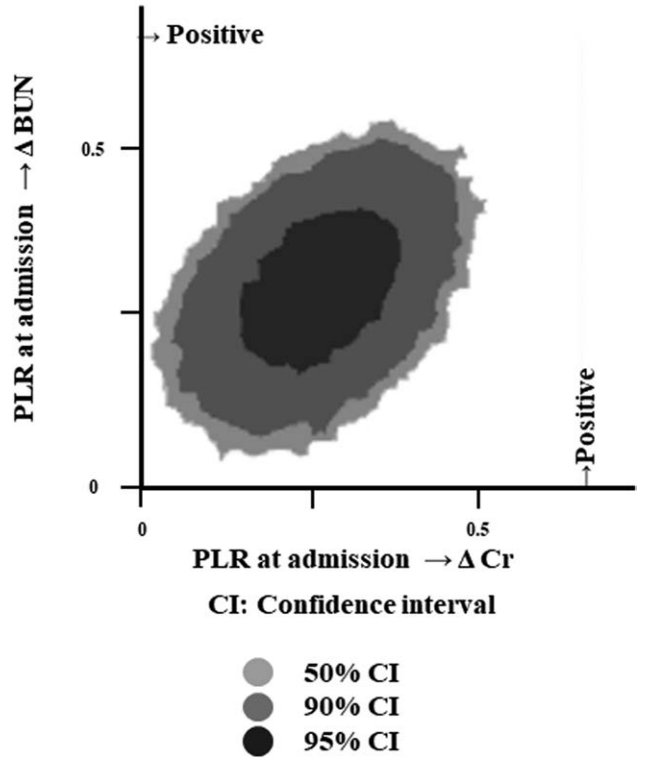

Figure 6. Bayesian estimation in structural equation modeling. This figure is based on a Bayesian estimation. At the center of each figure, there is a circular distribution of 3 colors, and the colors change from the center to the outside: black, dark gray, and light gray. Black, dark gray, and light gray indicate the 95%, 90%, and 50% confidence intervals, respectively. This figure shows the effect of PLR at admission on the ΔCr count (x-axis) and ΔBUN (y-axis). In the two-dimensional plot, the horizontal and vertical axes did not cross zero, indicating that both were strongly affected. BUN = blood urea nitrogen, CI = confidence interval, Cr = creatinine, PLR = platelet-to-lymphocyte ratio.

Additionally, we observed a significant positive correlation between Hb level at admission and ΔBUN, and a weak but significant negative correlation between NLR at admission and ΔBUN. However, the mechanisms underlying these relationships remain unclear and should be investigated further in future studies.

6. Study limitations

This study has several limitations, including the small sample size, its retrospective study design, and the use of various medications, including diuretics, which could have affected the results. In addition, PLR and NLR data were obtained at the time of admission and temporal trends were not examined, which should be investigated in future studies. In this study, SEM was used to create path diagrams, which are a useful tool for resolving complex relational hypotheses and allow for the exclusion of the influence of confounding factors and evaluation of the degree of influence among factors. However, path diagrams are highly flexible and can be modified to suit the author's intentions. Therefore, further validation using various path diagrams and other statistical methods is necessary.

7. Conclusions

The results of this study suggest that an elevated PLR at admission in AMI affects and exacerbates renal function. Our study findings highlight the importance of measuring PLR at admission, an easily obtainable and cost-effective marker that allows us to determine renal function in the chronic phase after treatment for AMI. Early intervention to disrupt cardiorenal syndrome is crucial for cardiac and renal protection and may have important implications for the treatment of patients with AMI.

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