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Association between mild renal insufficiency, inflammatory status on initial admission, and 1-year mortality following ST-segment elevation myocardial infarction

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The systemic inflammation tends to increase progressively as kidney function deteriorates. However, it remains unknown whether mild renal insufficiency affects inflammatory response at admission and subsequent clinical outcomes following ST-segment elevation myocardial infarction (STEMI). This study aimed to evaluate the joint, interactive, and mediating effects of estimated glomerular filtration rate (eGFR) and neutrophil-lymphocyte ratio (NLR) at admission on 1-year mortality in STEMI patients. Data were collected from 5,594 consecutive STEMI patients at seven centers (*NCT04996901*). Mildly reduced eGFR (60–89 mL/min/1.73m^2) was associated with both elevated NLR and increased 1-year mortality (β 0.55, 95%CI [0.07–1.02], $P = 0.024$; HR 2.18, 95%CI [1.55–3.08], $P < 0.001$; respectively). Inflammation at admission mediated a small but significant proportion of the association between mildly reduced eGFR and mortality risk (1.7%, $P = 0.030$). Incorporating eGFR and NLR into a predictive model significantly improved mortality prediction following STEMI compared with clinical risk factors alone (C-index, 0.799 vs. 0.730, $P < 0.001$; net reclassification index 0.334, $P < 0.001$). These findings support the identification of patients at risk who may benefit from intensive kidney function monitoring and early adjuvant intervention, while also highlighting the need for developing anti-inflammatory therapies for STEMI patients with renal insufficiency.

Keywords Renal insufficiency, Inflammation, STEMI, Mortality, Prognosis

Chronic kidney disease (CKD) has emerged as a major global public health challenge, with an increasing all-cause mortality reaching 52.2 per 1000 person-years in 2021 among younger adults[1]. It affects millions of individuals and imposes a substantial burden on healthcare systems and society[1,2]. Notably, cardiovascular disease rather than end-stage kidney disease is the leading cause of death in patients with CKD[3,4]. Previous studies have consistently demonstrated that individuals with low estimated glomerular filtration rate (eGFR) face a significantly elevated risk of adverse cardiovascular events[5–7]. It is attributed to a complex interplay of altered hemodynamics, electrolyte disturbances, vascular remodeling, and systemic inflammation in CKD patients[3].

CKD is known to be a state of chronic low-grade inflammation and an accelerator of cardiovascular aging, which exacerbates vascular dysfunction and accelerates atherosclerosis progression[3]. Inflammation is a key driver of atheroprogression and thromboembolic events, particularly in acute coronary syndrome such as ST-segment elevation myocardial infarction (STEMI)[8–10]. During STEMI, ischemia and reperfusion injury also trigger a robust inflammatory response characterized by the release of cytokines and activation of immune pathways, which exacerbates infarct expansion, myocardial remodeling, and poor clinical outcomes[11–14].

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Despite growing evidence linking renal dysfunction and inflammation to adverse cardiovascular outcomes, previous studies have several limitations. First, previous studies have predominantly focused on moderate to severe CKD and its association with cardiovascular outcomes[3,15,16], leaving a critical gap in understanding the impact of mild renal insufficiency, particularly in patients with STEMI. Second, while inflammation is a well-established prognostic factor in myocardial infarction, especially in patients with CKD or diabetes[17–20], the extent to which mild renal dysfunction exacerbates inflammatory activation at admission and its impact on long-term outcomes remains unexplored. To address these knowledge gaps, our study aims to investigate the joint, interactive, and mediating effects of mild renal insufficiency and inflammatory status on 1-year mortality following STEMI. By exploring these relationships, we seek to clarify whether even mild renal dysfunction contributes to cardiovascular risk, offering potential implications for risk stratification and management strategies in STEMI patients with renal insufficiency.

Methods

Data source and study population

Consecutive patients aged ≥ 18 years with STEMI who underwent primary percutaneous coronary intervention (PCI) between 2015 and 2021 at seven high-volume PCI centers in China were retrospectively enrolled (CSPR [The Chinese STEMI PPCI Registry] trial; Unique identifier: NCT04996901). STEMI was diagnosed based on the fourth universal definition of MI[21]. Principal exclusion criteria for further analyses were as follows: (1) STEMI with symptom-onset-to-balloon time > 24 h.; (2) Primary PCI was not successful or only underwent coronary angiography; (3) Missing key baseline laboratory data (neutrophil count, lymphocyte count, eGFR, etc.). The flowchart of patient enrollment in this study is displayed in Supplemental Fig. 1. Patient demographic characteristics, laboratory findings, medical history, and PCI procedure details were obtained from electronic medical records for further analyses. The CSPR trial was conducted in accordance with the Declaration of Helsinki and was approved by all institutional ethics and review committees (approval number: WDRY2021-K504). The individual informed consent was waived by Renmin Hospital of Wuhan University due to the opt-out policy of retrospective study.

Assessment of kidney function and inflammatory status

Kidney function was quantitatively assessed using the estimated glomerular filtration rate (eGFR), which was derived from inpatient serum creatinine measurements and calculated using the race-agnostic Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 Equation[22]. The eGFR was classified into three categories according to the definition of CKD and scale of the study population: normal or high, eGFR ≥ 90 mL/min/1.73m^2; mildly decreased, eGFR 60–89 mL/min/1.73m^2; moderately to severely decreased, eGFR < 60 mL/min/1.73m^2[23]. The inflammatory status at the onset of STEMI was assessed using the neutrophil-lymphocyte ratio (NLR), which was calculated as dividing the plasma neutrophil count ($\times 10^9$/L) by the plasma lymphocyte count ($\times 10^9$/L). NLR values were dichotomized into two groups based on the median value: low NLR < 7 and high NLR ≥ 7. Both eGFR and NLR values were obtained from medical records at admission, and patients with incomplete data on eGFR or NLR were excluded from the analysis.

Ascertainment of outcome

The primary outcome of this study was 1-year all-cause death, defined as death from any cardiac or non-cardiac cause occurring after admission. Clinical follow-up assessments were performed at 1, 6, and 12 months and every two years thereafter by outpatient clinical visits or telephone interviews. Follow-up was censored if events occurred after one year up to the latest available censor date (the end of February 2023).

Assessment of covariates

The following harmonized variables were included in the subsequent analysis based on their clinical relevance or statistical significance in baseline characteristics comparisons stratified by outcome: age, sex (female, male), hypertension (yes, no), diabetes (yes, no), hyperlipidemia (yes, no), smoking (yes, no), prior myocardial infarction (yes, no), prior stroke (yes, no), symptom-to-balloon time, anterior myocardial infarction (yes, no), post-procedural TIMI flow grade 3 (yes, no), multivessel disease (yes, no), and complete revascularization (yes, no). Multivessel disease was defined as the presence of significant stenosis (> 70%) in two or more major epicardial coronary arteries[24]. Complete revascularization was defined as the successful treatment of all lesions of anatomically significant stenosis[25]. The directed acyclic graphs (DAGs) were created to illustrate the relationships between exposure, outcome, and potential confounders (Supplemental Fig. 2).

Statistical analysis

Categorical variables were shown as counts (percentages) and compared using χ^2 tests or Fisher's exact tests, as appropriate. Continuous variables were presented as mean ± SD compared using Student's *t* tests.

To evaluate the association of eGFR and NLR with 1-year mortality, multivariable Cox proportional hazards models were fitted to estimate adjusted hazard ratios (HRs) as well as 95% confidence intervals (CIs). The proportionality assumption was tested by Schoenfeld residuals, and all Cox proportional hazard models met the assumption. Variance inflation factors (VIFs) were used to assess the collinearity of variables included in the multivariable model, and we did not find any collinear variables (all VIFs < 5). The Kaplan-Meier survival analyses with inverse probability of treatment weighting (IPTW) were used to assess the cumulative mortality risk for categorical eGFR and NLR on admission. Additionally, 4-knotted restricted cubic splines (RCS) were plotted to explore the potential exposure-response relationships between eGFR, NLR, and 1-year mortality.

To evaluate the joint effects of eGFR and NLR on 1-year mortality, patients were stratified into six distinct groups based on the categorized eGFR (≥ 90 mL/min/1.73m^2, 60–89 mL/min/1.73m^2, and < 60 mL/min/1.73m^2)

and NLR (< 7 and ≥ 7). All aforementioned covariables were included in the model for adjustment. To assess the addictive interaction, we use the R package "epiR" to calculate three distinct metrics: the relative excess risk due to interaction (RERI), attributable proportion due to interaction (AP), and the synergy index (SI). Meanwhile, the multiplicative interaction was also tested and considered as an absence of interaction if the value equals one.

To evaluate the mediating role of inflammatory status on admission on the association between renal insufficiency and all-cause death following STEMI, two-step regression analyses were performed using the R package "Mediation". A multivariate linear regression model was created to investigate the relationship between categorical eGFR and continuous NLR. Multivariate Cox regression models were constructed to assess the associations between eGFR, NLR, and 1-year mortality. The average causal mediation effect (ACME), average direct effect (ADE), and the percent mediated were then calculated using the quasi-Bayesian Monte Carlo simulation approaches (resampling 1,000 times). Additionally, we introduced a surrogate inflammatory marker, the systemic immune-inflammatory index (SII), calculated as platelet count × neutrophil count/lymphocyte count, to further validate the robustness of our conclusions. The optimal cut-off value of SII was determined by maximally selected rank statistics.

To evaluate the discriminant capabilities of predictive models to predict 1-year mortality following STEMI, the receiver-operating characteristic (ROC) curves were plotted and C-indexes with 95%CIs were compared. The incremental predictive implications of adding eGFR and NLR to a model with clinical risk factors compared to a model with clinical risk factors only were further assessed using integrated discrimination improvement (IDI) and the net reclassification index (NRI). Finally, decision curve analysis (DCA) was employed to compare the clinical net benefits against various threshold probabilities.

All statistical analyses were performed using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) and RStudio version 2023.12.1 + 402. A two-sided $P < 0.05$ was regarded as statistically significant.

Results

Baseline characteristics

A total of 4,778 patients with STEMI treated with primary PCI were enrolled in the analyses. The mean age was 61 ± 12 years, and 19.9% of the cohort were female. During 1-year follow-up, 266 (5.6%) deaths were documented (89 women and 177 men). The median (interquartile range) of eGFR was 96.6 (81.4, 106.1) mL/min/1.73m^2, while the median of NLR was 7 (4, 11). 26% of patients had mild renal insufficiency (eGFR 60–89 mL/min/1.73m^2), while 9.8% had moderate to severe renal insufficiency (eGFR < 60 mL/min/1.73m^2). Table 1 and Supplemental Table 1 present the baseline characteristics of the patients enrolled stratified by eGFR categories and NLR categories, respectively.

Association of eGFR and NLR with 1-year mortality

A consistent association of eGFR and NLR with 1-year mortality was observed across all three models (Table 2). Compared with patients with normal or high eGFR (≥ 90 mL/min/1.73m^2), the multivariate-adjusted HR among those with mildly decreased eGFR (60–89 mL/min/1.73m^2) was 2.18 (95% CI 1.55–3.08) in the fully adjusted model 3. Patients with moderately to severely decreased eGFR (< 60 mL/min/1.73m^2) exhibited an even higher1-year mortality risk, with an adjusted HR of 8.54 (95% CI 6.09–11.98). Compared with patients with low NLR < 7, those with high NLR ≥ 7 had a significantly increased 1-year mortality risk (adjusted HR 1.44, 95%CI 1.12–1.86, $P = 0.004$). Furthermore, the cumulative mortality risks were higher in patients with low eGFR and those with high NLR (both log-rank $P < 0.001$, Fig. 1). A nonlinear exposure-response association between eGFR and 1-year

Characteristics	Levels	Total (*N* = 4778)	eGFR ≥ 90 (*N* = 3067)	eGFR 60–89 (*N* = 1241)	eGFR < 60 (*N* = 470)	*P*
Age (years)	< 60	2113 (44.2%)	1715 (55.9%)	321 (25.9%)	77 (16.4%)	< 0.001
	≥ 60	2665 (55.8%)	1352 (44.1%)	920 (74.1%)	393 (83.6%)	
Gender	Male	3827 (80.1%)	2569 (83.8%)	930 (74.9%)	328 (69.8%)	< 0.001
	Female	951 (19.9%)	498 (16.2%)	311 (25.1%)	142 (30.2%)	
Hypertension	Yes	2334 (48.8%)	1317 (42.9%)	713 (57.5%)	304 (64.7%)	< 0.001
Diabetes	Yes	875 (18.3%)	534 (17.4%)	239 (19.3%)	102 (21.7%)	0.049
Hyperlipidemia	Yes	342 (7.2%)	246 (8%)	79 (6.4%)	17 (3.6%)	0.001
Smoking	Yes	2467 (51.6%)	1691 (55.1%)	590 (47.5%)	186 (39.6%)	< 0.001
Prior myocardial infarction	Yes	158 (3.3%)	84 (2.7%)	48 (3.9%)	26 (5.5%)	0.003
Prior stroke	Yes	308 (6.4%)	161 (5.2%)	96 (7.7%)	51 (10.9%)	< 0.001
Symptom-to-balloon time (h)	Mean ± SD	6.2 ± 4.8	6.1 ± 4.8	6.1 ± 4.8	6.9 ± 5.3	0.007
Anterior myocardial infarction	Yes	2409 (50.4%)	1602 (52.2%)	595 (47.9%)	212 (45.1%)	0.002
Post-procedural TIMI flow grade 3	Yes	4699 (98.3%)	3030 (98.8%)	1218 (98.1%)	451 (96%)	< 0.001
Multivessel disease	Yes	2450 (51.3%)	1500 (48.9%)	673 (54.2%)	277 (58.9%)	< 0.001
Complete revascularization	Yes	2779 (58.2%)	1867 (60.9%)	695 (56%)	217 (46.2%)	< 0.001

Table 1. Baseline characteristics for STEMI patients with different eGFR categories (mL/min/1.73m^2). *eGFR* estimated glomerular filtration rate, *STEMI* ST-segment elevation myocardial infarction, *TIMI* thrombolysis in myocardial infarction.

Characteristics	Levels	Stats	Model 1	Model 2	Model 3
			HR (95% CI)	HR (95% CI)	HR (95% CI)
eGFR (mL/min/1.73m^2)	Continuous	91.8 ± 23.2	0.97 (0.96, 0.97) $P < 0.001$	0.97 (0.96, 0.97) $P < 0.001$	0.97 (0.96, 0.97) $P < 0.001$
Normal or high	≥ 90	3067 (64.2%)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Mildly decreased	60–89	1241 (26.0%)	2.77 (2.01, 3.83) $P < 0.001$	2.13 (1.52, 2.99) $P < 0.001$	2.18 (1.55, 3.08) $P < 0.001$
Moderately to severely decreased	< 60	470 (9.8%)	12.23 (9.11, 16.43) $P < 0.001$	8.59 (6.18, 11.93) $P < 0.001$	8.54 (6.09, 11.98) $P < 0.001$
NLR	Continuous	8.7 ± 6.8	1.03 (1.02, 1.04) $P < 0.001$	1.03 (1.01, 1.04) $P < 0.001$	1.02 (1.01, 1.04) $P < 0.001$
Low	< 7	2360 (49.4%)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
High	≥ 7	2418 (50.6%)	1.64 (1.28, 2.10) $P < 0.001$	1.51 (1.18, 1.93) $P = 0.001$	1.44 (1.12, 1.86) $P = 0.004$

Table 2. Associations of eGFR and NLR with 1-year mortality risk following STEMI. Model 1 was not adjusted for any covariates; Model 2 was adjusted for adjusted for age, gender; Model 3 was further adjusted for age, gender, hypertension, diabetes, hyperlipidemia, smoking, prior myocardial infarction, prior stroke, symptom-to-balloon time, anterior myocardial infarction, post-procedural TIMI flow grade 3, multivessel disease, and complete revascularization. *CI* confidence interval, *eGFR* estimated glomerular filtration rate, *HR* hazard ratios, *NLR* neutrophil-lymphocyte ratio, *STEMI* ST-segment elevation myocardial infarction.

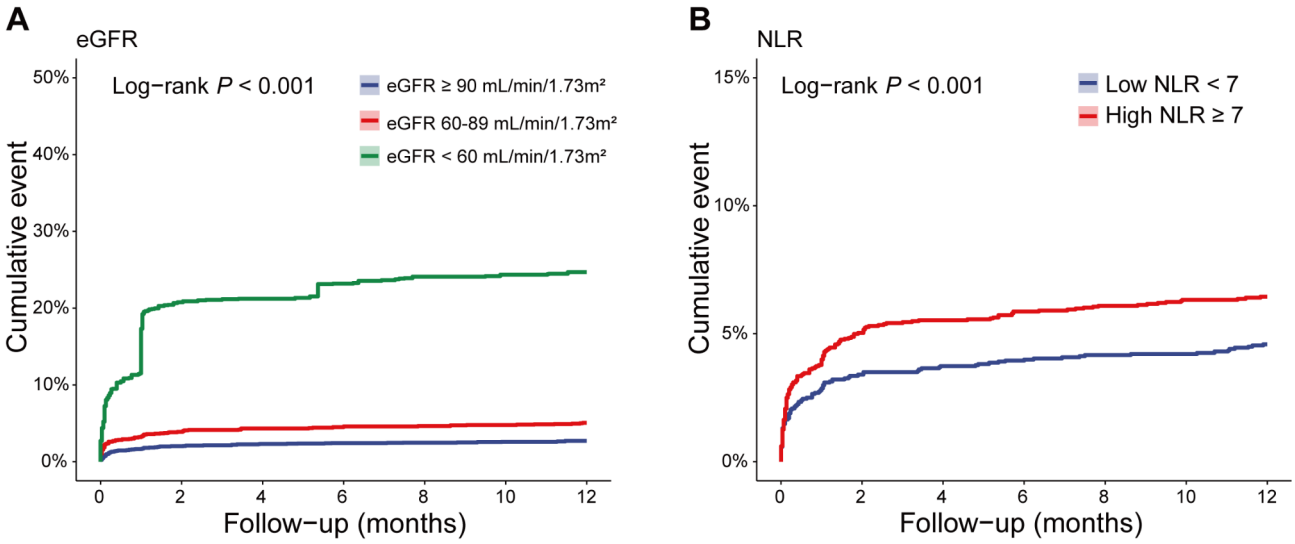

Fig. 1. Kaplan-Meier curves show the cumulative hazard of all-cause death following STEMI according to eGFR categories (**A**) and NLR categories (**B**), respectively. HRs were adjusted for age, gender, hypertension, diabetes, hyperlipidemia, smoking, prior myocardial infarction, prior stroke, symptom-to-balloon time, anterior myocardial infarction, post-procedural TIMI flow grade 3, multivessel disease, and complete revascularization using inverse probability of treatment weighting. *eGFR* estimated glomerular filtration rate, *NLR* neutrophil-lymphocyte ratio, *STEMI* ST-segment elevation myocardial infarction.

mortality using RCS regression analysis was found (P for nonlinearity < 0.001, Fig. 2A), whereas a monotonically increasing linear relationship between NLR and 1-year death events was observed (P for nonlinearity = 0.393, Fig. 2B). Additionally, there was a significant linear association between eGFR (as continuous and categorical exposure, respectively) and NLR (all $P < 0.05$, Supplemental Table 2).

Joint and interaction analyses of eGFR and NLR with mortality

The joint effects of eGFR and NLR on 1-year mortality are presented in Fig. 3. Reduced kidney function significantly aggravated the 1-year mortality following STEMI in both low and high NLR groups when compared to normal or high eGFR. Notably, even mildly decreased eGFR in patients with low NLR was associated with an increased mortality risk, with an adjusted HR 2.23 (95%CI 1.30–3.84). A similar result was observed in joint analysis of eGFR and SII with 1-year mortality (Supplemental Fig. 3). Furthermore, interactions between eGFR and NLR on 1-year mortality were further investigated. No additive but significant multiplicative interactions were found (Additive, RERI 0.54 [95%CI -0.82, 1.91] and 2.17 [95%CI -1.95, 6.28) in eGFR 60–89 mL/min/1.73m^2 and < 60 mL/min/1.73m^2 groups, respectively; Multiplicative, 3.37 [2.07, 5.50] and 12.40 [7.73, 19.90], respectively; Supplemental Table 3).

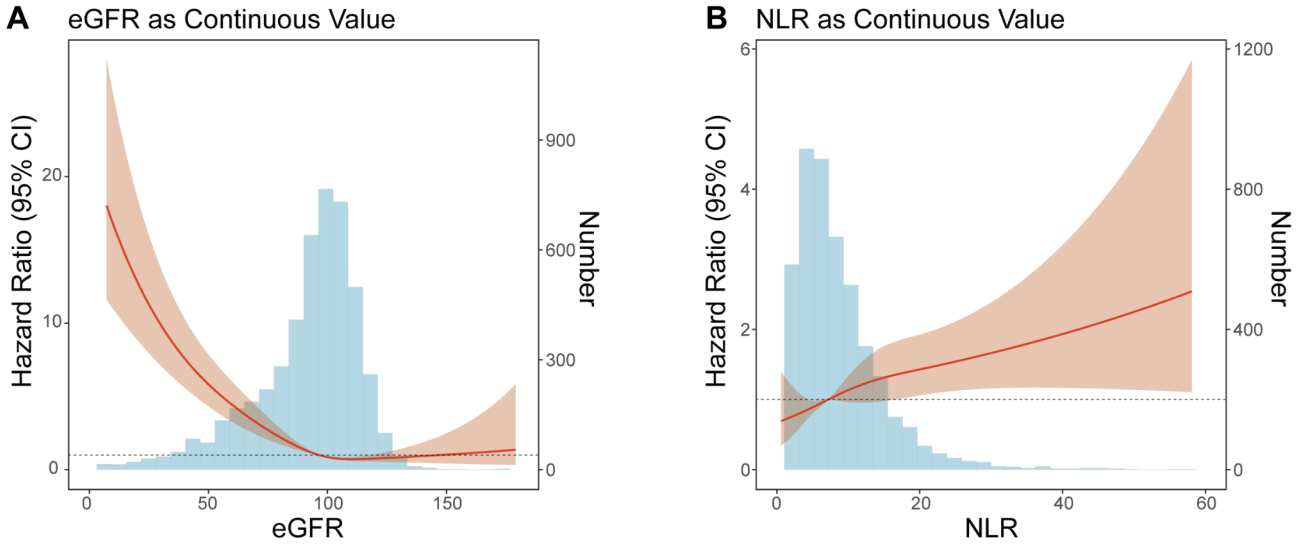

Fig. 2. Exposure-response relationships of eGFR (**A**), NLR (**B**) with the 1-year mortality risk following STEMI. HRs were adjusted for age, gender, hypertension, diabetes, hyperlipidemia, smoking, prior myocardial infarction, prior stroke, symptom-to-balloon time, anterior myocardial infarction, post-procedural TIMI flow grade 3, multivessel disease, and complete revascularization. *CI* confidence interval, *eGFR* estimated glomerular filtration rate, *NLR* neutrophil-lymphocyte ratio, *STEMI* ST-segment elevation myocardial infarction.

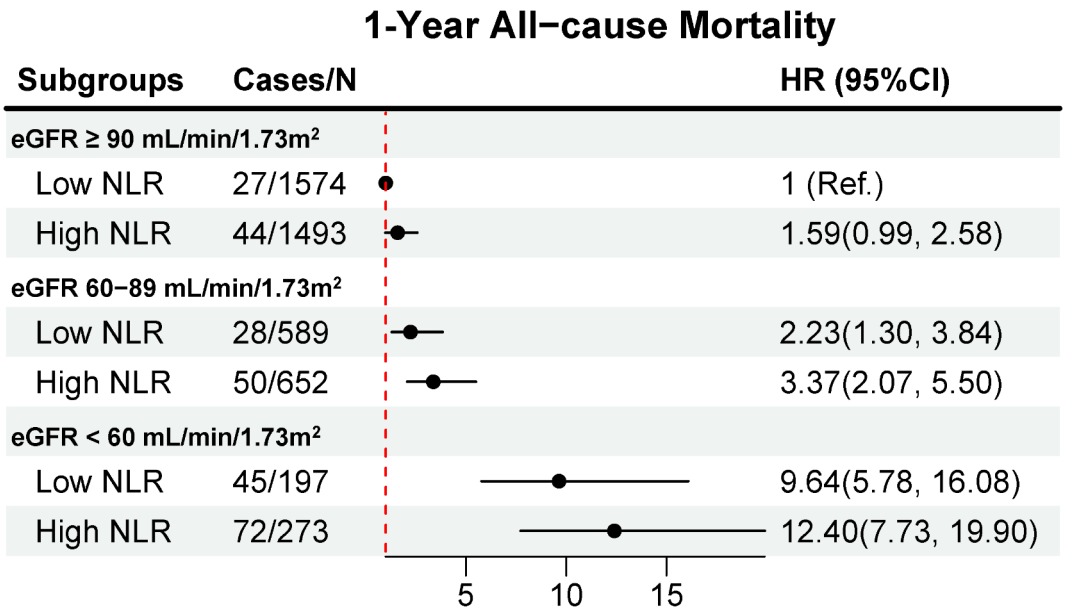

Fig. 3. Joint effects of eGFR and NLR on the 1-year mortality risk following STEMI. The model was adjusted for age, gender, hypertension, diabetes, hyperlipidemia, smoking, prior myocardial infarction, prior stroke, symptom-to-balloon time, anterior myocardial infarction, post-procedural TIMI flow grade 3, multivessel disease, and complete revascularization. *CI* confidence interval, *eGFR* estimated glomerular filtration rate, *HR* hazard ratios, *NLR* neutrophil-lymphocyte ratio, *STEMI* ST-segment elevation myocardial infarction.

Mediation analyses of NLR of eGFR with mortality

Table 3 shows the total, direct, and indirect associations between eGFR categories and 1-year mortality. We detected mediating effects through NLR were 1.7% (95%CI 0.1–4.5) for eGFR 60–89 mL/min/1.73m^2 group and 4.5% (95%CI 0.7–8.6) for eGFR < 60 mL/min/1.73m^2 group ($P = 0.03$ and $P = 0.01$, respectively). The small but significant proportion of mediation indicates that the NLR on admission was involved in the association between eGFR and 1-year mortality following STEMI. Similar mediating effects of NLR and SII were observed in the

	Total effect estimate	Direct effect estimate	Mediated estimate	% Mediated*	*P* value
eGFR 60–89 mL/min/1.73m^2	− 67779826.625 (− 349892361.771, − 4492128.069)	− 66474671.143 (− 341046323.935, − 4392416)	− 1305155.482 (− 7834902.16, − 23779.326)	1.7 (0.1, 4.5)	0.030
eGFR < 60 mL/min/1.73m^2	− 68846476.092 (− 327237947.601, − 4587182.16)	− 65441682.086 (− 310986658.323, − 4419777.602)	− 3404794.005 (− 17330301.103, − 85798.701)	4.5 (0.7, 8.6)	0.010

Table 3. Adjusted direct and indirect associations between eGFR and 1-year mortality risk and proportion mediated by admission NLR levels. All models were adjusted for age, gender, hypertension, diabetes, hyperlipidemia, smoking, prior myocardial infarction, prior stroke, symptom-to-balloon time, anterior myocardial infarction, post-procedural TIMI flow grade 3, multivessel disease, and complete revascularization. The group with eGFR > 90 mL/min/1.73m^2 was set as control. * Proportion mediated = mediated estimate/total effect estimate. *CI* confidence interval, *eGFR* estimated glomerular filtration rate, *NLR* neutrophil-lymphocyte ratio.

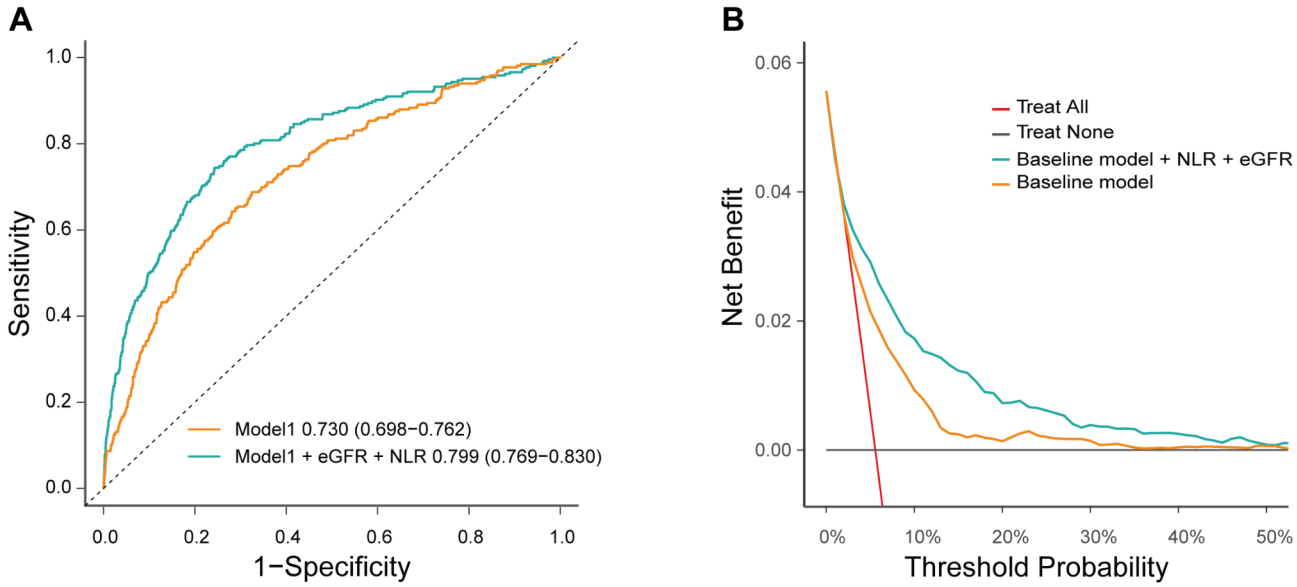

Fig. 4. Predictive performance of the combined eGFR and NLR for 1-year mortality risk following STEMI. (**A**) The receiver operating characteristic (ROC) curve for evaluating the discrimination power by calculating the AUC with 95%CI; (**B**) Decision curve analysis (DCA) to compare the clinical usefulness of the models for decision making. The y-axis measures the net benefits. The x-axis measures the threshold probability. *AUC* area under curve, *CI* confidence interval, *eGFR* estimated glomerular filtration rate, *NLR* neutrophil-lymphocyte ratio, *STEMI* ST-segment elevation myocardial infarction.

association between continuous eGFR and 1-year mortality (Proportion mediated, 1.3%, $P = 0.01$, Supplemental Fig. 4).

Incremental predictive value of eGFR and NLR in 1-year mortality

For discrimination ability for 1-year mortality, Fig. 4 shows incorporating additional eGFR and NLR can significantly improve the discriminant and reclassification indexes when compared with a model with clinical risk factors only (C-index, 0.799 vs. 0.730, $P < 0.001$; IDI, 0.062, $P < 0.001$; NRI, 0.334, $P < 0.001$). Meanwhile, the DCA compared the net benefit of patients and confirmed its clinical utility (Fig. 4B). The predictive value of eGFR alone, NLR alone, and the combined eGFR + NLR index was further assessed. The ROC curves indicated individual eGFR yielded a higher discriminant and reclassification abilities than NLR did (C-index, 0.771 vs. 0.587, $P < 0.001$; IDI, 0.078, $P < 0.001$; NRI, 0.405, $P < 0.001$; Supplemental Fig. 5). However, the combined eGFR + NLR did not significantly improve the predictive performance for 1-year mortality compared with eGFR alone (C-index, 0.776 vs. 0.771, $P = 0.172$; IDI, 0.002, $P = 0.352$; NRI, 0.075, $P = 0.100$; Supplemental Fig. 5).

Discussion

In this retrospective cohort study, we investigated the joint, interactive, and mediating effects of renal insufficiency and admission inflammatory status on 1-year all-cause mortality following STEMI. Our results demonstrated that even mildly decreased eGFR (60-89mL/min/1.73m^2) was consistently associated with higher admission inflammatory response and subsequent 1-year mortality, suggesting the withdrawal of kidney function and activation of inflammatory status on admission represent pivotal markers of poor outcome in STEMI patients.

Although no significant additive interactions were found between eGFR and NLR in relation to 1-year mortality, inflammatory status at initial admission mediated a small but significant proportion of the association between eGFR and mortality risk. Moreover, the inclusion of eGFR and NLR on admission improved the predictive performance for 1-year mortality risk following STEMI. These findings underscore the crucial need for early recognition and intensive monitoring of kidney function, even in patients with eGFR above 60 mL/min/1.73m^2, particularly in the context of STEMI.

Consistent with previous research, our findings provide additional evidence of a strong correlation between CKD and cardiovascular disease[3,5,26]. It is well acknowledged that individuals with CKD face an elevated risk of cardiovascular events. A previous study has reported that each 10-unit decrease in eGFR corresponded to a hazard ratio of 1.10 for adverse cardiovascular events, particularly when eGFR falls below 80 mL/min/1.73 m^2 [27]. Notably, our study revealed that even mild eGFR reduction (60–89 mL/min/1.73 m^2) was significantly associated with 1-year mortality following STEMI. In line with our findings, a recent study demonstrated that even modest reductions in renal function can increase the risk of adverse outcomes, including death, cardiovascular events, and kidney failure in younger adults[28]. These compelling findings emphasize the critical importance of proactive monitoring and early intervention for renal function decline, even before eGFR drops below 60 mL/min/1.73 m^2, especially among STEMI patients.

The strong causal association between decreased eGFR and adverse outcomes in STEMI patients may involve multiple pathophysiological pathways, with inflammation potentially playing a significant role. Studies have shown that impaired renal function contributes to systemic inflammation, oxidative stress, dysregulation of neurohormonal systems, and endothelial dysfunction, all of which can exacerbate cardiac injury, impair myocardial function, and increase the susceptibility to adverse cardiovascular events[3,7,29,30]. Inflammation plays a critical role in the crosstalk along the cardio-renal axis. On the one hand, CKD is recognized as a systemic inflammatory condition with multiple underlying causes[29]. Systemic inflammation tends to increase progressively as kidney function deteriorates. Proinflammatory factors in CKD include reduced cytokine clearance, infections, oxidative stress, accumulation of advanced glycation end-products and toxins absorbed in the gut, sodium overload, metabolic acidosis, insulin resistance, among others[29]. Moreover, increased sympathetic activity and autonomic imbalance in CKD can further trigger and modulate inflammation through pathways involving cytokines like interferon-γ, IL-6 and IL-10, exacerbating the overall inflammatory burden[31]. Our findings further confirm that renal insufficiency is associated with elevated inflammatory status at initial admission. On the other hand, inflammation plays a crucial role in cardiac repair and remodeling in patients with STEMI. Proinflammatory cytokines that drive inflammatory cascades are closely associated with endothelial function and clot formation[32,33]. While active suppression and resolution of inflammation mediate subsequent scar formation and cardiac repair, disproportionately prolonged and excessive inflammatory response can lead to improper wound healing, infarct expansion, adverse post-infarction remodeling, and ultimately heart failure[11,34,35].

In addition, we explored the interaction between eGFR and NLR with the 1-year mortality following STEMI. Contrary to our initial hypothesis, our results indicate no significant synergy effect between eGFR and NLR on mortality risk, though both factors independently contribute to adverse outcomes following STEIMI[27,36–38]. This finding adds complexity to our understanding of how eGFR and inflammation interact to influence all-cause mortality. One possible reason for the absence of a pronounced synergy effect is that renal insufficiency may affect the prognosis of STEMI primarily through pathways of inflammation.

Although no synergistic interaction was observed between eGFR and NLR, we identified a mediating effect of admission inflammatory status on the association between eGFR and 1-year all-cause mortality, illuminating the potential role of inflammation in linking renal insufficiency to adverse outcomes. Notably, even mild renal impairment affects STEMI prognosis through pro-inflammatory mechanisms. While the magnitude of this mediating effect was modest (1.7% and 4.5% for eGFR 60–89 mL/min/1.73m^2 and < 60 mL/min/1.73m^2, respectively), it suggests the intricate pathophysiological mechanisms underlying the relationship between renal function and adverse outcomes following STEMI.

Another notable finding is that incorporating both eGFR and NLR into the predictive model may improve predictive performance for 1-year mortality following STEMI compared with a model with clinical risk factors alone. This suggests that eGFR and NLR can provide a convenient tool for risk stratification in patients with STEMI, helping clinicians identify high-risk individuals who may benefit from targeted interventions and closer follow-up care. While close monitoring of kidney function is feasible, there are currently few anti-inflammatory therapies specifically clinically effective for myocardial infarction. Although several anti-inflammatory agents (e.g., canakinumab, pexelizumab) have been tested, they failed to conclusively confer a prognostic benefit in patients with acute myocardial infarction[13,39–41]. Further work is required to establish the viability of selective therapies targeting inflammatory response in acute myocardial infarction to mitigate the post-infarction complications. Overall, early identification and management of renal insufficiency, along with the development of potent anti-inflammatory agents, may help mitigate adverse effects and improve clinical outcomes in patients with STEMI.

There are some limitations that need to be addressed. Firstly, due to the nature of the retrospective study, it is subject to inherent biases and unmeasured confounding factors that could influence the observed associations. Secondly, the generalizability of our findings may be limited to Chinese population and the specific clinical setting in which the study was conducted. Further research involving diverse populations is warranted to validate our findings. Thirdly, the clinical predictive model developed in this study has not yet been evaluated by external validation though it showed a moderate-to-good accuracy (C-index 0.799). Fourth, circulating inflammatory markers reflecting the status of inflammatory processes, such as hs-CRP, procalcitonin, and interleukin family, were not measured in our study. Besides, we did not collect the urinary albumin-creatinine ratio and cannot simultaneously assess the two markers of kidney function to enhance the robustness of the results. Fifth, a second

measurement of inflammatory and renal function indicators 24 h after admission would have strengthened the reliability of the conclusions. Future prospective studies are needed to elucidate the underlying mechanisms and confirm the generalizability of our findings.

Overall, this study reveals that even mild renal insufficiency is consistently associated with an elevated admission inflammatory response and increased 1-year mortality following STEMI. Additionally, inflammatory status mediates a small but significant proportion of the association between renal insufficiency and 1-year mortality following STEMI. Incorporating both eGFR and NLR at admission into a predictive model with clinical risk factors significantly improves the predictability for risk of 1-year death following STEMI. Thus, it can help identify high-risk patients who may benefit from intensive kidney function monitoring and early adjuvant intervention after primary PCI. Moreover, the findings suggest potential benefits in developing targeted anti-inflammatory therapies for STEMI patients with renal insufficiency.

Data availability

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

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References

1. US Renal Data System. Annual Data Report. Accessed March 19, 2024. https://usrds-adr.niddk.nih.gov/2023/chronic-kidney-disease (2023).
2. Eckardt, K. U. et al. Evolving importance of kidney disease: from subspecialty to global health burden. *Lancet* **382** (9887), 158–169. https://doi.org/10.1016/S0140-6736(13)60439-0 (2013).
3. Jankowski, J., Floege, J., Fliser, D., Böhm, M. & Marx, N. Cardiovascular disease in chronic kidney disease: pathophysiological insights and therapeutic options. *Circulation* **143** (11), 1157–1172. https://doi.org/10.1161/CIRCULATIONAHA.120.050686 (2021).
4. Matsushita, K. et al. Epidemiology and risk of cardiovascular disease in populations with chronic kidney disease. *Nat. Rev. Nephrol.* **18** (11), 696–707. https://doi.org/10.1038/s41581-022-00616-6 (2022).
5. Lai, A. C. et al. A personalized approach to chronic kidney disease and cardiovascular disease: JACC review topic of the week. *J. Am. Coll. Cardiol.* **77** (11), 1470–1479. https://doi.org/10.1016/j.jacc.2021.01.028 (2021).
6. Association of estimated glomerular filtration rate. And albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* **375** (9731), 2073–2081. https://doi.org/10.1016/S0140-6736(10)60674-5 (2010).
7. Gansevoort, R. T. et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet* **382** (9889), 339–352. https://doi.org/10.1016/S0140-6736(13)60595-4 (2013).
8. K L, W. D Immunity and inflammation in atherosclerosis. *Circ. Res.* **124** (2). https://doi.org/10.1161/CIRCRESAHA.118.313591 (2019).
9. Kobiyama, K., Ley, K. & Atherosclerosis *Circ. Res.* ;**123**(10):1118–1120. https://doi.org/10.1161/CIRCRESAHA.118.313816 (2018).
10. Weber, C. & Noels, H. Atherosclerosis: current pathogenesis and therapeutic options. *Nat. Med.* **17** (11), 1410–1422. https://doi.org/10.1038/nm.2538 (2011).
11. Westman, P. C. et al. Inflammation as a driver of adverse left ventricular remodeling after acute myocardial infarction. *J. Am. Coll. Cardiol.* **67** (17), 2050–2060. https://doi.org/10.1016/j.jacc.2016.01.073 (2016).
12. Seropian, I. M., Sonnino, C., Van Tassell, B. W., Biasucci, L. M. & Abbate, A. Inflammatory markers in ST-elevation acute myocardial infarction. *Eur. Heart J. Acute Cardiovasc. Care.* **5** (4), 382–395. https://doi.org/10.1177/2048872615568965 (2016).
13. Seropian, I. M., Toldo, S., Van Tassell, B. W. & Abbate, A. Anti-inflammatory strategies for ventricular remodeling following ST-segment elevation acute myocardial infarction. *J. Am. Coll. Cardiol.* **63** (16), 1593–1603. https://doi.org/10.1016/j.jacc.2014.01.014 (2014).
14. Paolisso, P. et al. Hyperglycemia, inflammatory response and infarct size in obstructive acute myocardial infarction and MINOCA. *Cardiovasc. Diabetol.* **20** (1), 33. https://doi.org/10.1186/s12933-021-01222-9 (2021).
15. Chronic Kidney Disease Prognosis Consortium et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet Lond. Engl.* **375** (9731), 2073–2081. https://doi.org/10.1016/S0140-6736(10)60674-5 (2010).
16. Zoccali, C. et al. Cardiovascular complications in chronic kidney disease: a review from the European renal and cardiovascular medicine working group of the European renal association. *Cardiovasc. Res.* **119** (11), 2017–2032. https://doi.org/10.1093/cvr/cvad083 (2023).
17. Schunk, S. J. et al. Interleukin-1α is a central regulator of Leukocyte-Endothelial adhesion in myocardial infarction and in chronic kidney disease. *Circulation* **144** (11), 893–908. https://doi.org/10.1161/CIRCULATIONAHA.121.053547 (2021).
18. Batra, G. et al. Interleukin 6 and cardiovascular outcomes in patients with chronic kidney disease and chronic coronary syndrome. *JAMA Cardiol.* **6** (12), 1440–1445. https://doi.org/10.1001/jamacardio.2021.3079 (2021).
19. J L, X Q, X Z, et al. Prognostic implications of systemic immune-inflammation index in myocardial infarction patients with and without diabetes: insights from the NOAFCAMI-SH registry. *Cardiovasc. Diabetol.* ;**23**(1). (2024). https://doi.org/10.1186/s12933-024-02129-x
20. Kufazvinei, T. T. J., Chai, J., Boden, K. A., Channon, K. M. & Choudhury, R. P. Emerging opportunities to target inflammation: myocardial infarction and type 2 diabetes. *Cardiovasc. Res.* **120** (11), 1241–1252. https://doi.org/10.1093/cvr/cvae142 (2024).
21. Thygesen, K. et al. Fourth universal definition of myocardial infarction (2018). *Circulation* **138** (20), e618–e651. https://doi.org/10.1161/CIR.0000000000000617 (2018).
22. Inker, L. A. et al. New Creatinine- and Cystatin C-Based equations to estimate GFR without race. *N Engl. J. Med.* **385** (19), 1737–1749. https://doi.org/10.1056/NEJMoa2102953 (2021).
23. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int.* **102** (5S), S1–S127. https://doi.org/10.1016/j.kint.2022.06.008 (2022).
24. Thiele, H. et al. PCI strategies in patients with acute myocardial infarction and cardiogenic shock. *N Engl. J. Med.* **377** (25), 2419–2432. https://doi.org/10.1056/NEJMoa1710261 (2017).
25. Gaba, P., Gersh, B. J., Ali, Z. A., Moses, J. W. & Stone, G. W. Complete versus incomplete coronary revascularization: definitions, assessment and outcomes. *Nat. Rev. Cardiol.* **18** (3), 155–168. https://doi.org/10.1038/s41569-020-00457-5 (2021).
26. Writing Group for the CKD Prognosis Consortium et al. Estimated glomerular filtration rate, albuminuria, and adverse outcomes: an Individual-Participant data Meta-Analysis. *JAMA* **330** (13), 1266–1277. https://doi.org/10.1001/jama.2023.17002 (2023).

27. Anavekar, N. S. et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl. J. Med.* **351** (13), 1285–1295. https://doi.org/10.1056/NEJMoa041365 (2004).
28. Hussain, J. et al. Associations between modest reductions in kidney function and adverse outcomes in young adults: retrospective, population based cohort study. *BMJ* **381**, e075062. https://doi.org/10.1136/bmj-2023-075062 (2023).
29. Zoccali, C. et al. The systemic nature of CKD. *Nat. Rev. Nephrol.* **13** (6), 344–358. https://doi.org/10.1038/nrneph.2017.52 (2017).
30. Izumaru, K. et al. Reduced estimated GFR and cardiac remodeling: A Population-Based autopsy study. *Am. J. Kidney Dis.* **74** (3), 373–381. https://doi.org/10.1053/j.ajkd.2019.02.013 (2019).
31. Levick, S. P., Murray, D. B., Janicki, J. S. & Brower, G. L. Sympathetic nervous system modulation of inflammation and remodeling in the hypertensive heart. *Hypertens. Dallas Tex. 1979.* **55** (2), 270–276. https://doi.org/10.1161/HYPERTENSIONAHA.109.142042 (2010).
32. Kalinskaya, A. et al. Circulating cytokines in myocardial infarction are associated with coronary blood flow. *Front. Immunol.* **13** https://doi.org/10.3389/fimmu.2022.837642 (2022).
33. Kaptoge, S. et al. Inflammatory cytokines and risk of coronary heart disease: new prospective study and updated meta-analysis. *Eur. Heart J.* **35** (9), 578–589. https://doi.org/10.1093/eurheartj/eht367 (2014).
34. Prabhu, S. D. & Frangogiannis, N. G. The biological basis for cardiac repair after myocardial infarction: from inflammation to fibrosis. *Circ. Res.* **119** (1), 91–112. https://doi.org/10.1161/CIRCRESAHA.116.303577 (2016).
35. Frangogiannis, N. G. The inflammatory response in myocardial injury, repair, and remodelling. *Nat. Rev. Cardiol.* **11** (5), 255–265. https://doi.org/10.1038/nrcardio.2014.28 (2014).
36. He, J. et al. High neutrophil to lymphocyte ratio with type 2 diabetes mellitus predicts poor prognosis in patients undergoing percutaneous coronary intervention: a large-scale cohort study. *Cardiovasc. Diabetol.* **21** (1), 156. https://doi.org/10.1186/s12933-022-01583-9 (2022).
37. Suzuki, M. et al. Critical role of systemic inflammation in patients with ST-segment elevation myocardial infarction complicated with renal dysfunction. *Int. J. Cardiol.* **168** (3), 3062–3064. https://doi.org/10.1016/j.ijcard.2013.04.095 (2013).
38. van Diepen, S. et al. The systemic inflammatory response syndrome in patients with ST-Segment elevation myocardial infarction. *Crit. Care Med.* **41** (9), 2080–2087. https://doi.org/10.1097/CCM.0b013e31828a67b2 (2013).
39. Mewton, N. et al. Effect of Colchicine on myocardial injury in acute myocardial infarction. *Circulation* **144** (11), 859–869. https://doi.org/10.1161/CIRCULATIONAHA.121.056177 (2021).
40. Aimo, A. et al. Colchicine for the treatment of coronary artery disease. *Trends Cardiovasc. Med.* **31** (8), 497–504. https://doi.org/10.1016/j.tcm.2020.10.007 (2021).
41. Rymer, J. A. & Newby, L. K. Failure to launch: targeting inflammation in acute coronary syndromes. *JACC Basic. Transl Sci.* **2** (4), 484–497. https://doi.org/10.1016/j.jacbts.2017.07.001 (2017).

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Declarations

Competing interests

The authors declare no competing interests.

Ethics declarations

The CSPR trial was conducted in accordance with the Declaration of Helsinki and was approved by all institutional ethics and review committees.

Additional information

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