Am J Transl Res 2025;17(6):4754-4763
www.ajtr.org /ISSN:1943-8141/AJTR0164278

Original Article

Early initiation of sacubitril/valsartan in STEMI patients improves ventricular remodeling

Hongyuan Wang*, Yanping Wang*, Xinjun Zhang*, Qiuxian Liu, Kun Zhang

*Department of Cardiology, Jiangshan People's Hospital, Quzhou 450001, Zhejiang, China. *Equal contributors and co-first authors.*

Received March 2, 2025; Accepted May 20, 2025; Epub June 15, 2025; Published June 30, 2025

Abstract: Objective: To explore the effect of early administration (within 24 hours) of sacubitril/valsartan (Entresto) on left ventricular remodeling and prognosis in patients with ST-elevation myocardial infarction (STEMI). Methods: A retrospective study was conducted involving 150 STEMI patients diagnosed at Jiangshan People's Hospital between September 2021 and August 2023. Among them, 70 patients who received sacubitril/valsartan treatment were assigned as the observation group, and 80 patients treated with valsartan formed the control group. The echocardiographic parameters and biomarkers of cardiac injury were assessed in both groups. Results: The observation group exhibited improved left ventricular ejection fraction and reduced left atrial and ventricular diameters, along with a significant rise in stroke volume and reductions in left ventricular end-systolic and end-diastolic volumes. Cardiac injury biomarkers, including B-type natriuretic peptide and Troponin, significantly decreased in the observation group, while minimal changes were observed in the control group. Inflammatory markers, such as C-reactive protein, procalcitonin, and white blood cell count, were significantly reduced in the observation group. These findings underscore the efficacy of early sacubitril/valsartan treatment in improving outcomes for STEMI patients through enhanced ventricular function and reduced biomarkers of injury and inflammation. Conclusion: Early initiation of sacubitril/valsartan in STEMI patients significantly improves ventricular remodeling, as evidenced by enhanced echocardiographic parameters and reduced biomarkers, without increasing adverse events or compromising renal function.

Keywords: STEMI, sacubitril/valsartan, Entresto, ventricular remodeling, early treatment

Introduction

ST-elevation myocardial infarction (STEMI) remains one of the most common and life-threatening manifestations of coronary artery disease, contributing significantly to global morbidity and mortality [1]. Despite advances in early reperfusion strategies, such as primary percutaneous coronary intervention, STEMI patients still experience persistent left ventricular dysfunction, which can progress to heart failure, a major determinant of long-term prognosis. Ventricular remodeling (VR) following an acute myocardial infarction (MI) is associated with adverse clinical outcomes, including an increased risk of heart failure, arrhythmias, and mortality [2]. Thus, preventing or mitigating VR has become a critical therapeutic target in improving outcomes for STEMI patients.

The pathophysiology of VR in STEMI involves a complex interplay of cellular and molecular processes, including inflammation, fibrosis, and myocyte loss. Over time, these processes lead to dilatation and dysfunction of the left ventricle, ultimately resulting in heart failure [3-5]. While current standard therapies for STEMI, including reperfusion therapy, antiplatelet agents, and renin-angiotensin-aldosterone system inhibitors, have demonstrated some benefit in reducing the incidence of VR [6], these interventions are not sufficient to fully prevent or reverse the deleterious effects of VR. As a result, novel therapeutic approaches are urgently needed to target VR and improve the long-term prognosis in STEMI patients.

Sacubitril/valsartan, a combination of an angiotensin receptor blocker and a neprilysin inhibi-

https://doi.org/10.62347/NUKJ1589

tor, has emerged as a promising therapeutic agent for heart failure management [7]. The benefits of sacubitril/valsartan, marketed under the brand name Entresto, have been demonstrated in large-scale clinical trials, notably the PARADIGM-HF study, which established its superiority over traditional ACE inhibitors in reducing the risk of hospitalization and death in patients with heart failure [8]. The beneficial effects of sacubitril/valsartan are primarily attributed to its dual action of blocking the RAAS and enhancing the natriuretic peptide system, which improves hemodynamics, reduces fibrosis, and promotes myocardial healing. While sacubitril/valsartan has proven effective in chronic heart failure, its role in the acute phase of STEMI remains incompletely understood. The early initiation of sacubitril/valsartan during the acute phase of STEMI may represent a novel therapeutic strategy to mitigate VR before it becomes irreversible. Recent studies suggest that early initiation of sacubitril/valsartan might attenuate myocardial injury, reduce infarct size, and improve cardiac remodeling in the context of acute MI [9-11]. However, evidence regarding the timing, dosing, and overall effect of this therapy in the context of STEMI remains limited.

Therefore, this study compares the effects of early administration (within 24 hours of onset) of sacubitril/valsartan versus valsartan alone in STEMI patients. By evaluating changes in key indicators such as left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDd), and B-type natriuretic peptide (BNP) before and after treatment, the study aims to assess the clinical efficacy of sacubitril/valsartan in improving VR in the early treatment of STEMI patients.

Methods

Case selection

A retrospective study was conducted involving 150 STEMI patients diagnosed at Jiangshan People's Hospital between September 2021 and August 2023. Among them, 70 patients who received sacubitril/valsartan treatment were assigned to the observation group, while the remaining 80 patients who received valsartan treatment were included in the control group. The study protocol was approved by the Ethics Committee of Jiangshan People's Hospital.

All enrolled patients met the following inclusion criteria: they had a confirmed clinical diagnosis of STEMI according to established diagnostic criteria [12], possessed complete clinical records, and were able to attend regular follow-up visits; all participants were aged over 18 years. Patients were excluded from the study if they had contraindications to angiotensin II receptor blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor-neprilysin inhibitors, such as hypersensitivity or prior adverse reactions to angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or angiotensin receptor-neprilysin inhibitors. Other exclusion criteria included severe renal impairment defined as an estimated glomerular filtration rate (eGFR) below 30 mL/min/1.73m^2 or bilateral renal artery stenosis, pregnancy or lactation, and the presence of heart failure, severe renal dysfunction, autoimmune diseases, primary lung lesions, lung tumors, severe anemia, or blood diseases. Furthermore, patients with incomplete baseline data, unreliable medical histories, refusal to participate, or inability to complete follow-up were excluded.

Interventions

All participants in both the observation and control groups received standard pharmacologic treatment in line with the latest STEMI management guidelines, which included β-blockers, aspirin, statins, and other recommended medications. These treatments were initiated immediately after hospital admission to manage myocardial injury and prevent further complications. Patients in the observation group administered sacubitril/valsartan (Entresto), a combination of a neprilysin inhibitor and angiotensin receptor blocker, manufactured by Novartis (Product code: 063280). Treatment with sacubitril/valsartan was initiated within 24 hours of STEMI onset, with an initial dose of 24/26 mg twice daily (i.e., 24 mg of sacubitril and 26 mg of valsartan). The dose was progressively increased every 2 to 4 weeks based on the individual patient's tolerance, doubling the dose at each interval until the target dose of 97/103 mg twice daily (97 mg of sacubitril and 103 mg of valsartan) was reached or the maximum tolerated dose was attained. This intervention was maintained for a total duration of 12 months.

The control group, in contrast, received valsartan (Diovan), an angiotensin receptor blocker also manufactured by Novartis (Product code: 083182), following the same dosing regimen. The initial dose of valsartan was 40 mg twice daily, and the dose was similarly titrated every 2 to 4 weeks based on tolerance, ultimately reaching a maximum dose of 160 mg twice daily. Treatment in the control group continued for 12 months, mirroring the duration of the observation group's treatment.

Data collection and outcome measurement

After completing routine examinations, all enrolled patients were given standard pharmacologic treatment according to the STEMI treatment guidelines, including β-blockers, aspirin, statins, and other medications. On this basis, the observation group received an early (within 24 hours of onset) initial dose of Entresto, with the dose doubled every 2-4 weeks based on the patient's tolerance, until the target dose or maximum tolerated dose was reached. Similarly, the control group received valsartan alone (within 24 hours of onset), starting at an initial dose of valsartan. The dose was doubled every 2-4 weeks based on the patient's tolerance, until the target dose or maximum tolerated dose was reached, and continued treatment for 12 months. The intraoperative bleeding percentage and other related indicators were measured by the surgical team during the procedures. Specifically, intraoperative blood loss was quantified by recording both the volume of suctioned blood and the amount absorbed by surgical sponges. The bleeding percentage was then calculated as the ratio of total blood loss to the estimated total blood volume, which was adjusted based on body weight and relevant clinical factors. This percentage was used as an indicator of intraoperative bleeding for this study. The same procedure was followed for other blood loss-related indicators in this study.

The outcome measures in this study were designed to assess the efficacy and safety of sacubitril/valsartan treatment in STEMI patients. The primary outcomes included echocardiographic parameters (LVEF, left atrial diameter [LAd], LVEDd, right ventricular diameter [RVd], interventricular septal thickness [IVST], stroke volume [SV], cardiac output, left ventricular end-systolic volume [LVESV], and left ventricular end-diastolic volume [LVEDV]) and biomarkers of cardiac injury (BNP and troponin), all of which were assessed before and after the intervention. Secondary outcomes were used to assess renal function indicators (serum creatinine, estimated eGFR, uric acid [UA], and blood urea nitrogen [BUN]); inflammatory markers (C-reactive protein [CRP], procalcitonin [PCT], and white blood cell count [WBC]); blood lipid profiles (cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein); coagulation parameters (prothrombin time [PT], international normalized ratio [INR], activated partial thromboplastin time [APTT], and thrombin time [TT]); and the incidence of adverse events (hypotension, dizziness, and gastrointestinal discomfort). These measures were selected to provide a comprehensive evaluation of the treatment's effects on inflammation, cardiac and renal function, and overall safety.

Statistical analysis

Statistical analysis was performed using SPSS 25.0 software. For continuous variables, those with a normal distribution were expressed as mean ± standard deviation (X ± SD). Comparisons between two groups were performed using independent sample t-tests. For variables that did not follow a normal distribution, data were expressed as the median (M), 25th percentile (P25), and 75th percentile (P75), and comparisons were conducted using the Mann-Whitney U test or the Wilcoxon rank-sum test, as appropriate. For categorical variables, percentages (%) were used, and intergroup comparisons were made using the chi-square test or Fisher's exact test when applicable. For multiple group comparisons, one-way analysis of variance (ANOVA) was employed, followed by a Tukey's honestly significant difference (HSD) post hoc test to identify pairwise differences between specific groups. In cases where repeated measurements were taken from the same subjects, repeated measures ANOVA was applied to assess changes over time. In experiments involving more than two variables, a two-way ANOVA was used to evaluate interaction effects between factors. A P-value < 0.05 was considered significant. All statistical analyses were reviewed and verified by a statistician specializing in clinical research to ensure the accuracy and appropriateness of the methods.

Table 1. Comparison of general characteristics

Item	Control group (n = 80)	Observation group(n = 70)	χ^2/t	p
Female	20 (25.00%)	22 (31.43%)	0.765	0.382
Hypertension	48 (60.00%)	46 (65.71%)	0.521	0.470
Diabetes	24 (30.00%)	23 (32.86%)	0.142	0.707
Chronic kidney disease	14 (17.50%)	11 (15.71%)	0.086	0.770
Smoking	43 (53.75%)	34 (48.57%)	0.401	0.527
Drinking	38 (47.50%)	30 (42.86%)	0.325	0.569
Age	62.59 ± 4.04	61.24 ± 6.28	1.578	0.117
Hospitalization time (days)	12.41 ± 2.02	12.87 ± 2.44	1.261	0.209
Heart rate (bpm)	75.26 ± 6.30	75.76 ± 5.41	0.512	0.609
BMI (kg/m^2)	26.46 ± 2.51	26.81 ± 2.71	0.803	0.423
Atrial fibrillation	8 (10.00%)	6 (8.57%)	0.090	0.764
Stroke	5 (6.25%)	4 (5.71%)	0.019	0.890
Killip classification			0.087	0.993
Killip I	60 (75.00%)	52 (74.29%)		
Killip II	12 (15.00%)	10 (14.29%)		
Killip III	6 (7.50%)	6 (8.57%)		
Killip IV	2 (2.50%)	2 (2.86%)		

Note: BMI: body mass index.

Results

Comparison of general characteristics

No significant differences were found between the two groups in terms of gender distribution, presence of hypertension, diabetes, or chronic kidney disease, or in smoking and alcohol consumption habits (all $P > 0.05$). The mean age was comparable in both groups (with an average of 63 years), and there were no significant differences in the duration of hospitalization, heart rate, or body mass index (BMI). Additionally, the prevalence of atrial fibrillation and prior stroke history was similar between groups. Regarding the Killip classification, most patients were in Killip I, and no significant intergroup differences were found (**Table 1**). These results suggest that the baseline characteristics were well balanced between the observation and control groups, supporting a valid comparison of the effects of sacubitril/valsartan treatment.

Comparison of echocardiogram measurements

The observation group demonstrated significant improvements in echocardiographic parameters following treatment. LVEF increased from 48.8% to 57.4% ($P < 0.001$). LAd decreased from 41.6 mm to 38.2 mm, although this change was not statistically significant ($P = 0.345$). LVEDd significantly reduced from 56.0 mm to 48.2 mm ($P < 0.001$). RVd also showed a significant reduction, decreasing from 36.6 mm to 32.1 mm ($P < 0.001$). IVST slightly reduced from 9.95 mm to 9.89 mm, not a statistically significant change ($P = 0.987$). In addition, SV increased from 66.1 mL to 70.3 mL ($P < 0.001$). Both LVESV and LVEDV were significantly reduced, decreasing from 44.7 mL to 39.9 mL ($P < 0.001$) and from 47.5 mL to 41.2 mL ($P < 0.001$), respectively. In contrast, the control group exhibited minimal changes across all parameters. LVEF remained nearly unchanged at 47.4%, with no significant improvement observed ($P > 0.05$). Similarly, no notable changes were found in LAd or LVEDd ($P > 0.05$) (**Table 2**). These findings suggest that early sacubitril/valsartan treatment significantly improved ventricular function and remodeling in the observation group.

Comparison of renal function

Figure 1 illustrates the changes in renal function data in the control and observation groups before and after the intervention. Serum creatinine levels decreased in both groups, but no significant difference was observed between the two groups ($P > 0.05$). Similarly, eGFR showed improvement in both groups without a significant difference ($P > 0.05$). UA levels were

Table 2. Comparison of echocardiogram measurements

Index		Observation group (n = 70)	Control group (n = 80)	p
LVEF (%)	Before intervention	48.80 ± 3.13	48.80 ± 3.34	0.994
	After intervention	57.42 ± 3.35	47.44 ± 3.4	< 0.001
LAd (mm)	Before intervention	41.55 ± 3.32	42.29 ± 4.07	0.226
	After intervention	38.17 ± 3.45	38.69 ± 3.28	0.345
LVEDd (mm)	Before intervention	56.00 ± 3.76	55.92 ± 3.80	0.893
	After intervention	48.21 ± 3.00	54.44 ± 3.71	< 0.001
RVd (mm)	Before intervention	36.57 ± 2.50	37.17 ± 2.88	0.177
	After intervention	32.14 ± 2.98	35.77 ± 2.69	< 0.001
IVST (mm)	Before intervention	9.95± 1.05	10.28 ± 1.01	0.053
	After intervention	9.89 ± 0.90	9.90 ± 0.97	0.987
SV (ml)	Before intervention	66.08 ± 6.42	68.36 ± 8.11	0.061
	After intervention	70.32 ± 7.93	65.13 ± 6.74	< 0.001
CO (l/min)	Before intervention	4.27 ± 0.46	4.29 ± 0.47	0.714
	After intervention	4.20 ± 0.51	4.22 ± 0.52	0.823
LVESV (mm)	Before intervention	44.68 ± 4.20	46.00 ± 5.17	0.094
	After intervention	39.94 ± 4.67	44.01 ± 4.53	< 0.001
LVEDV (mm)	Before intervention	47.46 ± 4.10	46.54 ± 4.11	0.175
	After intervention	41.20 ± 3.89	47.02 ± 4.05	< 0.001

Note: LVEF (%): Left Ventricular Ejection Fraction; LAd (mm): Left Atrial Diameter; LVEDd (mm): Left Ventricular End-Diastolic Diameter; RVd (mm): Right Ventricular Diameter; IVST (mm): Interventricular Septal Thickness; SV (ml): Stroke Volume; CO (l/min): Cardiac Output; LVESV (mm): Left Ventricular End-Systolic Volume; LVEDV (mm): Left Ventricular End-Diastolic Volume.

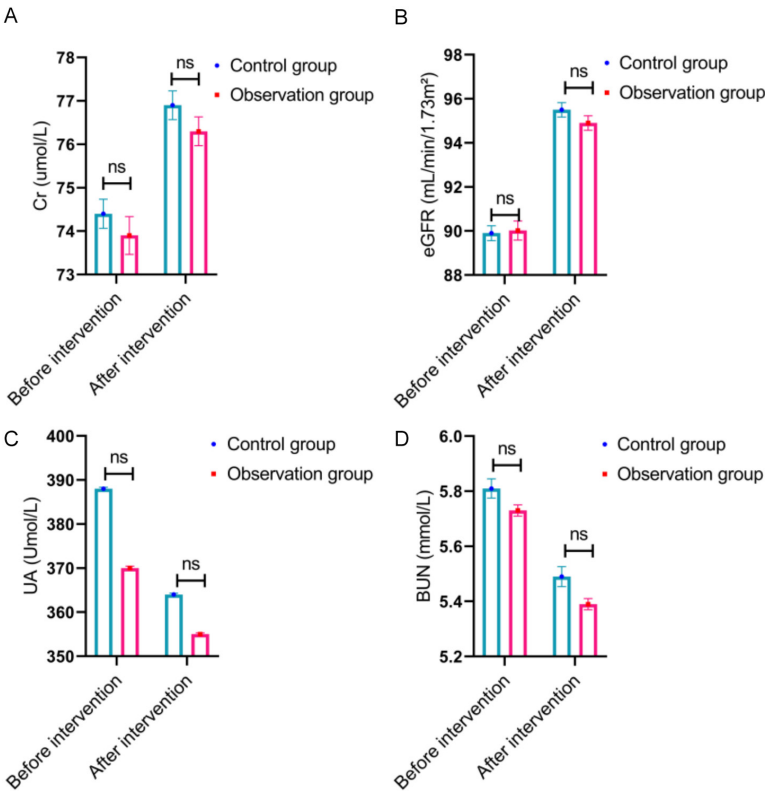

Figure 1. Comparison of renal function between two groups. A: Cr; B: eGFR; C: UA; D: BUN. Note: Cr: Creatinine; eGFR: Estimated Glomerular Filtration Rate; UA: Uric Acid; BUN: Blood Urea Nitrogen. ns, no significance.

reduced in both groups, with a slightly greater, but non-significant decrease noted in the control group ($P > 0.05$). BUN levels also declined in both groups, with no significant difference ($P > 0.05$). Overall, these findings indicate that both treatments had comparable effects on renal function over the 12-month treatment period.

Comparison of blood lipid indicators

Table 3 presents a comparison of blood lipid indicators between the observation and control groups. No statistically significant differences were observed in cholesterol, triglycerides, high-density lipoprotein, or low-density lipoprotein levels between the two groups ($P > 0.05$). These findings suggest that neither sacubitril/valsartan nor valsartan had a substantial effect

Table 3. Comparison of blood lipid indicators

	Observation group (n = 70)	Control group (n = 80)	t	*P*
CHO	3.82 ± 1.02	4.05 ± 0.56	1.743	0.083
TG	1.20 ± 0.69	1.35 ± 0.29	1.761	0.080
HDL	1.84 ± 0.32	1.79 ± 0.12	1.429	0.155
LDL	2.26 ± 0.42	2.35 ± 0.38	0.124	0.902

Note: CHO: cholesterol; TG: triglyceride; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Table 4. Comparison of coagulation-related indicator levels

	Observation group (n = 70)	Control group (n = 80)	t	*P*
PT	11.09 ± 1.49	10.33 ± 4.22	1.413	0.160
INR	1.19 ± 0.48	1.10 ± 0.06	1.614	0.109
APTT	28.20 ± 4.11	28.13 ± 3.72	0.108	0.914
TT	17.37 ± 1.50	17.64 ± 1.47	1.136	0.258

Note: PT: Prothrombin Time; INR: International Normalized Ratio; APTT: Activated Partial Thromboplastin Time; TT: Thrombin Time.

on the lipid profiles of the participants in the groups.

Comparison of coagulation-related indicator level

Table 4 summarizes the coagulation profiles of both groups following the intervention. No significant differences were found in PT, INR, APTT, or TT between the two groups (all $P > 0.05$). These results suggest that neither treatment regimen significantly altered coagulation values, indicating that the intervention did not interfere with the coagulation profiles in the studied population.

Comparison of adverse events

The incidence of adverse events during the 12-month follow-up period was comparable between the two groups. In the control group, 12.5% of patients experienced hypotension, 8.8% reported dizziness, and 7.5% developed gastrointestinal discomfort. In the observation group, the corresponding rates were 11.4% for hypotension, 8.6% for dizziness, and 7.1% for gastrointestinal discomfort. The overall incidence of adverse events did not differ significantly between groups ($P = 0.721$). None of these differences were statistically significant (all $P > 0.05$; see **Table 5**), indicating that adverse event rates in the groups were similar.

Comparison of biomarkers (BNP, Troponin)

Table 6 presents the comparison of BNP and Troponin levels between the observation and control groups. In the observation group, BNP levels decreased significantly after the intervention ($P < 0.001$), whereas no significant change was observed in the control group. Troponin levels also significantly decreased in the observation group ($P < 0.001$) after treatment, but no significant change was observed in the control group. These findings indicate that the treatment was associated with a significant reduction in BNP and Troponin levels.

Comparison of inflammatory markers

For CRP (panel A), a significant reduction was observed after intervention in the observation group (pink bar), but no significant change was noted in the control group (blue bar) ($P < 0.001$). PCT (panel B), both groups showed significant decreases after intervention ($P < 0.001$ for the observation group), but no significant difference was found between groups at either time point. As for WBC count (panel C), a significant decline in the observation group was seen after the intervention ($P < 0.001$), whereas the control group did not demonstrate a significant change (**Figure 2**). Overall, the observation group experienced a more pronounced improvement in inflammatory markers compared to the control group after the intervention.

Discussion

The early initiation of sacubitril/valsartan (Entresto) treatment in STEMI patients has shown promising results in improving ventricular remodeling (VR) and clinical outcomes. Our study found that this intervention led to significant improvements in echocardiographic parameters, inflammatory markers, and biomarkers of cardiac injury. These findings support the growing body of evidence suggesting the beneficial effects of sacubitril/valsartan in heart failure and acute myocardial infarction (MI). This section will discuss the study results in detail, integrating the findings with the existing literature, exploring potential mechanisms, and providing insight into the therapeutic implications for STEMI patients.

Table 5. Comparison of adverse events

Event Type	Control Group (%)	Observation Group (%)	X^2	*P*-Value
Hypotension	12.5	11.4	0.189	0.663
Dizziness	8.8	8.6	0.002	0.969
Gastrointestinal Discomfort	7.5	7.1	0.072	0.788
Total incidence	28.8	27.1	0.128	0.721

Table 6. Comparison of biomarkers (BNP, Troponin)

Group		Observation group (n = 70)	Control group (n = 80)	p
BNP (pg/mL)	Before intervention	663.17 ± 85.61	650.49 ± 76.24	0.839
	After intervention	491.00 ± 69.26	584.41 ± 72.94	< 0.001
Troponin (ng/mL)	Before intervention	0.14 ± 0.01	0.14 ± 0.03	0.080
	After intervention	0.05 ± 0.01	0.10 ± 0.02	< 0.001

Note: BNP: B-type Natriuretic Peptide.

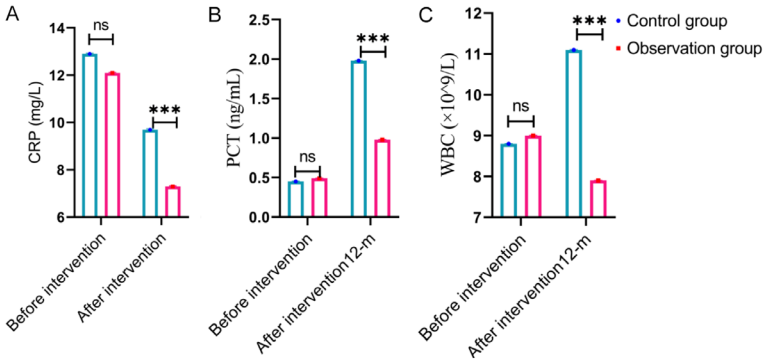

Figure 2. Comparison of inflammatory markers. A: CRP; B: PCT; C: WBC. Note: CRP: C-reactive protein; PCT: Procalcitonin; WBC: White blood cell count. ***P < 0.001.

The most striking finding from our study was the significant improvement in several echocardiographic parameters in the Observation group following early Sacubitril/Valsartan treatment. Specifically, the treatment led to a marked increase in LVEF and significant reductions in LAd and LVEDd. These changes are consistent with previous studies demonstrating that Sacubitril/Valsartan, a combination of an angiotensin receptor neprilysin inhibitor, exerts a beneficial effect on ventricular function and remodeling, particularly in patients with heart failure or acute coronary syndromes [13, 14]. The improvements observed in the current study suggest that Sacubitril/Valsartan may help attenuate adverse remodeling post-MI, which is a major determinant of long-term outcomes in STEMI patients. This effect can be attributed to the dual action of Sacubitril/Valsartan on the renin-angiotensin-aldosterone system and neprilysin inhibition. By blocking angiotensin II receptors and promoting the degradation of harmful neurohormones like angiotensin II, endothelin, and vasopressin, Sacubitril/Valsartan leads to reduced myocardial stress and improved myocardial relaxation [15]. Furthermore, neprilysin inhibition increases the levels of beneficial natriuretic peptides, which promote vasodilation, natriuresis, and anti-fibrotic effects, all contributing to better VR and function [15]. Our study also showed that the RVd and IVST were reduced significantly in the observation group. Right ventricular dysfunction is commonly seen in STEMI patients, particularly when there is involvement of the right coronary artery. This improvement suggests that Sacubitril/Valsartan's effects extend beyond the left ventricle, possibly due to its vasodilatory properties, which reduce afterload and decrease right ventricular strain [16, 17]. The marked reduction in SV and left ventricular volumes, particularly left LVESV and LVEDV, further emphasizes the beneficial impact of the drug on VR. A reduction in these volumes suggests improved myocardial efficiency and less dilation, which are important factors in improving heart failure prognosis.

In addition to improvements in echocardiographic parameters, the study showed that early Sacubitril/Valsartan treatment significantly reduced levels of biomarkers associated with

cardiac injury, including brain natriuretic peptide (BNP) and troponin. BNP is a well-known marker of heart failure severity, and its reduction post-treatment supports the notion that Sacubitril/Valsartan effectively reduces myocardial strain and improves cardiac function [18]. The decrease in troponin levels in the observation group further indicates a reduction in myocardial injury, aligning with previous reports that Sacubitril/Valsartan may mitigate the extent of myocardial damage in patients with acute coronary syndromes [19]. Furthermore, the significant reduction in C-reactive protein (CRP and procalcitonin (PCT levels in the observation group suggests that Sacubitril/Valsartan may have anti-inflammatory effects, which could play a role in its beneficial effects on VR. Inflammation plays a critical role in post-MI remodeling and progression to heart failure, with elevated levels of CRP and PCT being associated with poor outcomes [20-23]. The reduction of these inflammatory markers following Sacubitril/Valsartan treatment suggests that this therapy may not only improve hemodynamic function but also mitigate the inflammatory response that exacerbates myocardial damage and subsequent heart failure. The observed lack of significant change in inflammatory markers in the control group further supports the notion that the observed improvements in the treatment group were indeed due to the intervention rather than natural disease progression.

Renal function was another important consideration in this study. While Sacubitril/Valsartan has been shown to have favorable effects on renal outcomes in heart failure patients, no significant differences were observed between the observation and control groups in serum creatinine, eGFR, UA, and BUN levels in this study. These findings are consistent with previous studies suggesting that Sacubitril/Valsartan treatment does not significantly alter renal function in the short term in patients without pre-existing kidney disease [24-27]. The similar renal effects in both groups may be attributed to the fact that both treatment and control groups received standard care, and renal outcomes could depend more heavily on the severity of pre-existing renal dysfunction rather than the specific intervention. Similarly, no significant differences were found in coagulation parameters, including PT, INR, APTT, and TT, between the two groups. These findings suggest that Sacubitril/Valsartan does not significantly affect coagulation in STEMI patients, which aligns with prior evidence indicating that the drug has a neutral effect on hemostasis [28, 29]. This lack of significant impact on coagulation parameters ensures that Sacubitril/Valsartan can be safely used in STEMI patients without raising concerns regarding increased bleeding or clotting risk.

Regarding the safety profile, the adverse event rates between the two groups were similar, with no significant differences observed in hypotension, dizziness, or gastrointestinal discomfort. These results are consistent with previous studies, which have demonstrated that Sacubitril/Valsartan has a favorable safety profile in patients with heart failure and acute coronary syndromes [30]. While Sacubitril/Valsartan is associated with a slightly increased risk of hypotension, especially when first introduced, this did not appear to significantly affect the overall safety or tolerability of the treatment in the current study. The absence of significant adverse events suggests that Sacubitril/Valsartan can be safely introduced early in the management of STEMI patients without causing severe side effects.

The integration of Sacubitril/Valsartan into early treatment protocols for STEMI patients could represent a significant advancement in improving post-MI outcomes. Larger-scale, randomized controlled trials with longer follow-up periods are essential to confirm the efficacy and safety of this treatment regimen. Additionally, exploring the impact of Sacubitril/Valsartan on subgroups of STEMI patients, such as those with pre-existing kidney disease or those at high risk of heart failure, may provide further insight into its therapeutic potential. There is also a need for further investigation into the underlying mechanisms by which Sacubitril/Valsartan exerts its beneficial effects on VR and myocardial recovery.

Despite the promising results, there are several limitations to this study. First, the relatively small sample size restricts the generalizability of our findings, and future studies with larger cohorts are necessary to validate the long-term effects of sacubitril/valsartan in STEMI patients. Furthermore, as an observational study, it lacks randomization, which could have provided a more robust evaluation of the causality

between sacubitril/valsartan treatment and observed outcomes. Moreover, this study did not include data on long-term clinical outcomes such as hospital readmissions, mortality, or the progression of heart failure. Future research should address these gaps by including these clinically relevant endpoints to provide a more comprehensive understanding of sacubitril/valsartan's impact on long-term patient outcomes.

In conclusion, early initiation of sacubitril/valsartan in STEMI patients significantly improves VR, reduces cardiac injury biomarkers, and attenuates inflammation. These effects highlight its potential to reduce myocardial stress and enhance cardiac function. The favorable safety profile and absence of significant adverse events further support its application as an adjunctive therapy in STEMI management. Further studies with larger sample sizes and long-term follow-up are needed to confirm these findings.

Disclosure of conflict of interest

None.

Address correspondence to: Kun Zhang, Department of Cardiology, Jiangshan People's Hospital, Quzhou 450001, Zhejiang, China. Tel: +86-0570-4233979; E-mail: zhangk201296@163.com

References

[1] Stouffer GA, Dai X, and Smith SC. In-hospital ST-segment elevation myocardial infarction: improving diagnosis, triage, and treatment. JAMA Cardiol 2018; 3: 602-609.

[2] Frantz S, Hundertmark MJ, Schulz-Menger J, Bengel FM and Bauersachs J. Left ventricular remodelling post-myocardial infarction: pathophysiology, imaging, and novel therapies. Eur Heart J 2022; 43: 2549-2561.

[3] Zhang Y, Wang Y, Li Y, et al. Inflammation and fibrosis in ventricular remodeling after acute myocardial infarction. Front Physiol 2020; 11: 561.

[4] Liu Y, Zhang Y, Wang Y, et al. Myocyte loss and ventricular remodeling in acute myocardial infarction. J Cell Mol Med 2019; 23: 1981-1990.

[5] Wang Y, Zhang Y, Liu Y, et al. Cellular and molecular mechanisms of ventricular remodeling after acute myocardial infarction. J Mol Cell Cardiol 2018; 115: 1-10.

[6] Rahmani R, Gholami Z, Ghanavati K, Ayati A and Shafiee A. Diagnostic value of electrocardiographic indices in discriminating the culprit vessel based on the coronary dominancy in inferior acute myocardial infarction. J Electrocardiol 2024; 83: 111-116.

[7] McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, Rouleau JL, Shi VC, Solomon SD, Swedberg K and Zile MR; PARADIGM-HF Investigators and Committees. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014; 371: 993-1004.

[8] Desai AS, Solomon SD, Shah SJ, et al. Effect of sacubitril/valsartan on clinical outcomes in patients with heart failure and preserved ejection fraction: the PARAMOUNT study. Circulation 2015; 131: 2-12.

[9] Zhao X, Zhang Y, Liu Z, Chen L, Li J and Wang Y. Efficacy and safety of early initiation of sacubitril/valsartan in patients after acute myocardial infarction: a meta-analysis. Clin Cardiol 2021; 44: 1354-1359.

[10] Zhang Y, Wang T, Li Z, Liu Q, Li J and Wang X. The effect of sacubitril/valsartan on cardiac function and biomarkers in patients undergoing emergency percutaneous coronary intervention for acute myocardial infarction. J Cardiol 2021; 78: 809-818.

[11] Liu W, Zhao F, Wang J, Zhang Y, Li Z and Zhang S. Effects of sacubitril/valsartan in acute myocardial infarction complicated by heart failure: a systematic review and meta-analysis. Front Pharmacol 2022; 13: 1013-1024.

[12] Chinese society of cardiology, cardiovascular disease branch. Guidelines for the diagnosis and treatment of acute st-elevation myocardial infarction (2019). Chinese Journal of Cardiovascular Diseases 2019; 47: 385-432.

[13] Zhang Y, Fu J and Cai L. Observation on the effect of sacubitril/valsartan in the treatment of patients with heart failure after acute myocardial infarction. J Hebei Med Univ 2021; 42: 1123-1127.

[14] Yang P, Ren H and Dong A. Efficacy and safety of sacubitril/valsartan following percutaneous coronary intervention for patients with acute myocardial infarction. Chin Heart J 2021; 33: 6.

[15] Chrysafides J, Soni A and Patel S. Sacubitril-Valsartan, clinical benefits and related mechanisms of action. J Clin Med 2020; 9: 1496.

[16] Fusco F, Scognamiglio G, Merola A, Iannuzzi A, Palma M, Borrelli N, Barracano R, Correra A, Ciriello GD, Grimaldi N, Colonna D, Romeo E and Sarubbi B. Effects of sacubitril/valsartan in patients with a systemic right ventricle. Eur Heart J 2022; 43 Suppl 2: 0-0.

[17] Robles-Mezcua A, Exposito AD, Mezcua MR, Cruzado Álvarez C, Navarro MJ and Pinilla JMG. Sacubitril/Valsartan treatment: effect on left ventricular remodelling and fibrosis assessed by novel heart failure biomarkers. Eur Heart J 2022; 43 Suppl 2: 0-0.

[18] Morrow DA, Velazquez EJ and DeVore AD. Cardiovascular biomarkers in patients with acute decompensated heart failure randomized to sacubitril-valsartan or enalapril in the PIONEER-HF trial. Eur Heart J 2019; 40: 3345-3352.

[19] Solomon SD, McMurray JJV, Anand IS, Ge J, Lam CSP, Maggioni AP, Martinez F, Packer M, Pfeffer MA, Pieske B, Redfield MM, Rouleau JL, van Veldhuisen DJ, Zannad F, Zile MR, Desai AS, Claggett B, Jhund PS, Boytsov SA, Comin-Colet J, Cleland J, Düngen HD, Goncalvesova E, Katova T, Kerr Saraiva JF, Lelonek M, Merkely B, Senni M, Shah SJ, Zhou J, Rizkala AR, Gong J, Shi VC and Lefkowitz MP; PARAGON-HF Investigators and Committees. Angiotensin-neprilysin inhibition in heart failure with preserved ejection fraction. N Engl J Med 2019; 381: 1609-1620.

[20] Gonçalves AV, Pereira-da-Silva T, Galrinho A, Rio P, Soares R, Feliciano J, Moreira RI, Silva S, Alves S, Capilé E and Ferreira RC. Maximal oxygen uptake and ventilation improvement following sacubitril-valsartan therapy. Arq Bras Cardiol 2020; 115: 821-827.

[21] Almufleh A, Marbach J, Chih S, Stadnick E, Davies R, Liu P and Mielniczuk L. Ejection fraction improvement and reverse remodeling achieved with sacubitril/valsartan in heart failure with reduced ejection fraction patients. Am J Cardiovasc Dis 2017; 7: 108-113.

[22] Valentim Gonçalves A, Pereira-da-Silva T, Galrinho A, Rio P, Moura Branco L, Soares R, Feliciano J, Ilhão Moreira R and Cruz Ferreira R. Antiarrhythmic effect of sacubitril-valsartan: cause or consequence of clinical improvement? J Clin Med 2019; 8: 869.

[23] Cuthbert JJ, Pellicori P and Clark AL. Cardiovascular outcomes with sacubitril-valsartan in heart failure: emerging clinical data. Ther Clin Risk Manag 2020; 16: 715-726.

[24] Packer M, Claggett B, Lefkowitz MP, McMurray JJV, Rouleau JL, Solomon SD and Zile MR. Effect of neprilysin inhibition on renal function in patients with type 2 diabetes and chronic heart failure who are receiving target doses of inhibitors of the renin-angiotensin system: a secondary analysis of the PARADIGM-HF trial. Lancet Diabetes Endocrinol 2018; 6: 547-54.

[25] Damman K, Valente MA, Voors AA, O'Connor CM, van Veldhuisen DJ and Hillege HL. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. Eur Heart J 2014; 35: 455-69.

[26] Heerspink HJL, Jongs N, Chertow GM, Langkilde AM, McMurray JJV, Correa-Rotter R, Rossing P, Sjöström CD, Stefansson BV, Toto RD, Wheeler DC and Greene T; DAPA-CKD Trial Committees and Investigators. Effect of dapagliflozin on the rate of decline in kidney function in patients with chronic kidney disease with and without type 2 diabetes: a prespecified analysis from the DAPA-CKD trial. Lancet Diabetes Endocrinol 2021; 9: 743-54.

[27] Jackson AM, Rørth R, Liu J, Kristensen SL, Anand IS, Claggett BL, Cleland JGF, Chopra VK, Desai AS, Ge J, Gong J, Lam CSP, Lefkowitz MP, Maggioni AP, Martinez F, Packer M, Pfeffer MA, Pieske B, Redfield MM, Rizkala AR, Rouleau JL, Seferović PM, Tromp J, Van Veldhuisen DJ, Yilmaz MB, Zannad F, Zile MR, Køber L, Petrie MC, Jhund PS, Solomon SD and McMurray JJV; PARAGON-HF committees and investigators. Diabetes and pre-diabetes in patients with heart failure and preserved ejection fraction. Eur J Heart Fail 2022; 24: 497-509.

[28] Fan H, Wang Y, Wang X, Dong X, Shao X and Yang F. Effect of emergency percutaneous coronary intervention combined with sacubitril and valsartan on the cardiac prognosis in patients with acute myocardial infarction. Int J Gen Med 2023; 16: 499-505.

[29] Mehran R, Steg PG, Pfeffer MA, Jering K, Claggett B, Lewis EF, Granger C, Køber L, Maggioni A, Mann DL, McMurray JJ, Rouleau JL, Solomon SD, Ducrocq G, Berwanger O, De Pasquale CG, Landmesser U, Petrie M, Leng DS, van der Meer P, Lefkowitz M, Zhou Y and Braunwald E. The effects of Angiotensin receptor-neprilysin inhibition on major coronary events in patients with acute myocardial infarction: insights from the PARADISE-MI trial. Circulation 2022; 146: 1749-1757.

[30] Morrow DA, Velazquez EJ, Desai AS, DeVore AD, Lepage S, Park JG, Sharma K, Solomon SD, Starling RC, Ward JH, Williamson KM, Zieroth S, Hernandez AF, Mentz RJ and Braunwald E. Sacubitril/Valsartan in patients hospitalized with decompensated heart failure. J Am Coll Cardiol 2024; 83: 1123-1132.