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Original Article

Impact of sacubitril/valsartan on cardiac structure and function in post-acute myocardial infarction heart failure patients aged over 65: a single-center experience

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Abstract: Objectives: This study evaluates the impact of sacubitril/valsartan on cardiac structure and function in post- acute myocardial infarction (AMI) heart failure (HF) patients over 65 years. Methods: A retrospective analysis was conducted on 204 HF patients over 65 years who experienced AMI between January 2018 and December 2023. Patients were divided into two groups: sacubitril/valsartan treatment group (n = 103) and enalapril treatment group (n = 101). Baseline characteristics were comparable between the two groups. Echocardiographic evaluations, six-minute walk tests, treatment effects, adverse reactions, and patient satisfaction were assessed over a one-year follow-up period. Results: The sacubitril/valsartan group had bigger decreases in NT-proBNP ($P < 0.001$) and cTnI ($P = 0.030$). The sacubitril/valsartan group demonstrated significant improvements in left ventricular ejection fraction (LVEF) ($P = 0.002$), reduced left ventricular end-diastolic volume (LVEDV) ($P = 0.019$), and left ventricular end-systolic volume (LVESV) ($P = 0.002$) when compared to the enalapril group. A substantial increase in six-minute walk test distance was observed in the sacubitril/valsartan group ($P = 0.013$). The treatment was significantly more effective in the sacubitril/valsartan group compared to the enalapril group (51.46% v.s. 30.69%, $P = 0.011$). Patient satisfaction was also higher in the sacubitril/valsartan group ($P = 0.043$). Conclusion: Sacubitril/valsartan shows superior efficacy over enalapril in improving cardiac structure, function, exercise capacity, and patient satisfaction in elderly post-AMI HF patients, as evidenced by greater improvements in cardiac function and more pronounced reduction in stress-related biomarkers.

Keywords: Heart failure, acute myocardial infarction, sacubitril/valsartan, enalapril, cardiac function, elderly patients

Introduction

Heart failure (HF) following acute myocardial infarction (AMI) represents a critical and increasingly prevalent clinical challenge, particularly in the elderly population [1]. As lifespans extend and the risk factors for cardiovascular diseases - such as hypertension, diabetes, and obesity - persist, the incidence of AMI and subsequent HF in populations over 65 years has surged [2]. These patients often exhibit complex clinical profiles with more comorbidities, complicating treatments and necessitating tailored therapeutic strategies [3, 4]. Effective management of post-AMI HF in elderly patients is crucial to improving survival rates, combating morbidity, and enhancing quality of life [5].

In recent years, there has been increasing interest in novel pharmacological interventions that can positively influence cardiac remodeling, a process that underlies the progression of

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HF following AMI [6]. Cardiac remodeling involves changes in cardiac structure and function, including left ventricular dilation and myocardial fibrosis, which can ultimately lead to diminished cardiac output and symptomatic HF [7]. Traditional HF management strategies focus on mitigating symptoms and impeding further cardiovascular damage [8]. ACE inhibitors, beta-blockers, and mineralocorticoid receptor antagonists have long served as the cornerstone of post-AMI HF treatment. However, despite these treatments, the morbidity and mortality associated with HF remain substantial, highlighting the need for advancements in therapeutic options [9].

In this context, the introduction of angiotensin receptor-neprilysin inhibitors (ARNIs) has generated substantial interest [10]. Sacubitril/valsartan, an ARNI, combines the effects of inhibiting neprilysin, a neutral endopeptidase responsible for the degradation of natriuretic peptides, with blocking the renin-angiotensin system (RAS), thereby synergistically reducing myocardial stress and fibrosis while improving diuresis and vasodilation [11]. The PARADIGM-HF trial demonstrated the superiority of sacubitril/valsartan over enalapril in reducing both cardiovascular death and HF hospitalization in a chronic HF population with reduced ejection fraction (HFrEF) [12]. These findings have shifted the treatment paradigm in HFrEF management, endorsing sacubitril/valsartan as a first-line treatment.

Notably, while the efficacy of sacubitril/valsartan in chronic HF settings was well documented, its impact on cardiac structure and function in the context of post-AMI HF, particularly in an elderly cohort, continues to evolve [13]. The delicate interplay of aging, myocardial infarction, and the transition to HF presents a unique opportunity to explore the potential benefits of sacubitril/valsartan [13, 14]. Aging has been associated with intrinsic alterations in cardiovascular physiology, including increased vascular stiffness and altered myocardial compliance, which may exacerbate the progression of HF post-AMI [15].

This study aims to address this knowledge gap by evaluating the impact of sacubitril/valsartan on cardiac structure and function in HF patients over 65 years who have experienced an AMI. By examining a single-center cohort, this research seeks to provide insights into the practical application and outcomes of sacubitril/valsartan in a real-world elderly patient population.

Materials and methods

Case selection

A retrospective analysis was conducted on 204 HF patients aged ≥ 65 years who had experienced an AMI and were treated at Concept Verification Platform for Preclinical Verification and Risk Assessment of Animal Experiments between January 2018 and December 2023. Data were gathered from the medical records system, including baseline characteristics, laboratory test results, echocardiographic measurements, medication usage, and other pertinent information.

According to the World Medical Association (2013) *Declaration of Helsinki*, medical research involving human subjects must prioritize the safety and well-being of the individual [16]. This research was approved by Institutional Review Board and Ethics Committee of Tianjin International Travel Health Care Center, Concept Verification Platform for Preclinical Verification and Risk Assessment of Animal Experiments. Given that the study exclusively utilized de-identified patient information and posed no risk or influence on patient treatment, the requirement for informed consent was waived. This exemption from obtaining informed consent adhered to the regulatory and ethical standards set forth for retrospective studies.

Sample selection and grouping criteria

Inclusion criteria: (1) Age of 65 years or older; (2) Diagnosis of AMI, characterized by cardiac troponin (cTn) levels exceeding the normal upper limit at least once, combined with clinical signs of acute myocardial ischemia [17]; (3) Development of HF following AMI, indicated by abnormal cardiac structure and/or function impairing ventricular filling (diastolic function) and/or ejection capacity (systolic function) [18]; (4) High patient compliance with timely medication intake; (5) Regular follow-up attendance; (6) Availability of complete clinical data.

Exclusion criteria: (1) A history of significant heart diseases, including valvular heart dis-

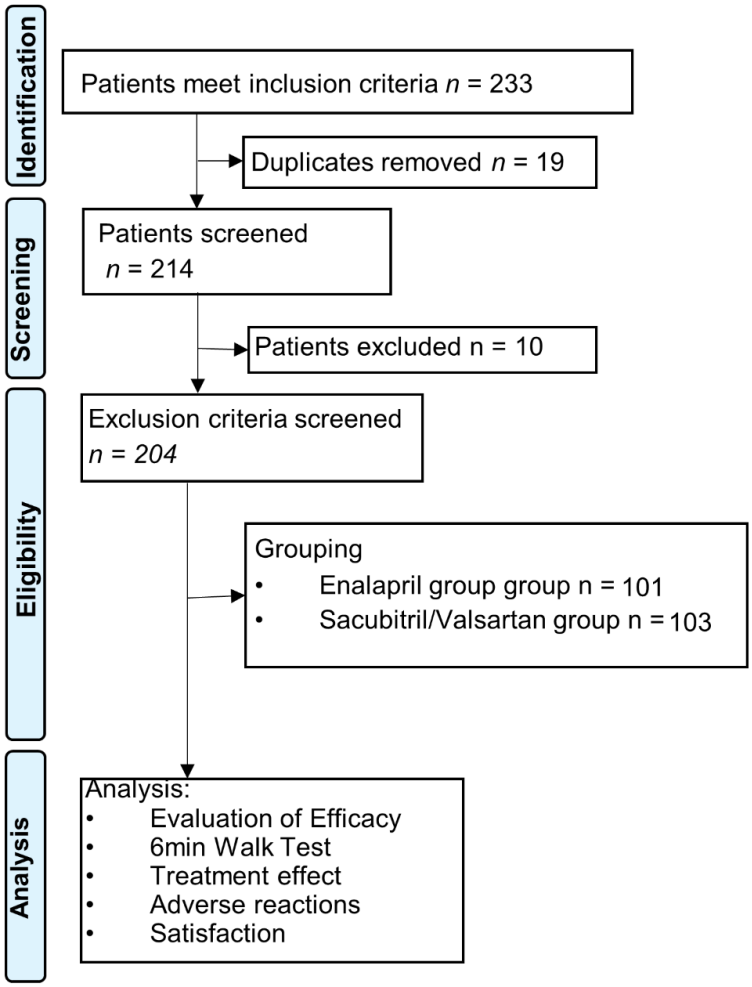

Figure 1. Study flowchart.

ease or rheumatic heart disease [19]; (2) Presence of renal dysfunction or end-stage renal disease, indicated by serum creatinine (sCr) levels exceeding 265 μmol/L [20]; (3) Serum potassium levels exceeding 5.2 mmol/L; (4) Intolerance to ACE inhibitors or angiotensin receptor blockers; (5) Severe comorbidities, such as malignant tumors or multiple organ failure; (6) Diagnosed neurological disorders, or mental/cognitive impairments.

A total of 233 patients were initially selected, of whom 10 patients were excluded based on exclusion criteria and 19 were excluded due to duplicated information, leaving 204 patients finally included in the study (**Figure 1**). Based on electronic medical records, patients were classified into two groups according to their prescribed therapeutic drugs: the sacubitril/valsartan group (n = 103) and the enalapril group (n = 101).

Treatment approach

Percutaneous coronary intervention (PCI) was performed early to achieve revascularization; if PCI was not feasible, early thrombolysis was considered [21]. All patients received standard post-myocardial infarction medical treatment, with diuretics used judiciously based on the individual patient's condition [22].

Patients in the sacubitril/valsartan group were administered sacubitril/valsartan, starting at 25 mg twice daily, with doses gradually increased to a target of 100 mg twice daily, depending on the patient's blood pressure and other clinical factors (Novartis Pharma AG, National Drug Approval Number: HJ20170363, Beijing). Conversely, patients in the enalapril group received 10 mg of enalapril once daily (Yangzijiang Pharmaceutical Group, National Drug Approval Number: H32026567, Guangzhou).

Follow-up assessments were conducted every three months, with a study endpoint of one year.

Basic information

Basic patient information was collected from the clinical case system, including age, sex, medical history, heart rate, blood pressure, laboratory test results, type of myocardial infarction, Killip classification, and New York Heart Association (NYHA) HF Classification.

The severity of myocardial infarction was assessed using the Killip classification as follows: Class I - no evident signs or symptoms of HF, with no wet rales in the lung fields; Class II - mild to moderate HF symptoms with moist rales present in less than 50% of the lung fields; Class III - severe HF accompanied by pul-

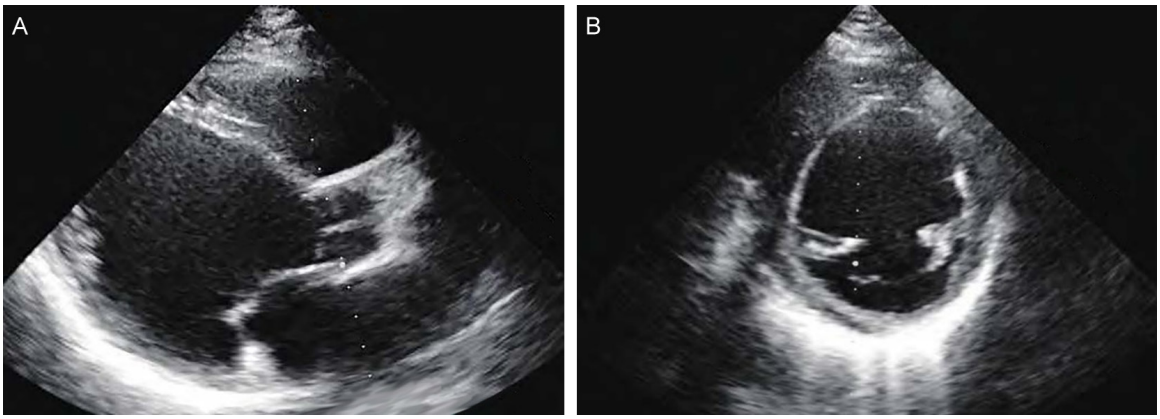

Figure 2. Typical echocardiographic images of heart failure patients after acute myocardial infarction. A. Long-axis view of the left ventricle for enalapril group; B. Short-axis view of the left ventricle for sacubitril/valsartan group.

monary edema, with moist rales in more than 50% of the lung fields; Class IV - cardiogenic shock characterized by varying degrees of hemodynamic instability, with blood pressure below 90/60 mmHg [23].

Patients' cardiac function was graded using the NYHA HF Classification: Class I - no limitation of physical activity, with ordinary activity not causing fatigue, palpitations, dyspnea, or angina; Class II - slight limitation of physical activity, with symptoms occurring during ordinary activities and remaining comfortable at rest; Class III - marked limitation of physical activity, with symptoms occurring during less-than-ordinary activities and remaining comfort only at rest; Class IV - inability to perform any physical activity without discomfort, with symptoms present even at rest [24].

Within 24 hours of admission, venous and arterial blood samples (5 ml each) were collected from patients. Venous blood was processed using a high-speed refrigerated centrifuge (TLD 12A, Xiangxi Scientific Instrument Factory, China) at 3000 rpm for 10 minutes, and the separated plasma was stored at -80°C. An automated biochemical analyzer (AU5811, Kehua Bio-engineering Co., Ltd., Shanghai) was used to measure serum cardiac troponin I (cTnI), serum creatinine (sCr), and N-terminal pro-B-type natriuretic peptide (NT-proBNP). Arterial blood gas analysis was performed using a blood gas analyzer (i-STAT 300G, Abbott, USA).

Echocardiography

Following three months of treatment, echocardiographic evaluations were conducted using the Aplio i800 ultrasound system (Canon, Japan) with a cardiac ultrasound probe (**Figure 2**). The following parameters were recorded:

Left Ventricular Ejection Fraction (LVEF): This was calculated using Simpson's rule from apical four-chamber and two-chamber views to determine the end-diastolic volume (EDV) and end-systolic volume (ESV). LVEF was calculated using formula [(EDV - ESV)/EDV] × 100%.

Left Ventricular End-Diastolic Volume (LVEDV) and Left Ventricular End-Diastolic Volume Index (LVEDVi): Measurements were taken at the end-diastolic and end-systolic phases using Simpson's rule, and the values were standardized by dividing by the body surface area (BSA), often calculated using the Du Bois formula or a similar method.

Left Ventricular End-Systolic Volume (LVESV) and Left Ventricular End-Systolic Volume Index (LVESVi): These were similarly adjusted for individual differences by dividing by BSA.

Left Ventricular Mass (LVM) and Left Ventricular Mass Index (LVMI): Wall thickness and internal diameter of the left ventricle were measured, and the Devereux formula or a comparable calculation was used to determine LVM, which was then standardized to BSA to obtain LVMI.

Left Atrial Volume (LAV) and Left Atrial Volume Index (LAVI): Calculations were conducted using the biplane Simpson's rule or single-plane area-length method from the apical four-chamber view, with results divided by BSA to obtain LAVI.

Left Atrial Width: This was measured directly as the maximum anteroposterior diameter of the left atrium in the parasternal long-axis view.

Peak Early Diastolic Tissue Velocity (e'): Measurements were obtained from the septal (e'sept) and lateral (e'lat) aspects of the mitral annulus, and the average (e'ave) was calculated.

Mitral Inflow Velocity: This was assessed using pulsed-wave Doppler from the apical four-chamber view.

Peak Tricuspid Regurgitation (TR) Velocity: This was determined from the continuous wave spectral Doppler envelope.

Six-minute walk test

Patients underwent the Six-Minute Walk Distance (6-MWD) test upon admission and at the three-month follow-up. This test was conducted in a flat 30-meter corridor, where patients were instructed to walk as far as possible within six minutes, with the option to pause if necessary. Upon test completion, the total walking distance was recorded, along with post-test vital signs and any symptoms experienced by the patients.

Adverse reactions and prognosis

Patients were evaluated three months after treatment to assess improvements in cardiac function. According to the NYHA, a two-grade or higher improvement in heart function was considered significantly effective, while a one-grade or higher improvement, combined with notable clinical symptom relief, was deemed an improvement. Failure to meet these criteria was classified as ineffective. Adverse reactions experienced by patients during this period were also recorded [25].

Additionally, patient satisfaction was assessed across four domains: disease recovery, medical process, hospital environment, and the attitude of medical staff. Each aspect was rated on a scale from 0 to 3, with higher scores reflecting greater satisfaction. The total score was calculated, with a maximum of 12 points. Scores of 0-3 indicated dissatisfaction, 4-6 indicated general satisfaction, 5-9 indicated moderate satisfaction, and 9-12 indicated high satisfaction.

Statistical analysis

Data were analyzed using SPSS 29.0 statistical software (SPSS Inc., Chicago, IL, USA). Categorical data were represented as [n (%)], and the chi-square test was employed. Continuous variables first underwent normality testing with the Shapiro-Wilk method. Normally distributed data were presented as ($\bar{X}$ ± sd) and analyzed using independent-sample t-test, whereas non-normally distributed data were presented as [median (25% quantile, 75% quantile)] and analyzed using the Wilcoxon rank-sum test. A *P*-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics of participants

As shown in **Table 1**, no significant difference in baseline characteristics were observed between the two groups, including age, body mass index, smoking and alcohol consumption history, marital status, educational level, ethnicity, and medical history of diabetes, hypertension, or previous myocardial infarction ($P > 0.05$). Types of myocardial infarction were similar between the two groups, with STEMI being the most prevalent, and there were no significant differences in heart rate, levels of cardiac biomarkers (cTnI and NT-proBNP), or sCr ($P > 0.05$). The Killip classification and NYHA HF classification were comparable between the groups, demonstrating similar severity at baseline ($P > 0.05$).

Serum biomarker levels

After treatment, cTnI levels significantly declined in the sacubitril/valsartan group (11.25 ± 2.62 vs. 12.06 ± 2.64, t = 2.189, P = 0.030), and NT-proBNP levels significantly increased (845.63 ± 279.35 vs. 1246.62 ± 294.15, t =

Table 1. Comparison of baseline information between the two groups

Parameters	Enalapril group (n = 101)	Sacubitril/Valsartan group (n = 103)	t/χ^2	P
Age (years)	73.15 ± 5.4	74.04 ± 5.62	1.156	0.249
Male/Female	59 (58.42%)/42 (41.58%)	61 (59.22%)/42 (40.78%)	0.014	0.907
Body Mass Index (kg/m^2)	23.49 ± 1.31	23.55 ± 1.26	0.364	0.716
Smoking history (Yes/No)	35 (34.65%)/66 (65.35%)	31 (30.1%)/72 (69.9%)	0.484	0.487
Alcohol consumption history (Yes/No)	39 (38.61%)/62 (61.39%)	35 (33.98%)/68 (66.02%)	0.474	0.491
Marital Status (Married/Unmarried)	86 (85.15%)/15 (14.85%)	84 (81.55%)/19 (18.45%)	0.475	0.491
Educational Level (Junior college graduate or lower/College graduate or higher)	77 (76.24%)/24 (23.76%)	73 (70.87%)/30 (29.13%)	0.754	0.385
Ethnicity (Han/Other)	89 (88.12%)/12 (11.88%)	91 (88.35%)/12 (11.65%)	0.003	0.959
Medical history				
Diabetes (Yes/No)	23 (22.77%)/78 (77.23%)	24 (23.3%)/79 (76.7%)	0.008	0.929
Hypertension (Yes/No)	34 (33.66%)/67 (66.34%)	35 (33.98%)/68 (66.02%)	0.002	0.962
Previous myocardial infarction (Yes/No)	8 (7.92%)/93 (92.08%)	9 (8.74%)/94 (91.26%)	0.045	0.833
Types of myocardial infarction			0.006	0.939
STEMI	75 (74.26%)	76 (73.79%)		
NSTEMI	26 (25.74%)	27 (26.21%)		
Heart rate, bpm	75.83 ± 11.60	75.51 ± 11.76	0.196	0.845
cTnI (ng/ml)	34.85 ± 6.21	33.41 ± 6.24	1.648	0.101
NT-proBNP (ng/L)	1575.94 ± 319.65	1493.24 ± 327.65	1.824	0.07
sCr (mg/dl)	4.45 ± 0.52	4.41 ± 0.57	0.481	0.631
Killip class			0.316	0.854
Class II	49 (48.51%)	51 (48.51%)		
Class III	43 (42.57%)	45 (42.57%)		
Class IV	9 (8.91%)	7 (8.91%)		
NYHA Heart Failure Classification			0.351	0.839
Class II	45 (44.55%)	45 (43.69%)		
Class III	45 (44.55%)	49 (47.57%)		
Class IV	11 (10.89%)	9 (8.74%)		

cTnI: Cardiac Troponin I; NT-proBNP: N-terminal pro-B-type natriuretic peptide; sCr: Serum creatinine; STEMI: ST-Elevation Myocardial Infarction; NSTEMI: Non-ST-Segment Elevation Myocardial Infarction; NYHA: New York Heart Association.

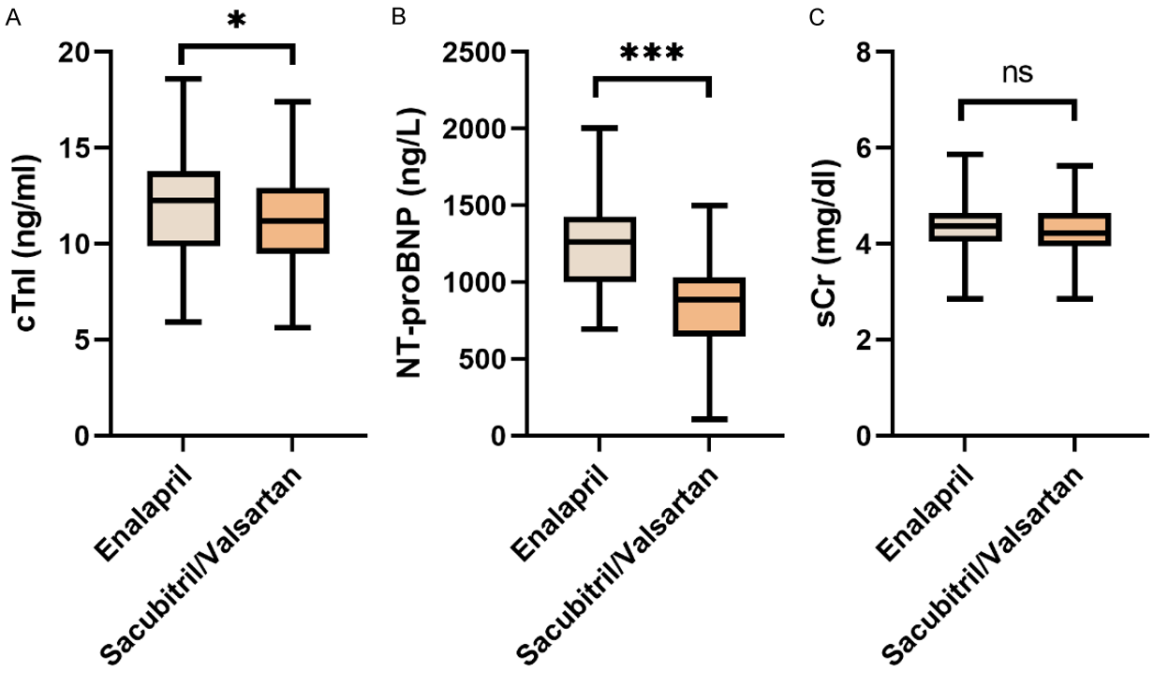

Figure 3. Comparison of post-treatment serum biomarker levels between the two groups. A. cTnI; B. NT-proBNP; C. sCr. cTnI: Cardiac Troponin I; NT-proBNP: N-terminal pro-B-type natriuretic peptide; sCr: Serum creatinine. ns: no significant difference; *: P < 0.05; ***: P < 0.001.

Table 2. Comparison of post-treatment LV structure and systolic function between the two groups

Parameters	Enalapril group (n = 101)	Sacubitril/Valsartan group (n = 103)	t	P
LVEF (%)	40.81 ± 11.07	45.91 ± 11.81	3.177	0.002
LVEDV (mL)	136.74 ± 36.28	124.35 ± 38.75	2.358	0.019
LVEDVi (ml/m^2)	63.18 ± 17.75	69.47 ± 22.23	2.236	0.026
LVESV (mL)	79.37 ± 17.92	72.26 ± 13.86	3.165	0.002
LVESVi (mL/m^2)	40.35 ± 10.33	37.07 ± 6.44	2.714	0.007
LV mass (g)	195.84 ± 32.21	189.44 ± 33.02	1.402	0.163
LVMi (g/m^2)	97.86 ± 25.36	100.27 ± 24.41	0.693	0.489

LVEF: Left Ventricular Ejection Fraction; LVEDV: Left Ventricular End-Diastolic Volume; LVEDVi: Left Ventricular End-Diastolic Volume Index; LVESV: Left Ventricular End-Systolic Volume; LVESVi: Left Ventricular End-Systolic Volume Index; LV mass: Left Ventricular Mass; LVMi: Left Ventricular Mass Index.

9.985, P < 0.001), compared with the enalapril group (**Figure 3**). Although there was no significant difference in sCr levels between the groups (P = 0.443), the sacubitril/valsartan group showed a trend towards lower sCr levels compared to the enalapril group.

Treatment efficacy

The LVEF increased substantially in the sacubitril/valsartan group (45.91% ± 11.81) compared to the enalapril group (40.81% ± 11.07, P = 0.002) (**Table 2**). Additionally, the sacubitril/valsartan group exhibited a significantly lower LVEDV (124.35 mL ± 38.75 vs. 136.74 mL ± 36.28, P = 0.019) and LVESV (72.26 mL ± 13.86 vs. 79.37 mL ± 17.92, P = 0.002). Furthermore, there was a notable reduction in LVESVi in the sacubitril/valsartan group (37.07 mL/m^2 ± 6.44 vs. 40.35 mL/m^2 ± 10.33, P = 0.007). The LVEDVi was higher in the sacubitril/valsartan group (69.47 mL/m^2 ± 22.23) compared to the enalapril group (63.18 mL/m^2 ± 17.75, P = 0.026). However, there were no significant differences between the groups in terms of LVM and LVMI (P = 0.163, 0.489, respectively). Overall, sacubitril/valsartan showed a favorable impact on key measures of cardiac structure and function.

The LAV (49.36 mL ± 11.31 vs. 49.45 mL ± 11.14, P = 0.954) and LAVI (24.74 mL/m^2 ± 8.62 vs. 25.43 mL/m^2 ± 9.94, P = 0.596) were

Table 3. Comparison of post-treatment LA structure between the two groups

Parameters	Enalapril group (n = 101)	Sacubitril/Valsartan group (n = 103)	t	P
LA volume (ml)	49.36 ± 11.31	49.45 ± 11.14	0.057	0.954
LAVi (ml/m^2)	24.74 ± 8.62	25.43 ± 9.94	0.531	0.596
LA width (cm)	3.7 ± 0.55	3.68 ± 0.59	0.206	0.837

LA volume: Left Atrial Volume; LAVi: Left Atrial Volume Index; LA width: Left Atrial Width.

Table 4. Comparison of LV diastolic measures between the two groups

Parameters	Enalapril group (n = 101)	Sacubitril/Valsartan group (n = 103)	t	P
E wave (cm/s)	70.36 ± 13.06	68.67 ± 13.5	0.91	0.364
TDI e'lat (cm/s)	6.93 ± 2.43	6.74 ± 2.41	0.548	0.584
E/e'lat	11.34 ± 3.22	11.35 ± 2.95	0.029	0.977
TDI e'sept (cm/s)	5.56 ± 1.71	5.34 ± 1.71	0.928	0.354
E/e'sept	13.97 ± 2.72	13.73 ± 2.15	0.699	0.485
TDI e'ave (cm/s)	6.21 ± 1.81	6.03 ± 1.82	0.681	0.497
E/e'ave	12.01 ± 3.02	12.24 ± 3.75	0.474	0.636
TR velocity (m/s)	2.59 ± 0.34	2.57 ± 0.39	0.424	0.672

E wave (cm/s): Early diastolic filling velocity of the mitral valve flow; TDI e'lat (cm/s): Tissue Doppler imaging early diastolic myocardial velocity at the lateral wall; E/e'lat: Ratio of early diastolic filling velocity (E wave) to early diastolic myocardial velocity at the lateral wall (e'lat); TDI e'sept (cm/s): Tissue Doppler imaging early diastolic myocardial velocity at the septal wall (in centimeters per second); E/e'sept: Ratio of early diastolic filling velocity (E wave) to early diastolic myocardial velocity at the septal wall (e'sept); TDI e'ave (cm/s): Tissue Doppler imaging average early diastolic myocardial velocity (in centimeters per second); E/e'ave: Ratio of early diastolic filling velocity (E wave) to average early diastolic myocardial velocity (e'ave).

similar between the two groups (**Table 3**). Additionally, the LA width remained comparable between the two groups (3.7 cm ± 0.55 vs. 3.68 cm ± 0.59, P = 0.837).

The early diastolic filling velocity (E wave) was comparable between the two groups (70.36 cm/s ± 13.06 vs. 68.67 cm/s ± 13.5, P = 0.364) (**Table 4**). Similarly, the Tissue Doppler Imaging (TDI) early diastolic myocardial velocities at the lateral wall (TDI e'lat) and septal wall (TDI e'sept) showed no significant differences (P = 0.584 and P = 0.354, respectively). Ratios such as E/e'lat and E/e'sept, as well as other diastolic parameters like TDI e'ave and TR velocity, also did not show significant variations between the groups (P > 0.05 for all). These findings suggest that sacubitril/valsartan did not produce detectable changes in LV diastolic function compared to enalapril in this patient population.

6-MWD

The 6-MWD results revealed that both groups demonstrated similar baseline walking distances before treatment (330.27 ± 34.97 meters vs. 332.54 ± 39.42 meters, P = 0.664) (**Table 5**). However, following treatment, there was a significant improvement in the 6-MWD in the sacubitril/valsartan group compared to the enalapril group (408.65 ± 34.13 meters vs. 395.41 meters ± 41.32, P = 0.013), indicating a superior enhancement in exercise capacity in the sacubitril/valsartan group.

Treatment effect

The sacubitril/valsartan group exhibited a significantly higher proportion of patients achieving a significant improvement compared to the enalapril group (51.46% vs. 30.69%, P = 0.011) (**Table 6**). Conversely, the proportion of patients showing improvement was higher in the enalapril group at 47.52% (48 patients) compared to 33.01% (34 patients) in the sacubitril/valsartan group. The proportion of patients experiencing ineffective treatment outcomes was similar between the two groups (21.78% vs. 15.53%). Overall, sacubitril/valsartan was more effective in yielding significant treatment effects in this patient population.

Adverse reactions

The incidence of hyperkalemia was slightly higher in the enalapril group, but the difference didn't reach statistical significance (1.98% vs. 0.97%, P = 0.986) (**Table 7**). Gastrointestinal reactions were slightly more frequent in the sacubitril/valsartan group at 2.91% compared to 1.98% in the enalapril group, though this difference was not statistically significant (P =

Table 5. Comparison of 6 min walk test between the two groups

Parameters		Enalapril group (n = 101)	Sacubitril/Valsartan group (n = 103)	t/χ^2	P
6 min walking distance	Before treatment	330.27 ± 34.97	332.54 ± 39.42	0.435	0.664
	After treatment	395.41 ± 41.32	408.65 ± 34.13	2.497	0.013

Table 6. Comparison of treatment efficacy between the two groups

Parameters	Enalapril group (n = 101)	Sacubitril/Valsartan group (n = 103)	t/χ^2	P
Significant effective	31 (30.69%)	53 (51.46%)	9.081	0.011
Improvement	48 (47.52%)	34 (33.01%)		
Ineffective	2 (21.78%)	16 (15.53%)		

1.000). Dizziness was reported at 2.97% of patients in the enalapril group and 0.97% in the sacubitril/valsartan group (P = 0.600). Weakness was observed at similar rates of 0.99% and 0.97% in the enalapril and sacubitril/valsartan groups, respectively (P = 1.000). The total adverse reaction rate was 7.92% in the enalapril group and 5.83% in the sacubitril/valsartan group, with no significant difference (P = 0.554). Overall, the incidence of adverse reactions was low and comparable between the two groups.

Satisfaction

The sacubitril/valsartan group reported a significantly higher satisfaction rate compared to the enalapril group (48.54% vs. 30.69%, P = 0.043) (**Table 8**). Moderate satisfaction was more frequently reported in the enalapril group at 39.6%, compared to 31.07% in the sacubitril/valsartan group. General satisfaction levels were similar, with 19.8% in the enalapril group and 16.5% in the sacubitril/valsartan group. Dissatisfaction rates were higher in the enalapril group, with 9.9% compared to just 3.88% in the sacubitril/valsartan group. These findings indicate a superior satisfaction level among patients treated with sacubitril/valsartan.

Discussion

In this study, we explored the effects of sacubitril/valsartan on cardiac structure and function among HF patients over 65 years old who had suffered AMI. The superior performance of sacubitril/valsartan in improving LVEF compared to enalapril may be attributed to its dual inhibition mechanism. Sacubitril/valsartan exerts its effects by simultaneously blocking the angiotensin II type 1 receptor (via valsartan) and inhibiting neprilysin (via sacubitril) [26]. This unique dual action provides a more comprehensive neurohormonal modulation than enalapril alone. Valsartan inhibits the detrimental effects of the renin angiotensin aldosterone system, such as vasoconstriction, sodium retention, and pro fibrotic signaling. Concurrently, sacubitril enhances the protective natriuretic peptide system by preventing the degradation of beneficial peptides like atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP). The resulting elevation in these peptides promotes vasodilation, natriuresis, and diuresis [27, 28]. The inhibition of neprilysin can also prevent fibrosis and pathological cardiac remodeling, thus improving cardiac function [29]. This comprehensive mechanism ultimately reduces cardiac afterload and volume overload more effectively and directly counteracts maladaptive remodeling. This explains why patients receiving sacubitril/valsartan exhibited greater enhancement in LVEF, an essential parameter of systolic function, and suggests its role in better preserving cardiac structure post AMI.

The reduction in LVEDV and LVESV in the sacubitril/valsartan group compared to the enalapril group further supports the notion that sacubitril/valsartan confers beneficial effects on cardiac geometry and mechanics. The observed improvement in LV volumes suggests that sacubitril/valsartan can more effectively minimize volume overload, a fundamental contributor to adverse cardiac remodeling [30, 31]. By reducing the heart's workload and pressure demands, sacubitril/valsartan may help in preventing the progression of HF symptoms more efficiently than enalapril.

Table 7. Comparison of adverse reactions between the two groups

Parameters	Enalapril group (n = 101)	Sacubitril/Valsartan group (n = 103)	t/χ^2	P
Hyperkalemia	2 (1.98%)/99 (98.02%)	1 (0.97%)/102 (99.03%)	0	0.986
Gastrointestinal reactions	2 (1.98%)/99 (98.02%)	3 (2.91%)/100 (97.09%)	0	1
Dizzy	3 (2.97%)/98 (97.03%)	1 (0.97%)/102 (99.03%)	0.275	0.6
Weakness	1 (0.99%)/100 (99.01%)	1 (0.97%)/102 (99.03%)	0	1
Total	8 (7.92%)/93 (92.08%)	6 (5.83%)/97 (94.17%)	0.35	0.554

Table 8. Comparison of patient satisfaction between the two groups

Parameters	Enalapril group (n = 101)	Sacubitril/Valsartan group (n = 103)	t/χ^2	P
Satisfaction	31 (30.69%)	50 (48.54%)	8.142	0.043
Moderate satisfaction	40 (39.6%)	32 (31.07%)		
General satisfaction	20 (19.8%)	17 (16.5%)		
Dissatisfaction	10 (9.9%)	4 (3.88%)		

The observed superior improvements in cardiac structure and function are strongly supported by the significant reductions in key serum biomarkers. The more pronounced reduction in NT-proBNP levels in the sacubitril/valsartan group provides direct molecular evidence of its enhanced efficacy in alleviating ventricular wall stress, a direct consequence of neprilysin inhibition and potentiation of the protective natriuretic peptide system. This profound neurohormonal modulation, achieved through dual inhibition of the renin-angiotensin system and neprilysin, represents the core molecular mechanism underpinning the superior clinical outcomes [32, 33]. The concurrent reduction in cTnI levels further suggests a potential favorable effect on mitigating ongoing myocardial injury, which may contribute to its overall cardioprotective benefits and the observed enhancement in functional capacity.

Interestingly, while sacubitril/valsartan showed significant advantages in systolic function, the study did not demonstrate a notable difference between the groups concerning diastolic measures, such as Tissue Doppler Imaging (TDI) velocities and E/e' ratios. This observation could be due to the complex nature of diastolic dysfunction measurement and the multifactorial causes underpinning these impairments in older patients [34, 35]. Sacubitril/valsartan's effects on diastolic parameters might require a longer duration to manifest or necessitate a larger cohort for significant differences to emerge. Nevertheless, the encouraging outcomes in systolic measures and overall patient exercise tolerance emphasize the need for further research into the potential long-term benefits sacubitril/valsartan may offer for both systolic and diastolic function.

The 6-MWD test, in which the sacubitril/valsartan group outperformed the enalapril group, provides clinical corroboration for the superior impact of sacubitril/valsartan on exercise capacity and physical endurance in elderly HF patients. The enhanced exercise performance was presumably linked to the reduced cardiac workload and improved cardiac efficiency afforded by sacubitril/valsartan's pharmacological action [36, 37]. This improvement was not only a surrogate marker for better clinical state but also translates into improved quality of life for the patients, an important consideration for aging individuals already burdened by multiple comorbidities [38].

Overall satisfaction and treatment effect perceptions were also notably higher among patients treated with sacubitril/valsartan. The higher satisfaction scores may partly result from reduced symptoms, allowing for greater participation in daily activities, and lessening the psychological burden associated with chronic HF management [39, 40]. In addition, the reduction in adverse reaction rates, although not statistically significant, might have contributed to this perceived improvement. Given that medication tolerance often impacts adherence, the slightly better safety profile of sacubitril/valsartan could enhance long-term treatment adherence, which was critical for sustained clinical benefits [41].

Our findings align with previous evidence demonstrating the positive impact of sacubitril/val-

sartan in HF management. Previous studies [38, 42], such as the PARADIGM-HF trial, established foundational evidence for the efficacy of sacubitril/valsartan in improving outcomes in HF with reduced ejection fraction (HFrEF). Our study confirms that these benefits extend to a specific subset of patients - elderly individuals recovering from AMI - demonstrating improvements in cardiac structure, function, and overall patient experience. Moreover, this single-center experience specifically illuminates its utility in real-world clinical settings, presenting sacubitril/valsartan as an attractive option for this patient population characterized by complex therapeutic needs due to age-related physiological changes and the presence of comorbidities. Enalapril was selected as the active comparator in this study because it served as the standard-of-care control in the pivotal PARADIGM-HF trial [43], which established the superiority of sacubitril/valsartan. This choice allows for a direct comparison within the conceptual framework of the landmark evidence and reinforces the validity of our results against a well-accepted therapeutic benchmark.

While the study provides valuable insights, certain limitations must be acknowledged. First, sacubitril/valsartan (Novartis) used was a brand-name drug, whereas enalapril (Yangzijiang) was a generic formulation. Although generic drugs approved for clinical use in China are required to demonstrate bioequivalence to their brand-name counterparts, we cannot entirely rule out potential, albeit unlikely, differences in excipients or manufacturing processes that might influence clinical outcomes. Second, the retrospective design inherently limits causal inferences, and the single-center setting may restrict the generalizability of the findings. Third, a longer follow-up period could better elucidate the potential differences in diastolic function and provide more detailed information regarding the long-term safety and effectiveness of sacubitril/valsartan in this population. Additionally, while the findings suggest better treatment effects and satisfaction rates with sacubitril/valsartan, further studies into cost-effectiveness and resource utilization compared to traditional therapies would provide a more holistic understanding of its role in HF management, especially within healthcare systems under varying economic constraints.

Conclusion

Sacubitril/valsartan offers significant improvements in cardiac structure and function, exercise capacity, and patient satisfaction as compared to enalapril in managing elderly patients with HF post-AMI, which are supported by an attenuation of neurohormonal stress as indicated by biomarker changes. These findings underline the importance of novel therapeutic approaches that address complex pathophysiological changes characteristic of this patient population. Going forward, sacubitril/valsartan emerges as a promising standard of care for elderly patients with HF post-AMI, warranting further prospective studies to corroborate these benefits and explore its impact on long-term cardiac health and mortality.

Disclosure of conflict of interest

None.

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