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Comparative effects of sacubitril/valsartan versus enalapril on QRS duration and cardiac function in heart failure patients undergoing left bundle branch area pacing

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Abstract: **Background**: Left bundle branch area pacing (LBBaP) has emerged as a physiological pacing strategy for cardiac resynchronization therapy in patients with heart failure (HF) and left bundle branch block (LBBB). However, evidence comparing different pharmacological regimens following LBBaP implantation remains limited. **Objectives**: To compare the effects of sacubitril/valsartan and enalapril on QRS duration and cardiac function in HF patients undergoing LBBaP. **Methods**: This retrospective cohort study included 106 patients with HF and LBBB who underwent successful LBBaP implantation at a single center between January 2022 and December 2023. According to the postoperative pharmacotherapy protocol, patients were divided into two groups: a control group receiving enalapril (n = 52) and an observation group receiving sacubitril/valsartan (n = 54). After six months of follow-up, QRS duration and amplitude, echocardiographic parameters (left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD)), functional capacity assessed by the 6-minute walk distance (6MWD), serum biomarkers (N-terminal pro-B-type natriuretic peptide (NT-proBNP) and cardiac troponin I (cTnI)) and major adverse cardiovascular events (MACE) were compared between the two groups. **Results**: Both groups showed improvements in electrophysiological and cardiac functional parameters after treatment. Compared with the enalapril group, patients receiving sacubitril/valsartan demonstrated significantly shorter QRS duration (125.45 ± 9.79 ms vs 150.23 ± 3.33 ms, $P < 0.001$), higher LVEF (57.03 ± 2.49% vs 50.29 ± 2.18%, $P < 0.001$) and smaller LVESD and LVEDD (all $P < 0.001$). In addition, the sacubitril/valsartan group showed greater improvement in exercise capacity (6MWD: 370.25 ± 17.64 m vs 349.51 ± 17.45 m, $P < 0.001$) and lower levels of NT-proBNP and cTnI. The incidence of MACE during the 6-month follow-up was also lower in this group (11.11% vs 26.92%, $P = 0.038$). **Conclusion**: Among HF patients with LBBB undergoing LBBaP implantation, treatment with sacubitril/valsartan was associated with greater short-term improvements in QRS duration, cardiac function and exercise capacity compared with enalapril. Larger prospective studies with longer follow-up are required to further evaluate long-term clinical outcomes.

Keywords: Cardiac resynchronization therapy; Heart failure; Left bundle branch area pacing; QRS duration; Sacubitril/valsartan

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INTRODUCTION

The prevalence of coronary atherosclerotic heart disease has continued to rise in China, leading to a growing population of patients who ultimately progress to heart failure (HF), which has become one of the leading causes of cardiovascular mortality (Zhang and Shan, 2022; Vijayaraman *et al*., 2023). HF represents the final stage of many cardiovascular diseases and is a complex clinical syndrome characterized by dyspnea, fluid retention and reduced exercise tolerance. This condition may lead to multisystem dysfunction and, in advanced stages, cardiac cachexia, thereby severely impairing quality of life and contributing to high rates of hospitalization and mortality (Vijayaraman *et al*., 2022).

During the development and progression of chronic HF, both electrical and mechanical dyssynchrony of the myocardium play critical roles. Among these conduction abnormalities, left bundle branch block (LBBB) is a common disorder that leads to asynchronous contraction between the left and right ventricles, thereby further worsening ventricular dysfunction and contributing to a vicious cycle of progressive cardiac deterioration (Vijayaraman *et al*., 2022). In addition, long-term right ventricular apical pacing (RVAP), which produces an electrical activation pattern similar to LBBB, may also induce or worsen HF. As a simple, noninvasive and widely available diagnostic tool, the electrocardiogram (ECG) provides the QRS duration, an important indicator of ventricular electrical synchrony. Previous studies have shown that prolonged QRS duration is closely associated with the severity of cardiac dysfunction and ventricular remodeling in HF and it is therefore considered an important prognostic marker (Sidhu *et al*., 2021; Richter *et al*., 2023).

The management of HF is fundamentally based on guideline-directed medical therapy (GDMT). In recent years, this pharmacological foundation has been substantially strengthened by the introduction of angiotensin receptor–neprilysin inhibitors (ARNIs), represented by sacubitril/valsartan, which have

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significantly improved outcomes in patients with heart failure with reduced ejection fraction (HFrEF) (Piña *et al*., 2021). Contemporary GDMT for HFrEF also includes β-blockers, mineralocorticoid receptor antagonists and sodium–glucose cotransporter-2 inhibitors. Although angiotensin-converting enzyme inhibitors (ACEIs), such as enalapril, were historically considered cornerstone therapies for HF, ARNIs are now recommended as a preferred treatment option in current clinical guidelines. Nevertheless, ACEIs remain widely used in routine clinical practice and are still frequently employed as comparators in studies evaluating newer pharmacological strategies.

For patients with HF accompanied by ventricular conduction abnormalities, device-based cardiac resynchronization therapy (CRT) has become an important therapeutic approach. Conventional CRT typically relies on biventricular pacing (BVP) to correct mechanical dyssynchrony; however, approximately 30% of patients show little or no response to this therapy in clinical practice (Palmisano *et al*., 2024). To overcome the limitations of BVP, including its non-physiological activation pattern and relatively high non-response rate, conduction system pacing (CSP) has emerged as a more physiological pacing strategy. Among these techniques, left bundle branch area pacing (LBBaP) directly captures the left bundle branch conduction system, resulting in a narrower QRS duration and improved ventricular electrical synchrony. In addition, LBBaP has several advantages, including stable pacing parameters, low capture thresholds and high procedural success rates (Vijayaraman *et al*., 2023; Palmisano *et al*., 2024).

Recent observational studies have begun to investigate the clinical outcomes of LBBaP combined with different pharmacological therapies in patients with HF. Previous studies have demonstrated that LBBaP combined with sacubitril/valsartan or enalapril significantly improves cardiac function and electrical synchrony in elderly patients with coronary heart disease and heart failure (Zhao *et al*., 2025). Additional retrospective evidence suggests that sacubitril/valsartan may provide greater improvements in ventricular remodeling and cardiac function than enalapril following LBBaP implantation (Wang *et al*., 2024). However, the currently available evidence remains limited by relatively small sample sizes, retrospective study designs and short follow-up durations.

Therefore, the present study aimed to further evaluate the clinical outcomes of sacubitril/valsartan compared with enalapril in patients with HF and LBBB undergoing LBBaP implantation. Specifically, the present study assessed changes in QRS duration, cardiac structure and function, exercise capacity and circulating biomarkers during a six-month follow-up period, with the aim of providing additional clinical evidence regarding pharmacological management in patients receiving LBBaP therapy.

MATERIALS AND METHODS

Study subjects and grouping

This retrospective observational cohort study was conducted at a single tertiary medical center. A total of 106 consecutive patients hospitalized in the Department of Cardiology between January 2022 and December 2023 who met the predefined inclusion and exclusion criteria and had indications for CRT due to HF with LBBB were retrospectively enrolled. All patients underwent successful implantation of an LBBaP system. Postoperative pharmacological therapy was determined by the treating physicians according to clinical judgment based on patients' blood pressure status, renal function, drug tolerance and economic accessibility. According to the medication administered after device implantation, patients were categorized into two groups: a control group (CG, n = 52) receiving enalapril maleate tablets and an observation group (OG, n = 54) receiving sacubitril/valsartan sodium tablets. Baseline demographic characteristics, cardiac function parameters and laboratory biomarkers were collected from medical records to assess comparability between the two groups. The baseline profiles of the two groups were comparable, as no significant differences were observed in sex distribution, mean age, disease duration, or cardiomyopathy etiology (ischemic vs dilated) (all $P > 0.05$) (Table 1). The participant selection, exclusion, treatment allocation and follow-up process are summarized in Fig. 1.

Inclusion and exclusion criteria

Inclusion criteria: (1) Diagnosis of heart failure consistent with the Chinese guideline recommendations; (2) New York Heart Association (NYHA) functional class II–III; (3) Chronic heart failure with reduced cardiac function accompanied by ventricular conduction delay and meeting the clinical indications for cardiac resynchronization therapy according to contemporary guideline recommendations (Glikson *et al*., 2021); (4) Availability of complete clinical data and the ability to complete electrocardiographic and echocardiographic follow-up examinations; (5) Clear consciousness with good communication ability and follow-up compliance.

Exclusion criteria: (1) Severe psychiatric disorders or coagulation dysfunction; (2) Missing key clinical data or withdrawal during the study period; (3) Concomitant chronic obstructive pulmonary disease, severe hepatic or renal insufficiency, or autoimmune disease; (4) History of permanent pacemaker implantation; (5) Contraindications or intolerance to the study medications.

Treatment methods

LBBaP procedure

A standardized LBBaP implantation protocol was applied to all enrolled patients. The procedure was performed under local anesthesia with vascular access obtained via the left subclavian vein. A SelectSecure 3830 pacing lead (69 cm) delivered through a C315His sheath (Medtronic, USA) was used for implantation. Under continuous fluoroscopic

guidance in the right anterior oblique projection, the delivery sheath was positioned against the right ventricular septum. The pacing lead was then advanced through the sheath and rotated clockwise to penetrate the interventricular septum toward the anatomical region of the left bundle branch. During the procedure, pacing parameters were continuously monitored, including pacing impedance (400–1000 Ω), pacing threshold (≤ 1.5 V at 0.4 ms) and R-wave sensing amplitude (≥ 5 mV). Successful left bundle branch capture was confirmed according to previously reported criteria (McCausland *et al*., 2022; Liu *et al*., 2021): (1) stimulus-to-left ventricular activation time (Sti-LVAT) recorded in leads V5 or V6 < 75 ms without further shortening during additional lead advancement; (2) paced QRS morphology showing a right bundle branch block pattern. Procedural parameters, including pacing threshold, sensing amplitude and lead impedance, were recorded immediately after implantation to evaluate device performance and procedural success. Representative electrocardiographic evolution during successful LBBaP implantation is illustrated in fig. 2.

Medication regimens

After LBBaP implantation, patients in the CG received enalapril maleate tablets (State Drug Approval No. H20083604). The initial dose was 5 mg once daily and was titrated according to blood pressure and drug tolerance to a target dose of 10–40 mg/day, divided into two to three doses, over 2–4 weeks. Patients in the OG received sacubitril/valsartan sodium tablets (Entresto; State Drug Approval No. J20171054) at an initial dose of 50 mg twice daily. After two weeks, if hypotension, renal dysfunction, or other contraindications were absent, the dose was titrated to a target maintenance dose of 200 mg twice daily. Both groups continued treatment and follow-up for six months.

Observation indicators and evaluation methods

Primary outcome measures

Electrocardiographic synchrony parameters were evaluated using standard 12-lead electrocardiography. Successful left bundle branch capture was characterized by a paced QRS complex in lead V1 showing a right bundle branch block morphology and a stimulus-to-left ventricular activation time in lead V6 of < 80 ms. In a subset of patients, direct recording of a left bundle branch potential preceding the QRS onset provided additional confirmation. QRS duration was defined as the interval from the onset of the QRS complex to the J point. Measurements were initially generated automatically by the ECG analysis system and subsequently manually verified by an experienced cardiologist, blinded to group allocation, to ensure measurement accuracy.

Secondary outcome measures

Cardiac function was assessed using both echocardiographic and functional parameters. Echocardiographic evaluation included measurement of left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF). Functional capacity was assessed using the standardized 6-minute walk test (6MWD) and NYHA functional classification. Serum biomarkers—including N-terminal pro-brain natriuretic peptide (NT-proBNP), cardiac troponin T (cTnT), fasting plasma glucose (FPG) and serum creatinine (SCr)—were measured at baseline before LBBaP implantation and again at the end of the six-month follow-up period. Laboratory analyses were performed using a Roche automatic chemiluminescence immunoassay analyzer and a bioMérieux immunofluorescence analyzer with the corresponding reagent kits. Baseline cardiac function parameters (LVEF, LVEDD and LVESD) were obtained from echocardiographic examinations performed prior to device implantation. Safety assessment included the occurrence of major adverse cardiovascular events (MACE) during the six-month follow-up period, including rehospitalization for angina, symptomatic tachyarrhythmia and sudden cardiac death. Drug-related adverse reactions were also monitored.

Statistical analysis

Statistical analyses were performed using SPSS software (version 23.0). The normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed data are presented as mean ± standard deviation, whereas non-normally distributed variables are expressed as median and interquartile range when appropriate. Comparisons between two independent groups were conducted using the independent samples t-test or the Mann–Whitney U test, depending on the data distribution. Paired t-tests were used to compare pre- and post-treatment values within groups. Categorical variables are presented as frequencies and percentages and were analyzed using the chi-square test or Fisher's exact test where appropriate. A two-sided P value < 0.05 was considered statistically significant. Given the exploratory nature of this retrospective study and the relatively limited sample size, adjustments for multiple comparisons were not applied.

RESULTS

Baseline characteristics of the two groups

The baseline demographic and clinical characteristics of the two groups were generally comparable. No significant differences were observed between the groups in age, sex distribution, NYHA functional class, or the prevalence of major comorbidities, including smoking history, hypertension and diabetes (all P > 0.05). Similarly, the use of background medications—such as β-blockers, mineralocorticoid receptor antagonists and diuretics—was comparable between the two groups. Baseline cardiac function parameters and laboratory biomarkers also showed no significant differences, indicating that the two study cohorts were well balanced at baseline (Table 1).

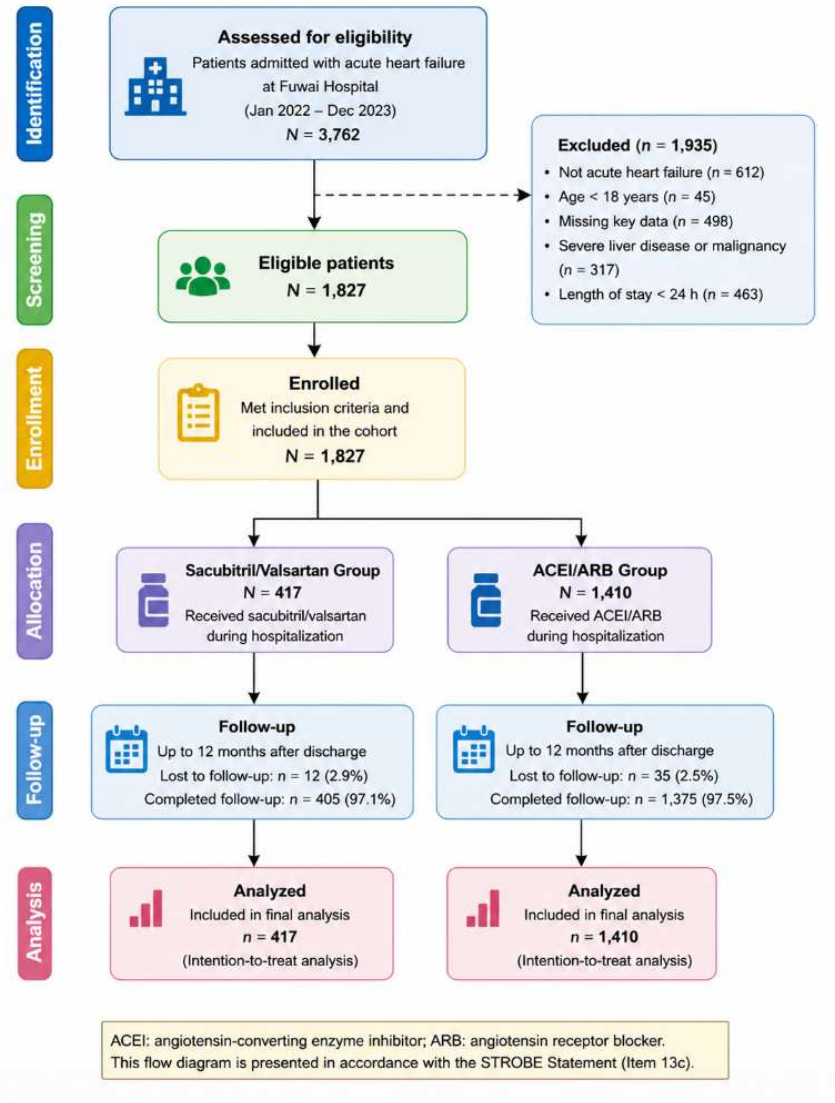

Fig. 1: Flow diagram of patient selection, grouping and follow-up.

Table 1: Baseline characteristics of the two groups [mean ± SD, n (%)].

Variable	CG (n=52)	OG (n=54)	t/χ^2	P
Age (years)	63.20 ± 7.59	63.28 ± 7.70	0.054	0.957
Male	28 (53.85)	26 (48.15)	0.350	0.554
NYHA class			0.259	0.879
II	6 (11.54)	5 (9.26)		
III	28 (53.85)	27 (50.00)		
IV	16 (30.77)	18 (33.33)		
Smoking history	9 (17.31)	8 (14.81)	0.128	0.72
Hypertension	6 (11.54)	5 (9.26)	0.152	0.697
Diabetes	5 (9.62)	6 (11.11)	0.069	0.793
Baseline medications				
Enalapril	15 (28.85)	15 (27.78)	0.016	0.899
Metoprolol	9 (17.31)	8 (14.81)	0.128	0.72
Spironolactone	15 (28.85)	15 (27.78)	0.016	0.899
Diuretics	5 (9.62)	4 (7.41)	0.177	0.674

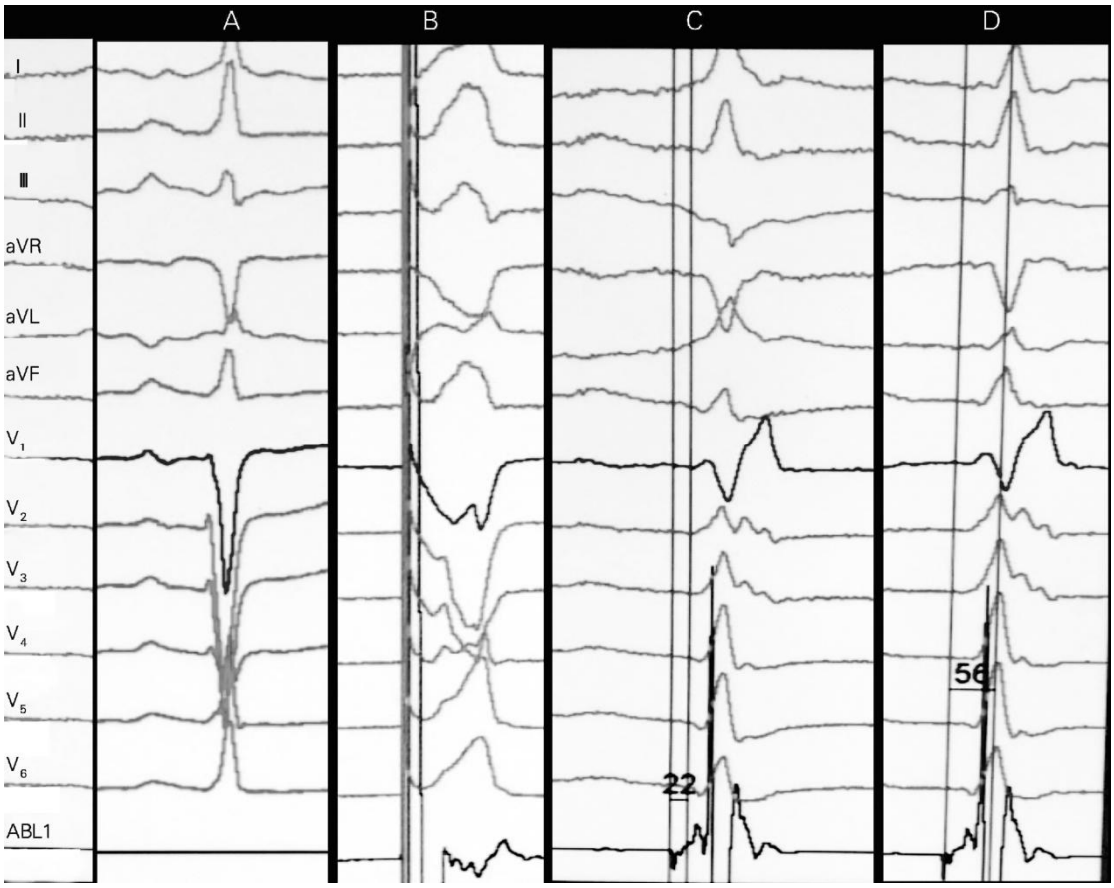

Fig. 2: Evolution of ECG during LBBaP implantation.
(A) Intrinsic rhythm showing left bundle branch block morphology; (B) Pacing ECG when the electrode was positioned at the right ventricular septum, showing left ventricular apical activation pattern; (C) Pacing ECG after successful left bundle branch capture, showing right bundle branch block morphology; stimulus-to-left bundle branch potential interval = 22 ms; (D) Surface ECG corresponding to (C), showing Sti-LVAT in lead V6 = 56 ms.

Table 2: Changes in electrophysiological parameters (mean ± SD)

Parameter	Group	n	Before treatment	After treatment	t	P
QRS duration (ms)	Observation	54	165.38 ± 10.25	125.45 ± 9.79	25.741	<0.001
	Control	52	164.92 ± 9.87	150.23 ± 3.33	10.552	<0.001
Between-group (after treatment)				t = –17.832, P < 0.001		
QRS amplitude (mV)	Observation	54	1.95 ± 0.52	9.32 ± 3.88	–14.725	<0.001
	Control	52	1.91 ± 0.49	6.89 ± 0.47	0.284	0.778
Between-group (after treatment)				t = 14.256, P < 0.001		

Changes in electrophysiological parameters

At baseline, QRS duration and QRS amplitude did not differ significantly between the two groups (P > 0.05). After six months of treatment, both groups demonstrated reductions in QRS duration and increases in QRS amplitude compared with baseline values. However, the magnitude of improvement was greater in the sacubitril/valsartan group. After treatment, patients receiving sacubitril/valsartan exhibited significantly shorter QRS duration and higher QRS amplitude compared with those receiving enalapril (P < 0.001) (Table 2).

Changes in cardiac structure, function and exercise capacity

Baseline measurements of cardiac structure, systolic function and exercise capacity were similar between the two groups (P > 0.05). After six months of treatment, both groups showed significant improvements in LVEDD, LVESD, LVEF and 6MWD compared with baseline (P < 0.05).

Table 3: Changes in cardiac structure, function, and exercise capacity (mean ± SD)

Parameter	Group	n	Before treatment	After treatment	t	P
LVESD (mm)	Observation	54	52.47 ± 5.18	43.22 ± 2.33	12.351	<0.001
	Control	52	52.31 ± 5.37	50.61 ± 2.19	1.908	0.062
Between-group (after treatment)				t = 17.905, P < 0.001		
LVEDD (mm)	Observation	54	61.32 ± 3.21	54.25 ± 2.38	13.801	<0.001
	Control	52	61.45 ± 3.29	58.48 ± 2.21	5.823	<0.001
Between-group (after treatment)				t = 9.587, P < 0.001		
LVEF (%)	Observation	54	46.32 ± 1.20	57.03 ± 2.49	–29.624	<0.001
	Control	52	46.30 ± 1.48	50.29 ± 2.18	–11.872	<0.001
Between-group (after treatment)				t = 15.204, P < 0.001		
6MWD (m)	Observation	54	265.31 ± 15.72	370.25 ± 17.64	–31.624	<0.001
	Control	52	268.05 ± 16.47	349.51 ± 17.45	–24.125	<0.001
Between-group (after treatment)				t = 6.112, P < 0.001		

Table 4: Changes in serum biomarkers (mean ± SD)

Parameter	Group	n	Before treatment	After treatment	t	P
cTnI (ng/L)	*Observation*	54	30.89 ± 7.86	20.15 ± 6.68	7.352	<0.001
	Control	52	32.35 ± 10.24	26.38 ± 8.82	3.128	0.003
Between-group (after treatment)				t = 4.215, P < 0.001		
NT-proBNP (ng/L)	*Observation*	54	3837.52 ± 991.45	1685.73 ± 992.18	10.894	<0.001
	Control	52	3731.48 ± 875.63	2245.79 ± 861.42	8.587	<0.001
Between-group (after treatment)				t = 3.102, P = 0.003		
FPG (mmol/L)	*Observation*	54	6.84 ± 1.42	6.35 ± 1.61	1.835	0.071
	Control	52	6.77 ± 1.53	6.25 ± 1.42	1.841	0.071
Between-group (after treatment)				t = 0.335, P = 0.738		
SCr (μmol/L)	*Observation*	54	101.52 ± 8.43	98.34 ± 9.61	1.805	0.076
	Control	52	109.63 ± 8.92	96.91 ± 9.28	1.522	0.134
Between-group (after treatment)				t = 0.788, P = 0.433		

Table 5: Incidence of MACE [n (%)]

Group	n	Rehospitalization for HF	Angina	Severe arrhythmia	Sudden cardiac death	Total incidence
Control	52	6 (11.54)	4 (7.69)	2 (3.85)	2 (3.85)	14 (26.92)
Observation	54	3 (5.56)	3 (5.56)	0 (0.00)	0 (0.00)	6 (11.11)
χ^2						4.316
P						0.038

However, the degree of improvement in these parameters was significantly greater in the sacubitril/valsartan group than in the enalapril group (P < 0.001) (Table 3).

Changes in serum biomarkers

Serum concentrations of cTnI and NT-proBNP decreased significantly from baseline in both groups after treatment (P < 0.01). The magnitude of reduction was greater in the observation group than in the control group (P < 0.01). In contrast, FPG and SCr levels remained relatively stable throughout the study period, with no significant changes observed either within or between the two groups (P > 0.05) (Table 4).

Incidence of MACE

During the six-month follow-up period, the incidence of MACE was lower in the sacubitril/valsartan group (11.11%) than in the enalapril group (26.92%) and the difference reached statistical significance (P < 0.05) (Table 5). However, given the relatively short follow-up duration and limited sample size, these findings should be interpreted with caution.

DISCUSSION

This retrospective cohort study evaluated the clinical outcomes of sacubitril/valsartan compared with enalapril in patients with HF and LBBB undergoing LBBaP implantation. The main findings of this study can be summarized as follows. Compared with patients receiving enalapril after device implantation, those treated with sacubitril/valsartan demonstrated greater improvements in

ventricular electrical synchrony, as reflected by changes in QRS duration and amplitude. In addition, more pronounced improvements were observed in cardiac structure and systolic function (LVEDD, LVESD and LVEF), exercise capacity assessed by 6MWD and circulating biomarkers of myocardial injury and cardiac stress (cTnI and NT-proBNP). Furthermore, the incidence of MACE during the six-month follow-up period was lower in the sacubitril/valsartan group. Taken together, these findings suggest that among patients undergoing LBBaP implantation, sacubitril/valsartan may provide additional short-term clinical benefits compared with enalapril.

Electrophysiological mechanisms and advantages of LBBaP in cardiac resynchronization

Conventional BVP activates the ventricles through a non-physiological conduction pathway and approximately 30% of patients demonstrate a suboptimal response to this therapy (Liang *et al*., 2024). In contrast, LBBaP, as a form of CSP, achieves a more physiological pattern of ventricular activation by directly capturing the left bundle branch and restoring conduction through the His–Purkinje system. In the present study, all patients underwent successful LBBaP implantation, which was characterized by a paced RBBB morphology and a shortened Sti-LVAT (<75 ms), consistent with previously reported criteria (Huang *et al*., 2020).

After treatment, QRS duration decreased in both groups, with a greater reduction in the sacubitril/valsartan group. This observation is consistent with previous reports indicating that LBBaP can produce narrower QRS complexes and improved electrical synchrony compared with conventional BVP in candidates for CRT (Gin *et al*., 2023). One potential explanation is that LBBaP bypasses the site of conduction delay and facilitates rapid activation of the Purkinje network, thereby improving ventricular electrical coordination (El Iskandarani *et al*., 2024). Improved electrical synchrony may subsequently contribute to better mechanical coordination and functional improvement. In the present study, patients treated with sacubitril/valsartan also exhibited more favorable changes in LVEF, LVEDD and LVESD. However, given the observational design of this study, these structural changes cannot be directly attributed to a specific electrophysiological mechanism.

Pharmacological effects of Sacubitril/Valsartan in patients undergoing LBBaP

Another important observation of the present study is that, despite all patients receiving successful LBBaP implantation, those treated with sacubitril/valsartan showed greater improvements in cardiac functional parameters than those treated with enalapril. Sacubitril/valsartan exerts its therapeutic effects through dual pharmacological mechanisms: valsartan blocks angiotensin II type 1 receptors and suppresses RAAS activation, while sacubitril inhibits neprilysin, thereby increasing circulating levels of endogenous natriuretic peptides (Cosentino *et al*., 2019; Chatur *et al*., 2024).

The clinical benefits of sacubitril/valsartan in HFrEF have been well established. The landmark PARADIGM-HF trial demonstrated that sacubitril/valsartan significantly reduced cardiovascular mortality and heart failure hospitalizations compared with enalapril (Chatur *et al*., 2024). In the present study, patients receiving sacubitril/valsartan exhibited greater reductions in NT-proBNP levels and lower post-treatment cTnI concentrations, which may reflect reduced myocardial stress and myocardial injury. These findings are generally consistent with previous reports demonstrating improvements in cardiac remodeling and biomarker profiles following sacubitril/valsartan therapy (Bayard *et al*., 2019; Khan *et al*., 2021). However, because the current study did not include advanced imaging parameters or mechanistic biomarkers, these observations should be interpreted as clinical associations rather than direct mechanistic evidence.

Clinical implications of device therapy combined with pharmacological management

Patients with HF often require both device-based and pharmacological interventions to optimize cardiac performance. LBBaP improves ventricular electrical synchrony, whereas pharmacological therapy targets neurohormonal pathways involved in HF progression (Butter *et al*., 2021; Akhtar *et al*., 2023). In the present study, patients receiving sacubitril/valsartan after LBBaP implantation demonstrated greater improvement in exercise capacity, as reflected by the 6-minute walk distance, compared with those receiving enalapril.

In addition, the incidence of MACE during the six-month follow-up period was lower in the sacubitril/valsartan group and no cases of sudden cardiac death or severe arrhythmia were reported in this group. These findings are broadly consistent with previous evidence indicating that sacubitril/valsartan may improve clinical outcomes in patients with HFrEF, while physiological pacing strategies, such as LBBaP, may provide a more favorable electrical substrate than conventional pacing approaches (Arnold *et al*., 2018; Allam *et al*., 2024). Nevertheless, given the relatively small sample size and short follow-up duration, these results should be interpreted with caution and should not be considered evidence of long-term prognostic benefit.

Study limitations

Several limitations should be acknowledged. First, this investigation was a retrospective single-center study and is therefore subject to potential selection bias and residual confounding. Second, the sample size was relatively small and the follow-up duration was limited to six months,

which restricts the ability to assess long-term clinical outcomes. Third, although electrocardiographic parameters, echocardiographic indices and circulating biomarkers were evaluated, advanced imaging techniques such as cardiac magnetic resonance imaging, myocardial strain analysis, or myocardial work assessment were not included. Consequently, the present study cannot provide direct mechanistic insights into the interaction between pharmacological therapy and electrical resynchronization. Future studies involving larger patient populations, longer follow-up durations and more comprehensive imaging and biomarker assessments are warranted to further clarify the clinical significance of pharmacological optimization in patients undergoing LBBaP therapy.

CONCLUSION

In conclusion, among patients with HF and LBBB undergoing LBBaP implantation, treatment with sacubitril/valsartan was associated with greater improvements in ventricular electrical synchrony, cardiac structure and function, exercise capacity and circulating biomarkers compared with enalapril. In addition, the incidence of MACE during the six-month follow-up period was lower in the sacubitril/valsartan group. However, given the retrospective design, limited sample size and relatively short follow-up duration, these findings should be interpreted cautiously. Further large-scale prospective studies are required to confirm these observations.

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Authors' contributions
Rui Wang and Cuijun Hao: Contributed to the study conception and design; Zhiqin Fang and Huahan Jing: Responsible for data collection and data analysis; Jinzheng Shi: Supervised the study and critically revised the manuscript. All authors read and approved the final manuscript.

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

Ethical approval
This study was approved by the ethics committee of the First Affiliated Hospital of Hebei North University (Approval No. K2024051). Informed consent was obtained from all study participants. All the methods were carried out in accordance with the Declaration of Helsinki. This study was performed in adherence with the STROBE guidelines. See supplementary file for the STROBE checklist.

Conflict of interest
The authors declare that they have no conflicts of interest related to this study.

Supplementary data
https://www.pjps.pk/uploads/2026/05/SUP1779448982.pdf

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