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Original Article

Vericiguat combined with standard therapy improves cardiac function, inflammatory markers, and exercise tolerance in patients with essential hypertension and chronic heart failure

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Abstract: Objective: Hypertension combined with chronic heart failure is associated with high morbidity and mortality. As a novel soluble guanylate cyclase stimulator, vericiguat has demonstrated therapeutic benefits in the treatment of heart failure. Methods: A retrospective study was conducted on 120 patients with essential hypertension complicated by chronic heart failure, who were divided into a combination therapy group (63 cases) and a conventional therapy group (57 cases). Myocardial injury markers, including N-terminal pro-B-type natriuretic peptide (NT-proBNP), soluble suppression of tumorigenicity 2 (sST2), and cardiac troponin I (cTnI); inflammatory and prognostic biomarkers, including C-reactive protein (CRP), galectin-3 (Gal-3), and fatty acid-binding protein 4 (FABP4); cardiac function parameters, including left ventricular ejection fraction (LVEF), left ventricular peak ejection rate (LVPER), and left ventricular end-diastolic dimension (LVDd); and cardiopulmonary exercise parameters, including anaerobic threshold oxygen uptake (VO_2AT), maximal oxygen uptake (VO_2max), and the 6-minute walk distance (6MWD), were measured. In addition, blood pressure, New York Heart Association (NYHA) functional class, and adverse reactions were recorded, and correlation analyses among biomarkers and clinical parameters were performed. Results: After treatment, the combination therapy group had significantly lower levels of myocardial injury and inflammatory biomarkers ($P < 0.05$), together with improved cardiac function, exercise tolerance, blood pressure, and NYHA functional class. The 6MWD was markedly longer in the combination therapy group ($P < 0.001$). No significant intergroup difference was observed in the incidence of adverse reactions ($P > 0.05$). CRP was positively correlated with NT-proBNP and negatively correlated with LVEF and 6MWD ($P < 0.001$). Conclusion: Vericiguat combined with standard therapy alleviates myocardial injury and inflammation and improves cardiac function, exercise tolerance, blood pressure control, and clinical symptoms in patients with hypertension complicated by chronic heart failure, with a favorable safety profile. Further multicenter studies are required to validate its broader clinical applicability.

Keywords: Hypertension complicated with chronic heart failure, vericiguat, cardiac function, myocardial injury, exercise tolerance

Introduction

Hypertension (HTN) is one of the most prevalent illnesses worldwide and it is a major risk factor for cardiovascular disorders [1]. Global statistics indicate that, about one-third of adults have hypertension, which has become an important contributor to cardiovascular and cerebrovascular diseases, kidney disease, and death [2]. When blood pressure elevation is not adequately controlled over a prolonged period, it can induce structural and functional cardiac abnormalities, eventually leading to heart failure (HF). HF is a complex clinical syndrome characterized by impaired cardiac pumping capacity, leading to inadequate organ and tissue perfusion. As hypertension is a major risk factor for HF, its management is of great significance for improving patient prognosis [3-5]. In clinical practice, patients with HTN may experi-

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ence a progressive decline in cardiac function, characterized by myocardial hypertrophy and the eventual development of HF. This process usually progresses gradually, and patients may initially remain asymptomatic. However, as hypertension persists, cardiac workload increases, eventually leading to varying degrees of HF. Cardiac structural abnormalities and functional impairment induced by sustained hypertension not only reduce patients' quality of life (QoL) but also increase hospitalization and mortality rates [6]. Therefore, effective control of hypertension to prevent HF remains an important clinical challenge.

With continuous advances in pharmacological therapy, a variety of novel drugs have been introduced into clinical practice, providing additional treatment options for patients with hypertension complicated by HF [7]. Vericiguat, a soluble guanylate cyclase stimulator, improves cardiovascular function by modulating the nitric oxide-cyclic guanosine monophosphate (NO-cGMP) signaling pathway and has attracted increasing attention in the field of HF treatment. Vericiguat directly stimulates soluble guanylate cyclase and enhances its sensitivity to nitric oxide (NO), thereby increasing intracellular cGMP levels and potentially improving myocardial relaxation and hemodynamic function [8, 9]. Studies have shown that vericiguat may improve cardiovascular hemodynamics, reduce cardiac workload, and exert beneficial effects on vascular and myocardial function. In patients with hypertension and HF, vericiguat may delay the progression of HF by improving blood pressure and reducing cardiac load [10].

Although previous studies have demonstrated therapeutic effects of vericiguat in HF patients, its effects on cardiac function in patients with concomitant HTN and HF remains unclear. More importantly, changes in circulating C-reactive protein (CRP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels following vericiguat treatment have not been comprehensively evaluated using standardized assessment frameworks in previous studies [11]. CRP and NT-proBNP are important inflammatory and cardiac injury markers reflecting systemic inflammation and cardiac stress, respectively, and may therefore help characterize the overall effects of vericiguat in these patients [12]. Therefore, evaluating the effects of vericiguat on these biochemical indicators may not only improve understanding of its potential therapeutic effects but also provide evidence for more individualized therapeutic regimens in clinical practice.

The present study retrospectively evaluated the therapeutic effects of vericiguat in patients with HTN and HF, with particular emphasis on cardiac function, circulating CRP levels, and NT-proBNP levels. Through this retrospective cohort analysis, we aimed to assess the potential role of vericiguat in improving cardiac function and modulating inflammatory responses, thereby providing further evidence for its clinical application in patients with hypertension complicated by HF. Ultimately, this study may provide new insights into the clinical management of these patients and contribute to improving patient prognosis and QoL.

Materials and methods

Subjects

This retrospective study included 120 patients with essential hypertension complicated by chronic heart failure who were admitted to Xingtai Central Hospital between May 2022 and May 2024. Based on the introduction of vericiguat into clinical practice at our hospital in June 2023, patients admitted between May 2022 and May 2023 were assigned to the conventional therapy group (57 cases), whereas those admitted between June 2023 and May 2024 were assigned to the combination therapy group (63 cases; conventional therapy plus vericiguat). The study protocol was approved by the Ethics Committee of Xingtai Central Hospital. All procedures were conducted in accordance with relevant ethical principles, with strict protection of patient confidentiality and personal data.

Based on the primary outcome results of the VICTORIA trial [13], a post-hoc power analysis was performed using PASS 15.0 software. In that study, the incidence of the composite endpoint of cardiovascular death or heart failure hospitalization was 35.5% in the vericiguat group and 38.5% in the placebo group (hazard ratio, 0.90). With a two-sided α level of 0.05 and the observed effect size, the statistical power of the present sample size of 120 patients was approximately 82% to detect a between-group difference.

Inclusion criteria: (1) patents aged 40-80 years; (2) a diagnosis of HTN, defined as either systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg; (3) a diagnosis of chronic heart failure with New York Heart Association (NYHA) functional class II-III; and (4) a documented history of HTN with heart failure-related symptoms, including dyspnea or fatigue, lasting for at least six months.

Exclusion criteria: (1) acute worsening of heart failure or an acute myocardial infarction within 30 days before enrollment; (2) severe hepatic dysfunction, such as cirrhosis or liver failure; (3) pregnancy or breastfeeding; (4) a documented allergy to vericiguat or any of its components; (5) severe renal impairment, defined as a serum creatinine levels > 2.5 mg/dl or an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m^2; and (6) incomplete clinical data or inability to complete the required follow-up assessments.

Treatment methods

The conventional therapy group received standard treatment, including antihypertensive agents, such as angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), and calcium channel blockers); β-blockers (e.g., metoprolol or bisoprolol), diuretics (e.g., furosemide or spironolactone), and heart failure-related therapies (including aldosterone antagonists and anticoagulation therapy). The goals of conventional therapy were to achieve adequate blood pressure control (target SBP < 140 mmHg and DBP < 90 mmHg), alleviate heart failure-related symptoms, and improve overall cardiac function. The combination therapy group received vericiguat (Bayer Aktiengesellschaft, Germany; National Drug Approval No. HJ20220050) in addition to the conventional therapy. Vericiguat was initiated at 2.5 mg once daily and subsequently titrated according to patient tolerance and therapeutic response. The dose was increased to 5 mg once daily, when tolerated, further increased to a maximum maintenance dose of 10 mg once daily.

All patients received treatment for at least 6 months. To standardize data collection and statistical analysis, the primary outcome assessment was performed 6 months after treatment initiation. Although the total treatment duration ranged from 6 to 12 months, all outcome measurements included in the present analysis were obtained at the 6-month follow-up visit to ensure a consistent observation period across all enrolled patients. Long-term follow-up data beyond 6 months were not included in this study and warrant further investigation in future studies.

Observational indicators

The primary endpoints were left ventricular ejection fraction (LVEF) and serum N-terminal pro-B-type natriuretic peptide (NT-proBNP), which were selected to evaluate the principal therapeutic effects of vericiguat on cardiac function and myocardial stress in patients with heart failure.

The secondary endpoints included other cardiac function parameters, including left ventricular peak ejection rate (LVPER) and left ventricular end-diastolic dimension (LVDd); inflammatory and prognostic markers, including CRP, soluble suppression of tumorigenicity 2 (sST2), cardiac troponin I (cTnI), galectin-3 (Gal-3), and fatty acid-binding protein 4 (FABP4); cardiopulmonary exercise testing parameters, including anaerobic threshold oxygen uptake (VO_2AT) and maximal oxygen uptake (VO_2max); 6-minute walk distance (6MWD); blood pressure; NYHA functional class; and adverse events.

(1) Demographic and clinical data, including age, sex, and comorbidities, were collected from the electronic medical record system.

(2) Fasting venous blood samples were collected before treatment and at 1 and 6 months after treatment initiation. Serum NT-proBNP concentrations were measured using a chemiluminescent immunoassay, whereas sST2, cTnI, CRP, Gal-3, and FABP4 levels were determined using enzyme-linked immunosorbent assay (ELISA).

(3) Echocardiographic parameters, including LVPER, LVEF, and LVDd, were recorded before treatment and at 1 and 6 months after treatment initiation.

(4) Cardiopulmonary exercise testing parameters, including VO_2AT and VO_2max, were obtained before treatment and at 1 and 6 months after treatment initiation.

Table 1. Comparison of baseline characteristics between the two groups

Indicator	Combination therapy group (n = 63)	Conventional therapy group (n = 57)	Statistic	*P* value
Age ($\bar{x}$ ± s, years)	55.26 ± 8.60	53.47 ± 7.25	t = 1.236	0.219
Sex [n (%)]			χ^2 = 0.317	0.573
Male	38 (60.32)	41 (71.93)		
Female	25 (39.68)	16 (28.07)		
Comorbidities [n (%)]				
Coronary heart disease	29 (46.03)	27 (47.37)	χ^2 = 0.023	0.879
Hyperlipidemia	31 (49.21)	30 (52.63)	χ^2 = 0.141	0.707

(5) SBP and DBP were measured before treatment and at 1 and 6 months after treatment initiation. Blood pressure was measured with patients in a seated position after resting in a quiet environment, and the average of three measurements was used for analysis.

(6) NYHA functional class was assessed before treatment and at 6 months after treatment initiation by two cardiologists.

(7) The 6-minute walk distance (6MWD), assessed using the 6-minute walk test (6MWT), was recorded before treatment and at 4, 8, and 12 weeks after treatment initiation. 6MWD can reflect short-term changes in exercise tolerance, whereas echocardiographic parameters, serum biomarkers, and blood pressure were assessed over a longer follow-up period of 6 months to evaluate changes in cardiac function and clinical status.

(8) Adverse events, including dizziness, hypotension, and fatigue, as well as laboratory parameters reflecting hepatic and renal function, were recorded throughout the 6-month observation period.

Statistical processing

SPSS 22.0 software was applied for all statistical analyses. Continuous variables conforming to a normal distribution were expressed as the mean ± standard deviation (SD), whereas categorical variables were presented as numbers and percentages (n, %). Repeated measures obtained at baseline, 1 month, and 6 months were analyzed using repeated-measures ANOVA to assess the effects of group, time, and group-by-time interaction. When a significant group-by-time interaction was identified, independent-samples t-tests or Mann-Whitney U tests were used for post hoc between-group comparisons at individual time points, as appropriate. Categorical variables were compared using the chi-square (χ^2) test. Pearson correlation analysis was performed to assess correlations between continuous variables. A two-sided *P* value < 0.05 was considered statistically significant.

For analyses involving the 6MWD, the 12-week measurement was used because it represented the final standardized follow-up time point available for this outcome in all enrolled patients. Correlation analyses involving 6MWD therefore used the 12-week 6MWD data, whereas serological and echocardiographic parameters were evaluated at their predefined follow-up time points. All 120 enrolled patients with complete data were included in the correlation analyses.

Results

Baseline characteristics of the study participants

Baseline characteristics, including age and sex, and comorbidities such as coronary heart disease and hyperlipidemia, did not differ significantly between the combination therapy group and the conventional therapy group (*P* > 0.05; **Table 1**).

Comparison of myocardial injury-related biomarkers before and after treatment

As shown in **Figure 1**, no significant differences were observed in NT-proBNP, sST2, or cTnI between the two groups at baseline (*P* > 0.05). The levels of these markers decreased over time in both groups. At 1 and 6 months after treatment initiation, the combination therapy group showed significantly lower NT-proBNP,

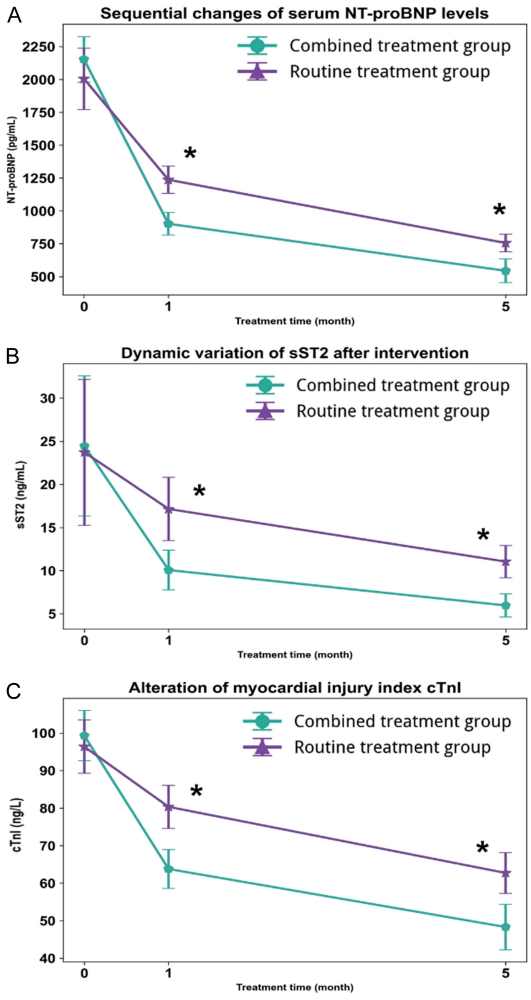


Figure 1. Comparison of myocardial injury-related indicators before and after treatment between the two groups. A. NT-proBNP; B. sST2; C. cTnI. Notes: *P < 0.05, versus the conventional therapy group. NT-proBNP: N-terminal pro-B-type natriuretic peptide; sST2: soluble suppression of tumorigenicity 2; cTnI: cardiac troponin I.

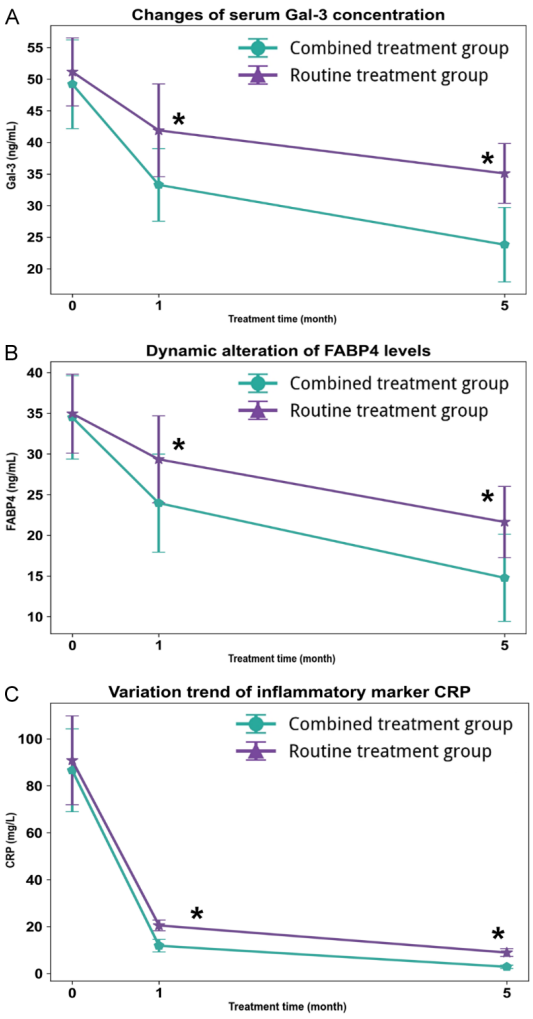


Figure 2. Comparison of prognosis-related indicators before and after treatment between the two groups. A. Gal-3; B. FABP4; C. CRP. Note: *P < 0.05, versus the conventional therapy group. Gal-3: Galectin-3; FABP4: Fatty acid-binding protein 4; CRP: C-reactive protein.

sST2, and cTnI levels than the conventional therapy group (P < 0.05).

Comparison of inflammatory and prognostic biomarkers before and after treatment

As shown in **Figure 2**, no significant differences were observed in the serum levels of CRP, Gal-3, or FABP4 between the two cohorts (P > 0.05). The levels of CRP, Gal-3, and FABP4 gradually decreased over time in both groups. At 1 and 6 months after intervention, these biomarker levels were significantly lower in the combination therapy group than in the conventional therapy group (P < 0.05).

Comparison of cardiac function parameters before and after intervention

As shown in **Figure 3**, there were no significant differences in baseline LVPER, LVEF, or LVDd values between the combination therapy group and the conventional therapy group. After treatment, both groups demonstrated increased LVPER and LVEF values and decreased LVDd values. At 1 and 6 months after treatment, the combination therapy group demonstrated significantly higher LVPER and LVEF and significantly lower LVDd compared with the conventional therapy group (all P < 0.05).

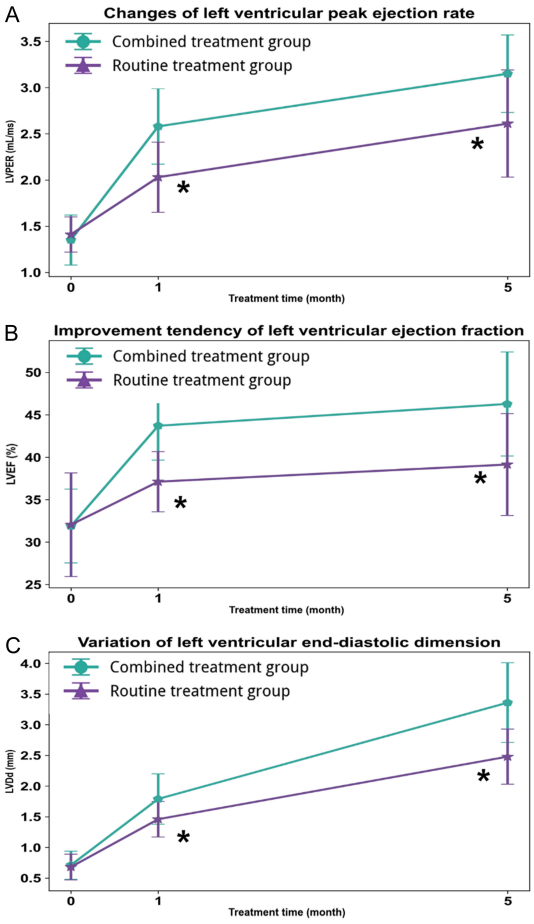


Figure 3. Comparison of cardiac function parameters before and after treatment between the two groups. A. LVPER; B. LVEF; C. LVDd. Note: $^{*}P < 0.05$, versus the conventional therapy group. LVPER: left ventricular peak ejection rate; LVEF: left ventricular ejection fraction; LVDd: left ventricular end-diastolic dimension.

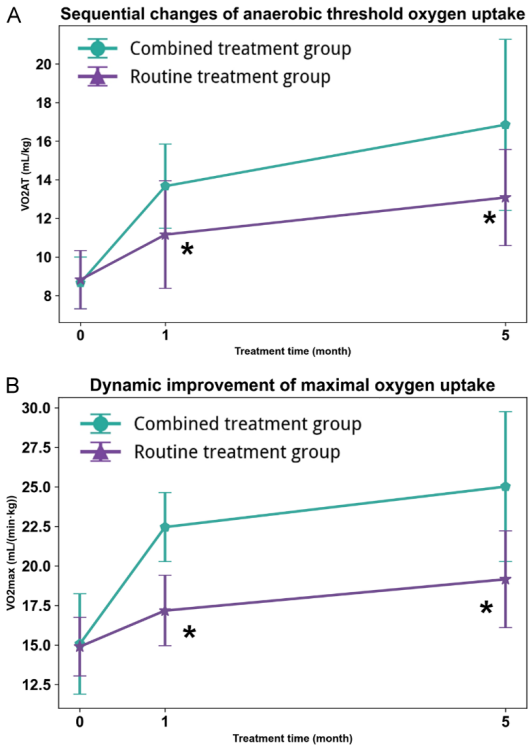


Figure 4. Comparison of VO_2AT (A) and VO_2max (B) before and after treatment between the two groups. Note: $^{*}P < 0.05$, versus conventional therapy group. VO_2AT: oxygen uptake at anaerobic threshold; VO_2max: maximal oxygen uptake.

Comparison of CPET parameters before and after treatment

As shown in **Figure 4**, there were no significant differences in baseline VO_2AT and VO_2max between the two groups ($P > 0.05$). Both VO_2AT and VO_2max of the subjects both increased over time, with the combination therapy group exhibiting significantly higher VO_2AT and VO_2max than the conventional group at 1 month and 6 months post-intervention ($P < 0.05$).

Comparison of SBP and DBP before and after treatment

Baseline SBP and DBP were comparable between the two groups ($P > 0.05$). Both SBP and DBP decreased after intervention in both groups. At 1 and 6 months after treatment initiation, the combination therapy group displayed significantly lower blood pressure than the conventional therapy group ($P < 0.001$; **Table 2**).

Comparison of NYHA functional class before and after treatment

At baseline, the distributions of NYHA Class II and III patients did not differ significantly between the two groups ($P > 0.05$). After 6 months of treatment, the proportion of patients classified as NYHA Class II increased, whereas the proportion of patients categorized as NYHA Class III decreased. The difference in NYHA functional class differed significantly between the two groups ($P = 0.011$; **Table 3**), indicating greater improvement in functional status in the combination therapy group.

6MWD

Within-group comparisons showed that 6MWD increased at 4, 8, and 12 weeks compared with baseline in both groups. Between-group com-

Table 2. Comparison of blood pressure levels between the two groups before and after treatment

Indicator	Time point	Combination therapy group (n = 63)	Conventional therapy group (n = 57)	t-value	*P*-value
SBP	Before treatment	152.3 ± 10.5	151.1 ± 9.8	0.645	0.520
	1 month after treatment	132.5 ± 8.2	139.6 ± 9.1	3.943	< 0.001
	6 months after treatment	128.4 ± 7.5	135.7 ± 8.4	4.370	< 0.001
DBP	Before treatment	92.6 ± 7.3	91.8 ± 6.9	0.618	0.538
	1 month after treatment	80.3 ± 5.6	85.1 ± 6.2	4.159	< 0.001
	6 months after treatment	77.2 ± 4.8	82.5 ± 5.3	5.209	< 0.001

Note: SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 3. Comparison of NYHA cardiac function classification between the two groups before and after treatment

Time point	NYHA class	Combination therapy group (n = 63)	Conventional therapy group (n = 57)	χ^2-value	*P*-value
Before treatment	Class II	35 (55.56)	36 (63.16)	0.720	0.396
	Class III	28 (44.44)	21 (36.84)		
6 months after treatment	Class II	49 (77.78)	39 (68.42)	6.502	0.011
	Class III	14 (22.22)	18 (31.58)		

Note: NYHA: New York Heart Association.

Table 4. Comparison of 6MWD before and after treatment between the two groups

Group	N	Before treatment	4 weeks after treatment	8 weeks after treatment	12 weeks after treatment
Combination therapy group	63	325.6 ± 42.3	378.5 ± 45.2	426.3 ± 48.6	468.2 ± 51.4
Conventional therapy	57	322.8 ± 43.1	346.2 ± 44.5	375.4 ± 46.3	402.5 ± 47.7
Inter-group F-value	-	-	12.364	15.728	18.415
P value	-	-	< 0.001	< 0.001	< 0.001

Note: 6MWD: 6-minute walking distance.

parisons showed that the combination therapy group had a significantly greater 6MWD than the conventional therapy group at each follow-up time point, with F values of 12.364 at 4 weeks ($P < 0.001$), 15.728 at 8 weeks ($P < 0.001$), and 18.415 at 12 weeks ($P < 0.001$; **Table 4**).

Analysis of safety

During the 6-month observation period, no serious adverse events occurred in either group, and no patient discontinued treatment due to adverse reactions. The most commonly recorded adverse events included mild dizziness, hypotension, and fatigue. Five adverse events occurred in the combination therapy group, corresponding to an overall incidence of 7.94% (5/63), including three cases of dizziness (4.76%) and two cases of hypotension (3.17%), with no cases of fatigue. In the conventional therapy group, four adverse events were recorded, corresponding to an overall incidence of 7.02% (4/57), including two cases of dizziness (3.51%) and two cases of fatigue (3.51%); no cases of hypotension were reported. Detailed data are presented in **Table 5**.

Correlation analysis

Pearson correlation analysis was performed to assess the relationships among serum CRP, NT-proBNP, LVEF, and 6MWD (**Table 6** and **Figure 5**). Serum CRP was positively correlated with NT-proBNP ($r = 0.726$, $P < 0.001$) and negatively correlated with LVEF ($r = -0.683$, $P < 0.001$) and 6MWD ($r = -0.642$, $P < 0.001$); NT-proBNP was negatively correlated with LVEF ($r = -0.751$, $P < 0.001$) and 6MWD ($r = -0.642$, $P < 0.001$).

Table 5. Comparison of safety profiles between the two groups

Group	N	Dizziness	Hypotension	Weakness	Overall incidence
Combination therapy group	63	3 (4.76%)	2 (3.17%)	0 (0.00%)	5 (7.94%)
Conventional therapy group	57	2 (3.51%)	0 (0.00%)	2 (3.51%)	4 (7.02%)
χ^2 value	-	-	-	-	0.125
P value	-	-	-	-	0.724

Table 6. Pearson correlation analysis of main observation indicators

Indicator pairing	Correlation coefficient r	Determination coefficient R^2	95% confidence interval	*P* value
CRP and NT-proBNP	0.726	0.527	0.612 - 0.811	< 0.001
CRP and LVEF	-0.683	0.466	-0.784 - -0.543	< 0.001
NT-proBNP and LVEF	-0.751	0.564	-0.835 - -0.632	< 0.001
CRP and 6MWD	-0.642	0.412	-0.753 - -0.491	< 0.001
NT-proBNP and 6MWD	-0.695	0.483	-0.792 - -0.561	< 0.001

Note: CRP: C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LVEF: left ventricular ejection fraction; 6MWD: 6-minute walking distance.

Discussion

The overall mortality rate in patients with hypertension complicated by chronic heart failure remains relatively high, and conventional treatment strategies are primarily aimed at controlling blood pressure, alleviating symptoms, and delaying disease progression [14]. Although standard medical therapy can effectively improve symptoms and maintain blood pressure stability, challenges remain in preventing disease progression and further improving long-term prognosis and quality of life [15]. Vericiguat, a soluble guanylate cyclase (sGC) stimulator, exerts its therapeutic effects in heart failure by modulating the NO-cGMP signaling pathway. To date, most clinical studies of vericiguat have focused on patients with heart failure with reduced ejection fraction, whereas real-world data regarding its use in patients with essential hypertension complicated by heart failure remains limited [16].

NT-proBNP, sST2, and cTnI are commonly used biochemical markers reflecting different aspects of cardiac stress, myocardial injury, and heart failure progression. Before treatment, there were no significant intergroup differences in the levels of these markers, indicating comparable baseline cardiac status between the two groups. At the 1- and 6-month follow-up visits, the levels of NT-proBNP, sST2, and cTnI were significantly lower in the combination therapy group than in the conventional therapy group, suggesting that the addition of vericiguat to conventional therapy can further reduce myocardial injury. This finding is consistent with existing evidence in heart failure management: conventional therapies, including ACE inhibitors, β-blockers, and diuretics, play important roles in controlling blood pressure, alleviating symptoms, but do not always improve clinical outcomes in all patients [17]. Vericiguat improves systemic hemodynamics and reduces cardiac workload by activating the NO-cGMP pathway, while also inhibiting myocardial fibrosis and systemic inflammatory responses. Its mechanisms of action in treating chronic heart failure mainly include improving vascular endothelial function, counteracting myocardial fibrosis, and suppressing inflammatory responses. Previous studies have shown that dysregulation of endothelin signaling may contribute to heart failure progression and myocardial injury [18]. After treatment, CRP, Gal-3, and FABP4 levels decreased in both groups, with significantly lower levels observed in the combination therapy group at the 1- and 6-month follow-up visits. These biomarkers are associated with different pathophysiological processes relevant to heart failure. CRP reflects systemic inflammatory activity, Gal-3 is associated with myocardial fibrosis, and FABP4 is involved in lipid metabolism and cardiometabolic dysfunction [19]. The greater reductions in these markers observed in the combination therapy group suggest that vericiguat-containing therapy can improve myocardial metabolic abnormalities and suppress persistent inflammation in patients with chronic heart failure; the simul-

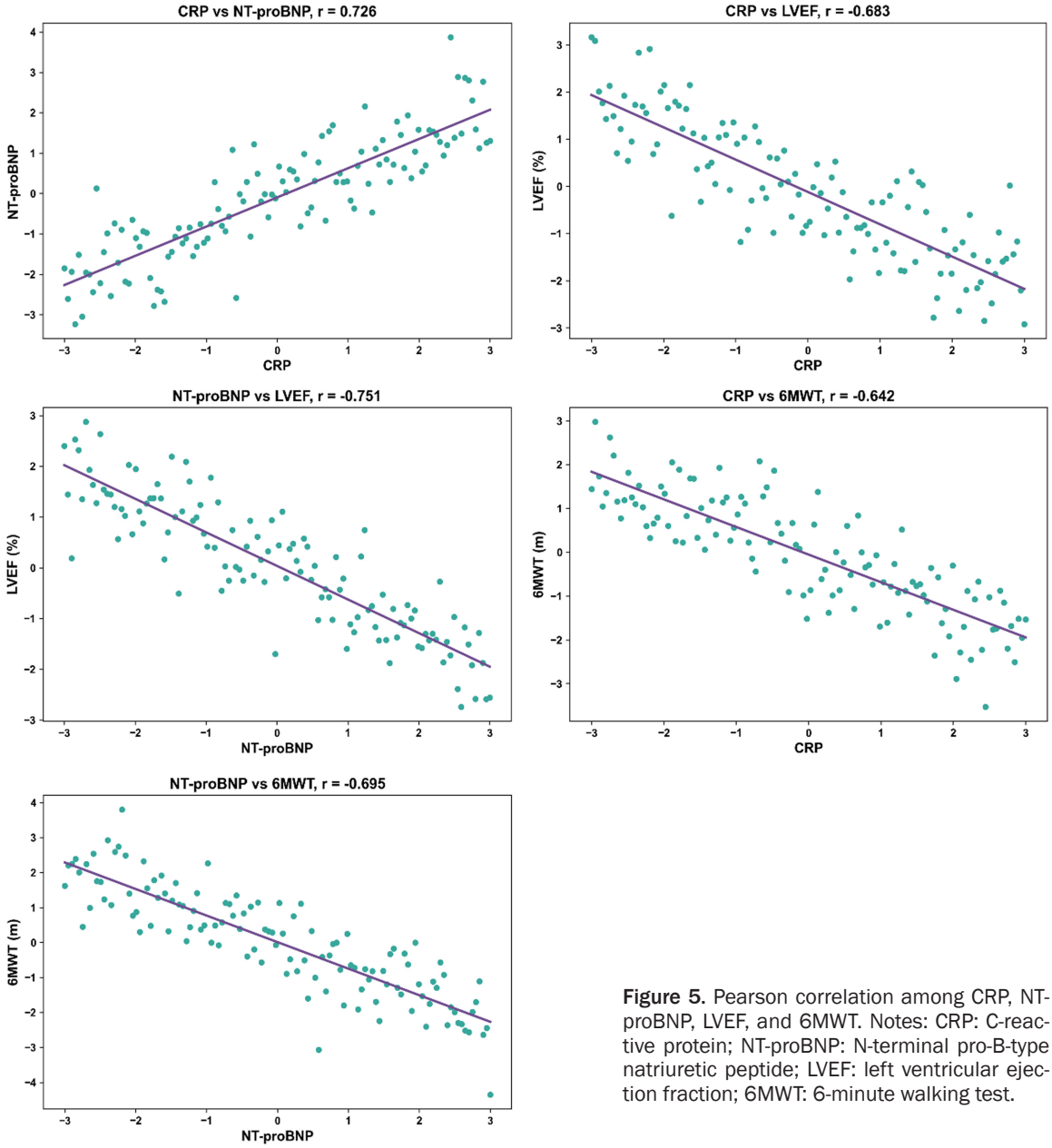


Figure 5. Pearson correlation among CRP, NT-proBNP, LVEF, and 6MWT. Notes: CRP: C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LVEF: left ventricular ejection fraction; 6MWT: 6-minute walking test.

taneous reduction in Gal-3 and FABP4 supports effective control of chronic inflammatory injury.

Cardiac function parameters are fundamental indicators for evaluating treatment efficacy in patients with heart failure. Our results showed that after treatment, LVPER and LVEF increased and LVDd decreased in the combination therapy group; at both 1 and 6 months, improvements in these cardiac function parameters were greater in the conventional therapy group than in the conventional therapy group. The increase in LVEF suggests an improvement in left ventricular systolic function and overall cardiac performance. Cardiopulmonary exercise testing (CPET) is a classic method for assessing cardiopulmonary reserve and exercise capacity in patients with heart failure. Multicenter studies have demonstrated that CPET parameters, such as VO_2AT and VO_2max, can objectively reflect the severity of cardiac dysfunction and response to treatment in patients with heart failure [20]. In our study, VO_2AT and VO_2max were significantly higher in the combination therapy group after treatment, consistent with the findings of a prospective

observational study by Zhan et al., who reported that vericiguat combined with standard heart failure therapy significantly increased peak oxygen uptake and anaerobic threshold, improved ventilatory efficiency, and enhanced overall exercise tolerance [21]. The improvements in oxygen uptake suggest enhanced cardiopulmonary reserve and exercise capacity, which may contribute to improved functional status and quality of life. Such benefits may be related to the hemodynamic effects of vericiguat through modulation of the NO-sGC-cGMP pathway, with potential improvements in ventricular function, vascular function, and circulatory efficiency, thereby helping to alleviate exercise intolerance, fatigue, and dyspnea in patients with heart failure.

We also observed improvements in blood pressure and NYHA functional class in both groups. Patients receiving vericiguat in addition to conventional therapy showed greater reductions in systolic and diastolic blood pressure during follow-up. By optimizing hemodynamics and reducing afterload, vericiguat exerts a synergistic hypotensive effect with conventional heart failure and antihypertensive drugs, further decreasing myocardial workload. After 6 months of treatment, the proportion of patients with NYHA class II was significantly higher in the combination therapy group, whereas the proportion with class III was significantly lower, indicating greater improvement in cardiac function compared with the conventional therapy group. The combination of stable blood pressure control and improved functional class demonstrates that adding vericiguat to standard therapy may provide additional benefits in terms of hemodynamic status, symptom burden, and functional capacity in patients with hypertension complicated by chronic heart failure. These findings may provide further clinical evidence supporting individualized treatment optimization in this population.

Our study further evaluated the 6MWT, adverse event profiles, inflammatory markers, and correlations among key clinical and biochemical parameters. At 4, 8, and 12 weeks post-intervention, the 6MWD was significantly longer in the combination therapy group than in the conventional therapy group. These findings suggest that the addition of vericiguat to standard therapy may further improve exercise tolerance and functional capacity in patients with hypertension complicated by heart failure by enhancing cardiac pumping capacity, reducing cardiac workload, and suppressing systemic inflammation. Regarding safety, the overall incidence of adverse events did not differ significantly between the combination therapy group and the conventional therapy group. The reported adverse reactions were mainly mild dizziness, hypotension, and fatigue, and no serious adverse events occurred during the study period. These findings suggest that vericiguat was generally well tolerated and are broadly consistent with the conclusions of a previous meta-analysis of soluble guanylate cyclase modulators [22].

Pearson correlation analysis showed that serum CRP was positively correlated with NT-proBNP, and negatively correlated with LVEF and 6MWD. These correlations suggest that greater systemic inflammatory activity and cardiac stress may be associated with poorer ventricular systolic function and reduced exercise capacity. As discussed in the mechanistic review by Bajec et al., activation of the NO-sGC-cGMP signaling pathway may exert beneficial effects on inflammation, fibrosis, ventricular remodeling, and cardiac stress [23]. This mechanistic framework may partially explain the concurrent improvements in biomarkers, cardiac function, and exercise capacity observed in the present study. By suppressing inflammation, reducing cardiac workload, and reversing ventricular remodeling, vericiguat simultaneously regulates cardiac function, inflammatory cytokine expression, and exercise capacity. Our findings provide additional real-world evidence supporting the potential clinical benefit and tolerability of vericiguat as an adjunct to standard therapy in patients with hypertension complicated by heart failure.

Nevertheless, the maximum follow-up duration for most observational parameters was only 6 months, whereas the 6MWT was followed for only 12 weeks. Therefore, the findings of this study primarily reflect the short-term effects of vericiguat combined with conventional therapy and cannot be extrapolated to long-term outcomes. Longer-term studies with extended follow-up (6 months or longer) are needed to further evaluate the durability of the observed therapeutic benefits. Furthermore, this is a retrospective, non-randomized study, and the use of historical medical records may have intro-

duced selection bias and other unmeasured confounding factors.

Conclusion

Vericiguat combined with conventional interventions was associated with greater improvements in cardiac function, exercise tolerance, blood pressure control, and overall clinical status, together with reductions in biomarkers related to cardiac stress and inflammation, in patients with essential hypertension complicated by chronic heart failure. This treatment was also well tolerated during the study period. However, these findings should be interpreted with caution. Larger prospective studies with longer follow-up are warranted to confirm the long-term efficacy and safety of vericiguat in this patient population.

Disclosure of conflict of interest

None.

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