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# The comparative study of the efficacy of recombinant human brain natriuretic peptide combined with vasoactive medications for elderly patients with heart failure and hypotension receiving injections

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## Abstract

**Background** Heart failure (HF) in elderly patients with concurrent hypotension presents a therapeutic challenge due to limited standard HF therapies' applicability. Recombinant human brain natriuretic peptide (rhBNP) and vasoactive medications have shown potential in HF management, but their combined efficacy in elderly patients with HF and hypotension remains understudied.

**Methods** This retrospective cohort study included elderly HF patients with hypotension who received rhBNP alone (Group A,  $n=68$ ), rhBNP with dobutamine (Group B,  $n=74$ ), or rhBNP with dopamine (Group C,  $n=71$ ). Biomarker responses, cardiac function, adverse events, and cost implications were compared among the groups using statistical analysis.

**Results** The combination therapy groups (B and C) showed significantly lower NT-proBNP levels compared to the rhBNP-alone group ( $P < 0.001$ ). Troponin I levels were also lower in the combination therapy groups compared to the rhBNP-alone group ( $P < 0.05$ ). Left ventricular ejection fraction (LVEF) was significantly higher in the combination therapy groups compared to the rhBNP-alone group ( $P < 0.05$ ). No significant differences were found in adverse events or cost implications among the groups.

**Conclusion** Combining rhBNP with vasoactive medications in elderly patients with HF and hypotension led to notable reductions in biomarkers and improvements in LVEF without significant differences in adverse events or cost implications. These findings support the potential utility of combined rhBNP and vasoactive medications therapy in optimizing HF management in this patient population, warranting further investigation through prospective studies.

**Trial registration** Not applicable.

**Clinical trial number** Not applicable.

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**Keywords** Efficacy, Recombinant human brain natriuretic peptide, Dopamine, Dobutamine, Elderly patients, Heart failure, Hypotension

## Introduction

Heart failure (HF) represents a significant public health challenge, with an expanding prevalence driven by aging populations and a rising burden of cardiovascular risk factors [1]. Despite advances in diagnostic and therapeutic strategies, the management of HF in elderly patients was complicated by distinctive clinical presentations, comorbidities, and altered pharmacokinetics, posing significant therapeutic challenges [2]. Among these challenges, concomitant hypotension in elderly patients with HF presents a particularly complex scenario, necessitating a delicate balance between optimizing cardiac function and preventing hemodynamic compromise [3].

The presence of hypotension in this population often limits the use of standard HF therapies, such as vasoactive medications and inotropic agents, due to the potential to exacerbate systemic hypoperfusion [4]. Consequently, the management of HF in elderly patients with concurrent hypotension remains a therapeutic conundrum, mandating the exploration of novel treatment modalities to establish effective and safe therapeutic regimens tailored to this vulnerable patient cohort.

The pharmacological landscape for HF therapy has evolved considerably, with the emergence of innovative treatment approaches targeting neurohormonal imbalances, ventricular remodeling, and hemodynamic optimization [5]. Recombinant human brain natriuretic peptide (rhBNP) has garnered attention as a promising therapeutic agent due to its vasodilatory, diuretic, and natriuretic properties, offering potential benefits in improving cardiac function and relieving symptoms in HF patients [6, 7]. However, the utilization of rhBNP in elderly patients with HF and hypotension poses unique considerations, as the delicate hemodynamic balance in these individuals requires a tailored therapeutic approach to confer clinical benefits without precipitating adverse events [8].

The significance of inotropic agents therapy in HF management has been well-established, particularly in the context of alleviating afterload and optimizing cardiac performance [9]. The vasoactive positive inotropic drugs dopamine and dobutamine, which agonize cardiac  $\beta$ -receptors, increase myocardial contractility, and increase cardiac output and ejection per beat, have demonstrated efficacy in decreasing systemic vascular resistance and decreasing ventricular afterload, and are reasonable adjunctive therapies to standard hypertension therapy, including rhBNP, in elderly patients with low blood pressure and impaired cardiac function [10].

Despite the theoretical rationale for combining rhBNP with positive inotropic agents with vasodilatory

properties in elderly patients with HF and hypotension, the clinical evidence supporting this treatment strategy remains limited (11, 12). Existing studies often lack comprehensive comparisons of the efficacy, safety, and cost implications of the combined therapy in this specific patient population. Furthermore, the dearth of evidence-based guidance on the optimal management of HF in elderly patients with hypotension underscores the critical need to rigorously evaluate the clinical impact of combining rhBNP with positive inotropic drugs.

Therefore, this comparative study aims to address the notable gaps in knowledge and practice by investigating the efficacy of combining rhBNP with positive inotropic drugs with vasoactive properties in elderly patients with HF and hypotension. This study seeks to provide robust evidence on the clinical utility of the combined therapy and its potential to optimize the management of HF in this vulnerable patient subset.

## Materials and methods

### Research object

This study was a retrospective cohort study. Clinical data of patients with HF (including ischemic heart disease, valvular disease, and cardiomyopathy) and hypotension admitted to our hospital from June 2022 to June 2023 were selected. The patients were grouped based on the different treatment methods used, namely rhBNP group (Group A,  $n=68$ ), rhBNP combined with dobutamine hydrochloride injection group (Group B,  $n=74$ ), and rhBNP combined with dopamine hydrochloride injection group (Group C,  $n=71$ ). The patient selection involved several steps to ensure that patient preferences were respected and considered. Firstly, the physicians provided comprehensive information about the existing treatment options, including their benefits and potential risks, in a clear and understandable manner to all patients, ensuring their full understanding of their choices. Subsequently, patients and physicians jointly made decisions, openly and honestly discussing the available treatment options, considering the patient's medical condition, personal values, and preferences. Importantly, all patient decisions were made within the framework of medical ethics, ensuring that patient autonomy and informed consent were effectively upheld throughout the decision-making process.

### Inclusion and exclusion criteria

Inclusion criteria: (1) Meet the diagnostic criteria for HF [11]; (2) Age > 60 years; (3) Systolic blood pressure  $\leq 110$  mmHg or mean arterial pressure  $\leq 65$  mmHg at the time

of enrollment; (4) Normal mental and cognitive function; (5) Completion of 3 days of treatment; (6) Complete case data.

Exclusion criteria: (1) Patients with malignant tumors or multiple organ failure; (2) Cardiogenic shock, cardiopulmonary disease; (3) Contraindications to experimental drugs; (4) Patients with recent surgery within 1 month, severe anemia, inadequate fluid volume, need for mechanical ventilation, aortic balloon counterpulsation, emergency intervention, etc.; (5) Pulmonary embolism or acute coronary syndrome; (6) Patients unable to tolerate inotropic drugs, leading to severe hypotension; (7) The patients did not have RV overload and hypotension caused by extrinsic factors.

### Treatment methods

Upon admission, all patients received standard treatment for HF, including bed rest, oxygen therapy, restricted salt and water intake, addressing the underlying causes, managing infections, and basic therapy with angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) and inotropic agents [12]. The aim was to raise systolic blood pressure to within 95–120 mmHg or maintain mean arterial pressure  $\geq 65$  mmHg.

Group A received rhBNP injection (National Drug Approval H20050033; Specification: 0.5 mg $\times$ 1 bottle/box). The administration method involved preparing a solution of 50 mg rhBNP injection mixed with 50 mL of normal saline, with a loading dose of 0.15 mL $\times$  body weight (kg) infused within 3 min, followed by a maintenance dose of 0.0075  $\mu$ g/(kg $\cdot$ min) for 24–72 h [13].

In addition to the treatment given to Group A, Group B received dobutamine hydrochloride injection (National Drug Approval H31021006; Specification: 1 mL:10 mg) at 100 mg mixed with normal saline to make a 50 mL solution, administered by micro-pump at a rate of 1 mL/h=2 mg/h, adjusted to maintain the target blood pressure [14].

Similarly, in addition to the treatment given to Group A, Group C received dopamine hydrochloride injection (National Drug Approval H44022388; Specification: 2 mL:20 mg) at a dose of 3 mg  $\times$  body weight (kg) mixed with normal saline to make a 50 mL solution, administered by micro-pump at a rate of 1 mL/h=1  $\mu$ g/(kg $\cdot$ min) to maintain the target systolic blood pressure. Throughout the treatment period, patient blood pressure was closely monitored, and the infusion rate was adjusted based on the patient's blood pressure and tolerance, with the aim of maintaining blood pressure above 90/60 mmHg following medication administration. All three groups of patients received continuous treatment for 3 days [15].

### Measurement parameters

#### Patient data

Patient general data was obtained through a systematic review of medical records, including age, gender, BMI, smoking history, alcohol consumption history, hypertension, diabetes, hyperlipidemia, heart rate, systolic pressure, diastolic pressure, cardiac output, pulmonary artery pressure, adverse reactions during patient treatment such as hypotension, arrhythmia, renal function impairment, atrial fibrillation, cardiogenic shock, ischemic events, infectious complications, bleeding events, as well as total hospitalization cost, total drug cost, total outpatient cost, and total cost per patient.

#### Blood tests

3 mL of fasting venous blood was collected from the elbow of the patient. After serum separation, dry fluorescence immunoassay analyzer (FS-301, Wondfo, China) was used for the detection of N-terminal pro-brain natriuretic peptide (NT-proBNP). Serum creatinine and BUN levels were measured using a fully automated biochemical analyzer (7060, Hitachi, Japan), and troponin I level was detected using chemiluminescence. C-reactive protein (CRP) level was measured using enzyme-linked immunosorbent assay (ELISA).

#### Cardiopulmonary function tests

A fully digital color Doppler ultrasound diagnostic instrument (Voluson E8, GE, USA) was used for the calculation of left ventricular ejection fraction (LVEF) using the biplane Simpson method. E/E' ratio and cardiac output were monitored using echocardiography, and cardiopulmonary exercise testing was performed using a cardiopulmonary exercise testing system (MasterScreen CPX, Jaeger, Germany) to measure peak oxygen consumption (VO<sub>2</sub> peak). Additionally, a 6-minute walk test (6MWT) was conducted with the patient's consent, measuring the distance covered in a 50-meter long corridor within 6 min in the cardiology ward after treatment.

### Statistical analysis

Data analysis was performed using SPSS 29.0 statistical software (SPSS Inc, Chicago, IL, USA). Categorical data were presented as [n (%)] format. For sample sizes  $\geq 40$  and theoretical frequency  $T \geq 5$ , the basic formula for chi-squared test was applied. When the sample size was  $\geq 40$  but the theoretical frequency was  $1 \leq T < 5$ , the chi-squared test was conducted using the corrected formula. For sample sizes  $< 40$  or theoretical frequency  $T < 1$ , statistical analysis was carried out using Fisher's exact probability method. The Shapiro-Wilk method was employed to assess the normality of continuous variables. Normally distributed continuous variables were expressed as ( $\bar{X} \pm s$ ) and analyzed using the t-test with corrected variance.

**Table 1** General information and demographic characteristics

Parameter	Group A (n = 68)	Group B (n = 74)	Group C (n = 71)	t/ $\chi^2$ (A vs. B)	PAvs.B	t/ $\chi^2$ (A vs. C)	PAvs.C
Age (years)	72.14 ± 3.21	72.25 ± 2.98	71.82 ± 3.57	0.222	0.824	0.554	0.580
Gender (M/F)	31 (45.59%) / 37 (54.41%)	36 (48.65%) / 38 (51.35%)	35 (49.30%) / 36 (50.70%)	0.039	0.844	0.072	0.789
BMI (kg/m <sup>2</sup> )	23.38 ± 2.14	23.86 ± 1.92	23.87 ± 1.98	1.391	0.167	1.401	0.163
Smoking history	19 (27.94%)	19 (25.68%)	18 (25.35%)	0.013	0.909	0.023	0.878
Drinking history	10 (14.71%)	12 (16.22%)	12 (16.90%)	0.000	0.987	0.015	0.903
Hypertension	13 (19.12%)	12 (16.22%)	12 (16.90%)	0.054	0.816	0.014	0.905
Diabetes	13 (19.12%)	13 (17.57%)	11 (15.49%)	0.000	0.983	0.116	0.733
Hyperlipidemia	9 (13.24%)	8 (10.81%)	8 (11.27%)	0.035	0.853	0.009	0.924
Heart rate (bpm)	78.51 ± 5.62	80.15 ± 6.93	79.41 ± 6.23	1.549	0.124	0.898	0.371
Systolic blood pressure (mmHg)	107.23 ± 10.56	106.27 ± 9.81	109.58 ± 11.25	0.561	0.576	1.272	0.206
Diastolic blood pressure (mmHg)	75.41 ± 4.67	76.82 ± 5.22	74.93 ± 4.96	1.694	0.093	0.596	0.552
Cardiac output (L/min)	3.45 ± 0.21	3.40 ± 0.17	3.49 ± 0.23	1.510	0.134	0.907	0.366
Pulmonary artery pressure (mmHg)	30.45 ± 2.56	29.98 ± 2.89	30.72 ± 2.34	1.025	0.307	0.648	0.518

**Table 2** Comparison of biomarker responses between the two groups

Parameter	Group A (n = 68)	Group B (n = 74)	Group C (n = 71)	t (A vs. B)	PAvs.B	t (A vs. C)	PAvs.C
NT-proBNP (pg/mL)	790.13 ± 50.14	692.54 ± 45.53	675.83 ± 55.14	12.106	< 0.001	12.796	< 0.001
Troponin I (ng/mL)	1.21 ± 0.16	1.27 ± 0.08	1.27 ± 0.12	2.865	0.005	2.450	0.016
Creatinine (mg/dL)	1.14 ± 0.15	1.11 ± 0.12	1.15 ± 0.18	1.328	0.186	0.442	0.659
BUN (mg/dL)	20.18 ± 2.03	19.73 ± 1.85	20.53 ± 2.23	1.374	0.172	0.959	0.339
CRP (mg/L)	3.14 ± 0.51	3.14 ± 0.45	3.07 ± 0.55	0.014	0.989	0.794	0.429

Non-normally distributed data were represented in the form of median (25th percentile, 75th percentile) and analyzed using the Wilcoxon rank-sum test. A two-tailed  $P < 0.05$  was considered statistically significant.

## Results

### General information and demographic characteristics

The demographic and baseline characteristics of the three groups (A, B, and C) were similar, as shown in Table 1. There were no statistically significant differences in age, gender distribution, BMI, smoking or drinking history, hypertension, diabetes, hyperlipidemia, heart rate, systolic and diastolic blood pressure, cardiac output, and pulmonary artery pressure among the three groups ( $P > 0.05$ ). Additionally, there were no significant differences in the baseline characteristics related to cardiovascular parameters among the three groups.

### Biomarker responses

The biomarker responses were compared between the groups (A, B, and C), as presented in Table 2. The NT-proBNP levels were significantly lower in the Group B and Group C compared to the Group A, with values of  $692.54 \pm 45.53$  and  $675.83 \pm 55.14$ , respectively, versus  $790.13 \pm 50.14$  pg/mL in the Group A ( $t = 12.106$ ,  $P < 0.001$  and  $t = 12.796$ ,  $P < 0.001$ , respectively) (Fig. 1). Troponin I levels showed a statistically significant difference between the Group A and Group B ( $t = 2.865$ ,  $P = 0.005$ )

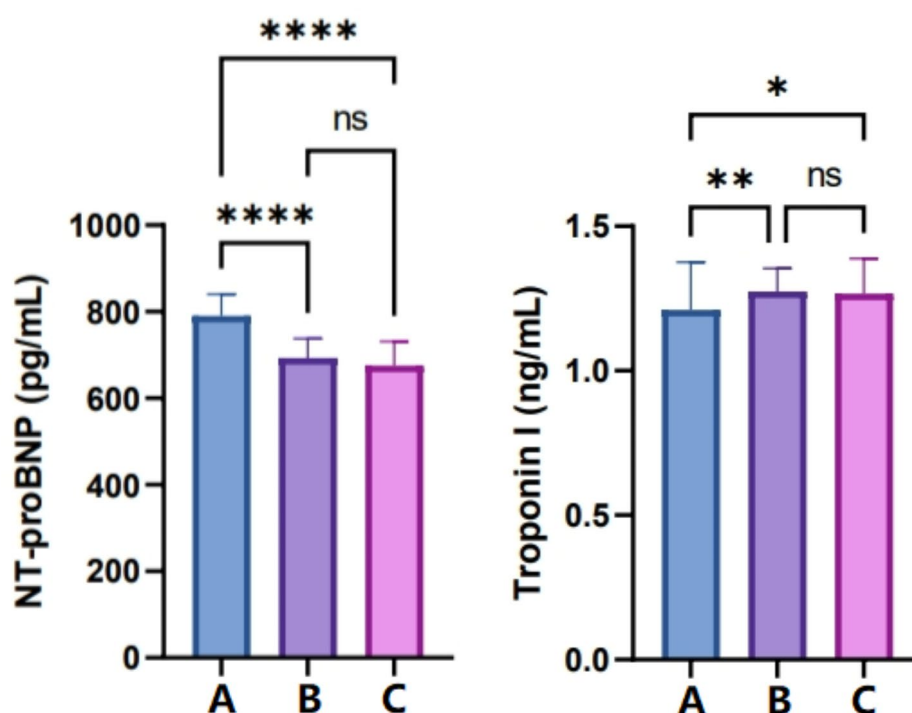
as well as between the Group A and Group C ( $t = 2.450$ ,  $P = 0.016$ ). However, there were no significant differences in creatinine, BUN, and CRP levels among the three groups. ( $P > 0.05$ )

### Efficacy of treatment on heart function

According to the analysis of treatment efficacy on heart function between the groups, a statistically significant difference was observed in the left ventricular ejection fraction, with group B ( $51.18 \pm 3.51$ ) and group C ( $51.28 \pm 3.27$ ) displaying higher values compared to group A ( $50.01 \pm 3.42$ ) ( $P = 0.047$  and  $P = 0.028$ , respectively) (Table 3). However, no statistically significant differences were found in cardiac output,  $E/e'$  ratio, peak  $VO_2$ , and six-minute walk distance among the three groups ( $P > 0.05$ ).

### Adverse events and safety profile

In the comparison of adverse events and safety profiles between the groups, no statistically significant differences were observed in the occurrence of hypotension, arrhythmias, renal impairment, atrial fibrillation, cardiogenic shock, ischemic events, infectious complications, or bleeding events among the three groups ( $P = 0.716$ ,  $0.763$ ,  $0.797$ ,  $0.643$ ,  $0.953$ ,  $0.947$ ,  $0.763$ ) (Table 4).



**Fig. 1** NT-proBNP levels and Troponin I levels

**Table 3** Comparison of efficacy of treatment on heart function between the two groups

Parameter	Group A (n = 68)	Group B (n = 74)	Group C (n = 71)	t (A vs. B)	PAvs.B	t (A vs. C)	PAvs.C
LVEF	50.01 ± 3.42	51.18 ± 3.51	51.28 ± 3.27	2.007	0.047	2.228	0.028
Cardiac output (L/min)	4.23 ± 0.31	4.16 ± 0.25	4.31 ± 0.35	1.521	0.131	1.397	0.165
E/e' ratio	12.56 ± 1.86	12.43 ± 1.73	12.65 ± 1.96	0.429	0.669	0.271	0.787
Peak VO <sub>2</sub> (mL/kg/min)	18.53 ± 1.25	18.45 ± 1.34	18.67 ± 1.15	0.392	0.696	0.699	0.486
Six-minute walk distance (m)	320.15 ± 25.14	315.26 ± 30.57	325.48 ± 20.36	1.043	0.299	1.369	0.173

LVEF: Left ventricular ejection fraction

**Table 4** Comparison of adverse events and safety profile between the two groups

Parameter	Group A (n = 68)	Group B (n = 74)	Group C (n = 71)	χ <sup>2</sup> (A vs. B)	PAvs.B	χ <sup>2</sup> (A vs. C)	PAvs.C
Hypotension (%)	5 (7.35%)	4 (5.41%)	4 (5.63%)	0.017	0.896	0.004	0.947
Arrhythmias (%)	2 (2.94%)	4 (5.41%)	4 (5.63%)	0.097	0.755	0.132	0.716
Renal impairment (%)	3 (4.41%)	5 (6.76%)	5 (7.04%)	0.058	0.809	0.091	0.763
Atrial Fibrillation (%)	4 (5.88%)	6 (8.11%)	6 (8.45%)	0.036	0.850	0.066	0.797
Cardiogenic shock (%)	1 (1.47%)	3 (4.05%)	3 (4.23%)	0.178	0.673	0.215	0.643
Ischemic events (%)	4 (5.88%)	3 (4.05%)	3 (4.23%)	0.013	0.909	0.003	0.953
Infectious complications (%)	5 (7.35%)	7 (9.46%)	4 (5.63%)	0.022	0.882	0.004	0.947
Bleeding events (%)	3 (4.41%)	5 (6.76%)	5 (7.04%)	0.058	0.809	0.091	0.763

### Cost analysis

In the comparison of cost analysis between the groups, no statistically significant differences were observed in total hospitalization cost, total medication cost, total outpatient visits cost, or total cost per patient among the three groups ( $P = 0.218, 0.582, 0.150, 0.207$ ) (Table 5).

### Discussion

This retrospective cohort study aimed to assess the efficacy of combining rhBNP with vasoactive medications in elderly patients suffering from HF and hypotension. A key finding of this study was the remarkable reduction in NT-proBNP levels in the groups receiving combination therapy with rhBNP and vasoactive medications



**Table 5** Comparison of cost analysis between the two groups

Parameter	Group A (n=68)	Group B (n=74)	Group C (n=71)	t (A vs. B)	PAvs.B	t (A vs. C)	PAvs.C
Total hospitalization cost	15002.57 ± 1005.26	15208.45 ± 1203.47	14811.12 ± 803.25	1.109	0.269	1.237	0.218
Total medication cost	2503.24 ± 202.31	2552.46 ± 180.35	2483.45 ± 220.46	1.525	0.130	0.552	0.582
Total outpatient visits cost	1202.28 ± 102.47	1215.52 ± 123.58	1179.23 ± 83.57	0.697	0.487	1.449	0.150
Total cost per patient	18704.46 ± 1304.35	19005.79 ± 1404.58	18400.00 ± 900.00	1.325	0.187	1.269	0.207

(dobutamine or dopamine) compared to the group receiving rhBNP alone. Elevated NT-proBNP levels were a well-established marker of cardiac dysfunction and were strongly linked to adverse clinical outcomes in HF patients [16].

The reduction in NT-proBNP levels observed in the combination therapy groups signifies an enhanced effect on cardiac function and underscores the potential role of inotropic agents in augmenting the impact of rhBNP in elderly patients with HF and hypotension. Additionally, the concurrent administration of rhBNP and inotropic agents may exert beneficial effects on the cardio-renal axis. rhBNP has been demonstrated to improve glomerular filtration rate and renal blood flow [17], while inotropic agents, by reducing systemic vascular resistance, may further enhance renal perfusion [18]. This dual action on the cardio-renal interaction may lead to improved renal function and fluid balance in elderly patients with HF and hypotension, contributing to the observed reductions in NT-proBNP levels and supporting the overall efficacy of combination therapy. The decrease of NT-proBNP also reflects the reduction of right heart load and is closely related to right heart function, diuretic effect and volume status. Studies have shown that elevated TAPSE indicates improved right ventricular systolic function and is positively correlated with decreased NT-proBNP [19]. Diuretic therapy can reduce right ventricular filling pressure and pulmonary artery pressure (PASP), thereby reducing right cardiac afterload and further promoting the decline of NT-proBNP [20]. In addition, the relief of volume overload (e.g. reduced venous return, decreased right atrial pressure) was also consistent with the decrease of NT-proBNP, and optimized volume management contributed to the improvement of right cardiac function [21]. Therefore, NT-proBNP can be used as an important biomarker to evaluate changes in right cardiac load and provide a reference for individualized management of patients with heart failure [22].

Similarly, the analysis of troponin I levels revealed notable differences between the group receiving rhBNP alone and the groups receiving combination therapy. Troponin I was a critical biomarker for myocardial injury and was indicative of adverse cardiovascular events in HF patients [23, 24]. The lower troponin I levels observed in the combination therapy groups suggest a potential reduction in myocardial injury, possibly attributed to the

hemodynamic effects of inotropic agents in conjunction with rhBNP.

The improvements in biomarker responses, particularly the reduction in NT-proBNP and troponin I levels, provide compelling evidence for the synergistic effects of combined rhBNP and vasodilator therapy in elderly patients with HF and hypotension. These findings highlight the potential of this treatment approach in ameliorating cardiac dysfunction and reducing the adverse clinical implications associated with elevated biomarker levels in this vulnerable patient population.

The combination of rhBNP and inotropic agents may lead to improved hemodynamic stability by reducing cardiac preload and afterload. When administered alongside inotropic agents such as dobutamine or dopamine, rhBNP's known promotion of natriuresis, diuresis, and vasodilation may further optimize cardiac performance and reduce strain on the failing heart [25–27].

The assessment of treatment efficacy on cardiac function revealed a significant improvement in LVEF in the combination therapy groups compared to the rhBNP-alone group. LVEF was a crucial measure of left ventricular contractile function and was widely used to assess cardiac performance in HF patients [28]. The observed improvement in LVEF in the combination therapy groups suggests a favorable impact on cardiac contractility and supports the notion that inotropic agents may potentiate the beneficial effects of rhBNP on myocardial function in elderly patients with HF and hypotension.

While no statistically significant differences were found in cardiac output, E/e' ratio, peak oxygen consumption (VO<sub>2</sub> peak), and six-minute walk distance among the three groups, the significant increase in LVEF in the combination therapy groups was clinically significant [29]. LVEF was a key determinant of both prognosis and therapeutic decision-making in HF patients and pivotal for assessing response to treatment [30]. The observed improvement in LVEF further strengthens the rationale for considering combination therapy with rhBNP and inotropic agents as a viable treatment option for elderly patients with HF and hypotension [31, 32].

Inotropic agents, through their vasodilatory effects, can contribute to the reduction of myocardial oxygen demand and potentially improve coronary perfusion [33]. The observed reductions in troponin I levels in the combination therapy groups suggest a potential attenuation

of myocardial injury, which underscores the myocardial preservation effects of the combined treatment. An essential aspect of evaluating the efficacy of any therapeutic intervention was the analysis of its safety profile and cost implications [34]. This study compared adverse events and safety profiles, demonstrating that the occurrence of adverse events such as hypotension, arrhythmias, renal impairment, atrial fibrillation, cardiogenic shock, ischemic events, infectious complications, and bleeding events was comparable among the three treatment groups. These findings indicate that the addition of inotropic agents to rhBNP therapy did not lead to a significant increase in adverse events, highlighting the tolerability and safety of the combination treatment in elderly patients with HF and hypotension. Furthermore, the cost analysis revealed no statistically significant differences in total hospitalization cost, total medication cost, total outpatient visits cost, or total cost per patient among the three groups. The comparable cost implications of the different treatment strategies suggest that the addition of inotropic agents to rhBNP therapy does not result in substantial differences in the financial burden associated with the management of HF in elderly patients with hypotension.

The findings of this study have several important clinical implications. Firstly, the demonstrated reductions in NT-proBNP and troponin I levels, along with the improvements in LVEF, support the potential utility of combined rhBNP and vasodilator therapy in elderly patients with HF and hypotension. These results signal a promising avenue for optimizing the management of HF in this patient population and warrant further exploration through larger prospective studies and clinical trials.

Additionally, the comparable safety profiles and cost implications of the different treatment strategies underscore the feasibility of incorporating inotropic agents into the existing treatment regimens for elderly patients with HF and hypotension. As such, future research endeavors should focus on elucidating the mechanistic underpinnings of the observed synergistic effects and conducting robust outcome-based studies to validate the long-term clinical benefits of combination therapy in this challenging patient cohort.

Despite the valuable insights provided by this study, certain limitations should be acknowledged. First, the retrospective nature of the study and the relatively small sample size limit the generalizability of the findings. Secondly, due to the existing clinical guidelines and our hospital ethics committee believe that positive inotropic drugs such as dopamine should be mainly used for cardiogenic shock, sufficient clinical samples could not be obtained in this retrospective study. This merits further investigation in prospective studies. Furthermore, the study did not evaluate long-term outcomes or survival

endpoints, which were integral for establishing the overall clinical efficacy and safety of the treatment strategies. Therefore, future research endeavors should encompass larger, prospective studies with long-term follow-up to validate the reproducibility and sustained benefits of combination therapy in elderly patients with HF and hypotension.

## Conclusion

In conclusion, this comparative study underscores the potential benefits of combining rhBNP with inotropic agents for the treatment of HF in elderly patients with hypotension. The observed reductions in biomarker levels, improvements in cardiac function, and comparable safety profiles and cost implications advocate for the consideration of combination therapy as a viable approach in the management of this challenging patient population. Future research endeavors should aim to corroborate these findings through robust clinical trials and investigate the long-term clinical impact of combination therapy on outcomes and survival in elderly patients with HF and hypotension.

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## Author contributions

All authors contributed to the study conception and design. Material preparation, data collection was performed by RM and XNL. The first draft of the manuscript was written by RM, XNL, HML and ZY. YLH commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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## Data availability

The data involved in the present study can be provided under reasonable request.

## Declarations

### Ethics approval and consent to participate

This study protocol was reviewed and approved by the Ethics Committee of Aerospace Center Hospital in accordance with regulatory and ethical guidelines and performed in accordance with the ethical standards set forth in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to conducting the study.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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