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Original Article

Effect of proton pump inhibitor (lansoprazole) on adverse drug reactions and rational drug use in elderly patients with chronic heart failure

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Abstract: Objective: To evaluate the efficacy and rationale of proton pump inhibitors (PPIs) for adverse drug reactions in elderly patients with heart failure (HF). Methods: From February 2019 to September 2021, 120 elderly patients with chronic heart failure (CHF) treated at Jintan First People's Hospital were enrolled as subjects. The patients were classified into a control group (n=60) and a research group (n=60). In addition to clopidogrel, the control group received cimetidine, while the research group received lansoprazole. Clinical efficacy, oxidative stress markers, echocardiographic indices, vascular endothelial function, cardiac function indicators, and adverse reactions were compared between the two groups. A cost-effectiveness analysis was also performed, and risk factors affecting patient efficacy were examined. Results: The clinical efficacy of the research group was remarkably superior to that of the control group (88.33% versus 63.33%, P<0.05). The combination of clopidogrel and cimetidine was identified as a risk factor affecting patient efficacy (P=0.003). Besides, the research group showed significant elevation in superoxide dismutase (SOD), glutathione peroxidase (GPx), left ventricular ejection fraction (LVEF), and nitric oxide (NO) after treatment, all higher compared to the control group (all P<0.05). Additionally, significant reductions in malondialdehyde (MDA), left ventricular end diastolic diameter (LVEDD), left ventricular end systolic dimension (LVSD), endothelin-1 (ET-1), N-terminal pro-B-type natriuretic peptide (NT-proBNP), creatine kinase (CK), lactate dehydrogenase (LDH), and free fatty acids (FFA) were observed in the research group, all lower than the control group (P<0.05). The incidence of bradycardia, hypotension and electrolyte disturbances in the research group was remarkably lower (P<0.05). Additionally, the research group demonstrated greater cost-effectiveness compared to the control group. Conclusion: The use of PPIs in elderly patients with HF not only improves efficacy but also enhances safety, making this drug treatment approach worth promoting.

Keywords: Proton pump inhibitor, lansoprazole, heart failure, adverse drug reactions

Introduction

Typical symptoms of heart failure (HF) include shortness of breath, ankle oedema, and fatigue, along with signs such as elevated jugular venous pressure, wet rales in the lungs, and peripheral oedema [1]. A retrospective study of 10,714 patients hospitalized with HF in China found that coronary heart disease was the leading cause [2, 3], followed by hypertension, while the proportion of rheumatic valve disease declined. The mortality rate for HF was higher across all age groups compared to other cardiovascular diseases during the same period. The main causes of death were left ventricular dysfunction (59%), arrhythmia (13%) and sudden death (13%) [4]. The "China Cardiovascular Disease Report 2017" outlines the rising incidence of cardiovascular diseases in China, estimating that 290 million individuals are affected, including 11 million with coronary heart disease and 4.5 million with HF. The mortality rate for cardiovascular diseases remains the highest, surpassing that of cancers and other diseases in 2015. Another survey of 15,518 people in 20 urban and rural areas in China

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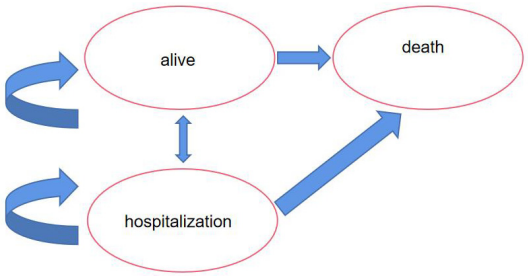

Figure 1. Steady state-hospitalization-death state model of elderly patients with HF.

indicated that the prevalence of chronic heart failure (CHF) in 2000 was 0.9% (0.7% in men and 1.0% in women) [5].

The prevalence of HF increases with age, meaning that as China's population ages, there will be an increasing number of elderly patients with HF. Due to the decline in physiological reserve function in elderly patients, which results in reduced stress resistance and limitation in medication options, HF will further reduce the life quality of elderly patients. In addition, the "Chinese Guidelines for the Diagnosis and Treatment of Heart Failure 2014" clearly states that the treatment goal of HF is not only to alleviate symptoms and improve life quality, but also to halt and delay myocardial remodeling, maintain cardiac function, and reduce mortality and hospitalization rates in HF patients [6] (**Figure 1**). Previous studies have shown that the rational use of proton pump inhibitors (PPIs) in conjunction with conventional therapy can improve clinical symptoms, exercise tolerance and life quality in patients with CHF, while also enhancing long-term prognosis of patients [8].

Antiplatelet drugs have become essential in the treatment of patients with cardiovascular diseases. With the development of evidence-based medicine, many clinical trials have provided robust evidence for the renewal and improvement of antiplatelet therapy. The combination of aspirin and clopidogrel has become the standard treatment following acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI), remarkably reducing the recurrence rate of adverse cardiovascular events [9]. However, nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin are commonly associated with gastrointestinal side effects. Oral administration of these drugs can directly irritate the gastric mucosa, leading to discomfort, nausea, and vomiting in the epigastric region. High doses can cause gastric mucosal damage and asymptomatic gastric bleeding. It is believed that the gastrointestinal ulcer and bleeding associated with clopidogrel are comparable to those caused by aspirin. While aspirin directly damages the mucosa, clopidogrel's anti-angiogenic effects may delay ulcer healing. In 2008, experts from the American College of Cardiology Foundation (ACCF), the American Gastroenterology Association (ACG), and the American College of Cardiology (AHA) recommended PPIs as the drug of choice to treat and prevent aspirin- and NSAID-related gastric and duodenal injuries [10, 11]. As a result, PPIs are commonly used in combination with dual anti-platelet agents to prevent gastrointestinal damage. However, there is limited research on the use of PPIs in elderly patients with CHF. To address this gap, this study aims to assess the effects of PPIs on adverse drug reactions and evaluate the rationality of their use in elderly patients with CHF, exploring the clinical value of PPIs in the treatment of HF in the elderly.

Materials and methods

General information

In this retrospective study, 120 elderly patients with CHF treated at Jintan First People's Hospital from February 2019 to September 2021 were enrolled. The patients were classified into a control group (n=60) and a research group (n=60). Both groups were treated with clopidogrel, with the control group additionally receiving cimetidine and the research group receiving lansoprazole. The trial was approved by the Medical Ethics Committee of Jintan First People's Hospital. The research flow chart is shown in **Figure 2**.

Inclusion criteria: 1) Patients met the diagnostic criteria for CHF [12]; 2) Patients aged ≥60 years; 3) Heart function was graded II to III according to the New York College of Cardiology (NHYA) classification.

Exclusion criteria: 1) Patients with acute HF; 2) Patients underwent hemodialysis; 3) Patients with severe systemic infection or hepatorenal

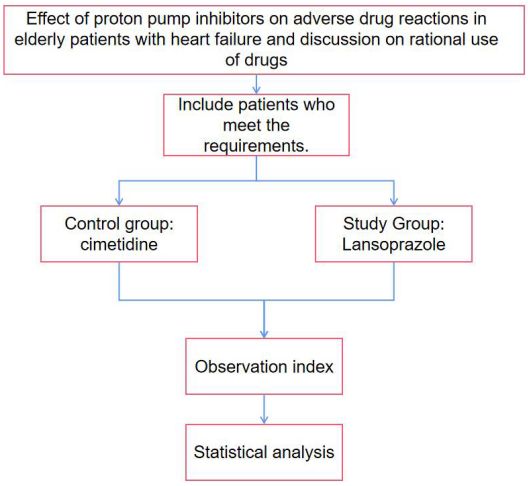

Figure 2. Research flow chart.

insufficiency; 4) Patients allergic to any PPIs; and 5) Patients with motor deficits in the lower limb due to a prior stroke.

Using a bilateral α of 0.05 and β of 0.2, the clinical curative effect (success rate) was taken as the effect index, with parameters set as P1=0.94, P2=0.77. The calculated sample size for each group was 54 cases minimally. Finaly, 60 patients were included in each group, for a total of 120 patients.

Equation for sample size calculation:

$$n_1 = \frac{[Z_{\alpha/2}\sqrt{p(1-p)(1+c)/c} + Z_{\beta}\sqrt{p_1(1-p_1)+p_2(1-p_2)/c}]^2}{(p_1-p_2)^2}$$

Treatment methods

All patients were treated with 300 mg of clopidogrel once a day. Additionally, the control group was given cimetidine capsules (specification: 0.2 g) twice a day with one tablet at a time, while the research group received lansoprazole (specification: 15 mg) once a day with two tablets. Both groups received continuous treatment for 28 days.

Observation indexes

Curative effect: The efficacy of treatment was evaluated 28 days after treatment [13]. Clinical symptoms such as dyspnea, fatigue, and retention of water and sodium were assessed for improvement. Cardiac function, as classified by the NYHA grading system, was compared to pre-treatment levels. Show effect: Compared with the pre-treatment condition, the symptoms including dyspnea, fatigue, and water and sodium retention were significantly alleviated, and there was an improvement of at least two grades in the NYHA classification; Effective: Improvement in symptoms (dyspnea, fatigue, and water and sodium retention) and an improvement of at least one grade in the NYHA classification compared to pre-treatment; Invalid: No improvement in clinical symptoms or NYHA classification; Aggravate: Worsening of clinical symptoms. Overall effective rate = (Show effect + Effective)/total number of patients.

Oxidative stress indexes: Fasting blood samples (5 ml) were collected from all patients before and 28 days after treatment. Blood samples were centrifuged at the 3000 r/min for 10 minutes, and the supernatant was removed. The levels of superoxide dismutase (SOD), glutathione peroxidase (GPx) and malondialdehyde (MDA) in the serum were detected by enzyme-linked immunosorbent assay (ELASA).

Echocardiographic indexes: Philips CX50 color Doppler ultrasound system with a 3.5 Hz probe was used for echocardiographic assessments before and 28 days after treatment. Patients were placed in the left lateral decubitus position, and two-dimensional ultrasound images were obtained from the long-axis, short-axis, and apical views of the left ventricle. Left ventricular end systolic dimension (LVSD), left ventricular end diastolic diameter (LVEDD), and left ventricular ejection fraction (LVEF) were obtained from the parasternal long-axis view. The echocardiographic examination was performed by the same physician who was blinded to the patient grouping.

Vascular endothelial function indexes: Plasma levels of endothelin-1 (ET-1) and nitric oxide (NO) were measured before and 28 days after treatment. ET-1 was determined by ELASA assay, and NO was measured using nitrate reductase method.

Cardiac function-associated indicators: Before treatment and 28 days after treatment, the levels of serum N-terminal pro-B-type natriuretic peptide (NT-proBNP), creatine kinase (CK), lactate dehydrogenase (LDH), and free fatty acids

Table 1. Comparison of general information between the two groups of patients

Factor	Control group (n=60)	Research group (n=60)	χ^2/t	*P*
Gender (male/female)	32/28	36/24	0.543	0.461
Age (years)	74.94±5.23	74.49±5.53	0.459	0.647
Disease course (years)	9.55±1.42	9.38±1.81	0.572	0.568
Body mass index (kg/m^2)	23.14±2.77	23.11±2.72	0.060	0.952
Years of education (years)	10.22±1.34	10.25±1.36	0.122	0.903

(FFA) were quantified. NT-proBNP was quantified using an electrochemiluminescence automatic immunoassay analyzer (Shanghai Tosoh Bioscience Co., Ltd., 0023651). The other indicators were determined using an automatic biochemical analyzer (Shanghai Yuduo Biotechnology Co., Ltd., H363ZS).

Adverse reactions: Adverse reactions occurring during treatment, including angioedema, bradycardia, hypotension, electrolyte disturbance, were recorded. Angioedema is defined as acute local oedema in the dermis, subcutaneous tissue, mucous membranes, and other loose connective tissues, characterized by poorly defined, locally tense swelling that resolves spontaneously. Bradycardia is defined as a heart rate of <60 beats/min; hypotension is defined as a systolic pressure <90 mmHg and a diastolic pressure <60 mmHg. Electrolyte disturbance is defined as abnormal levels of electrolytes, such as potassium, sodium, chloride, calcium and magnesium, in the blood.

Treatment cost: The cost-effectiveness ratio (CER) was employed to evaluate the cost-effectiveness of the two treatment protocols. The calculation formula is the net cost divided by the health outcomes (quality-adjusted life years, QALYs). A lower CER suggests that the particular therapeutic regimen is more cost-efficient from a financial perspective.

Statistical analysis

Data were analyzed and processed using SPSS21.0 statistical software. The normal distribution and variance homogeneity of the measurement data were first assessed. Data with a normal distribution or approximate normal distribution are presented as mean ± standard deviation (x±sd). Paired t-tests were used to compare data within the same group, while independent sample t-tests were applied to compare between the two groups. Categorical data are expressed as n (%), and the chi-square (χ^2) test was used for comparisons. Risk factors affecting patient efficacy were analyzed using binary logistic regression analysis. A *P*-value of <0.05 was considered statistically significant.

Results

Comparison of general information between the two groups of patients

In the control group, consisting of 32 men and 28 women, the patients' ages ranged from 64 to 84 years (mean: 74.94±5.23). The course of the disease ranged from 6 to 13 years, with an average of 9.55±1.42 years. The body mass index (BMI) ranged from 17.33 to 28.44 kg/m^2 (mean: 23.14±2.77 kg/m^2). The years of education ranged from 6 to 16 years (mean: 10.22±1.34 years).

In the research group, the patients' ages ranged from 65 to 86 years, with an average of 74.49±5.53 years. There were 36 men and 24 women, and the disease duration ranged from 6-12 years (mean =9.38±1.81 years). BMI ranged from 17.31 to 28.60 kg/m^2, with an average of 23.11±2.72 kg/m^2. The years of education ranged from 6 to 17 years, with an average of 10.25±1.36 years. No remarkable differences were found in general data between the two groups (P>0.05; **Table 1**).

Comparison of curative effect between the two groups of patients

In the research group, show effect was achieved in 14 patients, effective in 39 cases, invalid in 7, resulting in an overall effective rate of 88.33%. In the control group, show effect was achieved 2 patients, effective in 36 cases, invalid in 14, and aggravate in 8, resulting in an overall effective rate of 63.33%. The research

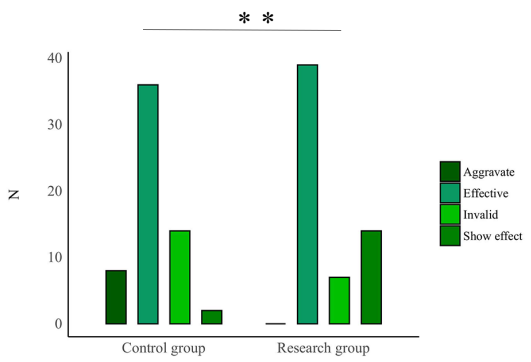

Figure 3. Comparison of curative effects. **P<0.01.

group showed a significantly higher overall effective rate (P=0.001, χ^2=10.231; **Figure 3**).

Multivariate analysis of factors affecting treatment efficacy

The clinical data, including gender, age, disease course, BMI, years of education, and treatment method, were considered as independent variables, while the efficacy was taken as the dependent variable. The variables were assigned values, as shown in **Table 2**. Binary logistic regression analysis revealed that gender, age, disease course, BMI, and years of education did not significantly affect treatment efficacy (all P>0.05), while the treatment method was found to be a significant factor influencing the efficacy (P=0.003). See **Table 3** for details.

Comparison of oxidative stress markers between the two groups of patients

No remarkable differences were observed in oxidative stress marker before treatment (P>0.05). After treatment, the levels of SOD and GPx elevated, while MDA levels decreased. Specifically, SOD and GPx levels were significantly higher in the research group, while MDA levels were significantly lower compared to the control group (all P<0.05). See **Table 4** for details.

Comparison of echocardiographic indices between the two groups of patients

In terms of echocardiographic indexes, no remarkable difference was found between the two groups before treatment (P>0.05). After treatment, the LVEDD and LVESD decreased, and the LVEF increased. Specifically, the research group had significantly lower LVEDD and LVESD, and higher LVEF compared to the control group (all P<0.05). See **Table 5** for details.

Comparison of vascular endothelial function between the two groups of patients

No remarkable differences were found in vascular endothelial function before treatment (P>0.05). After treatment, ET-1 levels decreased, while NO levels increased. The research group had significantly lower ET-1 and higher NO levels compared to the control group (both P<0.05). See **Table 6** for details.

Comparison of cardiac function-associated indicators between the two groups of patients

The two groups did not differ statistically in various cardiac function-associated indicators before treatment (P>0.05). After treatment, all indicators decreased in both groups (P<0.01), with even lower levels of NT-proBNP, CK, LDH, and FFA in the research group (P<0.05). The results of all data analyses are shown in **Figure 4**.

Comparison of adverse reactions between the two groups of patients

Regarding the incidence of adverse reactions, the incidences of bradycardia, hypotension and electrolyte disturbance in the research group were remarkably lower (P<0.05). See **Table 7** for details.

Cost-effectiveness analysis and comparison

As shown in **Table 8**, the CER of the research group compared with the control group was 837.21 yuan/QALYs. The treatment of senile HF with the research group has more cost-effectiveness advantages.

Discussion

The aging population has become a significant and challenging issue globally. Chinese epidemiological surveys indicate that the average life expectancy in 2015 was 76.34 years [4-15]. The demographic shift has led to an increase in chronic diseases, which pose a growing threat to the health of the elderly. The demand for healthcare in the elderly is increasingly urgent,

Table 2. Assignments

Factor	Variable	Assignment
Gender	X1	Male =0, female =1
Age (years)	X2	<75=0, ≥75=1
Disease course (years)	X3	<10=0, ≥10=1
Body mass index (kg/m^2)	X4	<23=0, ≥23=1
Years of education (years)	X5	<10=0, ≥10=1
Treatment method	X6	Lansoprazole treatment =0, Cimetidine treatment =1
Efficacy	Y	Effective =0, ineffective =1

Table 3. Multivariate analysis of factors affecting the treatment efficacy

Factor	β	S.E	Wald	P	OR	95% CI
Gender	-0.299	0.468	0.408	0.523	0.742	0.296-1.856
Age (years)	0.619	0.477	1.680	0.195	1.857	0.728-4.732
Disease course (years)	0.122	0.459	0.071	0.790	1.130	0.459-2.779
Body mass index (kg/m^2)	-0.103	0.462	0.050	0.823	0.902	0.365-2.229
Years of education (years)	-0.630	0.472	1.784	0.182	0.533	0.211-1.342
Treatment method	1.492	0.500	8.915	0.003	4.444	1.669-11.830

creating substantial challenges for both society and families. Among elderly inpatients, 91.36% suffer from two or more chronic diseases, with ischemic heart disease complicated by hypertension being the most common. As medical technology has advanced, patients with heart disease are living longer, resulting in a continuous rise in HF prevalence in China. HF is characterized by abnormal change in heart structure and function due to various reasons. It results in both systolic and diastolic dysfunction, leading to a complex range of clinical syndromes [16]. This condition significantly reduces patients' life quality [17-19].

CHF is a complex clinical syndrome in which cardiac ejection cannot meet the metabolic needs of various tissues and organs. It is the leading cause of death among patients with cardiovascular disease [20]. The primary pathophysiology of HF involves the overactivation of several neuroendocrine system, including the sympathetic nervous system, renin-angiotensin-aldosterone system (RAAS), endothelial system, and ventricular remodeling [21]. A global meta-analysis of CHF indicates that cardiovascular death remains the leading cause of mortality in heart failure [22]. Non-cardiovascular mortality is notably higher in patients with heart failure with preserved ejection fraction (HFpEF) compared to those with reduced ejection fraction (HFrEF), and this difference is linked to conditions such as hypertension and valvular disease. Notably, these three forms of heart failure - HFpEF, HFrEF, and mixed - can evolve into one another over time [23].

PPIs are among the most successful and widely used drugs for inhibiting gastric acid production, making them a cornerstone in gastroenterology. Clinically, PPIs are commonly prescribed for gastrointestinal conditions such as gastroesophageal reflux disease (GERD), peptic ulcer, eradication of Helicobacter pylori, upper gastrointestinal bleeding, and Barrett's esophagus, with remarkable therapeutic effects [24-26]. While the acid-suppressing ability and safety of PPIs are well established, their use can lead to various adverse effects. PPIs remarkably increase gastric pH and reduce hydrogen ion concentration in the stomach. This alteration disrupts the acidic environment of the stomach and duodenum which can affect calcium ionization and reduce calcium absorption, thereby increasing the risk of fracture [27]. Furthermore, bacterial reflux may result in bacterial colonization in the pharynx, and PPIs inhibit the H/K-ATP enzyme found on the surface of the larynx and lung glands. This action reduces the non-specific immunity of the respiratory tract, raising the risk of pulmonary infection. In addition, PPIs may cause adverse reactions in various systems, including the digestive

Table 4. Comparison of oxidative stress markers between the two groups of patients [$\bar{x}$±sd]

Group	N	SOD (μU/L)		GPx (U/L)		MDA (μmol/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	60	70.18±5.91	75.69±8.86*	90.18±12.84	103.85±5.85*	6.94±1.92	5.11±0.13*
Research group	60	70.81±5.52	85.19±9.91*	90.48±12.86	115.85±8.85*	6.91±1.85	4.19±0.94*
t		0.603	5.535	0.127	8.761	0.087	7.509
P		>0.05	<0.01	>0.05	<0.01	>0.05	<0.01

Note: *P<0.05, compare with before treatment. SOD, superoxide dismutase; GPx, glutathione peroxidase; MDA, malondialdehyde.

Table 5. Comparison of echocardiographic indices between the two groups of patients [$\bar{x}$±sd]

Group	N	LVEDD (mm)		LVESD (mm)		LVEF (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	60	54.83±5.91	50.48±5.91*	43.49±1.95	38.59±5.82*	43.19±4.91	48.59±5.58*
Research group	60	54.58±5.22	45.19±5.52*	43.85±1.84	32.59±5.58*	43.17±4.42	53.59±5.92*
t		0.245	5.066	1.040	5.764	0.023	4.760
P		>0.05	<0.01	>0.05	<0.01	>0.05	<0.01

Note: *P<0.05, compare with before treatment. LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic dimension; LVEF, left ventricular ejection fraction.

Table 6. Comparison of vascular endothelial function between the two groups of patients [$\bar{x}$±sd]

Group	N	NO (ng/L)		ET-1 (μmol/L)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	60	75.94±9.93	81.19±4.93*	91.48±9.84	84.81±5.85*
Research group	60	75.58±9.38	88.49±12.91*	91.38±9.44	70.18±9.92*
t		0.204	4.091	0.056	9.840
P		>0.05	<0.01	>0.05	<0.01

Note: *P<0.05, compare with before treatment. NO, nitric oxide; ET-1, endothelin-1.

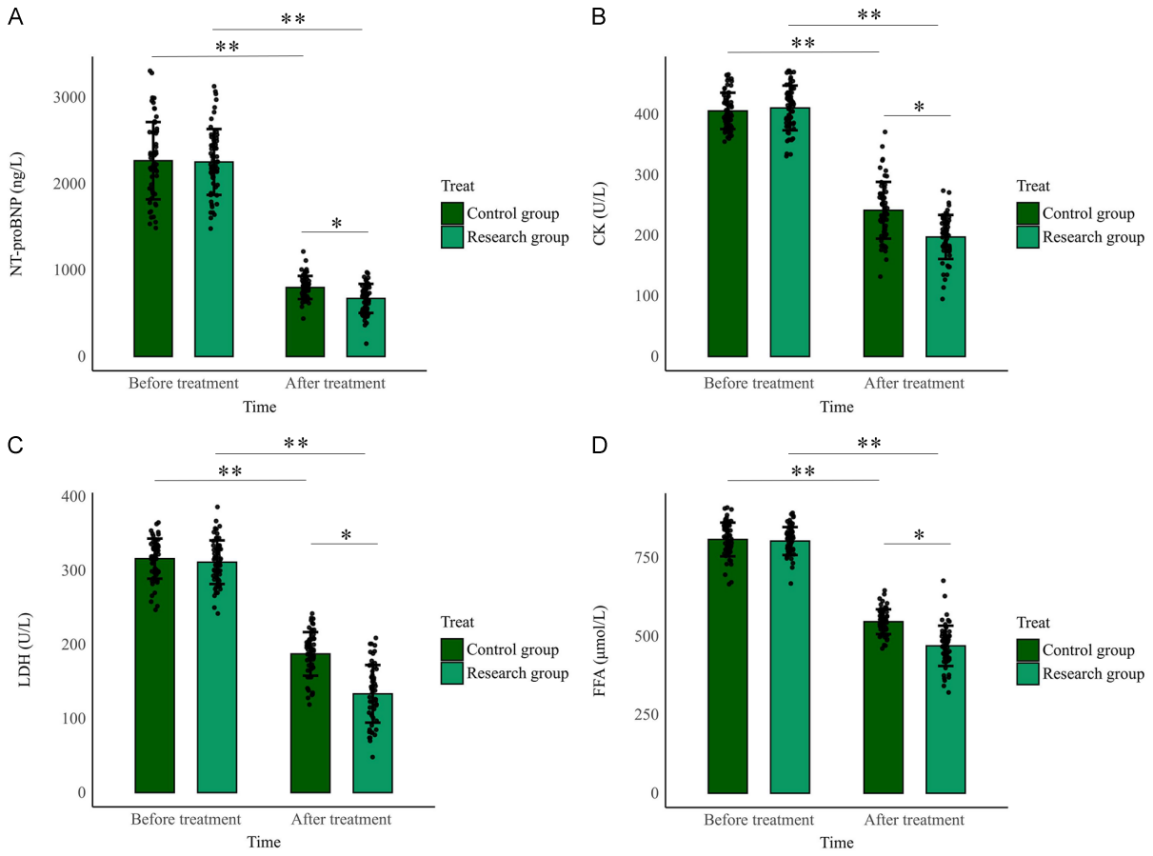

Figure 4. Comparison of cardiac function-associated indicators. A. Comparison of NT-proBNP levels between the two groups before and after treatment. B. Comparison of CK levels between the two groups before and after treatment. C. Comparison of LDH levels between the two groups before and after treatment. D. Comparison of FFA levels between the two groups before and after treatment. Note: **P<0.01, *P<0.05; NT-proBNP, N-terminal pro-B-type natriuretic peptide; CK, creatine kinase; LDH, lactate dehydrogenase; FFA, free fatty acids.

tract, circulatory system, and kidneys [28]. Common digestive symptoms include abdominal pain, diarrhea, nausea, and vomiting. Allergic reactions are generally manifested as itching and rashes, though in rare cases, severe anaphylaxis may occur. Cardiovascular side effects such as hypertension and arrhythmias are also observed, while acute renal impairment due to interstitial glomerulonephritis is another notable concern [29-32].

Some studies suggest that the use of PPIs increases the occurrence of cardiovascular events. A systematic review of 22,427 patients in the mortality dataset and 354,446 patients in the incidence dataset found a remarkable increase in both all-cause mortality and the incidence of major cardiovascular events in patients using PPIs [33]. Another study examined adverse cardiovascular events in patients who experienced their first myocardial infarc-

Table 7. Comparison of adverse reactions between the two groups of patients

Group	N	Vascular edema	Bradycardia	Hypotension	Electrolyte disturbance	Total
Control group	60	1 (1.67)	2 (3.33)	3 (5.00)	2 (3.33)	8 (13.33)
Research group	60	1 (1.67)	0 (0.00)	0 (0.00)	1 (1.67)	2 (3.33)
χ^2						3.927
P						0.048

Table 8. Cost-effectiveness analysis

Group	Cost (CNY)	Effect (QALYs)	CER (CNY/QALYs)
Control group (n=60)	7559.44	5.38	1405.10
Research group (n=60)	4855.84	5.80	837.21

Note: QALYs, quality-adjusted life years; CER, cost-effectiveness ratio.

tion (MI) between 1997 and 2006. This study followed patients for at least 30 days after their MI and treated them with aspirin combined with PPIs. The results indicated that 3,366 out of 19,925 patients who received both aspirin and PPIs experienced recurrent MI, stroke, or cardiovascular death. Notably, there was no elevated risk associated with the use of H2 receptor blockers, but an elevated risk of adverse cardiovascular events with the combination of PPIs and antiplatelet agents [34]. On the other hand, some studies have shown a positive correlation between PPI use and improved HF [35]. A study involving 1,191 HF patients classified them into three groups: the non-acid-suppressed group, the H2 receptor antagonists (H2RA) group, and the PPI group; Kaplan-Meier analysis and multivariate Cox proportional hazards analysis indicated that the PPI group may have better outcomes compared to the other two groups of HF patients [36].

In this study, higher efficacy was observed in the research group. Meanwhile, the treatment method was identified as a risk factor affecting treatment efficacy, suggesting that cimetidine treatment was associated with increased risk of ineffective treatment, and lansoprazole treatment should be preferred. After treatment, the research group exhibited higher levels of SOD and GPx, and lower levels of MDA, indicating an improvement in oxidative stress markers. Moreover, the research group demonstrated a decrease in LVEDD and LVESD, and an increase in LVEF. ET-1 was lower, and NO was higher in the research group. Following treatment, NT-proBNP, CK, LDH, and FFA levels were significantly reduced in the research group.

Regarding adverse reactions, the incidence of bradycardia, hypotension, and electrolyte disturbances in the research group was remarkably lower, suggesting that lansoprazole is more effective in reducing drug-related adverse reactions compared to cimetidine in elderly HF patients.

The selection of oxidative stress indicators such as SOD, GPx, and MDA is based on their strong representativeness of the pathological processes involved in HF. SOD and GPx, as antioxidants, are highly involved in many pathological processes of HF and are instrumental in predicting prognosis and facilitating risk stratification. MDA, a biomarker of lipid peroxidation, is also crucial in the pathogenesis of cardiovascular diseases, including HF [37, 38]. In a study by Hassanein EHM et al. [39], lansoprazole was shown to mitigate cyclophosphamide-induced oxidative stress and inflammation by modulating several key signaling pathways, including PPARγ, Nrf2/HO-1, and PI3K/AKT. This mechanism helps explain how lansoprazole affects oxidative stress in elderly HF patients.

Vascular endothelial dysfunction is another important factor in the progression of HF. Recurrent episodes of microvascular dysfunction may exacerbate myocardial injury and induce systemic inflammation, leading to disease exacerbation [40, 41]. ET-1 and NO, indicators of vascular endothelial dysfunction, are also closely related to the ongoing deterioration of cardiac function in HF patients [42]. A study by Onda K et al. [43] found that PPIs effectively alleviate tumor necrosis factor (TNF)-α-induced endothelial dysfunction by inhibiting the expression of vascular cell adhesion molecules, pre-

venting leukocyte adhesion to endothelial cells, and maintaining endothelial tube formation. These actions may help explain the positive effects of lansoprazole on vascular endothelial function in elderly HF patients.

The cost-effectiveness analysis indicated that the CER for the research group was 837.21 CNY/QALYs compared to 1405.10 CNY/QALYs in the control group, demonstrating that lansoprazole treatment for elderly HF patients is more cost-effective. The analysis indicates that PPIs, including lansoprazole, exert beneficial effects in senile HF by down-regulating pro-inflammatory cytokines, improving endothelial function, enhancing myocardial function, promoting vasodilation, and lowering blood pressure. The vasodilation induced by lansoprazole may be mediated by regulating NO production in the vasculature [44]. The vascular endothelium removal or addition of N(γ)-nitro-L-arginine methyl ester (L-NAME) (an endothelial nitric oxide synthase inhibitor) successfully inhibited the vasodilation effect of lansoprazole, but this inhibition was reversed after pretreatment [45]. The regulation of endothelial nitric oxide synthase (eNOS) and NO affects vascular dynamic balance. In some cases, L-NAME did not remarkably inhibit the vasodilation of lansoprazole in isolated arteries [46]. Therefore, the vasodilation effect of lansoprazole may not be related to NO regulation. More interestingly, the vasodilation effect of PPIs in a K+-free medium remained apparent, indicating that these effects may not be mediated by vascular H/K-ATPase. Subsequent studies also showed that lansoprazole inhibited Ca^{2+}-induced contraction in a high K+-Ca^{2+} free medium, indicating that intracellular Ca^{2+} regulation may be a potential mechanism. In isolated rat aortic rings, PPIs have been shown to inhibit contraction by increasing the level of cyclic guanosine mono phosphate (cGMP) or inhibiting voltage-dependent transduction pathways, thus further improving HF [47-49].

Conclusion

In conclusion, treatment with PPIs in elderly patients with HF appears to be both safe and effective in improving treatment outcomes. However, the study does have limitations, including a small sample size, absence of regional differences, and lack of follow-up. Future research should aim to conduct cross-regional, multi-center, and large-scale studies to provide more robust and generalizable evidence.

Disclosure of conflict of interest

None.

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