

# Evaluation of the Clinical Efficacy of Levothyroxine Combined with Irbesartan and Hydrochlorothiazide in the Treatment of Severe Heart Failure

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**Abstract:** Objective: To investigate the clinical efficacy of the combination of levothyroxine and irbesartan hydrochlorothiazide in the treatment of severe heart failure. Method: From February 2022 to May 2023, 66 patients with severe heart failure in our hospital were selected and randomly divided into a control group (treated with irbesartan and hydrochlorothiazide monotherapy) and a study group (treated with levothyroxine combined with irbesartan and hydrochlorothiazide) using a coin toss method. By comparing and analyzing the clinical efficacy indicators of two groups of patients, evaluate the differences in efficacy and application value of different treatment plans. Result: The overall therapeutic effect of the study group was significantly higher than that of the control group ( $P < 0.05$ ). The improvement level of key indicators of cardiac function in the study group was significantly higher than that in the control group ( $P < 0.05$ ). The levels of inflammatory factors and serological indicators in the research group were significantly improved compared to the control group ( $P < 0.05$ ). As for the occurrence of adverse reactions, no significant difference was observed between the two groups ( $P > 0.05$ ). Conclusion: The combined use of levothyroxine and irbesartan hydrochlorothiazide has shown significant therapeutic effects in the treatment of severe heart failure, indicating that this combination therapy has broad application prospects and promotion value in clinical practice.

**Keywords:** levothyroxine, irbesartan and hydrochlorothiazide, severe heart failure

## 1. Introduction

Heart failure refers to a pathological condition in which the diastolic and systolic functions of the heart are abnormal, resulting in insufficient arterial blood perfusion and venous blood retention. The incidence rate of the disease increases with age and is often accompanied by respiratory insufficiency, which may pose a threat to the life safety of patients in serious cases [1]. Severe heart failure usually represents the manifestation of various organic cardiovascular diseases entering the end-stage, and is one of the main causes of death among the elderly population in China. The pathogenesis of severe heart failure is extremely complex, involving multiple pathological and physiological changes. The patient's ventricular pumping efficiency and filling capacity significantly decrease, leading to a reduction in cardiac output [2]. These complex pathological conditions not only increase the burden on the heart but also seriously affect the patient's quality of life, making daily activities difficult.

Currently, the preferred strategy for treating severe heart failure is the combination of angiotensin II receptor blockers (ARBs) and diuretics [3]. The combination of irbesartan and hydrochlorothiazide is considered a typical representative, and the combination of the two can produce significant synergistic antihypertensive effects [4]. Some studies have also pointed out that for elderly patients with severe heart failure, relying solely on the treatment regimen of irbesartan combined with hydrochlorothiazide may have limited effectiveness in regulating endocrine and metabolic disorders and improving cardiac function. The myocardial injury of such patients is often accompanied by various changes in the neuroendocrine system, especially the possible decrease in thyroid hormone levels to varying degrees [5]. The levothyroxine sodium tablets, a type of thyroid hormone drug, have attracted much attention in clinical applications. This drug increases the concentration of thyroid hormones in the body, thereby enhancing the responsiveness of myocardial cells to adrenaline, helping to reduce the workload of the heart and demonstrating therapeutic effects against heart failure [6]. Given this background, the aim of this study is to investigate the efficacy of levothyroxine combined with irbesartan and hydrochlorothiazide in the treatment of severe heart failure in the elderly and its impact on endocrine function. The report is as follows.

## 2. Data and Methods

### 2.1 General Information

66 patients with severe heart failure admitted to our hospital from February 2022 to May 2023 were randomly divided

into two groups using the coin toss method (the coin positive group was the control group, and the coin negative group was the study group). After comparing and analyzing the baseline data, there was no significant difference in the basic indicators between the two groups ( $P>0.05$ ), indicating that the baseline characteristics were balanced and comparable (see Table 1 for details).

Inclusion criteria: clear indications for levothyroxine and irbesartan hydrochlorothiazide treatment, no history of drug allergies; Serum thyroid function indicators are within normal range or mildly abnormal; Left ventricular ejection fraction (LVEF)  $\leq 40\%$ .

Exclusion criteria: Patients with allergic reactions to levothyroxine or irbesartan hydrochlorothiazide; Individuals who have participated in other clinical research projects within the past three months; Accompanied by other serious diseases that may affect the test results or safety, such as malignant tumors, severe infections, etc.

## 2.2 Methods

Control group: The control group was treated with irbesartan hydrochlorothiazide tablets (specification 150.0mg/12.5mg x 7 tablets), 2 tablets each time, once a day, taken with meals.

Research group: The research group took levothyroxine tablets in addition to the control group, with an initial dose of 12.5  $\mu$ g/d, once a day. After 3 days, the dose increased to 25.0  $\mu$ g/d, once a day, for 14 consecutive days. The dose gradually decreased until discontinuation after 7 days. Both treatment groups have a duration of 2 months.

## 2.3 Observation indicators

(1) Cardiac function indicators: Both groups of subjects underwent echocardiography before and after treatment to observe fluctuations in left ventricular ejection fraction (LVEF), changes in left ventricular end systolic diameter (LVESD), and improvement in left ventricular end diastolic diameter (LVEDD).

(2) Inflammatory factors: Before and after treatment, enzyme-linked immunosorbent assay (ELISA) was used to detect the levels of tumor necrosis factor alpha (TNF -  $\alpha$ ), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1) in two groups of serum samples.

(3) Serological indicators: Serum brain natriuretic peptide (BNP) concentration was quantified using enzyme-linked immunosorbent assay (ELISA) before and after treatment, N-terminal brain natriuretic peptide precursor (NT proBNP) levels were measured using electrochemiluminescence immunoassay, and serum triiodothyronine (T3) and thyroxine (T4) levels were detected using radioimmunoassay.

(4) Adverse reactions: including but not limited to palpitations, bradycardia, gastrointestinal discomfort, headaches, etc.

(5) Efficacy evaluation criteria: Significant improvement in patient symptoms and signs, with an LVEF increase of  $\geq 10\%$ ; Effective relief of symptoms and signs with an LVEF increase of  $\geq 5\%$ ; Those who do not meet the above standards are considered invalid.

## 2.4 Statistical Methods

Statistical analysis was conducted using SPSS 26.0. Measurement data is expressed in ( $\pm$  s); Perform a t-test, with count data expressed as%, and perform a chi square test. The difference is statistically significant with  $P<0.05$ .

## 3. Results

### 3.1 Comparison of cardiac function indicators between two groups of patients

The LVEF of the research group was higher than that of the control group, while LVESD and LVEDD were lower than those of the control group, with significant differences ( $P<0.05$ ), as shown in Table 2.

### 3.2 Comparative analysis of inflammatory cytokine levels between two groups of patients

The decrease in inflammatory cytokine levels in the research group was significantly greater than that in the control group ( $P<0.05$ ), as shown in Table 3.

### 3.3 Comparison of serum indicators between two groups of patients

The study group showed significant differences ( $P<0.05$ ) in the degree of reduction of BNP and NT proBNP, as well as the degree of increase of T3 and T4, compared to the control group, as shown in Table 4.

### 3.4 Comparison of Adverse Reaction Rates between Two Groups of Patients

The incidence of adverse reactions between the two groups did not have statistical significance ( $P>0.05$ ), as shown in Table 5.

Table 1. General Information ( $\bar{x}\pm s$ )				
Group	Male/Female (Example)	Age (years)	BMI	Disease duration (months)
Study group(n=33)	15/18	52.68±2.52	22.23±2.02	3.24±1.23
Control group(n=33)	16/17	52.14±2.04	22.45±2.50	3.45±1.05
$\chi^2/t$	0.254	0.542	0.245	0.357
P	0.552	0.420	0.244	0.105

Table 2. Comparison of cardiac function indicators ( $\bar{x}\pm s$ ) between two groups of patients						
Group	LVEF(%)		LVESD(mm)		LVEDD(mm)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	Before treatment
Study group(n=33)	33.29±4.72	50.79±3.75	54.74±4.15	43.15±3.52	58.44±2.90	50.65±3.94
Control group(n=33)	33.69±4.68	46.94±3.83	54.82±4.07	46.10±3.74	58.56±2.93	54.20±4.06
t	0.345	3.913	0.074	3.134	0.161	3.436
P	0.732	<0.05	0.939	<0.05	0.875	<0.05

Table 3. Comparison of Inflammatory Factor Water ( $\bar{x}\pm s$ ) between Two Groups of Patients						
Group	TNF- $\alpha$ (ng/L)		IL-6(ng/L)		MCP-1(pg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group(n=33)	62.55±7.16	39.86±3.15	56.34±4.40	30.63±4.74	81.07±5.94	64.93±7.45
Control group(n=33)	60.29±6.34	43.25±4.78	56.82±4.87	37.55±5.32	81.56±6.23	67.84±6.33
t	1.742	4.362	0.542	7.173	0.437	2.195
P	0.084	<0.05	0.588	<0.05	0.661	<0.05

Table 4. Comparison of serum indicators ( $\bar{x}\pm s$ ) between two groups of patients								
Group	BNP(ng/L)		NT-proBNP(ng/L)		T3(nmol/L)		T4(nmol/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group(n=33)	326.79±23.14	132.52±13.80	5394.46±734.54	1543.44±354.65	0.74±0.19	1.06±0.12	93.94±11.85	115.80±11.04
Control group(n=33)	324.28±24.16	236.50±13.63	5325.34±738.46	2563.56±386.59	0.75±0.20	0.84±0.09	93.16±12.44	99.15±14.55
t	0.642	5.156	0.145	5.142	0.245	6.475	0.328	5.642
P	0.241	<0.05	0.321	<0.05	0.054	<0.05	0.541	<0.05

Table 5. Comparison of the adverse reactions of two groups of patients (n,%)					
Group	headache	Gastrointestinal reactions	bradycardia	palpitation	Always occurring
Study group(n=33)	1(3.03)	1(3.03)	0	1(3.03)	3(9.09)
Control group(n=33)	1(3.03)	2(6.06)	1(3.03)	1(3.03)	5(15.15)
$\chi^2$					0.513
P					0.571

3.5 Comparison of clinical efficacy between two groups of patients

The overall effective rate of the research group was significantly higher than that of the control group, and the difference was significant (P<0.05), as shown in Table 6.

Table 6. Comparison of Overall Efficacy between Two Groups (n,%)				
Group	Significant effect	effective	invalid	Total efficiency
Study group(n=33)	14(42.42)	18(54.5)	1(3.03)	32(96.97)
Control group(n=33)	12(36.36)	15(45.45)	6(18.18)	27(81.82)
$\chi^2$				4.325
P				<0.05

## 4. Discussion

Patients with severe heart failure often experience hypertrophic remodeling or abnormal dilation of the left ventricle due to the influence of ischemic pathological processes. This pathological change can further cause a decrease in ventricular filling capacity and impairment of ventricular ejection function [7]. This series of changes leads to a significant reduction in blood perfusion in the arterial system, ultimately resulting in abnormal cardiac function, hemodynamic disorders, and metabolic dysfunction, which seriously reduce the quality of life of patients and pose a significant threat to their safety. In the face of this situation, clinical treatment strategies are usually adopted with the main goals of enhancing cardiac function, adjusting hemodynamic balance, and optimizing endocrine and metabolic status [8].

Currently, the combination of irbesartan and hydrochlorothiazide is widely regarded as one of the standard drugs for treating heart failure. This drug achieves the goal of improving cardiac function by significantly relaxing vascular smooth muscle and effectively reducing peripheral vascular resistance [9]. However, relying solely on irbesartan and hydrochlorothiazide monotherapy may have limited effectiveness in correcting endocrine and metabolic disorders in patients and further improving cardiac function. Therefore, introducing thyroid hormone therapy is particularly important at this time. Thyroid hormones have a direct and positive impact on the pumping ability of the left ventricle, effectively reducing the resistance of myocardial blood vessels and significantly restoring the activity of the sympathetic adrenal system [10]. Thyroid hormones have shown significant clinical application value in improving the overall cardiovascular system function. This hormone also directly affects the energy metabolism process of the myocardium, significantly improving the contractility of the myocardium and activating electrolyte components such as sodium and potassium ions in myocardial cells, thereby optimizing the blood circulation of the myocardium [11].

The data analysis of this study revealed that the overall treatment efficacy of the study group was significantly higher than that of the control group ( $P < 0.05$ ). This finding indicates that the combination of levothyroxine sodium tablets and irbesartan hydrochlorothiazide tablets has shown definite therapeutic effects in the treatment of systolic heart failure, and the effectiveness of this combination therapy exceeds the traditional treatment method of using only irbesartan hydrochlorothiazide tablets. Further analysis of its mechanism of action reveals that in combination therapy, irbesartan hydrochlorothiazide tablets reduce the burden on the heart and optimize myocardial blood perfusion through their effective antihypertensive effect. This process is crucial for achieving the therapeutic goals of anti heart failure [12].

As a supplement to exogenous thyroid hormones, levothyroxine sodium tablets regulate the endocrine function of patients and promote the recovery of myocardial function. So when levothyroxine sodium tablets are combined with irbesartan hydrochlorothiazide tablets, both can fully exert their unique pharmacological mechanisms to further optimize and enhance the therapeutic effect. Research has shown that the improvement in heart function of patients in the study group after treatment is superior to that of the control group ( $P < 0.05$ ). This discovery reveals a significant effect of the combination of levothyroxine sodium tablets and irbesartan hydrochlorothiazide tablets in improving patients' cardiac function. The heart is one of the main target organs of thyroid hormones, and the T3 and T4 components in thyroid hormones not only affect the peripheral circulation status of the body, but also have important effects on the filling process, contraction function, and changes in hemodynamic levels of the heart [13]. The effective application of levothyroxine sodium tablets can significantly increase the concentration of thyroid hormones in the body, which helps prevent myocardial dysfunction caused by fluctuations in thyroid hormone levels. And the drug also has the effect of reducing systemic vascular resistance and increasing cardiac output, achieving significant improvement and optimization of myocardial function through these comprehensive effects. Related studies have pointed out that patients with severe heart failure often experience significant dysfunction of the neuroendocrine system, especially abnormalities in thyroid hormone metabolism. This situation can lead to a significant reduction in blood perfusion to various tissues and organs throughout the body, resulting in dysfunction of the circulatory system [14].

There is a close correlation between BNP and NT proBNP in plasma and ventricular systolic function, which has shown important clinical reference value in evaluating the severity of heart failure and predicting patient prognosis. The levels of T3 and T4 in patients with severe heart failure show a decreasing trend, which can reduce the responsiveness of blood vessels and myocardial tissue to adrenaline and have adverse effects on the recovery of cardiac function. The research results showed that after treatment, the study group showed better reductions in BNP and NT proBNP, as well as higher levels of T3 and T4, compared to the control group ( $P < 0.05$ ). This finding suggests that the combination of levothyroxine and irbesartan hydrochlorothiazide in the treatment of elderly patients with severe heart failure can effectively adjust their endocrine function, enhance the efficiency of the circulatory system, and have a positive effect on improving cardiac function. Levothyronine enhances the activity of  $\text{Na}^+ - \text{K}^+ - \text{ATPase}$  and sarcoplasmic reticulum  $\text{Ca}^{2+} - \text{ATPase}$  by regulating the energy metabolism of myocardial cells. This mechanism helps to strengthen the contractility of the myocardium, increase

cardiac output, and promote the improvement of coronary blood flow. The inflammatory cytokines such as TNF -  $\alpha$  and IL-6 in the serum of heart failure patients are often maintained at high concentrations. These diverse inflammatory mediators can induce damage to vascular endothelial cells and myocardial cells, thereby exacerbating the inflammatory response and promoting the pathological process of ventricular remodeling [15].

The data obtained from this study showed that the concentration of inflammatory factors in the study group was lower than that in the control group after treatment ( $P < 0.05$ ), indicating that the use of combination therapy can more effectively reduce the concentration of inflammatory factors in patients with severe heart failure. The application of irbesartan and hydrochlorothiazide can help alleviate cardiac stress, improve cardiac function, and be beneficial for the recovery of the cardiac microenvironment and the regulation of inflammatory cytokine levels in serum. Moreover, levothyroxine helps to reduce the production of inflammatory factors by affecting gene expression in myocardial cells and immune cells. During the research process, it was observed that there was no significant difference in the overall incidence of adverse reactions experienced by the two groups of participants during treatment, indicating that this combination therapy is safe and reliable.

The combined use of levothyroxine and irbesartan hydrochlorothiazide has been proven to significantly improve the treatment efficacy of elderly patients with severe heart failure. This will provide important reference for personalized medicine and ensure that each patient can receive the most suitable treatment plan according to their specific situation.

## References

- [1] Zhang Zhenen, Li Yukun, Chen Jia'an, etc The predictive value of the ratio of neutrophil count to lymphocyte count and platelet count for in-hospital mortality risk in sepsis patients [J]. Zhejiang Medical Journal, 2025, 47 (07): 712-716.
- [2] Jing Lijuan, Zhao Xiangmei, Xu Lijun, etc The value of ultrasound measurement of diaphragmatic activity and diaphragmatic superficial rapid breathing index in predicting successful weaning of mechanically ventilated patients with heart failure [J]. Journal of Medical Forum, 2025, 46 (05): 466-470.
- [3] Wang Dan, Li Weicheng The effect of ivabradine adjuvant conventional therapy on heart rate variability, plasma BNP, and serum miR-27b and miR-208 in patients with severe heart failure [J]. Clinical Medical Research and Practice, 2025, 10 (07): 70-73.
- [4] Wu Lei, Xiao Yuanyuan, Xia Qingqing Analysis on the nursing effect of PRECEDE nursing mode based on action research in patients with diabetes complicated with severe heart failure [J]. diabetes New World, 2025, 28 (03): 147-150.
- [5] Li Caihong, Lei Ruixin, Lin Xiaoyang The effect of dual level non-invasive positive pressure ventilation combined with recombinant human brain natriuretic peptide in the treatment of severe heart failure and its impact on patient hemodynamics and mMRC score [J]. Clinical Medicine, 2025, 45 (01): 68-70.
- [6] Luo Xinyao, Wan Dingyuan, Wang Ke, etc Explainable machine learning models predict short-term mortality in intensive care units for patients with heart failure complicated by acute kidney injury: a retrospective cohort study [J]. Journal of Sichuan University (Medical Edition), 2025, 56 (01): 183-190.
- [7] Liu Jianping, Liu Na, Nie Zhenyun The effect of Xinmailong injection combined with spironolactone tablets on BNP levels, exercise endurance, and cardiac function in patients with severe heart failure [J]. Drug Evaluation, 2024, 21 (11): 1394-1397.
- [8] Guo Mingkai, Zhang Donghong, Ma Liang, etc Clinical efficacy of dopamine combined with nitroprusside in the treatment of severe heart failure in elderly patients and its impact on CysC, Hcy, and BNP levels [J]. Clinical Medical Research and Practice, 2024, 9 (32): 55-58.
- [9] Mai Jiejian, Huang Tong The effect of recombinant human brain natriuretic peptide in the treatment of severe coronary heart disease with heart failure and its impact on patients' cardiac function, inflammatory factors, and adverse reactions [J]. Journal of Modern Medicine and Health Research, 2024, 8 (21): 57-60.
- [10] Xiong Xingjiang Connotation and Treatment Experience of Chest Bi Deficiency Syndrome and Ginseng Decoction Formula Syndrome Based on Severe Cases and Modern Pathophysiological Mechanisms in Treating Acute and Critical Illnesses such as Coronary Heart Disease, Wind Heart Disease, Heart Failure, Hypotension, and Pulmonary Hypertension. Chinese Journal of Traditional Chinese Medicine, 2025, 50 (06): 1706-1714.
- [11] Shi Shuai, Li Xiuwen, Zhao Yiting, etc Analysis of risk factors for severe infections and adverse cardiovascular events in patients with chronic renal failure and uremia undergoing hemodialysis maintenance treatment [J]. Advances in Modern Biomedicine, 2024, 24 (14): 2666-2671.
- [12] Fan Qun, Jiang Ping, Zhang Jinbian, etc The efficacy of recombinant human brain natriuretic peptide combined with dual level positive airway pressure ventilation in the treatment of severe AHF patients and its effects on cardiac function, hemodynamics, and antioxidant indicators [J]. Journal of Clinical and Experimental Medicine, 2024, 23 (04): 354-358.

- [13] Xie Hongming, Zheng Jiajia, Gong Yingying Observation of the Application Value and Improvement of Cardiac Function of Thyroxine Combined with Irbesartan and Hydrochlorothiazide in the Treatment of Severe Heart Failure [J]. Northern Pharmacy, 2024, 21 (06): 179-181.
- [14] Feng Xiaokai, Gao Xueliang The effect of recombinant human brain natriuretic peptide combined with low molecular weight heparin calcium on PaO<sub>2</sub> and CRP levels in patients with severe pulmonary heart disease and heart failure [J]. Journal of Shanxi Health Vocational College, 2024, 34 (02): 22-24.
- [15] Xu Xiao, Xu Huajuan, Li Ming, etc Correlation analysis of TNIP1 gene single nucleotide polymorphism and its mRNA expression level with pulmonary infection in elderly patients with chronic heart failure [J]. Journal of Xinjiang Medical University, 2024, 47 (04): 538-541+547.