Am J Transl Res 2026;18(8):7226-7235
www.ajtr.org /ISSN:1943-8141/AJTR0173536

Original Article

Trimetazidine combined with metoprolol improves therapeutic outcomes in patients with coronary heart disease complicated by heart failure

Xiaoyan Liang[1*], Feifei Wang[2*], Zechen Bai[3,4]

[1]Department of Cardiac Function, The First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, Xinjiang Uygur Autonomous Region, China; [2]The Second Affiliated Hospital of Xi'an Jiaotong University, Xinjiang Hospital (People's Hospital of Xinjiang Uygur Autonomous Region, Bainiaohu Hospital), Urumqi 830026, Xinjiang Uygur Autonomous Region, China; [3]College of Medical Engineering and Technology, Xinjiang Medical University, Urumqi 830017, Xinjiang Uygur Autonomous Region, China; [4]Institute of Medical Engineering Interdisciplinary Research, Xinjiang Medical University, Urumqi 830017, Xinjiang Uygur Autonomous Region, China. [*]Equal contributors and co-first authors.

Received April 23, 2026; Accepted July 3, 2026; Epub August 15, 2026; Published August 30, 2026

Abstract: Objective: To investigate the therapeutic efficacy and influencing factors of metoprolol combined with trimetazidine in the treatment of heart failure secondary to coronary heart disease (CHD). Methods: A retrospective analysis was performed on 142 patients with CHD complicated by heart failure (HF) who were treated at the First Affiliated Hospital of Xinjiang Medical University from July 2023 to July 2025. Patients were allocated into a control group (trimetazidine monotherapy, n=70) and a joint group (metoprolol combined with trimetazidine, n=72). Clinical outcomes were compared between the two groups, including overall treatment efficacy, QT dispersion (QTd) before and after treatment, heart rate (HR), hemodynamic parameters [hematocrit (Hct), plasma fibrinogen (Fib), plasma specific viscosity], vascular endothelial function markers [calcitonin gene-related peptide (CGRP), plasma endothelin (ET), nitric oxide (NO)], cardiac function indicators [left ventricular end-diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter (LVESD)], and incidence of adverse reactions. Logistic multivariate regression analysis was performed to identify independent factors affecting therapeutic efficacy in CHD patients complicated by HF. Results: The total effective rate was significantly higher in the joint group than the control group (86.11% vs. 71.43%, P=0.032). After treatment, QTd, HR, ET, and hemodynamic parameters were significantly decreased in both groups compared with baseline, whereas CGRP, NO, and LVEF were significantly increased. Moreover, the improvement in the joint group was significantly superior to that in the control group (P<0.05). There was no significant difference in the overall incidence of adverse reactions between the two groups (13.89% vs. 12.86%, P=0.857). Multivariate logistic regression analysis identified treatment regimen, diabetes mellitus, and age as independent factors affecting therapeutic efficacy (P<0.05). Conclusion: Trimetazidine combined with metoprolol demonstrates superior efficacy without increasing adverse reactions in CHD patients complicated by HF. This combination therapy may improve hemodynamic status, endothelial function, and cardiac function, supporting its clinical application.

Keywords: Metoprolol, trimetazidine, coronary heart disease with heart failure, cardiac function, safety

Introduction

Coronary heart disease (CHD) is primarily caused by lipid deposition in the coronary arterial wall, forming on the inner wall of the coronary artery, leading to plaque formation, luminal stenosis, or even vascular occlusion, resulting in insufficient myocardial perfusion and myocardial ischemia, hypoxia, or necrosis [1]. CHD is a leading contributor to the development of heart failure (HF). Patients with CHD-related HF not only present with symptoms such as chest tightness, fatigue, and dyspnea, but also frequently complicated by angina pectoris and myocardial infarction, posing a great threat to their life and safety [2]. Clinically, HF secondary to CHD is mainly managed with medication for improving cardiac function [3]. Although pharmacological treatment can partially alleviate symptoms, most patients are

https://doi.org/10.62347/WTNY7047

middle-aged or elderly and often present with diminished physical reserve and vascular sclerosis. Consequently, the therapeutic efficacy of conventional therapy remains suboptimal in this group [4, 5]. Therefore, the identification of more effective treatment strategies for CHD complicated by HF remains a hot issue for clinical investigation.

Trimetazidine is a myocardial energy metabolism regulator that improves cellular energy production efficiency under ischemic and hypoxic conditions by inhibiting free fatty acid β-oxidation and promoting glucose oxidation, thus protecting myocardial function [6]. However, due to the multifactorial nature of CHD and HF, monotherapy often fails to achieve satisfactory clinical outcomes, and combination strategies are increasingly applied in clinical practice. Metoprolol, as a selective β1-adrenergic receptor blocker, can effectively inhibits its sympathetic overactivation, reduces heart rate, and decreases myocardial oxygen consumption. It is recognized as one of the cornerstone medications in the treatment of HF [7, 8]. Previous studies have demonstrated that metoprolol can reduce cardiac workload and alleviate HF symptoms [9]. The combination of the two exert synergistic effects by simultaneously improving energy metabolism and regulating neuroendocrine, thereby providing a theoretical basis for improved therapeutic efficacy.

Currently, limited studies have investigated factors influencing the therapeutic efficacy of metoprolol combined with trimetazidine in CHD patients with HF. Therefore, this study aimed to analyze the independent predictors of treatment response to this combination therapy, with the aim of providing evidence for formulating more effective treatment plans in clinical practice. The innovation of this study lies in not only evaluating the clinical efficacy and safety of the drug combination, but also identifying independent predictors of therapeutic response through multivariate analysis, thereby providing an evidence-based foundation for individualized precision therapy.

Materials and methods

Patient selection

This retrospective study included 142 CHD patients complicated by HR who were treated at The First Affiliated Hospital of Xinjiang Medical University from July 2023 to July 2025. According to the actual treatment plan, patients were allocated into a control group (CG, trimetazidine monotherapy, n=70) and a joint group (JG, metoprolol combined with trimetazidine, n=72).

Inclusion criteria: (1) Diagnosis of CHD and chronic HF according to the Chinese Guidelines for the Diagnosis and Treatment of HR [10], with New York Heart Association (NYHA) functional class II-IV; (2) At least one major coronary artery stenosis ≥50% confirmed by coronary angiography; (3) Left ventricular ejection fraction (LVEF) <50%; (4) Age 18-80 years; (5) Complete clinical data available.

Exclusion criteria: (1) Acute myocardial infarction or unstable angina within the past 3 months; (2) Severe valvular heart disease, hypertrophic or restrictive cardiomyopathy, or acute myocarditis; (3) Cardiogenic shock or severe symptomatic hypotension (systolic blood pressure <90 mmhg); (4) Significant bradycardia (heart rate [HR] <50 beats/min) or grade II or above atrioventricular block without pacemaker implantation; (5) Severe hepatic or renal dysfunction; (6) Known allergy or contraindication to metoprolol or trimetazidine; (7) Malignancy, severe infection, thyroid disease, or autoimmune disease with an estimated life expectancy <1 year (**Figure 1**). The study was approved by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University, and conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

Treatment protocol

After admission, both groups received standard therapy, including diuretics, cardiotonic agents, medications for correction of water-electrolyte imbalance, lipid-lowering drugs, and vasodilators. On this basis, patients in the control group (CG) were administered trimetazidine (Beijing Wansheng Pharmaceutical, Co., Ltd., National Medical Products Administration [NMPA] approval No. H20065167, 20 mg/tablet) orally at a dose of 20 mg per administration, three times daily. Patients in the joint group (JG) additionally received metoprolol tartrate tablets (AstraZeneca Pharmaceutical Co., Ltd.). The dose was titrated upward every 7 days by 6.25-12.5 mg per administration based

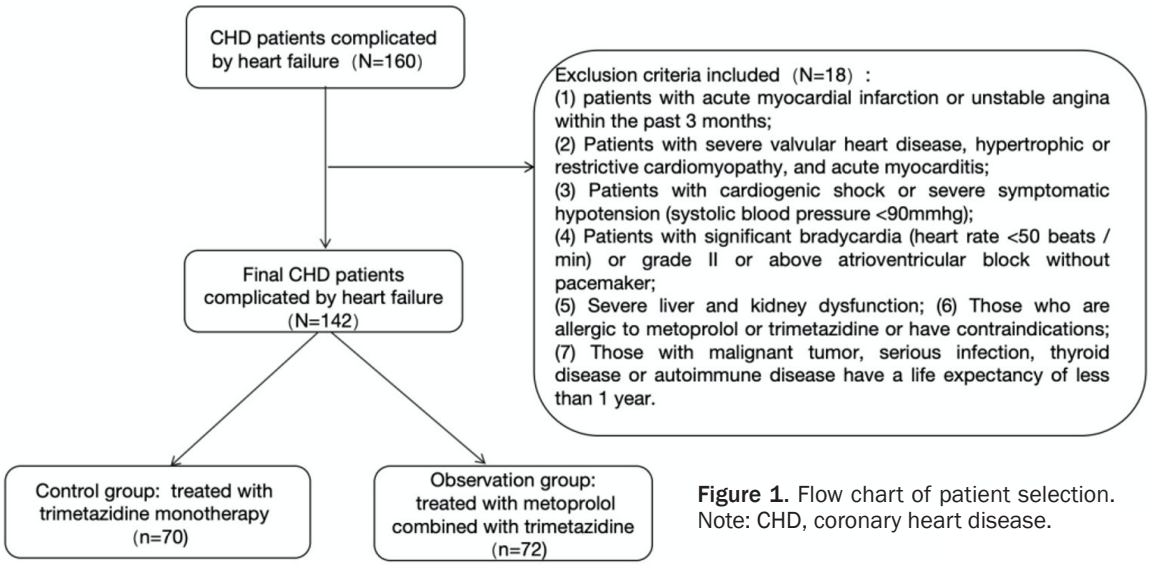

Figure 1. Flow chart of patient selection. Note: CHD, coronary heart disease.

on individual patient tolerance and clinical response, with a maximum daily dose below 300 mg. All patients were treated continuously for 2 months. Clinical indicators were measured before treatment and after 2 months of treatment.

Outcome measures

Primary endpoints: (1) The therapeutic efficacy was evaluated and compared between the two groups. Clinical response was categorized as markedly effective (complete resolution of clinical symptoms, with an improvement of ≥2 grades in cardiac function classification), effective (partial relief of clinical symptoms, with an improvement of 1 grade in cardiac function classification), and ineffective (failure to meet the aforementioned criteria, or worsening of clinical condition). The overall response rate (ORR) = (number of markedly effective cases + number of effective cases)/total number of cases × 100%. (2) QT dispersion (QTd) and HR were compared between the two groups before and after treatment. (3) Endothelial function was assessed and compared between the two groups before and after treatment. Peripheral venous blood (3 mL) was collected from patients before and after treatment, centrifuged for 10 minutes, and the supernatant serum was collected. Serum levels of nitric oxide (NO), calcitonin gene-related peptide (CGRP), and endothelin (ET) were measured using enzyme-linked immunosorbent assay (ELISA).

Secondary endpoints: (1) Hemodynamic parameters were measured and compared between the two groups before and after treatment using a Danish Innocor hemodynamic monitor, including hematocrit (Hct), plasma fibrinogen (Fib), and plasma specific viscosity. (2) Cardiac function parameters were evaluated using echocardiography and compared between the two groups, including left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), and left ventricular end-systolic diameter (LVESD). (3) The incidence of adverse reactions during treatment was recorded and compared between the two groups, including abnormal liver function, hypotension, sinus bradycardia, and gastrointestinal discomfort. (4) Clinical data were collected, and variables showing significant differences between the two groups were further included in a multivariable logistic regression analysis to identify independent factors affecting the therapeutic efficacy of metoprolol combined with trimetazidine in CHD patients with HF.

Sample size calculation

According to preliminary experimental data and previous literature results, the effective rate was estimated to be 70% in the control group and 87% in the joint group. With a two-sided significance level (α) of 0.05, a statistical power (1-β) of 0.80, and a 1:1 allocation ratio between groups, sample size calculation was performed using PASS software. The results indicated that at least 60 patients were required per group. Considering an anticipated attrition or incomplete data rate of approximately 10%, a total of 142 patients were ultimately enrolled in this study, which satisfied the required sample size.

Table 1. Comparison of baseline information between the joint and control groups

Factors	Joint Group n=72	Control Group n=70	X^2	P
Gender			0.001	0.977
Male	42 (58.33)	41 (58.57)		
Female	30 (41.67)	29 (41.43)		
Age (years)			0.031	0.861
≤65	35 (48.61)	33 (47.14)		
>65	37 (51.39)	37 (52.86)		
BMI (kg/m^2)			0.002	0.988
≤23	33 (45.83)	32 (45.71)		
>23	39 (54.17)	38 (54.29)		
History of smoking			0.002	0.965
Yes	45 (62.50)	44 (62.86)		
No	27 (37.50)	26 (37.14)		
Diabetes			0.005	0.943
Yes	50 (69.44)	49 (70.00)		
No	22 (30.56)	21 (30.00)		
Cardiac Function Classification			0.036	0.849
Class III	40 (55.56)	40 (57.14)		
Class IV	32 (44.44)	30 (42.86)		

Table 2. Comparison of clinical outcomes between the joint and control groups

Therapeutic effect	Joint Group n=72	Control Group n=70	X^2	P
Markedly effective	30 (41.67)	22 (31.43)	-	-
Effective	32 (44.44)	28 (40.00)	-	-
Ineffective	10 (13.89)	20 (28.57)	-	-
Overall Response Rate	62 (86.11)	50 (71.43)	4.592	0.032

Statistical methods

Statistical analyses were performed using SPSS 19.0. Categorical variables were presented as numbers and percentage (%) and compared using the χ^2 test. Continuous variables were expressed as mean ± standard deviation. Inter-group comparisons were conducted using independent-samples t-tests, while paired t-tests were applied for within-group comparisons before and after treatment. Post-hoc comparisons were conducted using the LSD/t-tests. Statistical significance was set at P<0.05.

Variables showing differences between groups were first subjected to univariate analysis. Variables with P<0.10 in univariate analysis were included in the multivariate logistic regression model. A forward stepwise regression method based on maximum likelihood estimation (forward LR) was used to determine the independent factors affecting the therapeutic efficacy. P< 0.05 was considered statistically significant.

Results

Baseline characteristics

No significant differences were observed in BMI, age, sex, or other baseline characteristics between the two groups (P>0.05, **Table 1**).

Comparison of treatment efficacy

After treatment, 30 patients were classified as markedly effective, 32 as effective, and 10 as ineffective in the joint group, and the corresponding numbers in the control group were 22, 28, and 20, respectively. The overall response rate (ORR) was higher in the joint group than in the control group (86.11% vs. 71.43%, P<0.05; **Table 2**).

Comparison of QTd and HR

No significant differences in QTd and HR were observed between the two groups before treatment (P>0.05). After treatment, both parameters improved in both groups, with more pronounced improvements observed in the joint

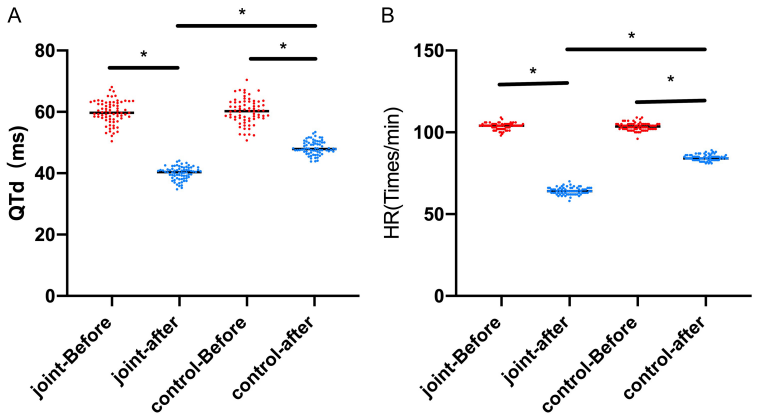

Figure 2. Comparison of QTd (A) and heart rate (B) between the two groups before and after treatment. *P<0.05. Note: QTd, QT interval dispersion.

group than in the control group (P<0.05; **Figure 2**).

Comparison of vascular endothelial function

No significant differences in vascular endothelial functions were observed between the two groups before treatment (P>0.05). After treatment, ET levels declined in both groups, while CGRP and NO levels increased in both groups. These changes were more significant in the joint group than the control group (P<0.05; **Figure 3**).

Comparison of hemodynamic parameters

Before treatment, no significant differences were observed between groups regarding the hemodynamic parameters, including Fib, Hct, and plasma specific viscosity (P>0.05). After treatment, all parameters decreased in both groups, with more pronounced reductions observed in the joint group compared with the control group (P<0.05; **Figure 4**).

Comparison of cardiac function

Before treatment, there were no significant differences in LVESD, LVEDD, or LVEF between the two groups (P>0.05). After treatment, cardiac function improved in both groups, with the joint group showing significantly lower LVESD and LVEDD and higher LVEF (P<0.05; **Figure 5**).

Comparison of adverse reaction

After treatment, adverse reactions in the joint group included abnormal liver function (n=3), hypotension (n=2), sinus bradycardia (n=2), and gastrointestinal discomfort (n=3), with a total incidence of 13.89, which was comparable to that of the control group (12.86%) (P>0.05; **Table 3**).

Factors influencing treatment efficacy

According to the treatment outcomes, patients were grouped into an effective group (n=112) and an ineffective group (n=30). Univariate analysis showed that age, diabetes, and treatment regimen were associated with therapeutic response (**Table 4**). Subsequent multivariate logistic regression analysis showed that diabetes, age, and treatment regimen were independent predictors of treatment efficacy in patients with CHD complicated by HF (P<0.05, **Tables 5**, **6**).

Discussion

Coronary heart disease (CHD) is one of the leading causes of heart failure (HF). With population aging, the prevalence of CHD complicated by HF has continued to increase, posing a serious public health problem worldwide [11]. The pathophysiological mechanism underlying CHD-related HF are complex, involving myocardial ischemia, impaired energy metabolism, neurohormonal overactivation, and progressive ventricular remodeling [12]. Currently, therapeutic strategies have shifted from simply relieving symptoms to comprehensive management aimed at delaying ventricular remodeling and improving long-term clinical outcomes [13].

In this study, the ORR in the joint group was evidently higher than that in the control group, consistent with previous findings. Feng et al. [14], in a study published in the *International Journal of General Medicine*, reported that trimetazidine combined with metoprolol significantly improved ORR in patients with CHD complicated by HF. In addition, another study [15] demonstrated that the ORR of the combination group was notably higher than that of the metoprolol alone group. Notably, the present study also found that improvement in QTd and HR were more pronounced in the joint group. QTd reflects the heterogeneity of ventricular repo-

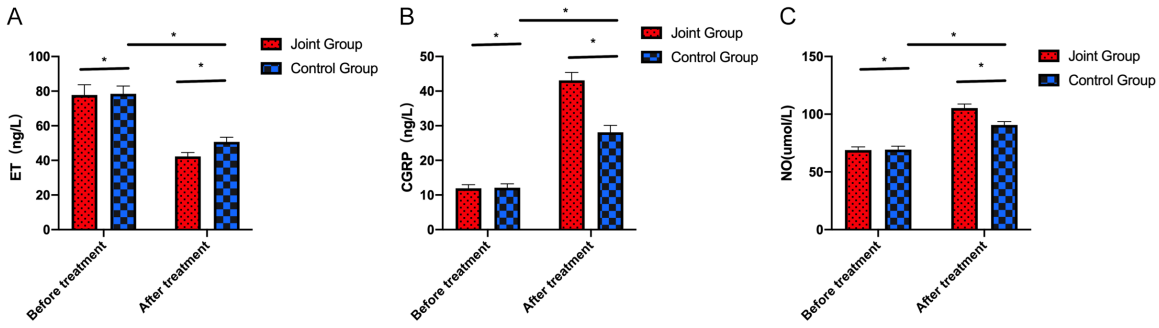

Figure 3. Comparison of vascular endothelial function between two groups before and after treatment. A: ET; B: CGPP; C: NO. Notes: *P<0.05. NO, nitric oxide; CGRP, calcitonin gene-related peptide; ET, plasma endothelin.

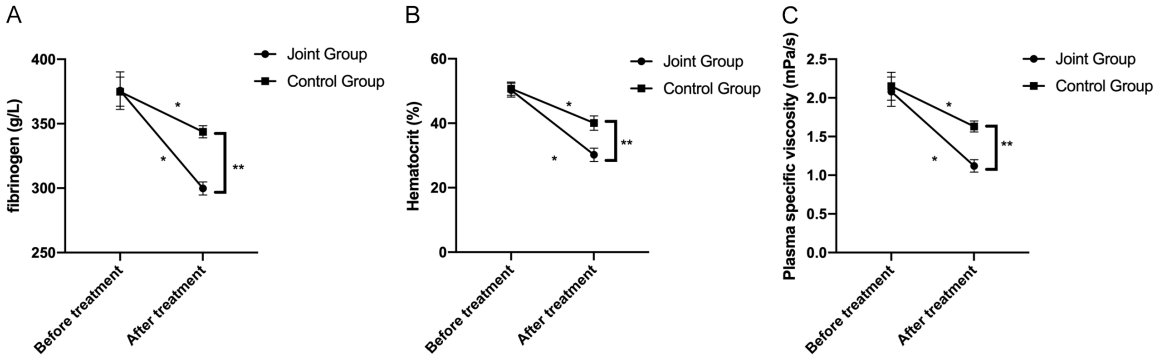

Figure 4. Comparison of hemodynamic parameters between the two groups before and after treatment. A: Plasma fibrinogen; B: Hematocrit; C: Plasma specific viscosity. Notes: *P<0.05, **P<0.001.

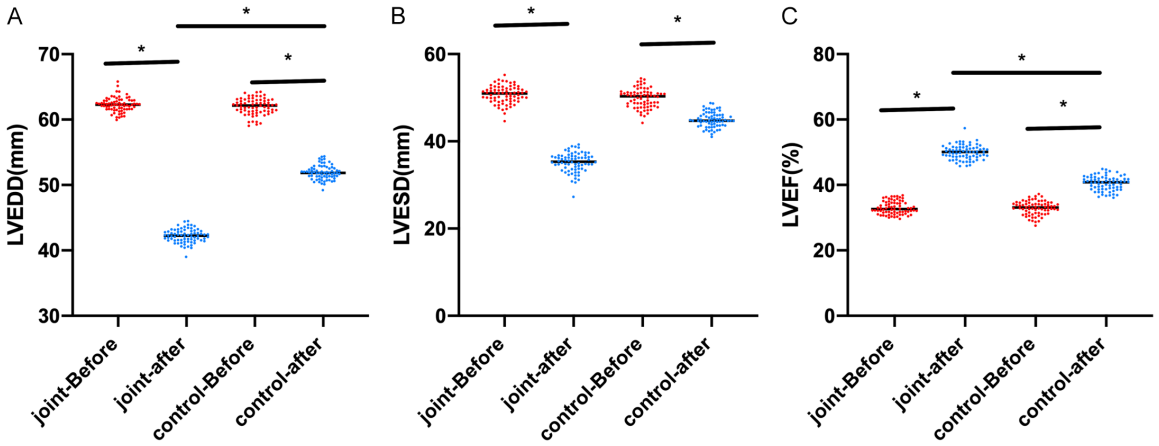

Figure 5. Comparison of cardiac function markers between the two groups before and after treatment. A: LVEDD; B: LVESD; C: LVEF. Notes: *P<0.05. LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter.

larization, and it is an important predictor for malignant ventricular arrhythmias [16]. This synergistic effect may stem from the complementarity of the two mechanisms: trimetazidine optimizes the energy supply of ischemic myocardium from the metabolic source and enhances the working efficiency of myocardium, while metoprolol inhibits the hyperexcitable sympathetic nerve, reduces the burden on the heart from the peripheral environment and improves ventricular remodeling. This dual mechanism can be conceptually understood as

Table 3. Comparison of the incidence of adverse reactions between the joint and control groups [n, (%)]

Adverse Reaction	Joint Group n=72	Control Group n=70	X^2	P
Abnormal liver function	3 (4.17)	3 (4.29)	-	-
Hypotension	2 (2.78)	2 (2.86)	-	-
Sinus bradycardia	2 (2.78)	2 (2.86)	-	-
Gastrointestinal discomfort	3 (4.17)	2 (2.86)	-	-
Adverse reaction rate	10 (13.89)	9 (12.86)	0.033	0.857

optimizing the "energy supply" to cardiomyocytes while simultaneously reducing the "energy demand", thereby improving overall cardiac efficiency and function [17, 18].

This study further demonstrated that, after treatment, ET levels were significantly lower in the joint group than in the control group, whereas NO levels were significantly higher, suggesting that combined medication can more effectively improve vascular endothelial function. These findings are consistent with the results reported by Qiu et al [15], who showed that serum Ang II and ET-1 levels were significantly reduced, while flow-mediated vasodilation (FMD) and NO levels were significantly increased in CHD patients after combined treatment with metoprolol and trimetazidine. ET has a strong vasoconstrictive effect, while NO mediates vasodilation; the balance between the two is crucial for maintaining vascular tone. CHD patients complicated by HF typically present endothelial dysfunction, manifested as increased ET secretion and decreased NO synthesis. Mechanistically, trimetazidine may exert endothelial protective effects indirectly by optimizing myocardial energy metabolism and attenuating ischemia-reperfusion injury, whereas metoprolol may provide additional vascular protective effect by reducing sympathetic overactivation and endothelial shear stress-induced endothelial injury [19, 20]. Moreover, patients in the joint group exhibited lower hemodynamic parameters, including plasma fibrinogen, hematocrit, and plasma specific viscosity than the control group after treatment. Patients with CHD and HF often present with increased blood viscosity, which contributes to elevated risk of thrombosis. Metoprolol can reduce sympathetic tone and reduce the adverse effects of catecholamines on blood rheology. When combined with trimetazidine, it further improves myocardial contractility and promotes hemodynamic stability [21]. In terms of ventricular remodeling, this study revealed that LVESD and LVEDD were significantly lower, whereas LVEF was significantly higher in the joint group compared to the control group. Ventricular remodeling is the core pathological basis for HF progression, manifested as ventricular cavity enlargement, ventricular wall thickening, and spherical deformation. Previous studies [22] have reported that combined treatment significantly improves LVEF while reducing LVEDD and LVESD in patients with CHD-related HF, which is consistent with our observation. The underlying mechanism may involve complementary pharmacological effects. Metoprolol delays or even partially reverses the process of ventricular remodeling by inhibiting excessive activation of the sympathetic nervous system and downregulating β1-adrenergic receptor signaling; while trimetazidine improves myocardial ATP synthesis efficiency and enhances myocardial contractility from a metabolic perspective [23]. This dual mechanisms therefore exert synergistic effects in attenuating or partially reversing ventricular remodeling.

Regarding safety, the incidence of adverse events was comparable between the two groups, which is consistent with existing literature reports. A previous study involving elderly patients with hypertension and chronic HF also confirmed that the overall rate of adverse events was similar between groups after treatment with metoprolol combined with trimetazidine [24]. Current guideline-guided drug therapy (GDMT) for HF emphasizes the importance of multidrug combination therapy; however, concerns remain regarding drug-drug interactions and increased risk of adverse reactions. The results of this study suggest that, under standardized dose titration and management, metoprolol combined with trimetazidine did not raise the risk of additional adverse events, and its safety profile was comparable to that of trimetazidine alone. Notably, no increase in the incidence of sinus bradycardia was observed in the joint group. This may be due to the structured dose titration strategy of metoprolol (starting at 6.25 mg/time, increasing every 7 days, with the daily dose controlled below 300

Table 4. Univariate analysis of factors associated with therapeutic efficacy

Variable	Effective group (n=112)	Ineffective group (n=30)	X^2	*P* value
Sex			0.038	0.846
Male (n=83)	65 (58.04)	18 (60.00)		
Female (n=59)	47 (41.96)	12 (40.00)		
Age			14.86	0.001
≤65 (n=68)	63 (56.25)	5 (16.67)		
>65 (n=74)	49 (43.75)	25 (83.33)		
BMI (kg/m^2)			0.511	0.475
≤23 (n=65)	53 (47.32)	12 (40.00)		
>23 (n=77)	59 (52.68)	18 (60.00)		
History of smoking			0.587	0.444
Yes (n=89)	72 (64.29)	17 (56.67)		
No (n=53)	40 (35.71)	13 (43.33)		
History of Diabetes			5.175	0.023
Yes (n=99)	73 (65.18)	26 (86.67)		
No (n=43)	39 (34.82)	4 (13.33)		
Treatment Regime			4.592	0.032
With Metoprolol (n=72)	62 (55.36)	10 (33.33)		
Without Metoprolol (n=70)	50 (44.64)	20 (66.67)		

Note: BMI, body mass index.

Table 5. Assignment of variables

Variable	Coding
Diabetes mellitus	Yes = 1, No = 0
Age	>65 = 1, ≤65 = 0
Treatment Regime	Without metoprolol = 1, With metoprolol = 0

mg), which allowed steady heart rate reduction while minimizing the risk of excessive bradycardia. Nevertheless, in clinical practice, dosage adjustments should be individualized according to patients' baseline heart rate, blood pressure, and concomitant medications, and close monitoring of heart rate and blood pressure is recommended during the early phase of treatment.

Finally, multivariate logistic regression analysis revealed identified diabetes mellitus, treatment regimen, and age as independent predictors of treatment efficacy. Patients with diabetes had poorer treatment outcomes, which may be associated with more extensive microvascular damage, increased oxidative stress, and more severe myocardial energy metabolism [25]. These findings highlight the advantages of combination therapy and support the paradigm shift from single-target intervention toward multi-target synergistic management in HF.

Conclusion

Metoprolol combined with trimetazidine greatly improves clinical efficacy in the treatment of CHD complicated with HF, enhancing electrophysiological parameters, vascular endothelial function, hemodynamic status, and ventricular remodeling indicators, with good safety profile.

Underlying disease (diabetes mellitus) and treatment regimen are independent predictors of treatment efficacy. Mechanistically, metoprolol exerts its effects primarily through neuroendocrine regulation, whereas trimetazidine improves myocardial performance by optimizing energy metabolism. The complementary and synergistic actions of these two agents demonstrate high clinical application value.

This study has several limitations. First, the retrospective design of this study may have introduced selection bias. Second, the relatively small sample size and single-center setting may limit the generalizability of the findings. In addition, the imbalance in sample size between groups may have influenced the robustness of the results. Future studies should focus on

Table 6. Multivariable analysis of independent predictors of therapeutic efficacy

Variable	B	S.E	Wals	P	Exp (B)	95% C.I	
						Lower limit	Upper limit
Diabetes mellitus	-1.689	0.677	6.232	0.013	0.185	0.049	0.696
Age	-2.109	0.557	14.312	0.001	0.121	0.041	0.362
Treatment Regime	1.029	0.501	4.219	0.040	2.798	1.048	7.475

multi-center, large-scale, prospective randomized controlled trials with extended follow-up periods. Moreover, individualized treatment strategies based on patient metabolic phenotypes and precision medicine approaches may further optimize therapeutic outcomes in this patient population.

Acknowledgements

This study was supported by the Natural Science Foundation of Xinjiang Uygur Autonomous Region (Grant No. 2023D01C44); National Natural Science Foundation of China (Grant No. 32460162); Talent Project of Tian-chi Doctoral Program in Xinjiang Uygur Autonomous Region and Special Funds for Talents of Xinjiang Medical University (Grant No. 0103010211); Hospital Project of People's Hospital of Xinjiang Uygur Autonomous Region (No. 20220109; No. 20210215); Health Science and Technology Project of Xinjiang Uygur Autonomous Region (No. 2025001CX-KYXM650026876).

Disclosure of conflict of interest

None.

Address correspondence to: Zechen Bai, College of Medical Engineering and Technology, Xinjiang Medical University, Urumqi 830017, Xinjiang Uygur Autonomous Region, China. Tel: +86-0991-2110400; E-mail: zc.bai@xjmu.edu.cn

References

[1] Carney RM, Freedland KE and Rich MW. Treating depression to improve survival in coronary heart disease: what have we learned? J Am Coll Cardiol 2024; 84: 482-489.

[2] Ciuca-Pana MA, Boulmpou A, Ileri C, Manzi G, Golino M, Ostojic M, Galimzhanov A, Busnatu S, Mega S and Perone F. Chronic heart failure and coronary artery disease: pharmacological treatment and cardiac rehabilitation. Medicina (Kaunas) 2025; 61: 211.

[3] Ski CF, Taylor RS, McGuigan K, Long L, Lambert JD, Richards SH and Thompson DR. Psychological interventions for depression and anxiety in patients with coronary heart disease, heart failure or atrial fibrillation: cochrane systematic review and meta-analysis. Eur J Cardiovasc Nurs 2025; 24: 194-204.

[4] Wang C, Xing J, Zhao B, Wang Y, Zhang L, Wang Y, Zheng M and Liu G. The effects of high-intensity interval training on exercise capacity and prognosis in heart failure and coronary artery disease: a systematic review and meta-analysis. Cardiovasc Ther 2022; 2022: 4273809.

[5] Sen P, Wang L, d'Ambrosio L, Bierschenk S, Hamers J, Ornek I, Sittig T, Zhang H, Zhang J and Merkus D. Coronary microvascular disease in heart failure with preserved ejection fraction. Physiol Rep 2025; 13: e70521.

[6] Nassiri S, Van de Bovenkamp AA, Remmelzwaal S, Sorea O, de Man F and Handoko ML. Effects of trimetazidine on heart failure with reduced ejection fraction and associated clinical outcomes: a systematic review and meta-analysis. Open Heart 2024; 11: e002579.

[7] Zhu T and Song Y. Efficacy of Sacubitril/Valsartan combined with metoprolol on cardiac function, cardiac remodeling, and endothelial function in patients with coronary heart disease and heart failure. Br J Hosp Med (Lond) 2025; 86: 1-16.

[8] Ren K, Feng J, Yang X, Ren B and Guo Y. Efficacy of metoprolol combined with torasemide in elderly patients with degenerative valvular heart disease and heart failure and its influence on NT-proBNP levels. Pak J Med Sci 2023; 39: 945-949.

[9] BioMed Research International. Retracted: observation of curative effect of trimetazidine combined with metoprolol in elderly patients with coronary heart disease complicated with heart failure and the effect of myocardial remodeling by integrated traditional chinese and western medicine. Biomed Res Int 2023; 2023: 9826080.

[10] Iaconelli A, Pellicori P, Dolce P, Busti M, Ruggio A, Aspromonte N, D'Amario D, Galli M, Princi G, Caiazzo E, Rezig AOM, Maffia P, Pecorini G, Crea F and Cleland JGF. Coronary revascularization for heart failure with coronary artery disease: a systematic review and meta-analy-

sis of randomized trials. Eur J Heart Fail 2023; 25: 1094-1104.
[11] Rush CJ, Berry C, Oldroyd KG, Rocchiccioli JP, Lindsay MM, Touyz RM, Murphy CL, Ford TJ, Sidik N, McEntegart MB, Lang NN, Jhund PS, Campbell RT, McMurray JJV and Petrie MC. Prevalence of coronary artery disease and coronary microvascular dysfunction in patients with heart failure with preserved ejection fraction. JAMA Cardiol 2021; 6: 1130-1143.
[12] Wang Z, Zhang Y, Wang Y, Liu L and Zhang J. Kinesiophobia and its associated factors in patients with coronary heart disease: a cross-sectional study based on latent feature analysis. BMJ Open 2023; 13: e072170.
[13] Gadomska B. Clinical and angiographic studies of the occlusion of arteria cerebri media and its branches. Wiad Lek 1972; 25: 663-672.
[14] Feng XH, Wang Y, Wang LY, Shen JF, You CY and Feng QT. Value of PTEN and echocardiography in predicting the efficacy of trimetazidine combined with metoprolol in the treatment of heart failure. Int J Gen Med 2021; 14: 10257-10263.
[15] Qiu QY, Dai M, Mou Y and Yu H. Effect of metoprolol combined with trimetazidine on serum angiotensin II and vascular endothelial function in patients with chronic heart failure. Journal of Clinical Medicine in Practice 2021; 25: 99-102
[16] Pestrea C, Cicala E, Ivascu M, Gherghina A, Ortan F and Pop D. Comparison of depolarization and repolarization parameters in left vs. right ventricular septal pacing-an intraprocedural electrocardiographic study. J Cardiovasc Dev Dis 2023; 10: 108.
[17] Journal of Healthcare Engineering. Retracted: metoprolol improves myocardial remodeling and cardiac function in patients with permanent pacemaker implantation. J Healthc Eng 2023; 2023: 9790631.
[18] Cheng YT, Lip GYH, Cheung BMY, Yiu KH, Tse HF and Chan YH. Trimetazidine is associated with ameliorated stroke risk in patients with both ischemic heart disease and atrial fibrillation. J Am Heart Assoc 2025; 14: e041629.
[19] van de Bovenkamp AA, Geurkink KTJ, Oosterveer FTP, de Man FS, Kok WEM, Bronzwaer PNA, Allaart CP, Nederveen AJ, van Rossum AC, Bakermans AJ and Handoko ML. Trimetazidine in heart failure with preserved ejection fraction: a randomized controlled cross-over trial. ESC Heart Fail 2023; 10: 2998-3010.
[20] Zheng H and Hu X. Calcium dibutyryl adenosine cyclophosphate enhances the effect of metoprolol in treating older adults with heart failure combined with arrhythmia. Sichuan Da Xue Xue Bao Yi Xue Ban 2024; 55: 699-707.
[21] Lu Y, Wang F, Ni H, Sun Y and Shi H. Observation of curative effect of trimetazidine combined with metoprolol in elderly patients with coronary heart disease complicated with heart failure and the effect of myocardial remodeling by integrated traditional chinese and western medicine. Biomed Res Int 2022; 2022: 6098799.
[22] Xu X, Yang Y, Zhou G, Du Z, Zhang X, Mao W and Cai H. Clinical efficacy of Qili Qiangxin capsule combined with western medicine in the treatment of chronic heart failure: a systematic review and meta-analysis. Evid Based Complement Alternat Med 2021; 2021: 9761159.
[23] Zhang L, Chen W and Gan D. Analysis of the physiological and pathological factors of hospitalized patients taking warfarin and the correlation between drug interactions and warfarin efficacy. Ann Palliat Med 2021; 10: 5400-5406.
[24] Tang X and Gong J. Assessment of trimetazidine treatment in acute myocardial infarction patients undergoing percutaneous coronary intervention. Cardiol Res Pract 2022; 2022: 7674366.
[25] Zarkasi KA, Abdul Murad NA, Ahmad N, Jamal R and Abdullah N. Coronary heart disease in type 2 diabetes mellitus: genetic factors and their mechanisms, gene-gene, and gene-environment interactions in the Asian populations. Int J Environ Res Public Health 2022; 19: 647.