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Effects of percutaneous coronary intervention *via* transradial artery access combined with metoprolol on cardiac function and vascular endothelial function in elderly patients with coronary heart disease

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Abstract. This research was designed to unveil the impacts of percutaneous coronary intervention *via* transradial artery access (TRA-PCI) combined with metoprolol on cardiac function and vascular endothelial function in elderly patients with coronary heart disease (CHD). Collectively, 112 CHD patients were enrolled and allocated into a control group (patients treated with TRA-PCI) and an observation group (patients treated with TRA-PCI and metoprolol) following the random number table method (n = 56 patients). The treatment outcome, cardiac function indicators, serum inflammatory factor indicators, vascular endothelial function indicators, and the occurrence of coronary restenosis were compared between the two groups. After treatment, elevated total effective rate was noted in CHD patients treated with TRA-PCI and metoprolol in contrast to TRA-PCI treatment alone. CHD patients treated with TRA-PCI and metoprolol alleviated cardiac function and vascular endothelial function and reduced inflammatory response and the occurrence of coronary restenosis in comparison to TRA-PCI treatment alone. TRA-PCI combined with metoprolol is effective in improving cardiac function and endothelial function, and reducing the degree of inflammation in the body and the occurrence of coronary restenosis in CHD patients.

Key words: Coronary heart disease — Percutaneous coronary intervention — Transradial artery access — Metoprolol — Cardiac function — Vascular endothelial function

Introduction

Coronary heart disease (CHD), featured with occlusion or narrowing of blood vessels resulting in myocardial hypoxia, ischemia, and necrosis, is a common risk parameter for cardiovascular disease and a chief public health issue worldwide (Dibben et al. 2021). The risk factors for CHD consist of advanced age, diabetes, smoking, dyslipidemia, obesity, as well as hypertension (Duggan et al. 2022). In the meantime, CHD causes influence on pulmonary function, activity ability, whole-body skeletal muscle function, and psychological status in addition to localized in the heart (Wang et al. 2017). Considerable progress has been made in clarifying the complicated mechanistic interactions among CHD-associated risk factors, yielding a wealth of success in preventive measures and the development of drugs to prevent and treat CHD (Shaya et al. 2022). Nevertheless, the prognosis of CHD is still very poor, and it is imperative to screen possible diagnostic markers together with therapeutic targets associated with CHD progression.

Nowadays, percutaneous coronary intervention (PCI) has been broadly applied in the clinic setting as a pivotal treatment for CHD that can effectively and rapidly open the occluded blood vessels together with restore the blood oxygen supply, with a short treatment course, less trauma, and remarkable effects (Lv et al. 2022). However, PCI treatment fails to eliminate the risk factors of CHD and reverse

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the coronary atherosclerosis development in clinical practice (Lv et al. 2022). Besides, PCI may contribute to the occurrence of major adverse cardiovascular events (MACEs), including angina pectoris recurrence, in-stent restenosis, repeated myocardial infarction, as well as cardiogenic death, resulting in failure to mitigate clinical symptoms and even life-threatening conditions (Lv et al. 2022). Transradial artery access (TRA) has been revealed to serve as an independent parameter of decreasing MACEs and bleeding events in consecutive CHD patients treated with PCI (Neumann et al. 2019; Ocsan et al. 2020). TRA-PCI technique has now been generally applied, and the feasibility and safety of it have been approved for bifurcation lesions, acute coronary syndrome (ACS), carotid artery stenting, chronic total occlusion, and unprotected left main lesions (Chen et al. 2015). Metoprolol is a selective β(1)-adrenergic antagonist that has been widely utilized since 1975, and its efficacy in decreasing mortality and cardiovascular events has been approved in CHD patients (Papadopoulos et al. 2009). It is reported that metoprolol can enhance cardiac autonomic function, slow heart rate, and suppress cardiac contractility. However, its efficacy is still unsatisfactory and is accompanied by multiple adverse events (Meng et al. 2022). Herein, this research was designed to unveil the impacts of TRA-PCI combined with metoprolol on cardiac function and vascular endothelial function in elderly patients with CHD.

Materials and Methods

Ethics statement

The study got approval from the ethics committee of Kunming Yan'an Hospital, and all patients signed a written informed consent form.

Study subjects

One hundred and twelve elderly patients with CHD admitted to Kunming Yan'an Hospital were recruited, and were allocated into a control group (n = 56) and an observation group (n = 56) using random numbers. Inclusion criteria: (1) patients met the Clinical Guidelines for Diagnosis and Treatment of Coronary Heart Disease, China: People's Medical Publishing House (PMPH) (2010); (2) patients were at II–IV stage following the New York Heart Association (NYHA) classification; (3) patients aged ≥60 years old. Exclusion criteria: (1) patients had coagulation disorders, blood disorders, immune system disorders, or severe infections; (2) patients had a history of stroke; (3) patients combined with other types of heart-associated diseases such as congenital heart disease, dilated cardiomyopathy, or heart valve disease; (4) patients had severe liver and kidney dysfunction; (5) patients were allergic to contrast agents and could not tolerate anticoagulants; (6) patients combined with malignancies; (7) patients had psychiatric disorders that prevented them from cooperating with treatment and those who were lost in the middle of the research.

Treatment methods

Patients in the control group were given a loading dose of 300 mg aspirin enteric-coated tablets (Bayer, Beijing, China; SFDA approval number: J20080078) and 300 mg clopidogrel (SALUBRIS, Shenzhen, China; SFDA approval number: H20000542) 1 day before surgery. The Allen test was performed on both palms before the procedure. The side of the hand with good circulation and the strongest radial artery pulsation was selected as the puncture site. The patient was placed in a lying position with the arm on the operated side abducted at approximately 35° and placed on a support plate. After disinfection, 10–15 ml of lidocaine injection (China National Pharmaceutical Group Rongsheng Pharmaceutical Co., Ltd., Henan, China; SFDA approval number: H20023544) was used for infiltration anesthesia. The puncture needle was slowly inserted into the vessel at 30°C to 45°C, the needle sheath was fixed and withdrawn at the same time to confirm entry into the radial artery, and the needle was immediately blocked with a guide wire when blood was ejected. The arterial dilatation sheath was inserted by guidewire guidance and injected with 3 ml of lidocaine, 0.2 ml of nitroglycerin (Shandong Xinyi Pharmaceutical Co., Ltd., Shangdong, China; SFDA approval number: H37021445), and 3 000 U of heparin (Jiangsu Datongmeng Pharmaceutical Co., Ltd., Jiangsu, China; SFDA approval number: H20163060) to prevent embolism and vascular smooth muscle spasm following irritation and disruption of the vessel wall by the guidewire. The catheter was X-rayed to confirm that it reached the opening of the right and left coronary arteries, and contrast was then injected separately. After identifying the location and condition of the coronary stenosis, a Judskin guiding catheter was inserted into the diseased coronary branch and the guidewire was delivered to the distal end of the stenotic vessel (for severe stenosis or significant calcification. First, the balloon was fully dilated, it was dilated 5 times at the calcified stenotic lesion, and the balloon dilatation time was 50 s, followed by delivering the stent to the lesion). After reconstitution of the coronary artery, the guidewire and sheath were withdrawn. The puncture site was dressed with pressure and an arterial hemostat was applied to the radial artery and removed 6 hours later. Postoperatively, the dose of oral clopidogrel was reduced to 75 mg/d twice a day on top of the usual preoperative dosing.

The patients in the observation group were treated with metoprolol tartrate on the basis of the control group. In

addition to aspirin enteric-coated tablets and clopidogrel, metoprolol sustained-release tablets were also given 12.5 mg/time, twice a day, 1 day before surgery. Then the patients underwent TRA-PCI treatment. After TRA-PCI treatment, in addition to aspirin enteric-coated tablets and clopidogrel, metoprolol sustained-release tablets were also administered 25 mg/time, twice a day.

Observation indicators and evaluation criteria

Evaluation criteria of curative effect

The ECG was reviewed after 2 months of treatment to assess the efficacy. Efficacy was determined as follows: significant effective, the ECG returned to the normal range; effective, the ST segment decreased and rose above 0.05 mV, but there was some difference from the normal level; the flat T wave changed to upright, the inverted T wave in the main ventricular leads became shallower, and there was some improvement in internal or atrioventricular block; ineffective, there was no change compared with the pre-treatment ECG. Total effective rate = (number of significant effective cases + number of effective cases)/total number of cases × 100%.

Cardiac function indicators

Cardiac function parameters, including left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), and left ventricular end-systolic diameter (LVESD) were measured by the same sonographer using cardiac Doppler ultrasound before treatment and after 2 months of treatment in the two groups.

Indicators of inflammatory factors and endothelial function

Peripheral venous blood (3–5 ml) was harvested both before and after treatment, and the serum was subjected to 10-min centrifugation at 3 000 rpm. Serum levels of hypersensitive C-reactive protein (hs-CRP), tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), endothelin-1 (ET-1), endothelial-specific molecule-1 (ESM-1), and nitric oxide (NO) were assessed by enzyme-linked immunosorbent assay (ELISA). ET-1, ESM-1, and NO kits were available from Shanghai Institute of Biological Products, and hs-CRP, TNF-α, and IL-6 kits were supplied by Wuhan Easy Diagnosis Biomedicine Co., Ltd. (Wuhang, China).

Occurrence of coronary artery restenosis

Patients were observed for the occurrence of in-stent coronary restenosis. A coronary angiogram showing > 50% lumen stenosis within the stent or within 5 mm of either end of the stent was considered to be coronary restenosis.

MACEs

Patients in both groups were followed up for 1 year and their MACEs, including malignant arrhythmias, heart failure, sudden cardiac death, and recurrent angina pectoris, were recorded.

Statistical methods

The data were statistically processed using SPSS 22.0 software. Measurement data were indicated as mean ± standard and compared by the t-test. Enumeration data were indicated as number of cases or percentage (%), and the comparisons between groups were processed by the chi-square test. $p < 0.05$ was considered a statistically significant difference.

Results

General data

There were 56 patients in the observation group and 56 patients in the control group. The average age of patients in the control group was 65.77 ± 3.83 years old, with 32 males and 24 females. The average age of patients in the observation group was 65.07 ± 4.06 years old, with 36 males and 20 females. No notable difference was witnessed in CHD patients between the two groups in terms of gender, age, duration of disease, number of hypertension, number of diabetes, and number of hyperlipidaemia (all $p > 0.05$), which were comparable (Table 1).

Therapeutic effects

Comparing the therapeutic effects of CHD patients in the control and observation groups disclosed that the total

Table 1. Comparison of general information between the control and observation groups

Parameter	Control group	Observation group	*p*
Age (years)	65.77 ± 3.83	65.07 ± 4.06	0.352
Gender (male/female)	32/24	36/20	0.439
NYHA classification			0.875
II	18	19	
III	28	29	
IV	10	8	
Course of disease (year)	4.93 ± 1.67	5.13 ± 1.51	0.516
Hypertension	25	21	0.442
Diabetes	28	31	0.570
Hyperlipidaemia	22	20	0.696

Data are mean ± SD.

Table 2. Comparison of treatment results between control and observation groups

Group	*n*	Significant effective (case)	Effective (case)	Ineffective (case)	Total effective rate (case (%))	*p*
Control	56	23	25	8	48 (85.71)	0.015
Observation	56	27	28	1	55 (98.21)	

effective rate of the control group was 85.71%, while the total effective rate of the observation group was 98.21%. Elevated total effective rate was noted in the observation group versus the control group ($p < 0.05$; Table 2). It is suggested that TRA-PCI combined with metoprolol is effective in treating elderly CHD patients.

Cardiac function

The cardiac function in CHD patients between the control and observation groups before and after treatment was compared. Before treatment, no statistical significance was observed in LVEF, LVEDD, and LVESD between the two groups ($p > 0.05$). After treatment, reduced LVEDD and LVESD and elevated LVEF were noted in the two groups; reduced LVEDD and LVESD and elevated LVEF were detected in the observation group in contrast to the control group ($p < 0.05$; Fig. 1). It is indicated that TRA-PCI combined with metoprolol improves cardiac function in elderly CHD patients.

Inflammatory factor levels

The inflammatory factor levels in CHD patients between the control and observation groups before and after treatment was compared. Before treatment, no statistical significance was noted in the serum levels of hs-CRP, TNF-α, and IL-6 between the two groups ($p > 0.05$). Decreased serum levels of hs-CRP, TNF-α, and IL-6 were witnessed in both groups after treatment ($p < 0.05$); after treatment, reduced serum levels of hs-CRP, TNF-α, and IL-6 were found in the observation group *versus* the control group ($p < 0.05$; Fig. 2). It is indicated that TRA-PCI combined with metoprolol reduces inflammatory reaction in elderly CHD patients.

Vascular endothelial function indicators

Comparing the serum vascular endothelial function indicators before and after treatment in the control and observation groups, the results demonstrated that before treatment, no statistical significance was noted in the serum levels of ET-1, ESM-1, and NO between the two groups ($p > 0.05$). Decreased serum levels of ET-1 and ESM-1 and elevated serum levels of NO were observed in both groups after treatment ($p < 0.05$); after treatment, decreased serum levels of ET-1 and ESM-1 and elevated serum levels of NO were found in the observation group versus the control group ($p < 0.05$; Fig. 3). It is summarized that TRA-PCI combined with metoprolol improves vascular endothelial function in elderly CHD patients.

Occurrence of coronary artery restenosis

The occurrence of coronary artery restenosis in the control and observation groups was compared. After treatment,

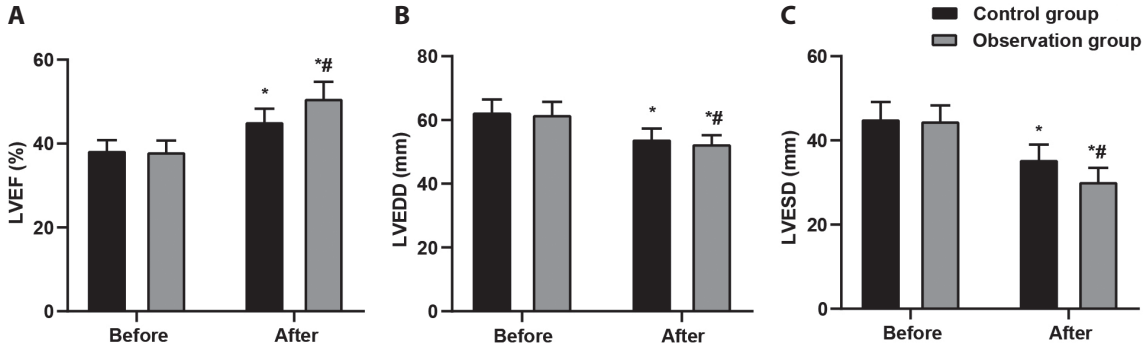

Figure 1. Comparison of pre-treatment and post-treatment cardiac function between the observation group and the control group. LVEF levels (**A**), LVEDD levels (**B**) and LVESD levels (**C**) before and after treatment in the control and observation groups. * $p < 0.05$ *vs.* Before treatment; # $p < 0.05$ *vs.* Control group. LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter. Control group, patients treated with TRA-PCI; Observation group, patients treated with TRA-PCI and metoprolol.

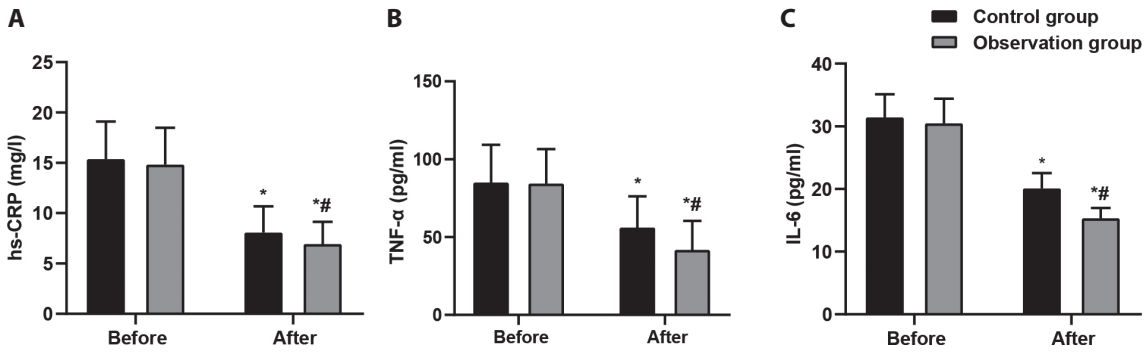

Figure 2. Comparison of pre-treatment and post-treatment serum inflammatory factors between the observation group and the control group. hs-CRP levels (**A**), TNF-α levels (**B**) and IL-6 levels (**C**) before and after treatment in the control group and observation groups. * $p < 0.05$ *vs*. Before treatment; # $p < 0.05$ *vs*. Control group. hs-CRP, hypersensitive C-reactive protein; TNF-α, tumour necrosis factor-α; IL-6, interleukin-6. Control group, patients treated with TRA-PCI; Observation group, patients treated with TRA-PCI and metoprolol.

10 cases (17.86%) of coronary restenosis occurred in the control group, which was higher than 2 cases (3.57%) in the observation group ($p < 0.05$; Table 3). It is indicated that TRA-PCI combined with metoprolol reduces the occurrence of coronary artery restenosis in elderly CHD patients.

Table 3. Comparison of the incidence of coronary restenosis in control and observation groups

Group	*n*	Incidence (case (%))	*p*
Control	56	10 (17.86)	0.014
Observation	56	2 (3.57)	

Incidence of MACEs

At one year follow-up, 5 cases of malignant arrhythmia, 4 cases of heart failure, 1 case of sudden cardiac death, and 5 cases of recurrent angina pectoris occurred in the control group, representing an incidence of MACEs of 26.79%. In the observation group, 4 cases of malignant arrhythmia, 4 cases of heart failure, 4 cases of sudden cardiac death, and 4 cases of recurrent angina pectoris occurred, with an incidence of MACEs of 17.86%. There was no significant difference in the incidence of MACEs in patients between the observation and the control groups ($p > 0.05$; Table 4).

Discussion

CHD is a frequent cardiovascular disease and a chief reason for death around the world (Xia et al. 2021). If not treated promptly, this disease can lead to heart failure, myocardial

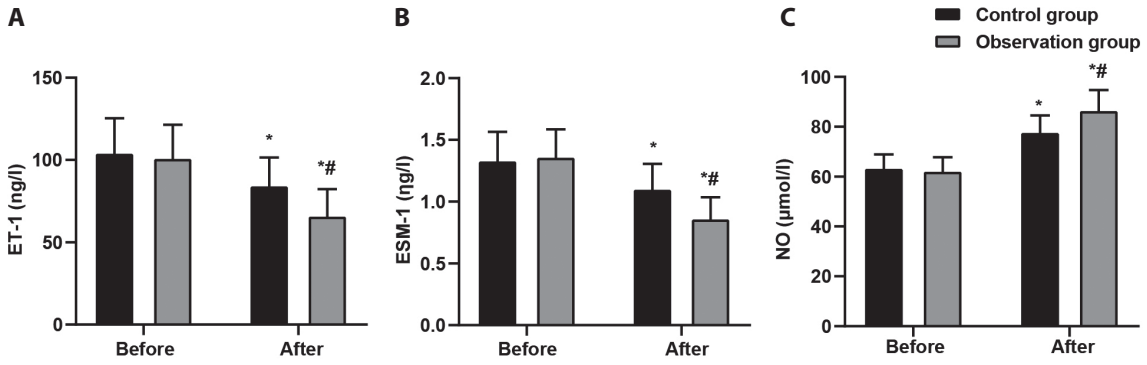

Figure 3. Comparison of pre-treatment and post-treatment vascular endothelial function indicators between the observation group and the control group. ET-1 levels (**A**), ESM-1 levels (**B**) and NO levels (**C**) before and after treatment in the control and observation groups. * $p < 0.05$ *vs*. Before treatment; # $p < 0.05$ *vs*. Control group. ET-1, endothelin-1; ESM-1, endothelial-specific molecule-1; NO, nitric oxide. Control group, patients treated with TRA-PCI; Observation group, patients treated with TRA-PCI and metoprolol.

Table 4. Comparison of the incidence of major adverse cardiovascular events between control and observation groups

Group	*n*	Malignant arrhythmia (case (%))	Heart failure (case (%))	Sudden cardiac death (case (%))	Recurrent angina pectoris (case (%))	Total incidence (case (%))	*p*
Control	56	5 (8.92)	4 (7.14)	1 (1.79)	5 (8.92)	15 (26.79)	0.256
Observation	56	4 (7.14)	1 (1.79)	1 (1.79)	4 (7.14)	10 (17.86)	

infarction, and even impact the life of patients in severe cases (Fan et al. 2021). Based on this, it is particularly significant to find novel treatment approaches for CHD. PCI is now extensively applied in treating CHD, while shorter hospital stays after PCI may influence patients' knowledge and succedent required lifestyle changes (Nolan et al. 2016). At present, TRA is the recommended route for coronary surgery due to its increased safety, while the radial artery occlusion (RAO) will increasingly impact patients receiving multiple procedures in their lifetimes (Aminian et al. 2022). Therefore, in this present work, we aimed to unearth the impacts of TRA-PCI combined with metoprolol on cardiac function and vascular endothelial function in elderly patients with CHD. The treatment outcome, cardiac function indicators, inflammatory factor indicators, vascular endothelial function indicators, the occurrence of coronary restenosis, and MACEs were compared between the control group (patients treated with TRA-PCI) and the observation group (patients treated with TRA-PCI and metoprolol).

Our work demonstrated that the treatment of TRA-PCI alone was effective in improving cardiac function and endothelial function, reducing the degree of inflammation in the body and the occurrence of coronary restenosis, and reducing postoperative MACEs in CHD patients. TRA is preferred for PCI due to its advantages of comfort and convenience, early ambulation, less related vascular complications, and short hospital stays (Corcos 2019; Lin et al. 2021). In the meantime, TRA reduces net adverse clinical events *via* decreasing major bleeding and all-cause mortality in ACS patients (Valgimigli et al. 2015), and is thus recommended by recent European guidelines as default regimen for coronary angiography and PCI (Neumann et al. 2019). Nevertheless, RAO is still the common complication of TRA, impeding the repeated utilization of arteriovenous fistula creation for hemodialysis, radial artery for coronary artery bypass grafting, as well as further catheterization (Bernat et al. 2019). In our work, we found that at one year follow-up, 5 cases of malignant arrhythmia, 4 cases of heart failure, 1 case of sudden cardiac death, and 5 cases of recurrent angina pectoris occurred in the control group, representing an incidence of MACEs of 26.79%. This result unveils that the incidence of adverse effects of TRA-PCI treatment alone for CHD is relatively high.

In addition, our study also revealed that TRA-PCI combined with metoprolol was more effective in improving cardiac function and endothelial function, reducing the degree of inflammation in the body and the occurrence of coronary restenosis, and reducing postoperative MACEs in CHD patients. β-blockers are a component of care in acute myocardial infarction patients due to their potency to decrease myocardial oxygen consumption *via* diminishing heart rate and myocardial contractility (Ndrepepa et al. 2013). In patients with ST-segment-elevation myocardial infarction (STEMI) undergoing primary PCI, evidence has shown that preprocedural β-blockade is related to remarkable improvement in clinical outcome, including decreased short-term mortality (Halkin et al. 2004; Valle et al. 2013). Metoprolol is the widely utilized cardiac selective β-blocker that serve as a mainstay drug in treating acute myocardial infarction, and metoprolol treatment following PCI has weakened the subsequent risk of MACEs (Li et al. 2021). Therefore, in this paper, we selected metoprolol for experiment. The cardioprotective effects of metoprolol are achieved through impeding the overactive adrenergic nervous system, decreasing oxygen demand and ventricular remodeling, and elevating cardiac perfusion (Hong et al. 2018). A recent article has disclosed that metoprolol can inhibit cardiac contractility, slow down heart rate, as well as decrease the resistance of peripheral circulation, blood viscosity, and myocardial oxygen consumption (Gourine et al. 2008). Wu et al. have supported that metoprolol can improve the left ventricle's structure and function, hinder inflammatory cytokine expression and enhance cardiac function in acute myocardial infarction patients (Wu et al. 2012). A recent study has unveiled that metoprolol can restrain the myocardial injury degree, oxidative stress, inflammatory reaction, and myocardial apoptosis, while improving myocardial ischemia in CHD rats (Fan et al. 2021). Moreover, prior research has indicated that metoprolol administration elevates IL-10 level but decreases TNF-α and IL-1β levels, as well as results in improved left ventricular function (Lu et al. 2011). At one year follow-up, in the observation group, 4 cases of malignant arrhythmia, 4 cases of heart failure, 4 cases of sudden cardiac death, and 4 cases of recurrent angina pectoris occurred, with an incidence of MACE of 17.86%, suggesting a reduced adverse events for CHD. Similarly, Li et al. have stated that metoprolol treatment post-PCI-related periprocedural myocardial infarction diminishes the subsequent risk of MACEs, especially the risk of recurrent myocardial infarc-

tion and revascularization in the real-world setting (Li et al. 2021).

In summary, this work underscores that TRA-PCI combined with metoprolol is more effective than TRA-PCI alone for the treatment of elderly patients with CHD. It is safe and feasible to use TRA-PCI combined with metoprolol in treating CHD in clinical setting. This paper offers a basis for the clinical treatment of cardiovascular disease, especially CHD. Therefore, high-quality studies with a larger sample size are imperative to validate and generalize the results. Meanwhile, the efficacy of TRA-PCI combined with metoprolol treatment in male and female patients will be further analyzed in future research.

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Availability of data and material. The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

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