https://doi.org/10.31925/farmacia.2025.2.24 **ORIGINAL ARTICLE**

EFFICACY OF *SALVIA MILTIORRHIZA* EXTRACT INJECTION ON PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH CORONARY ATHEROSCLEROTIC HEART DISEASE

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Abstract

Salvia miltiorrhiza extract, rich in salvianolic acid, has anti-inflammatory and microcirculatory benefits. This study evaluated its effects in coronary atherosclerotic heart disease (CAHD) patients' post-percutaneous coronary intervention (PCI). One hundred patients were randomised into a control group (CG) receiving isosorbide dinitrate and an experimental group (EG) receiving *Salvia miltiorrhiza* extract in addition. EG showed a higher treatment success rate (92% *vs*. 74%) and greater improvements in heart rate, angina, cardiac function, lipid profile, endothelial function and cardiovascular biomarkers. Significant reductions were observed in LDL-C, troponin, CK-MB, hs-CRP, GDF-15 and GRACE scores, with better outcomes in the EG. Adverse events were fewer in the EG ($p < 0.05$). *Salvia miltiorrhiza* extract injection proved clinically effective in improving cardiovascular outcomes and reducing disease progression in CAHD patients after PCI.

Rezumat

Acest studiu a evaluat efectele administrării extractului de *Salvia miltiorrhiza* la pacienți cu boală cardiacă aterosclerotică coronariană (CAHD) după intervenție coronariană percutanată (PCI). O sută de pacienți au fost randomizați într-un grup de control (GC), care a primit dinitrat de izosorbid, și un grup experimental (GE), care a primit suplimentar extract injectabil de *Salvia miltiorrhiza*. Grupul experimental a prezentat o rată mai mare de succes terapeutic (92% față de 74%) și îmbunătățiri semnificative ale frecvenței cardiace, simptomatologiei anginoase, funcției cardiace, profilului lipidic, funcției endoteliale și markerilor cardiovasculari. S-au observat reduceri semnificative ale valorilor LDL-C, troponinei, CK-MB, hs-CRP, GDF-15 și scorurilor GRACE, cu rezultate favorabile în GE. Evenimentele adverse au fost mai puțin frecvente în grupul experimental ($p < 0,05$). Injecția cu extract de *Salvia miltiorrhiza* s-a dovedit eficientă clinic în îmbunătățirea parametrilor cardiovasculari și în încetinirea progresiei bolii la pacienții cu CAHD după PCI.

Keywords: percutaneous coronary intervention, coronary atherosclerotic heart disease, *Salvia miltiorrhiza* extract

Introduction

Coronary atherosclerotic heart disease (CAHD) is a common heart disease [1]. It typically results from damage to the endothelial cells in patients, leading to the deposition of lipids, collagen and calcium in the arterial wall. As the plaques gradually enlarge, they block the coronary arteries, causing myocardial ischaemia and infarction [2, 3]. Common treatments for CAHD include medication, cardiovascular rehabilitation, coronary artery bypass grafting and percutaneous coronary intervention (PCI) [4, 5]. The primary goal of PCI is to widen narrowed or blocked coronary arteries. It offers advantages such as minimal trauma and rapid efficacy, but inevitably affects the coronary arteries [6-9].

Salvia miltiorrhiza extract injection is a traditional Chinese medicine formulation derived from *Salvia miltiorrhiza* (*Lamiaceae* family). These components impart various pharmacological effects to *Salvia miltiorrhiza* extract injection, including antioxidant, anti-inflammatory, anticoagulant, vasodilatory and microcirculatory promotion [10, 11]. In clinical applications, this injection is extensively used in the treatment of cardiovascular disease (CVD), in particular showing significant supportive effects in conditions such as coronary heart disease and angina pectoris. By modulating the release of inflammatory mediators and signalling pathways in inflammation, it helps to alleviate inflammatory responses, reduce tissue inflammatory levels and has potential in the treatment of inflammatory diseases [12-14]. Injection of *Salvia miltiorrhiza* extract helps to improve the function of the cardiovascular system and to some extent prevents the occurrence of cardiovascular events. In the treatment of ischaemic cerebrovascular disease, *Salvia miltiorrhiza* extract injection shows potential benefits. Its vasodilatory and microcirculatory properties help to improve blood supply to the brain, alleviating situations of cerebral tissue ischaemia and hypoxia [15]. Components such as salvianolic acid in *Salvia miltiorrhiza* extract have strong antioxidant properties, capable of scavenging

free radicals in the body and slowing down oxidative stress reactions. By neutralising free radicals caused by oxidative stress, it reduces oxidative damage and helps maintain the normal function of cells and tissues [16, 17]. This protective effect is beneficial in conditions such as CVD and diabetes where damage is caused by oxidative stress. Studies suggest that the use of *Salvia miltiorrhiza* extract may reduce cerebral ischaemia-reperfusion injury, which may have a beneficial effect on recovery from cerebral vascular disease, including stroke [18]. Research by Xie *et al*., found that *Salvia miltiorrhiza* extract had a protective effect on animal models of cerebral ischaemic injury by reducing inflammation, oxidative stress and inhibiting cell apoptosis [19]. By promoting the release of nitric oxide (NO), it can dilate blood vessels, improve blood flow and enhance tissue oxygenation. This has a beneficial effect on the circulation in patients with cardiovascular disease [20].

In this work, the application of *Salvia miltiorrhiza* extract injection was systematically observed in patients with CAHD undergoing PCI. The aim is to comprehensively evaluate its effects on clinical efficacy, cardiac function, lipid metabolism levels, vascular endothelial function (VEF) and serum inflammatory factor (SIF) levels. Through in-depth research, the aim is to provide CAHD patients with more comprehensive and personalised treatment approaches and to provide new directions and theoretical foundations to improve the effectiveness of PCI treatment.

Materials and Methods

Analysis and determination of Salvia miltiorrhiza extract

The *Salvia miltiorrhiza* extract injection (from Guangdong Leiyunshang Pharmaceutical Co., Ltd., China) was precisely withdrawn, totalling 540 μL, and blended with 60 μL of deuterated water containing 0.05% anhydrous trisodium phosphate (Aladdin, USA) in a 2 mL centrifuge tube. The solution was thoroughly blended to prepare the *Salvia miltiorrhiza* extract injection for the test sample. A precise amount of 13.12 mg of calcium formate (Shanghai Haohong Biomedical Technology Co., Ltd., China) was weighed into a 10 mL volumetric flask, followed by the addition of deuterated water to make up the volume. It was fully dissolved and mixed uniformly. Subsequently, 1 mL of the deuterated water containing calcium formate was precisely withdrawn and transferred to another 10 mL volumetric flask, where it was made up to volume with deionised water (Thermo Fisher, USA). This resulted in a standard sample with a concentration of 1.01 mmol/L of calcium formate. Subsequently, a defined quantity of control substances, including valine, isoleucine, proline, γ-aminobutyric acid, acetic acid, propanoic acid, glutamic acid, succinic acid, malic acid, succinic acid, glucose, fructose, lactose, sucrose, raffinose, maltose, uridine, lithospermic acid, salvianolic acid A, salvianolic acid B, salvianolic acid, rosmarinic acid, formic acid and catechol, were precisely weighed. They were then diluted with a deuterated solvent (Thermo Fisher, USA) to create the control solution. The control solution was further diluted in a deuterated solvent to obtain dilutions with concentrations of 1/2, 1/4, 1/8 and 1/16 of the original solution concentration. The test samples and standard samples were separately analysed using a Bruker Advanced III 600 nuclear magnetic resonance (NMR) spectrometer (Bruker, Germany). The residual water peak was suppressed using a presaturation water peak suppression pulse sequence, resulting in one-dimensional H NMR (^{1}H NMR) spectra for both test and standard samples.

The ^{1}H NMR data was collected with the following parameters: probe temperature set to 288 K; pulse sequence NOESYGPPR1D; solvent containing 90% H_2O + 10% D_2O for field locking; spectral width of 9.9974 ppm; centre frequency at 4.696 ppm; relaxation delay time of 15.0 s; acquisition time of 2.27 s; mixing time of 50 ms; number of scans set to 32; gain value at 40.3; and a data point detection of 64 K. The acquired raw spectra were processed using an exponential function window function with a line broadening of 0.30 Hz. Fourier transformation was then applied to the free induction decay (FID) signals. The resulting spectra were imported into the MestReNova software, with TSP (0.0) serving as the chemical shift reference for calibration. Automated baseline correction and phase correction were carried out. The concentration of chemical components was calculated using the PULCON method.

General data of patients

From October 2021 to October 2022, 100 post-PCI (Percutaneous Coronary Intervention) patients with CAHD were assigned and enrolled, encompassing 63 male and 37 female patients. They were 43 to 72 years old, which was averaged as (63 ± 7) years. The duration of illness (DOI) varied from 1 to 7 years, which was averaged as (5.3 ± 2.6) years. The cohort included 63 cases of stable angina, 24 cases of ST-segment elevation myocardial infarction (MI), and 13 cases of non-ST-segment elevation myocardial infarction. Baseline comorbidities comprised 47 cases of hypertension, 5 cases of diabetes and 11 cases of hyperlipidaemia. This work received approval from the ethics committee of Hunan Provincial People's Hospital (First Affiliated Hospital of Hunan Normal University), China.

Patients enrolled had to satisfy all the following conditions: (i) met the diagnostic criteria for CAHD as outlined in the *Naming and Diagnostic Criteria for Ischemic Heart Disease* and confirmed through coronary angiography; (ii) patients aged 18 years or older; (iii) those without history of previous mental illness or uncapable of independently participating in

the study and (iv) patient and their family members who have both signed an informed consent form.

Those with any of following conditions had to be excluded: (i) patients with severe aortic stenosis, sick sinus syndrome, hypertrophic cardiomyopathy, and a history of previous myocardial infarction; (ii) those who were allergic to the drugs used in this work; (iii) patients with malignant tumours; (iv) patients with abnormal liver or kidney function and (v) those with a history of vascular reconstruction treatments such as PCI or CABG.

Grouping and treatments

The patients were assigned into a control group (CT) and an experimental group (EG), each consisting of 50 cases, according to the random number table method. No visible differences were observed in general patient characteristics between different groups ($p < 0.05$). All patients underwent PCI for CAHD treatment. Postoperatively, CG patients received oral treatment with Isosorbide Dinitrate Tablets and Enteric-coated Aspirin Tablets (Beijing Hengsheng Pharmaceutical Co., Ltd., China) at 5 mg and 100 mg *per* administration, three times and once a day, respectively. During the treatment period, patients were required to rest in bed, maintain blood glucose levels, and receive continuous low-flow oxygen. Real-time electrocardiographic monitoring was implemented. In the event of an acute attack, patients were instructed to sublingually take nitroglycerin (Shanxi Zhendong Anxin Biopharmaceutical Co., Ltd., China) at 0.5 mg until relief.

In addition to the aforementioned treatments, EG patients received *Salvia miltiorrhiza* extract injection (Guangdong Leiyunshang Pharmaceutical Co., Ltd., China) on top of the CG treatment. This injection was administered intravenously, with 10 mL of *Salvia miltiorrhiza* extract injected into a 200 mL solution of 10% glucose injection once a day.

The treatment course consisted of continuous treatment for 10 days as one cycle, and three cycles were administered consecutively with a 5-day interval between each cycle.

Observation indicators and clinical efficacy assessment

Heart rate and angina pectoris attacks

The changes in heart rate and the frequency (times *per* day) and duration (minutes) of angina pectoris attacks were compared for patients from different groups before and after they were treated.

Clinical efficacy

Patients in CG and EG were compared for clinical efficacy after three cycles of treatment. The criteria for determining clinical efficacy were as follows: marked improvement: a reduction in the frequency and duration of angina pectoris attacks by more than 80%, and flattening of the T-wave in electrocardiogram; improvement: a reduction in the frequency and duration of angina pectoris attacks by more than 50%, with a great improvement in electrocardiogram; and ineffectiveness: a reduction in the frequency and duration of angina pectoris attacks by less than 20%, accompanied by ST-segment depression in electrocardiogram. The calculation method for clinical efficacy was described in Equation (1) [21].

$$effectiveness = \frac{Apparent\ effect + Effective}{Total\ number\ of\ people} \times 100\%. \quad (1)$$

Cardiac function evaluation

The cardiac function of patients in CG and EG was compared before and after they were treated. A colour Doppler ultrasound (CDUS) instrument (Jiangsu Xinrui Medical Technology Co., Ltd., China) was employed to assess left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), and left ventricular fractional shortening (FS). The cardiac function was assessed based on the New York Heart Association (NYHA) cardiac function classification. It categorizes the clinical presentation of heart failure (HF) patients into 4 grades [22]: Grade I (mild): patients have no apparent cardiac symptoms in daily life and can perform normal physical activities. Grade II (mild to moderate): patients experience mild cardiac symptoms in normal life but can complete light physical activities. Grade III (moderate): patients feel significant cardiac symptoms in daily life, can perform light physical activities, but need rest during moderate activities. Grade IV (severe): patients experience obvious cardiac symptoms even at rest, feel extreme discomfort during any physical activity, and may exhibit symptoms while at rest. The assessment of cardiac function was conducted by evaluating these NYHA grades.

Lipid metabolism levels

The lipid metabolism levels were compared for patients in CG and EG before and after they were treated. In the early morning (6:00 ~ 8:00), 5 mL of fasting venous blood (FVB) was collected from the patients, placed in a centrifuge, and centrifuged at 3,000 rpm for 15 min. After supernatant discharging, the remaining sample was stored at -80°C. A fully automatic biochemical analyser (Weir Medical Equipment Co., Ltd., China) was utilised to measure the levels of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol and triglycerides.

Vascular endothelial function (VEF)

Furthermore, the levels of flow-mediated dilation (FMD), nitric oxide (NO), and endothelin-1 were compared. A CDUS instrument was utilised to measure FMD in the brachial artery using the method outlined in Equation (2) [23].

$$FMD = \frac{D_{max} - D_{baseline}}{D_{baseline}} \times 100\%. \quad (2)$$

In the above expression, D_{max} referred to the maximum arterial diameter during diastole after congestion (widest diameter) and $D_{baseline}$ denoted the arterial diameter at baseline.

For both pre- and post-treatment assessments, 5 mL of FVB was collected from the patients at 6:00 ~ 8:00.

The blood samples were placed in a centrifuge (manufactured by Hunan Kaida Scientific Instrument Co., Ltd., China) for a 15-min centrifugation at 3,000 rpm. The resulting supernatant was then stored at -80°C until further analysis. Nitric oxide levels were assessed using the Enzyme-Linked ImmunoSorbent Assay (ELISA) method (Abcam, UK). Endothelin-1 levels were measured using a fully automatic biochemical analyser (Weir Medical Equipment Co., Ltd., China).

Myocardial markers

Additionally, levels of high-sensitivity cardiac troponin T (hs-cTnT), creatine kinase-MB (CK-MB), and high-sensitivity C-reactive protein (hs-CRP) were compared for patients before and after treatment differently to visualize their changes. Specifically, hs-cTnT and hs-CRP were measured using the chemiluminescent immunoassay sandwich method with electrochemiluminescence technology, while CK-MB activity was detected using an enzymatic assay. The concentration of CK-MB was measured using a UV-7 UV-visible spectrophotometer (Mettler Toledo, Switzerland).

Blood indicators

In addition, changes in growth differentiation factor-15 (GDF-15), soluble ST2 (sST2) and cardiac troponin I (cTnI) were analysed. For both pre- and post-treatment assessments, 5 mL of FVB was collected from the patients in the early morning (6:00 ~ 8:00) and subsequently centrifuged at 3,000 rpm for 15 min. The resulting supernatant was then positioned at -80°C until further analysis. The levels of GDF-15 and sST2 were measured using ELISA assay kits (Abcam, UK). The concentration of cTnI was detected using a TSQ AItis triple quadrupole mass spectrometer (Thermo Fisher, USA).

Serum inflammatory factors (SIF) levels

The SIF levels were compared between patients in CG and EG before and after treatment. For both pre- and post-treatment assessments, 5 mL of FVB was subjected to a 15-min centrifugation at 3,000 rpm. The resulting supernatant was next stored at -80°C until further analysis. Using the ELISA method, the levels of C-reactive protein (CRP), interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α) and homocysteine (Hcy) were measured in the patients (Abcam, UK).

Safety evaluation

The GRACE scores and the incidence of adverse events (IoAR) were comparatively analysed for patients before and after different interventions. The GRACE score [24] is a scoring system used to assess the prognosis risk of patients with acute coronary syndrome (ACS). The scoring components include age, heart rate, blood pressure, myocardial markers, ST-segment depression on electrocardiogram, HF, and others. The scoring details are as follows: low risk: < 108 points; moderate risk: 108 ≤ score < 140; and high risk: ≥ 140.

Methods for statistical analysis

Data were processed using SPSS 26.0 (IBM, USA). Continuous variables were presented as mean ± standard deviation ($\bar{x} \pm s$), and between-group comparisons were implemented using the t-test. Categorical data were expressed as frequencies or percentages and compared with the chi-square test. $P < 0.05$ was considered statistically significant.

Results and Discussion

Compositions of Salvia miltiorrhiza extract

After preprocessing, the ^{1}H NMR spectrum of the test sample revealed a total of 40 chemical components, including 12 amino acids, 7 small organic acids, 8 sugars and their degradation products, 7 salvianolic acid compounds and 6 nucleoside compounds, as detailed in Figure 1A. Quantitative analysis was performed on 20 chemical components exceeding the quantitative limit, as presented in Figure 1B. Among these components, salvianolic acid was the most abundant, with a concentration of 0.8334 mg/mL, excluding sugars.

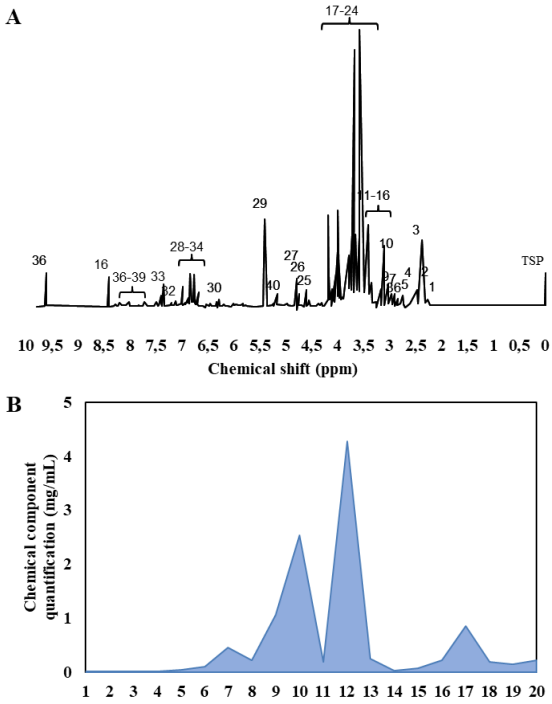

Figure 1.

Compositions in *Salvia miltiorrhiza* extract injection (A: ^{1}H NMR fingerprint spectrum of *Salvia miltiorrhiza* extract injection; B: Content chart of components in *Salvia miltiorrhiza* extract injection)

1: valine; 2: isoleucine; 3: proline; 4: gamma-aminobutyric acid; 5: acetic acid; 6: propanoic acid; 7: glutamic acid; 8: succinic acid; 9: glucose; 10: fructose; 11: lactose; 12: sucrose; 13: raffinose; 14: uridine; 15: lithospermic acid; 16: salvianolic acid B; 17: salvianolic acid; 18: rosmarinic acid; 19: formic acid; and 20: catechol

Clinical efficacy

In EG patients, the clinical efficacy showed 70% (35/50) and 22% (11/50) as marked improvement and improvement, respectively, yielding an overall effective rate (OER) of 92% (46/50). In CG patients, the clinical efficacy exhibited 48% (24/50) and 26% (13/50) as marked improvement and improvement, respectively, generating an OER of 74% (37/50). Meanwhile, the clinical efficacy in EG patients was higher in contrast to that in CG ($p < 0.05$), as demonstrated in Figure 2.

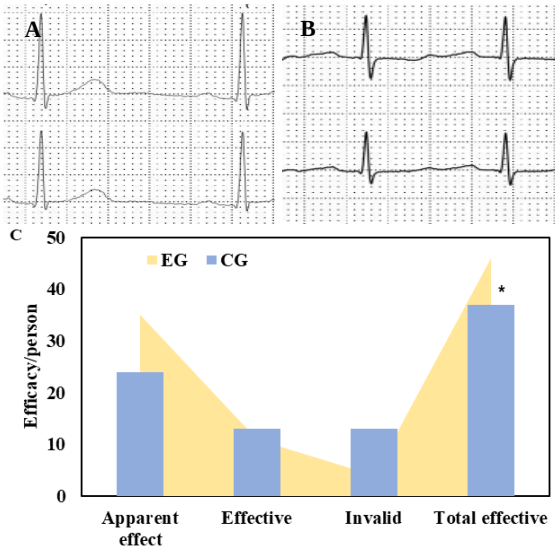

Figure 2.

Clinical efficacy in two groups of patients (A: normal electrocardiogram; B: abnormal ST-Segment electrocardiogram; C: distribution of clinical efficacy)

*Compared with CG, $p < 0.05$.

Heart rate and angina pectoris attacks

Before treatment, heart rate and angina attacks were similar in the different groups ($p > 0.05$). After treatment, the heart rate of all patients decreased significantly compared to the pre-treatment heart rate, and that of the EG patients was much lower than that of the CG patients, with a significant difference for both ($p < 0.05$). After treatment, there was a significant reduction in angina pectoris attacks for all patients in both CG and EG, showing a large difference with $p < 0.05$ compared to that before treatment. The frequency and duration of angina pectoris attacks in EG patients were significantly lower with visible differences to those in CG patients ($p < 0.05$) (Figure 3).

Cardiac function

Figure 4 shows the ultrasound images for LVEF, LVEDD, SF and NYHA classification of patients, and the specific values of these indicators were further compared in Figure 5. The pre-treatment LVEF, LVEDD, SF and NYHA classification of the patients showed a large gap before treatment ($p > 0.05$). After treatment, however, all patients showed a significant improvement in LVEF and LVEDD, with the improvement in EG patients being much greater ($p < 0.05$). FS decreased after the different treatments, and the decrease was greater in EG patients, showing a significant difference from CG patients ($p < 0.05$). Meanwhile, the pre- and post-treatment NYHA classification of the EG patients showed no obvious changes ($p > 0.05$), but the NYHA classification of the EG patients was lower compared to that of the CG ($p < 0.05$).

Lipid metabolism levels

The levels of lipid metabolism were comprehensively compared in Figure 6 below. Prior to treatment, there was no obvious difference in the levels of LDL-C, HDL-C, total cholesterol and triglycerides between patients in CG and EG ($p > 0.05$). The post-treatment levels of LDL-C, total cholesterol and triglycerides were strongly downregulated in all patients, regardless of the group they were in, and showed large differences compared with the pre-treatment levels ($p < 0.05$), and visible differences were observed for these four indicators between EG and CG patients ($p < 0.05$). In addition, HDL-C levels in both the EG and CG groups showed a clear upward trend after treatment, with a marked difference from pre-treatment levels ($p < 0.05$), and a higher level in the EG patients ($p < 0.05$).

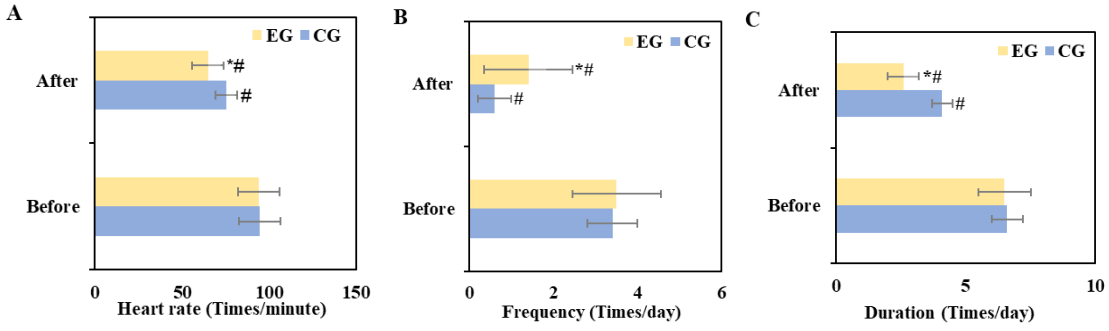

Figure 3.

Changes in heart rate and angina pectoris attacks (A: heart rate; B: angina pectoris attacks frequency; C: angina pectoris attacks duration)

*Compared with CG, $p < 0.05$; # compared with the pre-treatment value, $p < 0.05$

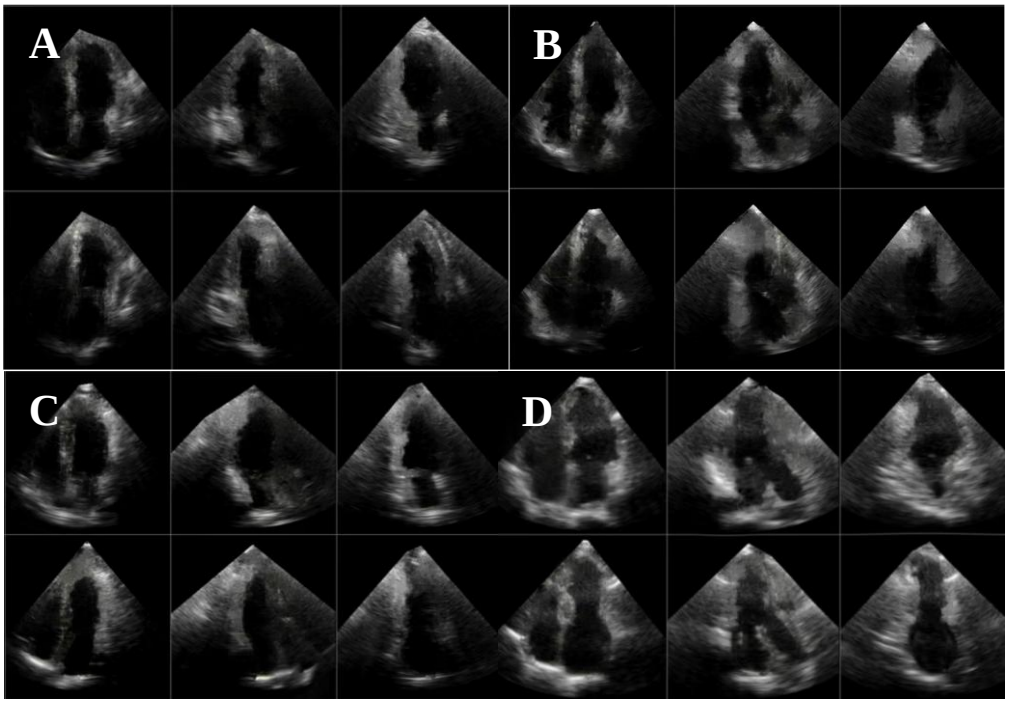

Figure 4.
Cardiac function ultrasonogram images (A: pre-treatment image for patients in CG; B: pre-treatment image for patients in EG; C: post-treatment image for patients in CG; D: pre-treatment image for patients in EG)

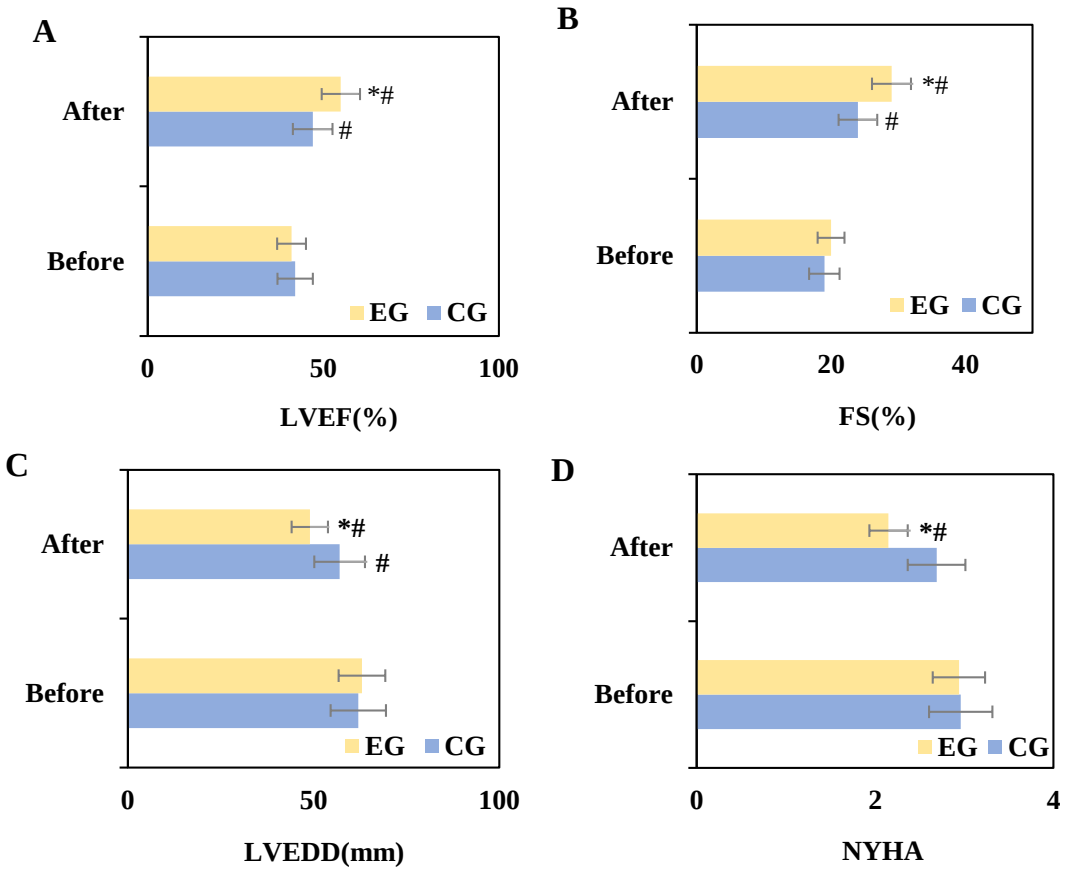

Figure 5.
Changes in cardiac function of patients (A: LVEF; B: FS; C: LVEDD; D: NYHA)
* Compared with CG, $p < 0.05$; # compared with the pre-treatment value, $p < 0.05$

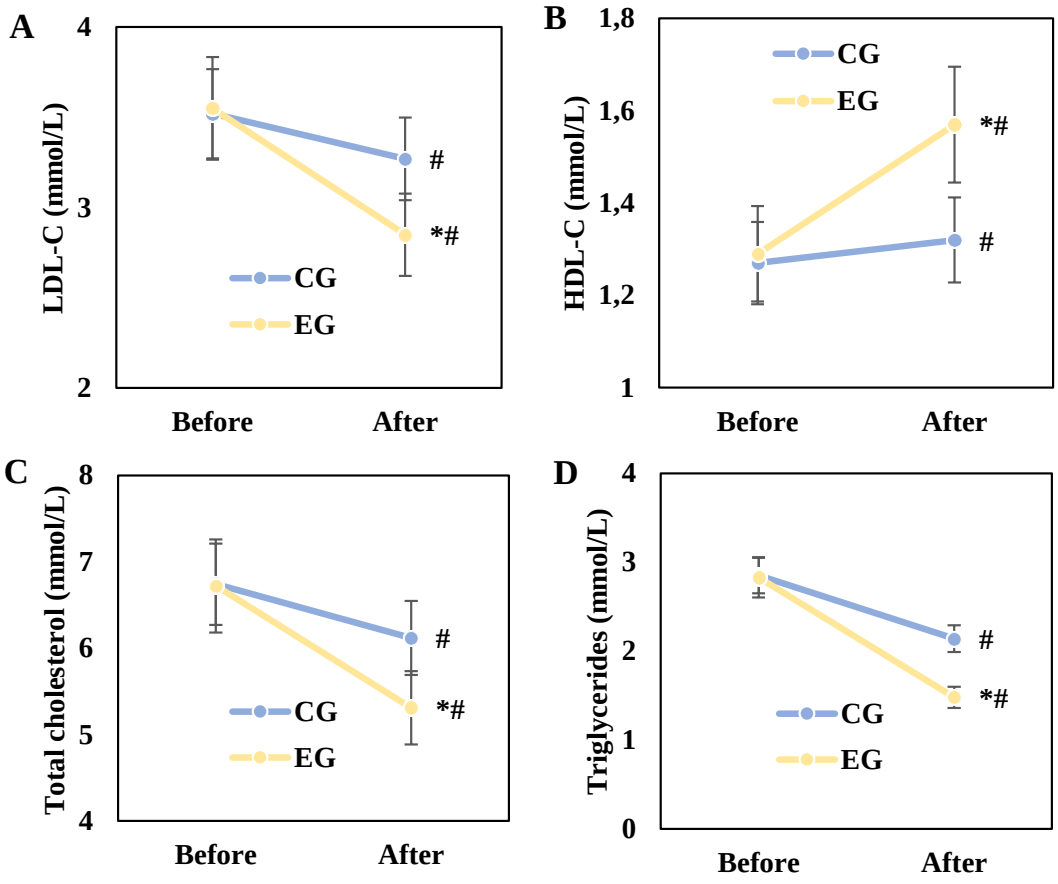

Figure 6.
Changes in lipid metabolism levels (A: LDL-C; B: HDL-C; C: total cholesterol; D: triglycerides)
*Compared with CG, $p < 0.05$; # compared with the pre-treatment value, $p < 0.05$

Vascular endothelial function

The results of the VEF assessment of patients in CG and EG are shown in Figure 7. Patients had similar levels of FMD, nitric oxide and endothelin-1 before the t interventions ($p > 0.05$). However, they experienced a marked increase in FMD and nitric oxide levels after the intervention ($p < 0.05$), with EG patients having extremely higher levels than CG patients ($p < 0.05$). Similarly, all patients experienced a decreasing trend in endothelin-1 levels, with EG patients having much lower levels, with both comparisons showing $p < 0.05$.

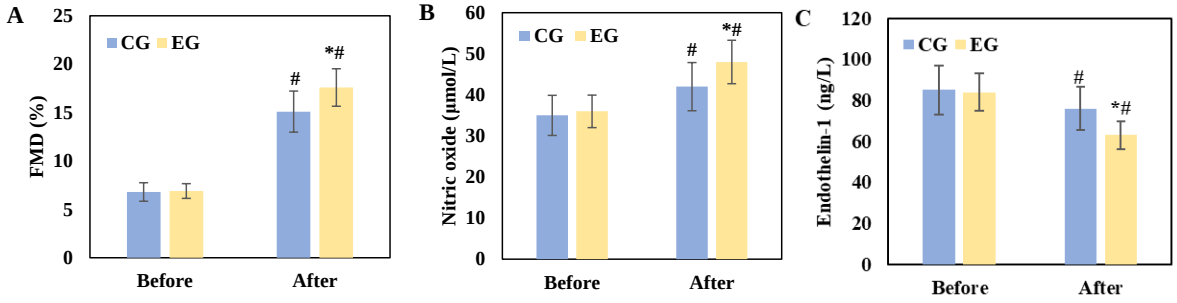

Figure 7.
Changes in VEF of patients (A: FMD; B: nitric oxide; C: endothelin-1)
*Compared with CG, $p < 0.05$; # compared with the pre-treatment value, $p < 0.05$

Myocardial markers

The comparison of myocardial marker levels is shown in Figure 8. It shows that before treatment, differences in hs-cTnT, CK-MB and hs-CRP were not obvious in all patients ($p > 0.05$) and were at relatively high levels. In addition, all patients showed a remarkable decrease in the levels of these three indicators ($p < 0.05$), with the levels in EG patients being significantly lower than those in CG patients ($p < 0.05$).

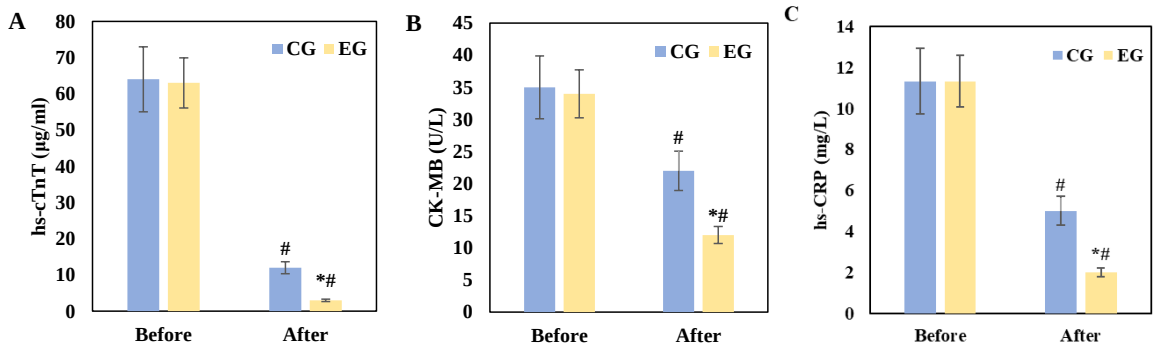

Figure 8.

Changes in myocardial markers of patients (A: hs-cTnT; B: CK-MB; C: hs-CRP)

*Compared with CG, $p < 0.05$; # compared with the pre-treatment value, $p < 0.05$

Blood indicators

Figure 9 shows a comparison of the patients' blood indicators. There was no visible difference in GDF-15, sST2 and cTnI in patients before treatment ($p > 0.05$). After the patients were treated, they showed a decreasing trend in GDF-15, sST2 and cTnI levels, with large differences from the pre-treatment levels ($p < 0.05$). Levels in EG patients were significantly lower than those in CG patients ($p < 0.05$).

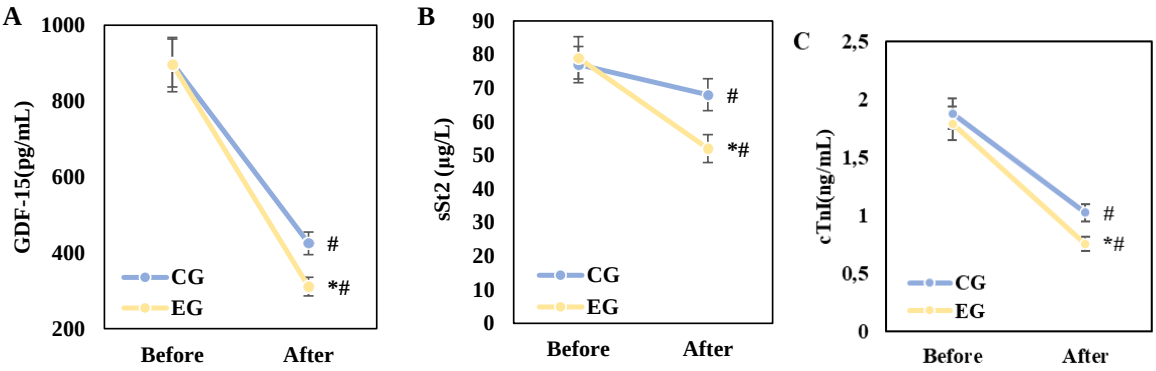

Figure 9.

Changes in blood indicators of patients (A: GDF-15; B: sST2; C: cTnT)

*Compared with CG, $p < 0.05$; # compared with the pre-treatment value, $p < 0.05$

Serum inflammatory factors

The comparison of SIF between patients before and after treatment is shown in Figure 10. CRP, IL-6, TNF-α and Hcy were measured at similar levels in patients before treatment ($p < 0.05$). However, after treatment, patients in both CG and EG showed a decreasing trend in these indicators, with significant differences from the corresponding pre-treatment levels ($p < 0.05$). Furthermore, the reduction in the above indicators was greater in patients with EG compared to the conditions in EG ($p < 0.05$).

Safety assessment results

The safety of *Salvia miltiorrhiza* extract injection was assessed by GRACE scores and IoAR, as shown in Figure 11. GRACE scores were similar in all patients before treatment ($p > 0.05$) but decreased after treatment ($p < 0.05$), with EG patients having significantly lower scores than CG patients ($p < 0.05$). In the CG group, 10% (5/50) experienced HF, 22% (11/50) angina, 6% (3/50) myocardial infarction, 6% (3/50) dizziness and 4% (2/50) gastrointestinal reactions. In the EG group, however, 4% (2/50) had HF, 8% (4/50) had angina, 2% (1/50) had myocardial infarction, 2% (1/50) reported dizziness and 2% (1/50) had gastrointestinal reactions. Therefore, it was evident that the IoAR in EG patients was much lower and showed a visible difference to that in CG patients ($p < 0.05$), indicating the safety of using *Salvia miltiorrhiza* extract injection in the treatment of CAHD after PCI intervention.

This work investigated the potential therapeutic efficacy of *Salvia miltiorrhiza* extract injection in patients with CAHD undergoing PCI. By studying 100 post-PCI CAHD patients, it was observed that patients in the EG showed significantly better clinical efficacy compared to those in the CG after applying different treatment regimens. In addition, positive results were observed in various aspects including cardiac function, lipid metabolism and VEF in EG patients.

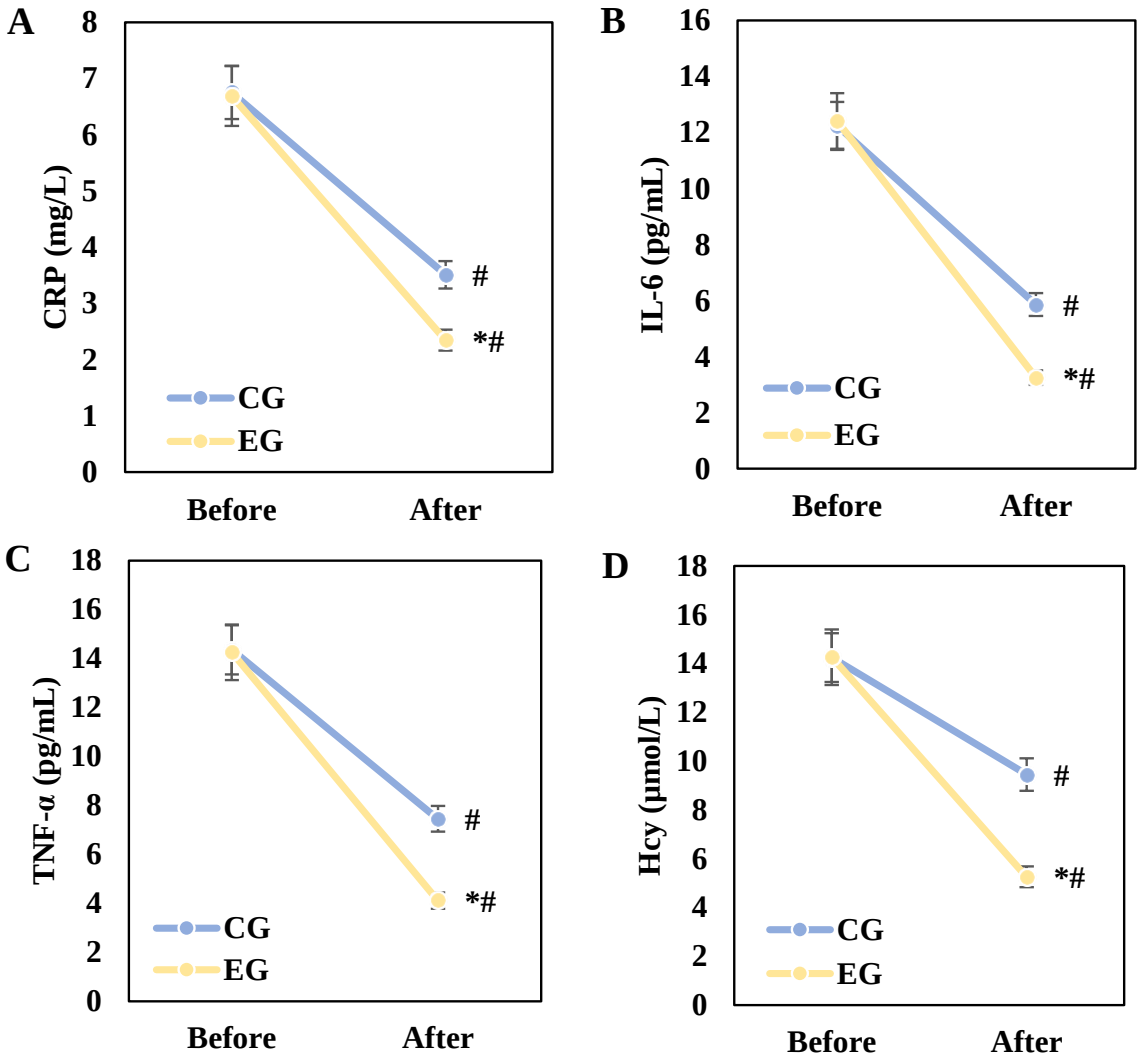

Figure 10.
Changes in SIF of patients in various groups (A: CRP; B: IL-6; C: TNF-α; D: Hcy)
*Compared with CG, $p < 0.05$; # compared with the pre-treatment value, $p < 0.05$

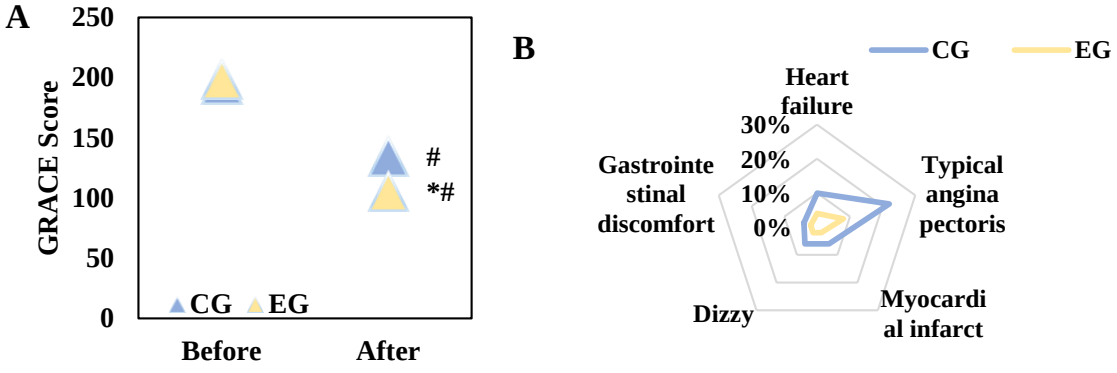

Figure 11.
Safety of *Salvia miltiorrhiza* extract injection (A: GRACE score; B: IoAR)
*Compared with CG, $p < 0.05$; # compared with the pre-treatment value, $p < 0.05$

The main component of *Salvia miltiorrhiza* extract injection is *Salvia miltiorrhiza*, which is known for its blood-activating, congestion-relieving and heart-nourishing properties [25]. Studies have shown that regional denervation occurs in the area of myocardial infarction after myocardial infarction, leading to an abnormal distribution of sympathetic nerves and the ventricular repolarisation dispersion. This significantly affects left ventricular systolic function, resulting in an increase in end-diastolic and end-systolic volumes

and a decrease in LVEF [26]. The results of the present study showed a significant improvement in LVEF and FS ($p < 0.05$) after the patients were treated differently. Post-treatment LVEDD and NYHA classification also decreased in all patients ($p < 0.05$), with extreme differences compared to CG ($p < 0.05$). *Salvia miltiorrhiza* extract is rich in antioxidants such as salvianolic acid, which helps to protect myocardial cells from oxidative damage by scavenging free radicals and reducing oxidative stress. Improving myocardial oxidative status may contribute to improved cardiac contractile and relaxation function [27]. Research has shown that irregular blood lipids are a significant factor leading to angina attacks in CAHD patients. Optimizing lipid metabolism may slow atherosclerosis, stabilise plaques and reduce mortality and disability in CAHD angina [28]. LDL-C is known as the "bad" cholesterol that transports cholesterol to cells, and elevated levels are associated with increased atherosclerosis and CVD risk. HDL-C, on the other hand, is considered "good" cholesterol and is responsible for removing excess cholesterol. Total cholesterol is the sum of lipids, including LDL-C and HDL-C, and triglycerides, which store and provide energy [29, 30]. Monitoring these indicators helps to assess metabolic health and CVD risk [31, 32]. This work showed that injection of *Salvia miltiorrhiza* extract effectively lowered LDL-C, total cholesterol and triglycerides while upregulating HDL-C ($p < 0.05$). These results are consistent with those of Guo *et al*. [33]. CRP is a blood marker of inflammation produced by the liver, and elevated levels usually indicate inflammation or infection. IL-6 and TNF-α are common SIFs involved in the regulation of inflammation and immune responses, with elevated levels reflecting the activity of the inflammatory process. Hcy is a metabolite of amino acids and elevated levels may be associated with the onset and progression of several diseases such as CVD and neurological disorders [34-37]. In addition, this work revealed the greatly reduced SIF levels in the EG patients ($p < 0.05$), which is consistent with existing literature reports on the potential benefits of *Salvia miltiorrhiza* extract in the treatment of CVD [38]. Therefore, the use of *Salvia miltiorrhiza* extract injection significantly improves the clinical efficacy of patients, supporting the potential cardiovascular benefits of *Salvia miltiorrhiza* extract as reported in previous literature.

Although research on *Salvia miltiorrhiza* extract in relation to heart health is relatively extensive, its use in PCI treatment remains an under-explored area. By evaluating FMD, nitric oxide and endothelin-1 to assess VEF, the measurement of FMD indirectly reflects the state of endothelial health. Higher levels of FMD are typically associated with good vascular function and cardiovascular health [39]. Nitric oxide is an important molecule produced by endothelial cells that plays a role in regulating vascular tone and inhibiting thrombus formation [40]. Endothelin-1 is secreted by endothelial cells and is involved in the regulation of vascular tone. Elevated levels of endothelin-1 are usually associated with vascular pathologies and serve as indicators of vasoconstriction and inflammation [41]. The results here showed that both FMD and nitric oxide were increased in patients after different treatments, with levels in the EG exceeding those in the CG ($p < 0.05$). Endothelin-1 levels decreased in both the CG and EG after the different treatments, with levels in the EG lower than those in the CG ($p < 0.05$). The active constituents, such as salvianolic acid, which are abundant in *Salvia miltiorrhiza* extract injection, confer potent antioxidant properties that help to alleviate oxidative stress-induced damage and thus protect endothelial cells. In addition, *Salvia miltiorrhiza* extract has been shown to promote the production of nitric oxide, a key regulator of vascular tone. Increased levels of nitric oxide contribute to enhanced vasodilation, which is reflected in increased FMD levels [42]. *Salvia miltiorrhiza* extract regulates vascular tone by inhibiting the excessive release of endothelin-1 by endothelial cells, reducing the occurrence of vascular spasms and promoting the maintenance of optimal vascular function [43]. Its anti-inflammatory effects help to reduce vascular damage caused by inflammatory responses, further improving VEF.

Conclusions

This paper evaluates the efficacy of *Salvia miltiorrhiza* extract injection in patients with CAHD undergoing PCI. Significant potential benefits of *Salvia miltiorrhiza* extract injection in the treatment of CVD were observed in a randomised controlled trial of 100 post-PCI CAHD patients. Patients in the EG showed significantly better clinical efficacy compared to those in the CG, suggesting a positive impact on the overall recovery of patients undergoing PCI treatment with *Salvia miltiorrhiza* extract. The optimization of cardiac function, the regulation of lipid metabolism levels and the improvement of VEF together suggested its multifaceted action. This comprehensive effect was expected to provide holistic therapeutic support for CAHD patients, effectively slowing the progression of the disease. In particular, treatment with *Salvia miltiorrhiza* extract was effective in reducing myocardial markers and SIF levels, indicating its crucial role in alleviating myocardial damage and inhibiting inflammatory responses. This has important clinical implications for reducing the risk of coronary events and improving patients' quality of life.

The injection of *Salvia miltiorrhiza* extract demonstrated extensive and remarkable clinical efficacy in patients with CAHD undergoing PCI. This provided a solid foundation for its use in the treatment of CVD and strong support for broader and more in-depth research in the future.

Conflict of interest

The authors declare no conflict of interest.

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