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Efficacy of Yangxin Recipe in Combination with Conventional Western Medicine in Treatment of Angina Pectoris of Coronary Heart Disease

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Abstract

Objective: To study the efficacy of Yangxin Recipe (YXR) in patients with stable angina pectoris of coronary heart disease and its impacts on coronary CT angiography.

Methods: A total of 78 patients with coronary heart disease and angina pectoris were randomly divided into a control group (n = 39) and a YXR group (n = 39). The control group adopted conventional Western medicine while the YXR group received conventional western medicine + oral administration of YXR. After six months of continuous treatment, the clinical efficacy, traditional Chinese medicine (TCM) syndrome scores, Pittsburgh Sleep Quality Index (PSQI), and the level of coronary CT vascular stenosis were observed.

Results: After treatment, the total effective rate of YXR was 92.31%, which was higher than ($P < 0.01$) that of the western medicine control group. The total score of TCM syndromes in the YXR group was (14.44 ± 9.87), which was significantly lower than ($P < 0.001$) that in the simple western medicine control group (22.44 ± 13.87). The degree of coronary stenosis in the YXR group decreased to (49.87 ± 7.82) %, which was significantly lower than ($P < 0.001$) that in the western medicine control group (57.05 ± 9.92) %.

Conclusion: The efficacy of YXR + conventional western medicine in treating coronary heart disease and angina pectoris is significantly improved compared with the simple conventional western medicine.

Keywords

yangxin recipe, qi stagnation and blood stasis, angina pectoris, clinical effect, coronary computed tomography angiography

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Introduction

Coronary heart disease (CHD) refers to vascular stenosis or obstruction caused by coronary atherosclerosis (AS), resulting in myocardial ischemia, hypoxia, necrosis, and heart disease.[1] Its clinical manifestations include sudden precardiac pain that is mostly paroxysmal colic or squeezing pain. It is an important cause of health problems and death in China and globally. Chinese medicine believes that non-obstructive CHD in patients is mostly related to qi stagnation, blood stasis, and collaterals obstruction. Blood stasis is a necessary characteristic. The etiology and pathogenesis of the liver qi stagnation are vital. Therefore, the major treatments should focus on soothing the liver and regulating qi, promoting blood circulation, removing blood stasis, and dredging collaterals.

Additionally, coronary CT angiography has become a unique non-invasive technique to exclude coronary artery

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stenosis and identify non-obstructive coronary artery disease. Recently, coronary CT has been used as a technique that can study the anatomical and functional significance of stenosis via evaluating the partial blood flow reserve measured by myocardial perfusion or CT (FFR-CT) after drug stress.[2]

Based on this, the present study firstly investigated whether YXR (YXR) could performed beneficial efficacy on patients with angina pectoris of CHD by improving clinical efficacy, TCM syndrome scores, Pittsburgh Sleep Quality Index (PSQI) and the degree of coronary artery CT stenosis, which aimed to provide research-based evidence for the clinical application of YXR.

1. Materials and Methods

1.1 General Information

A total of 78 patients with stable angina pectoris of CHD (Qi stagnation and blood stasis syndrome) admitted to Shanghai University of TCM Shanghai TCM-Integrated Hospital from January 2017 to December 2019 were recruited into this study. They were divided into two groups: control group (n = 39) and YXR group (n = 39). 23 males and 16 females were included in control group, with age from 43 to74 and an average age at (57.6 ± 5.2). 24 males and 15 females were included in YXR group, with age from 44 to72 and an average age at (57.8 ± 5.1). There was no significant difference in general data between the two groups ($P > 0.05$), and the data were comparable.

This study was conducted with approval from the Ethics Committee of Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine (No:2020SHL-KYYS-134), and all patients were informed of the study and voluntarily signed an informed consent form. Participant progress through this study was shown in Figure 1.

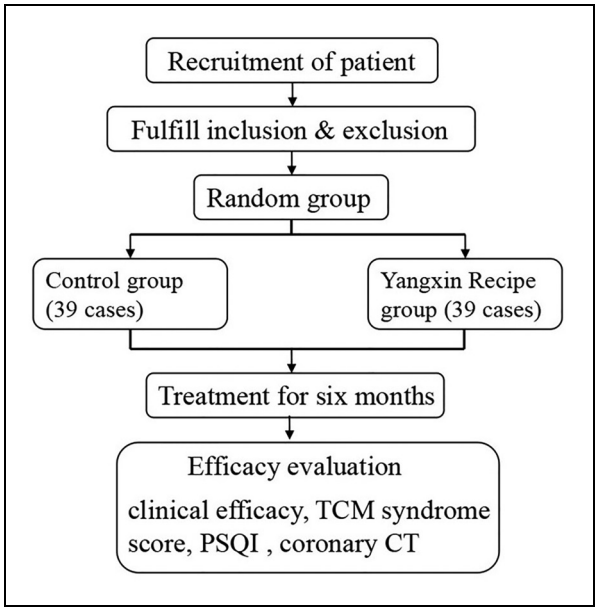

Figure 1. Flow diagram of this trial.

1.2 Diagnostic Criteria

1.2.1 The diagnostic criteria of western medicine. Diagnostic criteria were devised by referring to the 2013 ESC guidelines on the management of stable coronary artery disease.[3] ① Symptoms such as chest discomfort or chest pain occurred under emotional or exertional conditions and rapidly disappeared within a few minutes when these causal factors abate. ② These symptoms above mentioned could be relieved quickly after proper rest or sublingual nitroglycerin.

1.2.2 The diagnostic criteria of TCM. According to the dialectical points of qi stagnation and cardiothoracic syndrome of thoracic obstruction (angina pectoris) in the Chinese Traditional Internal Medicine[4] in combination with the dialectical standard[5] of stable angina pectoris of CHD with patterns of qi stagnation and blood stasis formulated by the Cardiovascular Branch of the Chinese Society of Traditional Chinese Medicine in 2019: ① cardiothoracic stuffiness, paroxysmal distending pain, and fixed pain; ② liver qi stagnation, easy to induce or aggravate when having affect-mind dissatisfaction; ③ distension in stomach duct, abdomen, and both flanks, feeling comfortable after flatus or belching; ④ purple or dark red tongue and small and wiry pulse.

1.3 Inclusion Criteria

① Patients who meet the above western and TCM diagnostic criteria; ② Those aged from 30 to 75; ③ Those with Disease duration 1 to 6 years; ④ Those who voluntarily participate in the study and sign the informed consent form; ⑤ Those who can ensure the treatment and follow-up.

1.4 Exclusion Criteria

① Patients with severe heart disease (unstable angina pectoris, acute myocardial infarction within six months, etc), severe cardiopulmonary insufficiency (cardiac function grade IV, severe abnormal pulmonary function); ② those with poor control of hypertension (post-treatment systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg); ③ those who used or were using cardiac pacemakers; ④ those with severe liver and kidney dysfunction complications, or other severe primary diseases such as hematopoietic system diseases and psychosis. ⑤ women who were pregnant, lactating, or planning pregnancy; ⑥ those who have engaged in other clinical studies within three months; ⑦ those wo with allergic constitution or being allergic to known components of the study drug; ⑧ those who researchers thought they were not suitable to participate in a clinical study; ⑨ those with severe arrhythmia (rapid atrial fibrillation, atrial flutter, paroxysmal ventricular tachycardia), sinus bradycardia (heart rate < 55 beats per minute) atrioventricular heart-block above type III; ⑩ those with major

surgery on the head, chest, and abdomen, and bleeding tendency within four weeks.

1.5 Interventions

1.5.1 Preparation of YXR. YXR was composed of Salvia Miltiorrhiza (20 g), Astragalus (30 g), Salidroside (15 g), Pseudo-Ginseng (15 g), Angelica Sinensis (20 g), Radix Bupleuri (15 g), Rhizoma Cyperi (10 g), Radix Paeoniae Alba (15 g), Poria Cocos (20 g), Fructus Alpiniae Oxyphyllae (15 g), Caulis Polygoni Multiflori (15 g), Cortex Albizziae (15 g), Polygala Tenuifolia (15 g), Juncus (3 g), Coptidis Rhizoma (6 g) and Cinnamon (6 g). The YXR was decocted with water divided into two equal parts for further use.

1.5.2. Grouping and treating. Patients were randomly divided into control group and YXR group, respectively. Both control group and YXR group were intervened with routine treatment of western medicine for six successive months, including aspirin enteric-coated tablets (Bayer HealthCare Co., Ltd GYZ Zi J20130078, 100 mg, po, qd) and isosorbide dinitrate tablets (Shanghai Fudan Fuhua Pharmaceutical Co., Ltd GYZ Zi H31021370,10 mg, po, tid). Meanwhile, patients in YXR group were also treated with YXR twice daily in combination with routine western medicine.

1.6 Observation Indicators

The clinical efficacy, TCM syndrome scores, PSQI and the degree of coronary artery CT stenosis were observed and recorded before and after treatment in both groups.

1.6.1 Clinical efficacy. The clinical efficacy of control and YXR groups was compared by referring to the Guiding Principles of Clinical Research on New Traditional Chinese Medicine.[6] Significant effectiveness: angina pectoris symptoms disappear, and ECG returns to normal. Effectiveness: Angina pectoris alleviates, and ECG results show that the ischemic S-T segment increases between 0.05 to 0.1 mV. Ineffectiveness: angina pectoris symptoms do not improve, and ECG does not change.

1.6.2 TCM syndrome scores. The TCM syndrome in both control and YXR groups was scored according to the Guiding Principles of Clinical Research on New Traditional Chinese Medicine.[6] Scoring methods: TCM syndromes are divided into four categories: nil, mild, medium, and severe. The primary symptoms (palpitation, chest pain and chest tightness) and secondary symptoms (fatigue, shortness of breath and dark purple complexion) are divided into 0, 1, 2, and 3 points depending on the severity of symptoms, respectively. The tongue is dark with ecchymosis and little or thin coating. The pulse is deep and thin, or uneven, or promotes knotting, and is divided into 0 points and 1 point. Significant effectiveness: The score is reduced by more than 70%. Effectiveness: The score is reduced to 70%–30%. Ineffectiveness: The score is reduced to less than 30%.

1.6.3 PSQI scores. The PSQI was used for reflecting different aspects of sleep and composed of seven items such as subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleep medication use, and daytime dysfunction. Each of afore-mentioned seven items ranges from 0 to 3. The total score was the sum of the score for each item. The higher PSQI score was related to the more worsen sleep quality. The subjects complete quizzes that last around 5 to 10 minutes.[7]

1.6.4 Coronary CT examination. The CT examination equipment used was Siemens 64-row CT coronary artery. Observational method for the levels of artery stenosis: The patients were examined by coronary CT before treatment and after six months of treatment to compare the stenosis level and plaque size of each coronary artery lumen before and after treatment. If there were multiple coronary artery lesions, the mean value was taken. Evaluation of coronary artery stenosis: Under the visual diameter method,[8] the lumen is completely blocked, or the diameter of the lumen is reduced by $\geq$90% for occlusion. The diameter of the lumen reduced by <90% and $\geq$75%, <75% and $\geq$50% and <50% represented severe stenosis, moderate stenosis and mild or normal stenosis, respectively.

1.7 Sample Size Calculation

The sample size of each group was calculated according to the following formulation.

$$n = \frac{2(\mu_\alpha + \mu_\beta)^2 \sigma^2}{\delta^2}$$

$\mu_\alpha = 0.05$, $1\text{-}\mu_\beta = 0.8$, $\sigma = 0.1$, δ (Two-sample mean difference) = 0.07. The estimated sample size and loss-visit rate were 70 cases and 10%, respectively. Adjusted sample size = estimated sample size / (1-lost-visit rate). Based on this, the sample size was calculated as 78 cases.

1.8 Follow-up

Following enrollment, all subjects will be followed up at post-treatment month 1, months 3 and months 6 for hospital visits. The corresponding items including the changes in TCM syndrome scores, liver function, renal function and PSQI score were measured and further analysis.

1.9 Data Analyses

The SPSS20.0 software was used for statistical analysis. The measurement data with normal distribution analyzed by Shapiro-Wilk test and homogeneous variances of each subject for different treatment groups were expressed as mean ± standard deviation ($\bar{x} \pm s$), and the t-test was used to compare the

differences between the two groups. The changes before and after treatment in both control and YXR groups has been analyzed by $\chi 2$ test, and the count data were expressed as frequency (constituent ratio, %). $P < 0.01$ was considered as a significant difference, and $P < 0.001$ was used as the criterion for judging the extremely significance of the difference.

2. Results

2.1 The Risk Factors of Coronary Heart Disease

Shown as Table 1, no significant difference could be found in the patients between control group and YXR treatment group in both basic diseases and the location of coronary stenosis. Of note, patients with stenosis of the left anterior descending coronary artery showed a higher percentage of all patients collected in clinic, mainly manifested as simply left anterior descending branch stenosis or combined stenosis of the left anterior descending branch and right coronary artery.

2.2 Clinical Efficacy

From Table 2, the effective rate of the patient treated with YXR in combination with conventional western medicine was 92.31%, which showed remarkable elevation ($P < 0.01$) as compared with that of in control group (64.10%), suggesting the beneficial efficacy of YXR on coronary heart disease and angina pectoris.

Table 1. The baseline characteristics of all the risk factors of coronary heart disease

Risk factors	N	Class	control group	YXR group	P
Hypertension	39	Yes	26	27	0.808
		No	13	12	
Hyperglycaemia	39	Yes	8	9	0.784
		No	31	30	
Dyslipidaemia	39	Yes	22	25	0.488
		No	17	14	
Left anterior coronary artery with descending branch stenosis	39	Yes	30	28	0.604
		No	9	11	
Right main coronary artery stenosis	39	Yes	24	26	0.637
		No	15	13	

Table 2. Comparative analysis of the clinical effective rate of two groups before and after treatment (%, n = 39)

Groups	Markedly effective	Effective	Ineffectiveness	Total effective rate
Control group	15 (38.46)	10 (25.64)	14 (35.90)	25 (64.10)
YXR group	20 (51.28)	16 (41.03)	3 (7.69)	36 (92.31)
X^2	9.101			
P value	0.003*			

Note:*: Compared with before treatment, $P < 0.01$; △: Compared with the control group after treatment, $P < 0.01$.

2.3 TCM Syndrome Scores

Table 3 and Figure 2 shows that no significant differences could be found between control and YXR groups. After treatment, the TCM syndrome scores of both groups were significantly lower ($P < 0.001$) than those before treatment. It could also be seen that the TCM syndrome scores of YXR in combination with the routine western medicine group was significantly lower than that of the simple western medicine control group ($P < 0.001$) after treatment, suggesting that YXR could performed positive efficacy on improving the symptoms of qi stagnation and blood stasis of patients with angina pectoris of CHD.

2.4 PSQI Scores

Subjective sleep quality: The difference of YXR is statistically significant ($P < 0.01$) after the treatment compared with the control group. Sleep latency: Before and after treatment, there is no obvious abnormality in the two groups. This is probably because many uncontrollable factors affect the patients' sleep latency. Therefore, the difference is not significant ($P > 0.01$). Sleep duration: The YXR group is lower than the control group after treatment, and the difference is statistically significant ($P < 0.01$). Habitual sleep efficiency: There is a significant difference between YXR and control group ($P < 0.05$) after treatment. Sleep disturbances: There is a slight difference between YXR and control group before treatment. The control group after treatment is slightly lower than before treatment. The YXR group is significantly lower than before treatment ($P < 0.01$). The difference is statistically significant ($P < 0.01$). Sleep medication use: Before treatment, the patients in the YXR group took hypnotic drugs more frequently than the control group. After treatment, the utilization rate of hypnotic drugs in the control group increases, while the utilization rate of hypnotic drugs in the YXR group decreases significantly. The difference is statistically significant ($P < 0.01$). Daytime dysfunction: After treatment, the scores of the two groups

Table 3. Comparison of TCM syndrome points of patients with coronary heart disease and angina pectoris between the two groups ($\bar{x} \pm s$, score)

Groups	n	Before treatment	After treatment	P
Control group	39	38.33 ± 3.06	22.44 ± 13.87	<0.001*
YXR group	39	39.10 ± 2.56	14.44 ± 9.87	<0.001*
P value		0.232	0.004△	
Intervention D value		−15.90 ± 14.32	−24.67 ± 10.09	0.003△

Note:*: Compared with before treatment, $P < 0.001$; △: Compared with the control group after treatment, $P < 0.001$.

decreases significantly, and the difference is statistically significant ($P < 0.01$). (Table 4)

2.5 Coronary CT

Table 5 shows that the degree of coronary stenosis in YXR in combination with routine western medicine or simple western medicine group decreases ($P < 0.001$) after treatment. Of note, a lower degree of coronary artery stenosis could be observed in patients treated with YXR in combination with western medicine as compared with that of simple western medicine group ($P < 0.001$). The visualized results have been shown in Figure 3.

3. Discussion

Coronary artery disease (CAD) is a slowly progressing disease and the most common cause of death worldwide. Recent studies have confirmed that the inflammation plays an important role in the overall progression of CAD.[9] Stable coronary heart disease (SCAD) and angina pectoris is a clinical syndrome of acute and temporary myocardial ischemia and hypoxia in which the myocardial load is increased by fatigue, emotional agitation, satiety, cold, and other factors based on coronary artery stenosis, spasm, or decreased circulating blood volume. It mainly manifests as oppressive chest pain and is usually accompanied by shortness of breath, palpitations, spontaneous sweating, etc It is the most common type of CHD.[10] Statins, antiplatelet drugs that inhibit angiotensin-converting enzymes, and calcium channel blockers are clinically used for the treatment of SCAD. However, existing Western medicine methods are not perfect for the treatment of SCAD, even for coronary intervention, its effect is also unknown.[11] In recent years, Chinese herbal medicine has been shown to be effective in the treatment of CHD and angina pectoris and can prevent its recurrence.[12] Other studies have shown that poor sleep may increase physical and mental fatigue and hinder the ability of daily activities in patients with CHD.[13] Some scholars believe that patients with heart disease, poor sleep quality, and daytime dysfunction are more likely to experience depression.[14] However, even if depression is controlled clinically, poor subjective sleep quality in patients with CHD may lead to myocardial risk and increase infarction, heart-related surgery, and death.[15] Therefore, subjective sleep quality has a great impact on the treatment and prevention of CHD and angina pectoris patients. A 64-slice spiral CT has good diagnostic value for moderate and severe coronary artery stenosis. It meets the diagnostic needs of CHD and helps avoid invasive coronary angiography in patients with healthy coronary arteries or who require non-interventional treatment.[16] Coronary CT imaging technology has the advantages of safety, non-invasive procedures, high accuracy, high negative predictive value, and low examination cost. It has important diagnostic value in the positioning and qualitative diagnosis of moderate and severe coronary stenosis and atherosclerotic plaques. It has important clinical significance for early prediction, diagnosis, and treatment of CHD and can be used as the first choice for clinical diagnosis of CHD.[17]

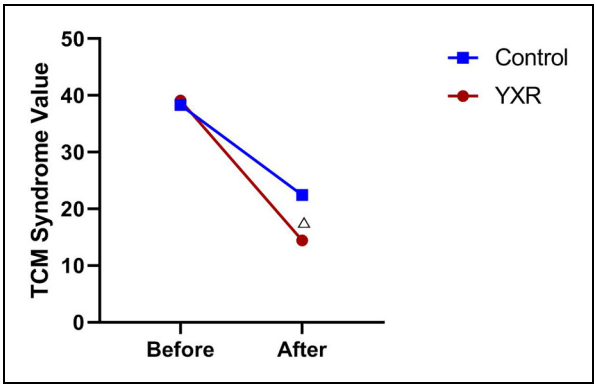

Figure 2. Comparison of TCM syndrome scores between control and Yangxin Recipe (YXR) groups before and after treatment (△, P < 0.001).

Stable angina pectoris belongs to the TCM category of "chest obstruction, cardiac pain" and "long-term cardiac pain." Patients with CHD may suffer from oppressive pain in the precordial region. These severe patients may have chest pain radiating to the back, back pain radiating to the heart, fixed pain, and pain just like needling and so on blood stasis syndrome. They may also have clinical manifestations such as qi stagnation, congealing cold, qi, and blood yin and yang

Table 4. Comparison of PSQI before and after treatment between the two groups ($\bar{x} \pm s$, score)

	Control group		YXR group	
Items	Before treatment	After treatment	Before treatment	After treatment
Subjective sleep quality	2.410 ± 0.677	2.487 ± 0.506	2.436 ± 0.680	1.692 ± 0.468*△
Sleep latency	2.487 ± 0.756	2.359 ± 0.903	2.385 ± 0.782	2.333 ± 0.701
Sleep duration	2.539 ± 0.682	2.590 ± 0.498	2.564 ± 0.680	1.564 ± 0.502*△
Habitual sleep efficiency	2.436 ± 0.718	2.564 ± 0.502	2.539 ± 0.505	1.539 ± 0.505*△
Sleep disturbances	2.205 ± 0.615	2.103 ± 0.680*	2.410 ± 0.677#	1.462 ± 0.505*△
Sleep medication use	1.897 ± 0.598	2.308 ± 0.766*	2.282 ± 0.647#	1.410 ± 0.498*△
Daytime dysfunction	2.462 ± 0.720	2.282 ± 0.647*	2.359 ± 0.668	1.256 ± 0.442*△
PSQI total score	16.462 ± 4.322	16.795 ± 3.948	16.974 ± 4.145#	11.256 ± 2.446*△

Note:*: Compared with before treatment, $P < 0.01$; △: Compared with the control group after treatment, $P < 0.01$; #: Compared with the control group before treatment, $P < 0.01$.

Table 5. Comparison of coronary CT before and after treatment between two groups ($\bar{x} \pm s$, %)

Groups	n	Before treatment	After treatment	P
Control group	39	69.87 ± 13.25	57.05 ± 9.92	<0.001*
YXR group	39	71.92 ± 9.43	49.87 ± 7.82	<0.001*
P value		0.433	0.001△	
Intervention D value		−12.82 ± 9.58	−22.05 ± 11.91	<0.001△

Note:*: Compared with before treatment, $P < 0.001$; △: Compared with the control group after treatment, $P < 0.001$.

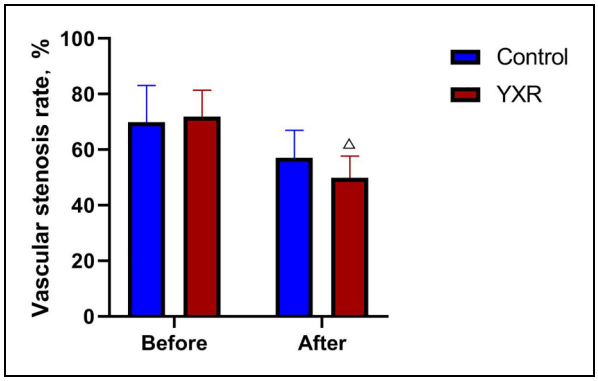

Figure 3. Comparison of vascular stenosis rate between control and Yangxin Recipe (YXR) groups before and after treatment (△, P < 0.001).

deficiency. Blood stasis syndrome is common in CHD. Blood stasis syndrome is not only the etiology and pathogenesis of CHD but also the pathological product.

YXR is a common clinical prescription for the treatment of angina pectoris of CHD summarized by the prestigious Chinese physician Yaorong Dong based on the experience of doctors of all dynasties. With the development of TCM, some scholars have carried out experimental studies on the extracts of single Chinese herbs. They have found that the unused medicine has a protective effect on the cardiovascular system or myocardial cells. These include drugs that promote blood circulation and remove blood stasis in YXR, including *Aalvia Miltiorrhiza*, *Astragalus*, *Salidroside*, *Pseudo-Ginseng*, and *Angelica Sinensis*. *Salvia Miltiorrhiza* is also known as the root of red-rooted salvia (named Danshen in Chinese). It has attracted worldwide interest due to its substantial impact on CHD. Salvianic acid (SA) is one of the main active components of Salvia Miltiorrhiza in CHD. SA is widely used in the treatment of CHD.[18] Xu et al.[19] synthetized a new DSS derivative DEX-018 under the esterification of the carboxyl group of SA and edaravone to achieve a protective effect and overcome the structural defects of SA. It proves that DEX-018 plays a role in anti-oxidation and anti-apoptosis in human umbilical vein endothelial cells (HUVECs) induced by tert-butyl hydroperoxide. *Astragalus*: Astragalus polysaccharides can promote the proliferation and migration of vascular endothelial cells and promote angiogenesis and tissue repair. Ma et al.[20] have found that the isoflavone Foronetin extracted from astragalus can significantly reduce the development of atherosclerosis in APOE knockout mouse models with a high-fat diet. This indicates that Foronetin may be a new treatment for inhibiting atherosclerosis. *Salidroside*: Salidroside (SAL) is known as "oriental god grass" and "plateau ginseng." The salidroside is one of its main effective components. The main ingredient of rhodiola is rhodiola rosea, which has been used in traditional Chinese medicine for decades. Multiple studies have demonstrated the protective effects of SAL on myocardial ischemia. Chen et al.[21] have confirmed through a study that SAL therapy is a pathological process that may reduce the mortality of *in vivo* myocardial infarction (MI) mice, improve cardiac function, and reduce myocardial remodeling in MI mice. Furthermore, oral SAL attenuates myocardial inflammation and apoptosis and promotes angiogenesis. SAL down-regulates the expression of TNF-α, TGF-β1, IL-1β, and Bax, and up-regulates the expression of Bcl-2, VEGF, Akt, and eNOS. The findings reveal that SAL may be a potentially effective treatment for clinical ischemic cardiovascular disease. *Pseudo-Ginseng*: Panax notoginseng saponins (PNS) is the main bioactive compound of notoginseng, which has been widely accepted and has a significant effect on CHD. Dong et al.[22] have found that the PNS can inhibit early apoptosis and protect HUVECs from H_2O_2-induced oxidative stress by up-regulating VEGFA mRNA expression. They have validated this through pharmacological prediction and experimental verification. *Angelica Sinensis*: Niu[23] has elucidated the mechanism of angelica polysaccharide (ASP) in the treatment of acute myocardial infarction in rats using network pharmacology analysis. The ASP can significantly reduce endoplasmic reticulum stress-induced apoptosis in rats with *in vivo* and *in vitro* ischemic injury. ASP treatment reduces the infarct area and preserves cardiac function. The experimental data suggest that ASP attenuates the stress of harmful endoplasmic reticulum proteins by activating transcription factor 6 (ATF6) to protect the heart from ischemic injury. The role of ASP can be achieved by activating AMPK-$PGC_{1\alpha}$ pathways. In addition to the above-mentioned TCM herbs commonly used to promote blood circulation and blood stasis in the treatment of CHD, YXR has added *Radix Bupleuri*, *Rhizoma Cyperi*, and *Radix Paeoniae Alba* for regulating qi movement to relieve stagnation. It can substantially promote qi and blood circulation. It can relieve muscle tension, especially smooth muscle tension, and promote smooth muscle normal peristalsis and pulsation, thereby improving the function of arterial vessels. YXR tranquilizes to aid sleep, improve sleep quality, and extend sleep duration, thereby moderately decreasing the brain excitability, reducing anxiety, balancing plant neural functions, and inhibiting the overexcited sympathetic nervous system. It does so in combination with *Poria Cocos*, *Bitter Cardamon*, *Tuber Fleece flower stem*, *Cortex Albizziae*, *Polygala Tenuifolia*, *Juncus*, and *Rhizoma Coptidis* from Sichuan of China, and cinnamon for restoring normal coordination between the heart and the kidneys.

Based on afore-mentioned information, we further investigated the efficacy of YXR combined with western medicine

on clinical efficacy, TCM syndrome scores, PSQI and coronary CT of patients with angina pectoris of CHD. In clinical practice, we used CT coronary imaging, research finding the efficacy of routine western medicine treatment may be improved substantially when combined with YXR in the treatment of patients with qi stagnation and blood stasis. YXR noticeably improves It shows that it is necessary to combine YXR with routine Western medicine treatment. Through clinical observation, we believe that the therapeutic effect of routine Western medicine + YXR has been improved because the medicine calms the heart and tranquilizes the mind if it is added in the YXR based on promoting blood circulation to remove blood stasis, thereby strengthening the therapeutic effect on angina pectoris of CHD. The results obtained in this study also showed that YXR combined with western medicine were more effective than western medicine alone for treating patients diagnosed with angina pectoris of CHD by improving these symptoms, suggesting the definite clinical efficacy of YXR. Additionally, some issues including whether YXR could exert its efficacy by improve others important indicators such as mean platelet volume (MPV)[24,25] and how YXR performed efficacy have not be explored in present study, which will be developed in further study.

Conclusion

In summary, this study, for the first time, demonstrated the remarkably protective effects of YXR on improving the coronary stenosis, various TCM symptoms of qi stagnation and blood stasis, subjective sleep quality of patients with CHD and angina pectoris and clinical efficacy, which not only provides a theoretical basis for our clinical treatment of angina pectoris of CHD with qi stagnation and blood stasis, but also applied research-based evidence on using UXR for the clinical application of CHD. Additionally, the results obtained in present study also suggested that YXR could be given on the basis of conventional western medicine treatment for patients with angina pectoris of CHD in future.

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Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Author Contributions

JLL, YRD and XZH conceived the idea and conceptualised the study. JLL, YRD and XZH collected the data. JLL, YRD and XZH analysed the data. JLL, YRD and XZH drafted the manuscript, then JLL, YRD and XZH reviewed the manuscript. All authors read and approved the final draft.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Informed Consent

All participants signed a document of informed consent.

Trial Registration

Trial Registration: 2020 SHL-KYYS-134

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References

1. Michalsen A, Grossman P, Lehmann N, et al. Psychological and qualityof life outcomes from a comprehensive stress reduction and lifestyle program in patients with coronary artery disease: results of a randomized trial. *Psychother Psychosom*. 2005;74(6):344-352.
2. Trabattoni D, Mushtaq S, Andreini D. Role of coronary computed tomography angiography and computed tomography-derived fractional flow reserve in coronary artery disease. *Article in Italian*. 2020;21(4):5-11.
3. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the task force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J*. 2013;34(38):2949-3003.
4. Zhou ZY. *Internal Medicine of Traditional Chinese Medicine*. China traditional Chinese Medicine Press; 2005:142-148.
5. Cardiovascular disease branch of Chinese society of traditional Chinese Medicine. Guidelines for diagnosis and treatment of stable angina pectoris of coronary heart disease. *Zhong Yi Za Zhi*. 2019;60(21):1880-1890.
6. Zheng XY. *Guiding Principles for Clinical Research of new Drugs of Traditional Chinese Medicine*. China Medical Science and Technology Press; 2002:78-79.
7. Tan JJL, Tay HY, Lim CKS, et al. Measurement structure of the Pittsburgh sleep quality Index and Its association with health functioning in patients with coronary heart disease. *J Clin Psychol Med Settings*. 2020;27(4):677-685.
8. Feng XR, Liang LH, Wu JF, et al. 64-Slice Spiral double-low CT to evaluate the degree of stenosis and plaque composition in diagnosing coronary artery disease. *Exp Ther Med*. 2017;14(4):3088-3092.
9. Moreira DM, da Silva RL, Vieira JL, et al. Role of vascular inflflammation in coronary artery disease: potential of anti-inflflammatory drugsin the prevention of atherothrombosis. Inflflammation and anti-inflflammatory drugs in coronary artery disease. *Am J Cardiovasc Drugs*. 2015;15(1):1-11.

10. Jia S, Liu Y, Yuan J. Evidence in guidelines for treatment of coronary artery disease. *Adv Exp Med Biol*. 2020;1177:37-73. doi: 10.1007/978-981-15-2517-9_2
11. Mitchell JD, Brown DL. Update on percutaneous coronary intervention in stable coronary artery disease. *JAMA Intern Med*. 2016;176(12):1855-1856.
12. Gong P, Li Y, Yao C, et al. Traditional Chinese medicine on the treatment of coronary heart disease in recent 20 years. *J Altern Complement Med*. 2017;23(9):659-666.
13. Johansson A, Windahl M, Svanborg E, et al. Perceptions of how sleep is influenced by rest, activity and health in patients with coronary heart disease: a phenomenographical study. *Scand J Caring Sci.* 2007;21(4):467-475.
14. Norra C, Kummer J, Boecker M, et al. Poor sleep quality is associated with depressive symptoms in patients with heart disease. *Int J Behav Med.* 2012;19(4):526-534.
15. Leineweber C, Kecklund G, Janszky I, et al. Poor sleep increases the prospective risk for recurrent events in middle-aged women with coronary disease: the Stockholm female coronary risk study. *J Psychosom Res.* 2003;54(2):121-127.
16. Wang J. Application of 64-slice spiral CT in coronary artery imaging. *J Pak Med Assoc*. 2020;70(9):2-8.
17. Yang FB, Guo WL, Sheng M, et al. Diagnostic accuracy of coronary angiography using 64-slice computed tomography in coronary artery disease. *Saudi Med J*. 2015;36-(10):1156-1162.
18. Huo MQ, Wang ZX, Wu DX, et al. Using coexpression protein interaction network analysis to identify mechanisms of danshensu affecting patients with coronary heart disease. *Int J Mol Sci*. 2017;18(6):1298.
19. Xu HL, He K, Li Y, et al. Cytoprotective effects evaluation of a novel danshensu derivative DEX-018 against oxidative stress injury in HUVECs. *Biol Pharm Bull*. 2020;43(5):801-809.
20. Ma C, Xia R, Yang S, et al. Formononetin attenuates atherosclerosis via regulating interaction between KLF4 and SRA in apoE -/- mice. *Theranostics*. 2020;10(3):1090-1106.
21. Chen PS, Liu J, Ruan HY, et al. Protective effects of salidroside on cardiac function in mice with myocardial infarction. *Sci Rep*. 2019;9(1):18127.
22. Dong Y, Duan L, Chen HW, et al. Network pharmacology-based prediction and verification of the targets and mechanism for Panax Notoginseng saponins against coronary heart disease. *Evid Based Complement Alternat Med*. 2019;3:6503752. doi: 10.1155/2019/6503752.
23. Niu XW, Zhang JJ, Ni JR, et al. Network pharmacology-based identification of major component of Angelica sinensis and its action mechanism for the treatment of acute myocardial infarction. *Biosci*. 2018;38(6):BSR20180519.
24. Sincer I, Gunes Y, Mansiroglu AK, et al. Association of mean platelet volume and red blood cell distribution width with coronary collateral development in stable coronary artery disease. *Adv Interv Cardiol*. 2018;14(3):263-269.
25. Aktas G, Kocak MZ, Tuba Taslamacioglu Duman, et al. Mean Platelet Volume (MPV) as an inflammatory marker in type 2 diabetes mellitus and obesity. *Bali Medical Journal*. 2018;7(3):650-653.