

STATE-OF-THE-ART REVIEW

Translational Research and Clinical Application of Traditional Chinese Medicine in Cardiovascular Diseases



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ABSTRACT

Luobing theory is based on the principles of traditional Chinese medicine (TCM) and focuses on the regulation of blood circulation. The translation of Luobing theory into clinical practice has shown promising results in the treatment of cardiovascular diseases (CVDs). Studies have reported the benefits of using Luobing theory in the treatment of metabolic syndrome, atherosclerosis, arrhythmia, and heart failure. This review article provides an overview of the evidence-based application of TCM Luobing theory in the treatment of CVDs. It also highlights the challenges and opportunities of translating TCM into clinical practice and provides valuable insights for future CVD research. (JACC Asia. 2024;4:711-720) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality worldwide, posing significant challenges to health care systems. Although modern medicine has made substantial advances in the diagnosis and treatment of these conditions, traditional Chinese medicine (TCM) offers complementary and alternative approaches that have been practiced for centuries.¹ Among these, the Luobing theory, also known as collateral disease theory, provides a unique framework for understanding and treating CVDs.

By bridging traditional practices with contemporary medical research, the current review highlights the potential of TCM to contribute to the evolving landscape of cardiovascular health care. This review integrates TCM with modern cardiovascular research, highlighting its potential in advancing cardiovascular

health care. Focusing on the Luobing theory, we explore its translational research and clinical applications in CVD. By analyzing key clinical studies and TCM formulas such as Jinlida, Tongxinluo, Shenson-gyangxin, and Qiliqiangxin, we show how integrating Luobing theory with modern practices can improve treatment and management of metabolic syndrome, coronary artery disease, arrhythmia, and heart failure.

THE ORIGIN AND RESEARCH OF LUOBING THEORY

The Luobing theory, previously referred to as the collateral disease theory, constitutes a pivotal aspect of the TCM academic framework. It centers on the study of the collaterals network (Luo), which are small blood vessels or channels that branch off from

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**ABBREVIATIONS
AND ACRONYMS****AF** = atrial fibrillation**AMI** = acute myocardial infarction**CVD** = cardiovascular disease**JLD** = Jinlida granules**MACCE** = major adverse composite cardiovascular event(s)**MI** = myocardial infarction**QLQX** = Qiliqiangxin capsules**SSYX** = Shensongyangxin capsules**STEMI** = ST-segment elevation myocardial infarction**TCM** = traditional Chinese medicine**TXL** = Tongxinluo capsule

the primary meridians in the human body. The *Yellow Emperor's Inner Canon* and *Synopsis of the Golden Chamber* laid the groundwork for this theory, which delves into pathologic alterations stemming from collateral vessel damage, along with associated diagnostic and therapeutic principles.² Luobing or collateral disease denotes a pathologic condition induced by various pathogenic factors compromising the integrity of the collateral vessels. The health of these collaterals is crucial for maintaining overall physiological balance and preventing disease. Blockages or dysfunctions within the collaterals can lead to various pathologies, including those affecting the cardiovascular system.

Under the leadership of Professor Yiling Wu from Hebei Medical University, State Key Laboratory for Innovation and Transformation of Luobing Theory, a research team systematically developed the theory of vessels and collaterals, establishing a novel theoretical paradigm guiding the prevention and treatment of CVD.³ They posited that vessels and collaterals extend from the blood vessels, fostering systemic nourishment throughout the body via a networked system. Furthermore, leveraging insights from both TCM and modern medical science, interdisciplinary research, using modern scientific methods and evidence-based approaches, has unveiled a promising avenue for managing CVD, with TCM serving as the primary framework.

Understanding Luobing theory is crucial for comprehending how TCM approaches the treatment of CVD. By focusing on the health of the collaterals and ensuring the smooth flow of Qi and blood, TCM offers a holistic and effective way to manage and treat these conditions. This theory provides the basis for many clinical applications and research studies in TCM, helping to bridge traditional practices with modern medical insights.

**CARDIOVASCULAR CONTINUUM AND
LUOBING THEORY**

Dzau and Braunwald⁴ proposed the concept of the “cardiovascular continuum,” describing the developmental process and consequences of CVD. It emphasizes that endothelial damage triggered by multiple risk factors is the initiating factor of the event chain. Metabolic syndrome, vulnerable plaques, acute myocardial infarction (AMI), reperfusion injury, recurrent atrial fibrillation (AF), and chronic heart failure play crucial roles in this process. Single

treatment methods are often unable to cover the management of CVDs, and an integrative approach to CVD prevention and treatment that considers the different pathophysiological aspects is now incorporated in our modern conventional treatment. However, there is still ample room for optimization in terms of patient treatment and prognosis.⁵

The Luobing theory in TCM offers a unique perspective on CVDs by highlighting the significance of collaterals in maintaining overall health. According to TCM principles, these collaterals serve as crucial pathways for the circulation of Qi, blood, and body fluids throughout the body. Dysfunction or blockages within these pathways can contribute to various cardiovascular pathologies. Understanding and applying Luobing theory enables practitioners to not only address symptoms but also target underlying imbalances affecting cardiovascular health. This approach complements modern medical interventions by providing holistic insights into disease prevention and management, thereby enhancing the continuum of cardiovascular care.

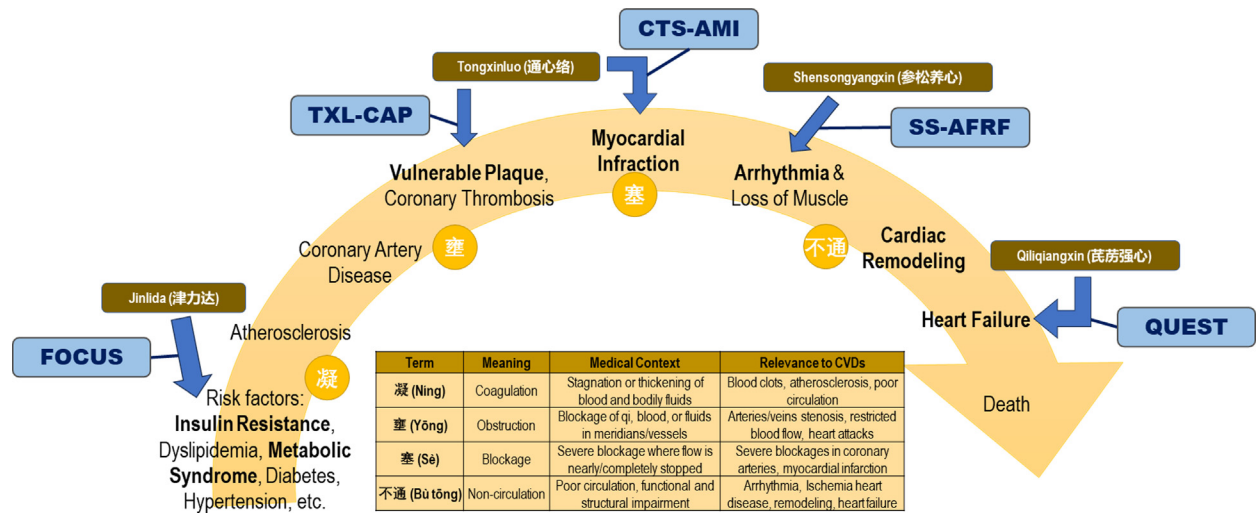
The application of Luobing theory provides a distinctive approach to understanding and treating these conditions. CVDs often involve issues such as poor circulation, blood stasis, and imbalances in Qi and blood, all of which align with the pathogenesis described in Luobing theory. Drawing on the TCM principle of “treating before the disease manifests,” innovative herbal medicines have been developed guided by this theory.⁶ Recent extensive research supports the clinical efficacy of these drugs, showing their value in preventing and treating CVDs across the continuum of care (**Central Illustration**).

TRANSLATION FROM TCM TO MODERN MEDICINE

With its unique theoretical framework and treatment modalities, TCM offers new perspectives and directions for the prevention and management of CVDs, presenting broad prospects for application. However, the integration of TCM and modern contemporary management faces challenges due to a lack of rigorous scientific research, differences in theoretical foundations, and skepticism toward TCM.^{7,8}

To advance this integration, performance of large-scale, randomized controlled trials is essential to validate TCM treatments and provide the necessary scientific evidence for their efficacy. Standardizing TCM protocols will ensure consistency in clinical settings, and fostering interdisciplinary collaboration between TCM practitioners and modern medical professionals will bridge knowledge gaps. Biomedical and pharmacologic research can elucidate the

CENTRAL ILLUSTRATION Progression and Interventions With Traditional Chinese Medicine of Cardiovascular Diseases



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The graphic outlines the progression from risk factors to heart failure in cardiovascular diseases (CVDs) and the intervention points of traditional Chinese medicines (TCM). Downward arrows represent progression of CVD, and yellow circles indicate disease stages based on TCM. The TCMs used include Jinlida (JLD), Tongxinluo (TXL), Shensongyangxin (SSYX), and Qiliqiangxin (QLQX) target-specific stages to mitigate disease progression, marked in brown square. Light blue squares represent the evidence-based trial conducted in the recent years include: FOCUS (Interventional study of Jinlida treatment for abnormal glucose metabolism in metabolic syndrome), TXL-CAP (A randomized, double-blind, placebo parallel controlled, multi-center clinical study of Tongxinluo capsule in the treatment of acute coronary syndrome with atherosclerotic plaque), CTS-AMI (China Tongxinluo Study for Myocardial Protection in Patients With Acute Myocardial Infarction), SS-AFRF (Shensongyangxin Capsule Regulates Persistent Atrial Fibrillation After Radiofrequency Catheter Ablation), and QUEST (Qiliqiangxin in Heart Failure: Assessment of Reduction in Mortality).

molecular mechanisms of TCM treatments, enhancing our understanding of their effects. Establishing regulatory frameworks will ensure that safety and quality standards are met in integrated health care systems. Translational research efforts can lead to the development of innovative therapies that combine the strengths of both medical traditions. By pursuing these strategies, the integration of TCM and modern medicine can result in more comprehensive and effective CVD management, ultimately improving patient outcomes and expanding treatment options.

TRANSLATIONAL RESEARCH AND APPLICATION OF LUOBING THEORY

Although TCM has made significant strides in the realm of health care, continuous efforts are essential for further advancements. Despite the considerable progress made in research and clinical applications, areas remain in which TCM could benefit from ongoing exploration and refinement. In addition, the field awaits the publication of pending research findings, which could potentially provide valuable insights into the efficacy and mechanisms of various

TCM interventions. Therefore, sustained dedication to research, coupled with the dissemination of forthcoming publications, will be crucial in enhancing our understanding and utilization of TCM for the betterment of global health care.

In view of the application of TCM in CVDs, a number of evidence-based translational studies have been conducted in recent years on drugs based on the Luobing theory: Jinlida granules (JLD), Tongxinluo capsules (TXL), Shensongyangxin capsules (SSYX), and Qiliqiangxin capsules (QLQX) (Table 1). The following section summarizes the series of randomized, double-blind, placebo-controlled, multicenter clinical studies conducted on these drugs corresponding to the cardiovascular continuum.

INTERVENTIONAL STUDY OF JINLIDA FOR DIABETES PREVENTION IN IMPAIRED GLUCOSE TOLERANCE AND MULTIPLE METABOLIC ABNORMALITIES: FOCUS RANDOMIZED CLINICAL TRIAL. Metabolic syndrome serves as the primary pathologic link in the cardiovascular continuum, and its coexistence with impaired glucose tolerance significantly increases the risk and accelerates the progress of CVDs. Proactive prevention and control efforts aid in achieving

TABLE 1 Components of the TCM Set Prescription and its Effects on CVDs

Set Prescription	No. of Components	Species	Effects on Cardiovascular Diseases	
Jinlida granules	17	<ul style="list-style-type: none"> • Panax ginseng C.A. Mey • Polygonatum kingianum Coll. et Hemsl • Atractylodes lancea (Thunb.) DC • Sophora flavescens Ait. • Ophiopogon japonicus (L.f) Ker-Gawl • Rehmanniag lutinosa Libosch • Polygonum multiflorum Thunb. • Cornus officinalis Sieb. et Zucc • Poria cocos (Schw.) Wolf 	<ul style="list-style-type: none"> • Eupatorium fortune Turcz • Coptis chinensis Franch. • Anemarrhena asphodeloides Bge. • Epimedium brevicornum Maxim • Salvia miltiorrhiza Bge. • Lycium chinense Mill. • Pueraria lobata (Willd.) Ohwi. • Litchi chinensis Sonn. 	Improves glucose metabolism, reduces blood lipid levels, and enhances microcirculation; beneficial for patients with diabetes-related cardiovascular issues
Tongxinluo capsule	12	<ul style="list-style-type: none"> • Panax ginseng C.A. Mey. • Paeonia lactiflora Pall. • Ziziphus jujuba Mill. Var. spinosa (Bunge) Hu ex H.F. Chou • Santalum album L. • Dalbergia odorifera T.C. Chen • Steleophaga plancyi (Boleny) 	<ul style="list-style-type: none"> • Scolopendra subspinipes mutilans L. Koch • Hirudo nipponica Whitman • Cryptotympana pustulata Fabricius • Buthus martensii Karsch • Boswellia carteri • Borneolum syntheticum 	Protects endothelial function, reduces myocardial ischemia, prevents atherosclerosis, and improves blood circulation
Shensongyangxin capsule	12	<ul style="list-style-type: none"> • Panax ginseng C.A. Mey. • Salvia miltiorrhiza Bge • Nardostachys jatamansi Dc. • Cornus officinalis Sieb. et Zucc. • Taxillus chinensis (DC.) Danser • Paeonia lactiflora Pall. 	<ul style="list-style-type: none"> • Schisandra sphenanthera Rehd. et Wils. • Coptis chinensis Franch. • Ophiopogon japonicas (Thunb.) Ker-Gawl. • Polypodiodes chinensis • Eupolyphaga sinensis Walker • Ziziphus jujuba Mill. var. spinosa (Bunge) Hu ex H.F. Chou 	Stabilizes heart rhythm, reduces palpitations, treats arrhythmias, and enhances myocardial perfusion
Qiliqiangxin capsule	11	<ul style="list-style-type: none"> • Astragalus membranaceus (Fisch) Bge. Var. mongholicus (Bge.) Hsiao. • Panax ginseng C.A. Mey. • Aconitum carmichaelii Debx. • Salvia miltiorrhiza Bge. • Lepidium apetalum Willd. • Alisma orientalis (Sam.) Juzep. 	<ul style="list-style-type: none"> • Polygonatum odoratum (Mill.) Druce • Carthamus tinctorius L. • Periploca sepium Bge. • Cinnamomum cassia Prest • Citrus reticulata Blanco 	Reduces heart failure symptoms, improves cardiac function, reduces inflammation, and enhances myocardial energy metabolism

CVD = cardiovascular disease; TCM = traditional Chinese medicine.

comprehensive management of multiple risk factors and controlling them at the source. Insulin resistance is a crucial link in the disorder of glucose and lipid metabolism and is also a major contributor to the development of obesity-related metabolic diseases.^{9,10}

With the holistic perspective in TCM representing a more comprehensive management of chronic diseases, JLD aim at improving glucose metabolism and enhancing microcirculation. In TCM, impaired glucose metabolism is often associated with damp-heat or phlegm-dampness obstructing Qi and blood flow.

JLD are a multitargeted hypoglycemic medication composed of danshensu sodium, puerarin, salvianolic acid B, epimedin B, epimedin C, icariin, and ginsenosides Rb1, Rc, and Rb2. Pharmacologic and bench research evidence has revealed their potential mechanisms, including the protection of islet β -cells, alleviation of oxidative stress, regulation of blood glucose-related hormones, and protection of vascular endothelial cells. Furthermore, JLD can reduce insulin resistance and inflammation by promoting skeletal muscle gene expression and regulating lipid metabolism, thus playing a pivotal role in the antidiabetes effect.¹¹⁻¹⁴

Several pilot clinical randomized controlled trials have reported the efficacy of JLD as an adjunct therapy to antidiabetic agents for the treatment of type 2 diabetes mellitus.¹⁵⁻¹⁷ Building upon prior research, a meta-analysis incorporating 15 clinical studies comprising 1,810 patients revealed that the combination of JLD further reduced fasting blood glucose, postprandial blood glucose, and glycosylated hemoglobin in patients with type 2 diabetes.¹⁸ Results supported an improved role of JLD in abnormal glucose and lipid metabolism.

A further exploration trial, the FOCUS (Jinlida for Diabetes Prevention in Impaired Glucose Tolerance and Multiple Metabolic Abnormalities; ChiCTR1900023241) study enrolled 889 participants aged 18 to 70 years with impaired glucose tolerance and multiple metabolic abnormalities from 35 centers in 21 cities in China from June 2019 to February 2023.¹⁹ Individuals with impaired glucose tolerance and metabolic syndrome (defined as abdominal obesity [ie, male waist circumference ≥ 90 cm, female waist circumference ≥ 85 cm]) received JLD or placebo on the basis of lifestyle intervention. The primary outcome was the incidence of type 2 diabetes during the intervention period, which was determined by the results of 2 consecutive oral glucose tolerance tests.

After a median observation period of 2.20 years, participants in the JLD group displayed a 41% lower risk of developing diabetes compared with those in the placebo group. In addition, JLD led to improvements in metabolic syndrome (eg, as reflected by the waist circumference, fasting blood glucose, postprandial 2-hour blood glucose, fasting triglycerides), insulin resistance (triglyceride-glucose index), and ankle-brachial index.²⁰

Based on existing evidence-based research, JLD may serve as adjunctive therapy for metabolic syndrome and prediabetic metabolic abnormalities. Further exploration and summarization of the potential mechanisms should be conducted to provide patients with better overall management strategies.

TXL IN THE TREATMENT OF ACUTE CORONARY SYNDROME WITH ATHEROSCLEROTIC PLAQUE.

Atherosclerosis-related ischemic vascular diseases continue to show an increasing incidence and mortality rate annually. Platelet aggregation and thrombus formation resulting from the progression and rupture of vulnerable plaques are fundamental pathologic mechanisms of acute coronary syndrome. Vulnerable plaque rupture accounts for 70% of acute coronary syndromes.^{21,22}

TXL are believed to unblock collaterals, particularly focusing on improving blood circulation, reducing blood stasis, and promoting the flow of Qi in TCM. Studies have also shown that TXL exhibits multiple mechanisms of action in the treatment of coronary heart disease. Studies indicate that use of TXL lowers lipid levels, exhibits anti-inflammatory and anticoagulant properties, protects vascular endothelium, increases fibrous cap thickness of plaques, reduces lipid deposition within plaques, and effectively stabilizes vulnerable plaques.

In apolipoprotein E^{-/-} mice, TXL reduced early atherosclerotic plaque burden by lowering plasma total cholesterol and low-density lipoprotein concentrations and inhibiting local inflammatory factor expression and intraplaque neovascularization, thus suppressing inflammation and reducing plaque load. In addition, TXL inhibits late-stage atherosclerotic plaque neovascularization, reduces inflammation, and decreases the vulnerability index, thereby stabilizing vulnerable plaques.²³⁻²⁶

Regarding other aspects, the previous evidence-based randomized controlled study on the effect of TXL in carotid artery plaques, known as the CAPITAL (Carotid Artery Plaque Intervention with Tongxinluo Capsule) study, found a significant reduction in the average intima-media thickness in 12 locations of bilateral carotid arteries after 2 years of TXL

treatment.²⁷ It also showed a decrease in plaque area, improvement in carotid artery vascular remodeling, and a reduction in major cardiovascular clinical events.

To further explore the effect of TXL plaques stability, the TXL-CAP (a randomized, double-blind, placebo parallel controlled, multi-center clinical study of Tongxinluo capsule in the treatment of acute coronary syndrome with atherosclerotic plaque) study led by Qilu Hospital of Shandong University investigated the intervention of TXL on coronary artery vulnerable plaques in 220 patients from 18 institutions (ChiCTR1900025842). The study enrolled patients with non-ST-segment elevation acute coronary syndrome and coronary artery vulnerable plaques (fibrous cap thickness <100 μm) characterized by using optical coherence tomography. The primary outcome measure was the thickness of the fibrous cap of target vessel plaque after 1 year of placebo or TXL in addition to conventional treatment. Unpublished results (<http://10.0.82.211/rs.3.rs-2451089/v1> Peili Bu) showed that TXL led to a decrease in fibrous cap thickness increase by 27.42 μm compared with the control group, improvement in lipid core angle, reduction in severity grading of angina pectoris, and improvement in quality of life (measured by using Seattle Angina Questionnaire score), showing a favorable trend in reducing composite endpoint events (eg, all-cause death, nonfatal MI, stroke, hospitalization due to angina pectoris).

Although these study results provide effective intervention for stabilizing vulnerable plaques and reducing cardiovascular events, research in this area only includes a certain spectrum of patients and medium/large vessel pathologic changes. Therefore, further studies targeting ST-segment elevation MI (STEMI) and related microvascular changes are needed.

CHINA TONGXINLUO STUDY FOR MYOCARDIAL PROTECTION IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION.

STEMI is caused by acute thrombotic occlusion of the coronary artery supplying the myocardium. The optimal treatment is coronary reperfusion therapy, including emergency percutaneous coronary intervention or thrombolytic therapy, to restore coronary blood flow and myocardial tissue reperfusion, salvage ischemic myocardium, and reduce infarct size, thereby lowering mortality and improving long-term prognosis.²⁸ However, even after successful coronary recanalization in patients with STEMI, patients often remain in a no-reflow state or poor distal targets.^{29,30}

Concurrently, advances in the understanding of coronary microvascular circulation have shed light on its crucial role in mitigating the adverse effects of myocardial no-reflow and reperfusion injury in STEMI patients.^{31,32} With series of bench studies and clinical exploration extended from this aspect, the efficacy of TXL was further validated in a multicenter clinical trial involving patients with STEMI undergoing primary revascularization. The ENLEAT (no-reflow protection and long-term efficacy for acute myocardial infarction with Tongxinluo: a randomized double-blind placebo-controlled multicenter clinical trial) study showed that TXL significantly improved ST-segment resolution on electrocardiography, reduced myocardial no-reflow, and enhanced myocardial microcirculation blood flow perfusion.³³ TXL significantly enhanced myocardial microvascular perfusion in these patients, indicating its potential clinical relevance in improving outcomes after MI. Moreover, TXL contributed to the preservation of endothelial structure and function in ischemia-reperfusion myocardial microvessels, ultimately leading to reduced apoptosis, improved barrier function, and decreased infarct size. In vitro experiments showed its ability to reduce endothelial cell apoptosis through the induction of autophagy. In addition, TXL exhibited protective effects on cardiomyocytes against hypoxia/reoxygenation injury and myocardial ischemic/reperfusion injury in animal models. Overall, the integration of TXL therapy represents a promising approach in the management of MI and its associated complications.³⁴⁻³⁸ These findings provide valuable insights into potential therapeutic strategies aimed at improving outcomes and reducing morbidity in patients with MI.

In the CTS-AMI (China Tongxinluo Study for Myocardial Protection in Patients With Acute Myocardial Infarction; [NCT03792035](#)) study, the impact of using TXL was evaluated in 3,797 patients with AMI and treated with the guideline-directed medications such as coronary reperfusion and dual antiplatelet treatment. A total of 124 institutions, including Fuwai Hospital of the Chinese Academy of Medical Sciences, jointly completed this randomized, double-blind, placebo-controlled, multicenter clinical study. The primary endpoint was the occurrence of major adverse composite cardiovascular events (MACCEs [cardiovascular death, recurrent infarction, urgent coronary revascularization, and stroke]).³⁹ Results showed that the 1-month MACCEs were reported among 64 recipients of TXL (3.4%) vs 99 placebo recipients (5.2%) (relative risk: 0.6; risk difference: -1.8%). In addition, individual MACCE components, including 1-month cardiovascular

mortality (56 vs 80; relative risk: 0.7; risk difference: 1.2%), were significantly lower among the TXL group compared with the placebo group.⁴⁰

This study published in *JAMA* represents a significant breakthrough in the treatment of AMI over the past decade.⁴⁰ In addition, the findings suggest the potential role of traditional medicine with TXL in the treatment of AMI and provide a basis for further exploration of its underlying mechanisms.

SHENSONGYANGXIN CAPSULE REGULATES PERSISTENT ATRIAL FIBRILLATION AFTER RADIOFREQUENCY CATHETER ABLATION. AF is the most common arrhythmia, significantly affecting patients' quality of life and prognosis. Catheter ablation is considered the preferred treatment for rhythm control and is significantly superior to antiarrhythmic drugs. However, the high recurrence rate after catheter ablation affects patients' postoperative quality of life.⁴¹ Although the SARA (Study of Ablation Versus Antiarrhythmic Drugs in Persistent Atrial Fibrillation) study revealed that catheter ablation was superior to medical therapy for the maintenance of sinus rhythm in patients with persistent AF at 12-month follow-up, there were a high recurrence rate of 39.8% postablation.⁴² There are no effective drugs internationally available to reduce the recurrence of persistent AF after radiofrequency ablation.

SSYX are known in TCM for their heart-calming and blood-nourishing properties. This formulation addresses arrhythmias by stabilizing heart rhythm and enhancing myocardial perfusion. They can regulate atrial structural remodeling, electrical remodeling and autonomic nervous function, and reduce the susceptibility to AF. Further bench research has shown that SSYX can reduce L type calcium-channel currents and transient outward potassium currents. These findings collectively suggest a complex modulation of cardiac ion channels by SSYX, which may contribute to their electrophysiological effects. Simultaneously, studies have shown that SSYX protect myocardial microvascular endothelial cells and initiate myocardial protective effects by activating Akt signaling pathways.⁴³⁻⁴⁸ Previous evidence-based research has also shown that SSYX have similar efficacy to propafenone in treating paroxysmal AF and can improve ventricular rate.⁴⁹

To explore whether the long-term use of SSYX after catheter ablation for persistent AF can effectively and safely reduce the recurrence of AF, the SS-AFRF (Shensongyangxin Capsule Regulates Persistent Atrial Fibrillation After Radiofrequency Catheter Ablation; [ChiCTR1900026912](#)) study was conducted; it included 920 patients with post-radiofrequency ablation persistent AF. The primary endpoint of the

trial was the recurrence of AF following a blanking period of 3 months within 1-year postablation.⁵⁰ The results showed that SSYX significantly reduced the risk of AF recurrence by 40.4% within 1-year postablation, decreased AF burden at 3 and 6 months' postablation, delayed the occurrence of first atrial flutter/AF events postablation by 24.8 days, significantly improved health-related quality of life, and exhibited good profile of safety.

Results suggest that SSYX could reduce the risk of AF recurrence post-radiofrequency ablation, providing evidence-based support for addressing the clinical challenge of AF recurrence postablation and offering potential optimization strategies for current post-AF ablation drug therapy.

QILIQIANGXIN IN HEART FAILURE: ASSESSMENT OF REDUCTION IN MORTALITY. Chronic heart failure represents the final stage and nexus of various CVDs, with a standardized prevalence rate of 1.1% in China and an incidence rate of 275 per 100,000 person-years. This imposes a significant public health burden, posing a severe threat to human life and quality of life.^{51,52} Despite the advancements in heart failure management and the implementation of guideline-directed medical therapy, some limitations and challenges remain that need to be addressed to further optimize management strategies and improve patient outcomes.⁵³

QLQX are a commercially available TCM formulation comprising 11 different plant ingredients, containing active compounds such as astragaloside IV, tanshinone IIA, ginsenosides (Rb1, Rg1, and Re), and periplocymarin. From the perspective of TCM, heart failure is often associated with Qi and Yang deficiency, leading to water retention and blood stasis. QLQX focuses on tonifying Qi, invigorating Yang, and promoting blood circulation. Previous studies have shown that QLQX exert cardioprotective effects by preserving microvasculature, improving myocardial energy metabolism, inhibiting myocardial inflammatory responses and fibroblast-to-myofibroblast transition, and attenuating ventricular remodeling via the modulation of peroxisome proliferator-activated receptor gamma and the coactivator-1 α signaling pathway in diverse experimental models of acute and congestive cardiac injury and stress.⁵⁴⁻⁵⁹ Previous clinical research involving 512 cases of chronic heart failure treated with QLQX or placebo for 12 weeks found that adjunctive therapy with QLQX significantly reduced serum N-terminal pro-B-type natriuretic peptide levels, improved quality of life, and reduced the absolute incidence of endpoint events when added to standard treatment.⁶⁰

To further assess long-term efficacy when using QLQX compared with placebo for patients with heart failure with reduced ejection fraction, the QUEST (Qiliqiangxin in Heart Failure: Assessment of Reduction in Mortality; ChiCTR1900021929) study was conducted. It was a randomized, double-blind, placebo-controlled, multicenter clinical trial involving 3,119 patients with heart failure with reduced ejection fraction (NYHA functional class II-IV, left ventricular ejection fraction \leq 40%, and N-terminal pro-B-type natriuretic peptide levels \geq 450 pg/mL). The primary endpoint was a MACCE of cardiovascular death and hospitalization of heart failure.⁶¹ During a median follow-up of 18 months, results showed that QLQX significantly reduced the risk of MACE by 22% compared with the placebo group. Specifically, the risk of CVD was reduced by 17%, and the risk of hospitalization for heart failure was reduced by 24%.⁶²

These results align with the philosophical concept of TCM balance modulation and the current understanding that the health of cardiomyocytes depends on achieving a balance between opposing neurohormonal systems and opposing signals of nutrient surplus and deprivation. QLQX may be viewed less as a multifaceted holistic medicine and more as a targeted pharmacologic tool capable of elucidating pathways relevant to the development and progression of heart failure. The research findings on QUEST have strengthened our understanding of the mechanisms underlying heart failure and its significant clinical implications.

DISCUSSION

Currently, there is a relative lack of information from evidence-based medicine regarding the use of TCM. Despite the accumulation of extensive clinical experience in TCM, these experiences are absent the rigorous scientific research needed to prove their efficacy. The majority of TCM treatment methods lack large-sample, randomized controlled clinical trials, thus hindering comprehensive scientific validation. Furthermore, they differ in theoretical foundations, diagnostic methods, and treatment modalities. The integration of the 2 concepts to achieve complementary advantages requires collaborative efforts and exchanges among medical professionals.

The theoretical bases of these formulas, rooted in TCM concepts such as Qi flow and Yin-Yang balance, provide a framework for understanding their mechanisms of action. Our systemic and rigorous clinical trial and bench studies showed the potential efficacy of the 4 TCM formulas across different stages of the cardiovascular continuum. JLD seem suitable for early

HIGHLIGHTS

- Integrating a traditional approach with modern cardiovascular medicine promises holistic care but needs more research and clinical trials.
- TCM formulas (JLD, TXL, SSYX, and QLQX) show efficacy in early metabolic disorders to advanced heart failure.
- The theoretical basis of TCM formulas in Qi and Yin-Yang aids understanding their cardiovascular disease mechanisms.
- TCM formulas offer adjunctive potential in cardiovascular care, warranting further study and standardization.

intervention, particularly in managing metabolic syndrome and diabetes-related cardiovascular risks, by improving glucose metabolism and reducing blood lipid levels. TXL show promise in intermediate stages, addressing atherosclerosis and myocardial ischemia, effective in preventing acute cardiovascular events. SSYX show applicability across various stages to stabilize heart rhythm and improve myocardial perfusion, particularly in managing arrhythmias. QLQX have emerged as a therapeutic option for heart failure, reducing the risk of severe adverse events.

The ability of these formulas to address different stages of the cardiovascular continuum suggests a complementary role to conventional treatments. However, the generalization of TCM in the treatment of CVD also faces certain obstacles, as some individuals harbor doubts and conservative attitudes toward TCM treatment for CVDs. Therefore, further research and exploration are needed to enhance our understanding and integrate the comprehensive management.

CONCLUSIONS

The translational research and clinical application of the TCM Luobing theory represent a promising

avenue in the treatment of CVDs. This comprehensive review of the literature and clinical trials offers unique insights into the pathogenesis and management of CVDs. By integrating ancient wisdom with modern scientific approaches, we have been able to elucidate their mechanisms of action and therapeutic potential. From preclinical studies to clinical trials, evidence continues to accumulate supporting the efficacy and safety of these interventions. Furthermore, the holistic nature of this traditional approach addresses not only the symptoms but also the underlying imbalances, providing a comprehensive framework for personalized patient management. As we advance in our understanding, it holds the promise of contributing significantly to the management of CVD, thereby improving patient outcomes and quality of life.

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