

Exploring the Complementary Role of Traditional Chinese Medicine in Enhancing Percutaneous Coronary Intervention Outcomes: Mechanisms, Benefits, and Future Research Directions

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Background: Percutaneous coronary intervention (PCI) is a cornerstone treatment for coronary artery disease (CAD), yet opportunities remain to improve clinical outcomes, symptom management, and long-term prognosis. Traditional Chinese Medicine (TCM), with its multi-target and multi-pathway mechanisms, offers a promising complementary approach to enhance PCI efficacy.

Methods: A systematic search was conducted in PubMed and Web of Science using the terms: (“Percutaneous Coronary Intervention” AND “Traditional Chinese Medicine”) and (“Percutaneous Coronary Intervention” AND “Chinese Herbal Drugs”). Randomized controlled trials (RCTs) with ≥ 100 participants were included to evaluate TCM's clinical efficacy in PCI. Pharmacological studies were also reviewed to explore underlying mechanisms.

Results: A review of 20 RCTs showed that TCM plays multiple roles in CAD treatment during PCI. Specific interventions such as Danhong Injection, Tongxinluo Capsule, and Shenzhu Guanxin Granule were found to alleviate angina symptoms, restore cardiac function, reduce cardiac biomarkers, prevent no-reflow/slow-flow phenomena, inhibit in-stent restenosis, and improve prognosis while reducing complications. Mechanistically, TCM exerts its effects through antiplatelet action, anti-inflammation, inhibition of smooth muscle proliferation, vasodilation, microcirculation improvement, and endothelial protection.

Conclusion: This systematic review highlights the complementary benefits of TCM in PCI for CAD patients. Effective interventions such as Danhong Injection and Tongxinluo Capsule contribute to symptom relief, cardiac function restoration, restenosis inhibition, and prognosis improvement. These benefits are linked to TCM's multi-target mechanisms, including anti-inflammatory and antiplatelet effects. Future high-quality studies are needed to further validate these findings and refine clinical applications.

Keywords: coronary artery disease, traditional Chinese medicine, percutaneous coronary intervention, randomized controlled trials, clinical efficacy, mechanisms of action

Introduction

Coronary artery disease (CAD) remains a leading cause of cardiovascular morbidity and mortality globally, significantly impacting public health.¹ It is characterized by the accumulation of atherosclerotic plaques in coronary arteries, reducing blood flow and increasing the risk of heart attacks.² The prevalence and mortality of cardiovascular diseases have been increasing over the past 30 years due to population growth and aging.³ CAD is a complex disease influenced by both environmental and genetic factors.⁴ In response to the growing prevalence of CAD, modern medicine has developed various interventions, including percutaneous coronary intervention (PCI), to alleviate symptoms and improve patient outcomes.⁵ PCI, which involves the insertion of a catheter to open blocked arteries, has proven effective in managing CAD;⁶ however, it does not address all aspects of the disease and can be accompanied by complications.

Traditional Chinese Medicine (TCM) offers a complementary approach to conventional treatments, with a long history of use in managing cardiovascular conditions.⁷ TCM encompasses a range of practices, including herbal medicine, acupuncture, and dietary recommendations, aimed at restoring balance and promoting overall well-being.⁸ Recent studies suggest that TCM may provide additional therapeutic benefits to CAD patients undergoing PCI by enhancing clinical outcomes and reducing adverse effects. Despite these promising findings, there has been a lack of comprehensive reviews synthesizing the role of TCM in this context.

This systematic review evaluates the clinical efficacy of TCM as an adjunctive therapy for CAD patients undergoing PCI. To bridge existing knowledge gaps, we conducted an extensive search of PubMed and Web of Science databases to identify relevant RCTs and pharmacological studies. The analysis includes diverse patient populations, such as elderly individuals, patients with diabetes, and those with acute coronary syndromes, covering varying CAD severity, including stable angina, unstable angina, and acute myocardial infarction. By examining TCM's role in symptom relief, cardiac function improvement, and potential mechanisms of action, this review clarifies how TCM can complement modern PCI treatments. Consolidating current evidence, it offers insights into the benefits of integrating TCM with conventional therapies and identifies areas for future research.

Percutaneous Coronary Intervention and Traditional Chinese Medicine in CAD

Treatment Strategies for CAD

CAD is a multifactorial condition primarily caused by the accumulation of atherosclerotic plaques within the coronary arteries, leading to reduced blood flow to the heart muscle and an increased risk of myocardial infarction. The management of CAD involves a combination of lifestyle modifications, pharmacological interventions, and, in more severe cases, revascularization procedures. The overarching goal of these strategies is to alleviate symptoms, improve quality of life, and reduce the risk of cardiovascular events.

Lifestyle Modifications: The cornerstone of CAD management begins with lifestyle modifications aimed at controlling risk factors such as hypertension, hyperlipidemia, diabetes, and smoking.⁹ Patients are encouraged to adopt a heart-healthy diet, engage in regular physical activity, and maintain a healthy weight. Additionally, stress management and cessation of tobacco use are critical components of lifestyle intervention.¹⁰ These measures not only help in slowing the progression of atherosclerosis but also enhance the effectiveness of other treatment modalities.

Pharmacological Interventions: Pharmacotherapy plays a critical role in the management of CAD, with several classes of drugs employed to address the underlying pathophysiology. Antiplatelet agents, such as aspirin and P2Y12 inhibitors, are routinely prescribed to prevent thrombus formation and reduce the risk of acute coronary events.¹¹ Statins are widely used to lower low-density lipoprotein (LDL) cholesterol levels and stabilize atherosclerotic plaques.¹² Additionally, angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and calcium channel blockers are used to manage blood pressure, reduce myocardial oxygen demand, and prevent adverse cardiac remodeling.¹³ In patients with significant ischemic symptoms, anti-anginal medications such as nitrates, ranolazine, and ivabradine may be prescribed to alleviate chest pain and improve exercise tolerance.¹⁴

Revascularization Procedures: For patients with severe CAD, especially those with significant stenosis or multiple vessel involvement, revascularization procedures are often necessary to restore adequate blood flow to the heart. PCI and coronary artery bypass grafting (CABG) are the primary revascularization strategies.¹⁵ PCI involves the use of balloon angioplasty and stent placement to open narrowed arteries, while CABG involves surgically creating a bypass around blocked arteries using grafts from other vessels.¹⁶ The choice between PCI and CABG depends on the extent of coronary disease, patient comorbidities, and anatomical considerations.

Integrative Approaches: In recent years, there has been growing interest in integrative approaches that combine conventional treatment strategies with complementary therapies, such as TCM. TCM offers a holistic approach to managing CAD by addressing not only the physical symptoms but also the underlying imbalances in the body's systems. Herbal formulations, acupuncture, and lifestyle recommendations based on TCM principles are increasingly being

studied for their potential to enhance the efficacy of conventional therapies, reduce adverse effects, and improve overall patient outcomes.

In summary, the treatment of CAD requires a multifaceted approach that integrates lifestyle changes, pharmacotherapy, and, when necessary, revascularization procedures. As the understanding of CAD continues to evolve, there is increasing recognition of the potential benefits of combining modern medicine with complementary approaches like TCM to optimize treatment outcomes and improve the quality of life for patients.

Roles of PCI in CAD

PCI has become a cornerstone in the management of CAD, offering a minimally invasive alternative to surgical revascularization. PCI encompasses a range of procedures designed to restore adequate blood flow to the heart muscle by addressing obstructed coronary arteries. The roles and benefits of PCI in CAD are multifaceted, addressing both acute and chronic aspects of the disease.

Acute Coronary Syndrome Management

In patients presenting with acute coronary syndrome (ACS), including unstable angina and myocardial infarction, PCI plays a critical role in rapidly restoring coronary blood flow. The primary goal of PCI in ACS is to alleviate ischemia and prevent myocardial damage. By performing angioplasty and deploying stents, PCI helps to reduce the size of the infarct, minimize cardiac muscle damage, and improve survival rates. The timely intervention of PCI in the setting of an acute myocardial infarction (MI) can significantly enhance patient outcomes by reducing mortality and morbidity associated with the event.¹⁷

Symptom Relief and Improved Quality of Life

For patients with chronic stable angina, PCI offers significant symptomatic relief by improving coronary blood flow and reducing the frequency and severity of anginal episodes.¹⁸ By alleviating the obstruction in coronary arteries, PCI can enhance exercise tolerance, reduce chest pain, and improve overall quality of life. The procedure helps to address the limitations imposed by CAD on daily activities and work performance, allowing patients to return to their normal routines with fewer restrictions.

Long-Term Benefits and Prognostic Impact

PCI not only provides immediate symptomatic relief but also offers long-term benefits in terms of prognosis. The deployment of drug-eluting stents (DES) has further enhanced the long-term efficacy of PCI by reducing the risk of in-stent restenosis and the need for repeat revascularization.¹⁹ PCI has been shown to improve long-term survival and reduce the incidence of major adverse cardiovascular events (MACE) in patients with significant coronary artery disease.²⁰ Moreover, recent advancements in PCI technology, such as improved stent designs and pharmacological coatings, have contributed to better clinical outcomes and lower complication rates.²¹

Integrating PCI with Medical Therapy

PCI is often used in conjunction with medical therapies to achieve optimal outcomes in CAD management. The combination of PCI with antiplatelet therapy, statins, and other cardiovascular medications enhances the effectiveness of the intervention and reduces the risk of adverse events.²² In patients with complex CAD or multiple vessel involvement, PCI may be combined with medical management to address residual risk factors and achieve comprehensive treatment goals.

Challenges and Considerations

Despite its advantages, PCI is not without limitations and potential complications. Issues such as restenosis, stent thrombosis, and the need for dual antiplatelet therapy pose challenges that must be carefully managed.²³ Additionally, PCI may not be suitable for all patients, particularly those with advanced coronary disease or significant comorbidities.²⁴ In such cases, alternative or adjunctive therapies, including CABG and complementary approaches like TCM, may be considered to address the complex needs of CAD patients.

In summary, PCI plays a pivotal role in the management of CAD by providing effective treatment for both acute and chronic coronary conditions. Its ability to restore coronary blood flow, alleviate symptoms, and improve long-term prognosis makes it a valuable tool in the cardiology arsenal. Continued advancements in PCI technology and technique, coupled with an integrative approach that includes complementary therapies, hold promise for further enhancing patient outcomes and addressing the evolving needs of CAD management.

Adjunctive Therapy of Traditional Chinese Medicine in CAD

Recent studies highlight the growing importance of TCM in treating CAD. A cross-sectional study found that 69.1% of CAD patients in Beijing used complementary and alternative medicine (CAM), with patent herbal medicine being the most common.²⁵ A systematic review and meta-analysis revealed that Chinese herbal medicine (CHM) as an adjunctive therapy for CAD patients undergoing PCI significantly reduced major adverse cardiovascular events and improved various clinical outcomes.²⁶ Another study of 5284 CAD patients in China showed that integrative medicine (IM) therapy, combining TCM and conventional medicine, was a protective factor against adverse events.²⁷ Additionally, a meta-analysis of 24 randomized controlled trials demonstrated that acupuncture as an adjunctive treatment significantly increased the markedly effective rate in CAD patients with angina.²⁸ These findings suggest TCM's potential benefits in CAD management.

Roles and Mechanisms of TCM in PCI: Evidence in the Past Decade

Search for Literature

We conducted a search in the PubMed database using the following queries: 1. (“Percutaneous Coronary Intervention” [Mesh]) AND “Medicine, Chinese Traditional” [Mesh] and 2. (“Percutaneous Coronary Intervention” [Mesh]) AND “Drugs, Chinese Herbal” [Mesh]. Additionally, we searched the Web of Science database with the queries: 1. (TS= (Percutaneous Coronary Intervention)) AND TS= (Traditional Chinese Medicine) and 2. (TS= (Percutaneous Coronary Intervention)) AND TS= (Chinese Herbal). The search results from both databases over the past decade were pooled, and duplicates were removed. RCTs with a sample size of at least 100 individuals were included to evaluate the clinical efficacy of TCM on PCI. Meanwhile, all pharmacological studies were included to explore the mechanisms of action (Figure 1).

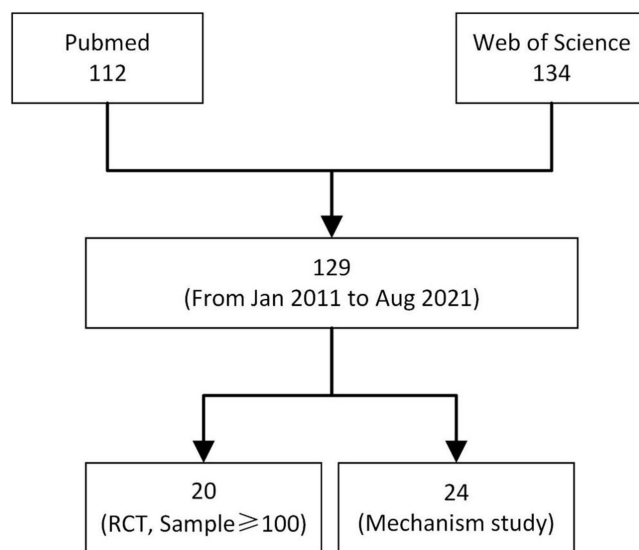


Figure 1 Literature search process and results.

Clinical Evidences

Alimenting Symptoms

A RCT demonstrated that adding Shenzhu Guanxin Granule—comprising Radix Ginseng, Rhizoma Atractylodis, Radix Notoginseng, Rhizoma Pinelliae, Hirudo, Radix Panacis quinquefolium, and Folium Nelumbinis, a formulation derived from the expertise of Prof. DENG Tie-tao, a renowned master of Chinese medicine—to GDMT could alleviate angina symptoms after PCI without increasing the risk of coronary events.²⁹ Another study found that administering Shuangshen Tongguan Capsule, which includes Salvia miltiorrhiza Bunge, Radix Ginseng, Rhodiola Crenulatae Radix et Rhizoma, Radix Notoginseng, and Lignum Dalbergiae Odoriferae, alongside GDMT for six months in patients with ST-Elevation Myocardial Infarction (STEMI) post-PCI led to notable improvements in TCM symptoms, cardiac function, and Seattle Angina Scale scores, suggesting enhanced clinical outcomes and quality of life.³⁰

Restoring Cardiac Functions and Biomarkers Level

Compared with GDMT alone, treatment with GDMT and Danhong Injection (derived from Salvia miltiorrhiza Bunge and Carthamus tinctorius L.) for one week during the perioperative period reduced cardiac troponin (cTn) T and creatine kinase-MB (CK-MB) levels, while also improving ventricular wall motion strain and strain rate after PCI.³¹ Another study demonstrated that using Danhong Injection for two weeks in combination with Naioxintong Tablet (a three-month treatment), a fine powder mixture containing Astragali Radix, Paeoniae Radix Rubra, Salviae Miltiorrhizae Radix Bunge, Persicae Semen, Angelicae Sinensis Radix, Achyranthis Bidentatae Radix, Chuanxiong Rhizoma, Spatholobi Stem, Cinnamomi Ranulus, Carthami Flos, Mori Ramulus, Olibanum, Myrrha Scorpio, Pheretima, and Hirudo, postoperatively alongside GDMT, improved cardiac function and reduced serum sCD40L levels in acute coronary syndrome (ACS) patients undergoing PCI after three months.³² Similarly, when compared with the control group, treatment with Fangshuan Capsule (containing Salvia miltiorrhiza Bunge, Radix Ginseng, Rhodiola Crenulatae Radix et Rhizoma, Radix Notoginseng, and Lignum Dalbergiae Odoriferae) for two weeks alongside GDMT improved cTnI, CK-MB, and myoglobin expression levels within 24 hours post-PCI, indicating that this treatment could reduce myocardial injury in patients with unstable angina (UA) undergoing PCI.³³ Another trial revealed that treatment with Xinyue Capsule (containing Panax quinquefolius saponin extracted from the leaves and stems of Panax quinquefolium L.) and Fufang Chuanxiong Capsule (containing Angelica Sinensis Radix and Chuanxiong Rhizome) significantly improved N-terminal pro b-type natriuretic peptide and high-sensitivity C-reactive protein (hs-CRP) levels at six months and one year after PCI in ACS patients, while also restoring heart function and reducing the incidence of major adverse cardiac events (MACEs).³⁴

Preventing No Recurrent Flow/Slow Blood Flow

A report indicated that administering Compound Danshen Dripping Pills (comprising Radix Salviae Miltiorrhizae, Radix Notoginseng, and Borneol) within one year before surgery significantly reduced the incidence of no-reflow during direct PCI compared to the control group (13.2% vs 26.3%).³⁵ Although a meta-analysis has suggested that combining GDMT with herbal interventions may lower the incidence of no-reflow and slow flow post-PCI and improve clinical outcomes, further evaluation through additional RCTs is required due to the small sample sizes and unclear baseline conditions of the included trials.^{36,37}

Reducing Complications

Intravenous hydration is believed to reduce the risk of contrast-induced nephropathy (CIN) and may also show a trend toward reducing all-cause mortality.³⁸ Additionally, TCMs have been reported to prevent CIN. An analysis of 846 patients who received contrast agents revealed that Danhong Injection could reduce the incidence of contrast-induced acute kidney injury (2.4% vs 5.7%).³⁹ Prophylactic treatment with Cordyceps Sinensis (Chinese caterpillar fungus) has shown a preventive effect against CIN in ACS patients undergoing elective PCI.⁴⁰ A report focusing on the prevention and treatment of CIN after PCI indicated that the TCM drugs currently studied primarily focus on blood-activating and stasis-transforming properties. These mechanisms are mainly attributed to their ability to dilate arterial blood vessels, improve microcirculation, provide anti-coagulation and antioxidant effects, and protect vascular endothelial cells.⁴¹ However, the precise mechanisms of action remain unclear, necessitating further urgent studies.

Another study revealed that the incidence of Qi deficiency and blood stasis syndrome in TCM symptoms was closely associated with post-PCI bleeding.⁴² The same research team found that the Supplementing Qi and Hemostasis Formula (comprising Astragalus, Radix Pseudostellariae, charred Radix Et Rhizoma Rhei, Rhizoma Bletillae, Cuttlebone, and Pseudoginseng) was comparable to Pantoprazole Sodium Enteric-Coated Capsules in terms of hemostasis and gastric mucosal protection in patients with CAD undergoing PCI, with superior effects in improving TCM syndrome manifestations.⁴³ Despite the low level of evidence, an analysis of 16 RCTs involving a total of 1443 patients found that TCMs showed a potentially beneficial effect on depressive symptoms and related clinical outcomes after PCI.⁴⁴

Inhibiting In-Stent Restenosis

The addition of Xiongshao Capsule (a formulation of Rhizoma Ligusticum Wallichii and Radix Paeoniae Rubra, derived from the traditional Xuefu Zhuyu Decoction as modified by Academician Chen Keji) to GDMT in elderly patients with CAD undergoing PCI significantly improved the minimum lumen diameter of coronary vessels (2.15 ± 0.84 mm vs 1.73 ± 0.91 mm) and showed a tendency to reduce in-stent restenosis one year post-surgery (24.32% vs 38.71%).⁴⁵ Additionally, a small-sample meta-analysis indicated that supplementing GDMT with Xiongshao Capsule and other TCM treatments reduces the incidence of in-stent restenosis following PCI.^{46,47}

Improve Prognosis

Xinyue Capsule combined with GDMT significantly reduces the incidence of the primary composite endpoint (cardiac death, nonfatal MI, and emergency revascularization) at 12 months post-procedure in patients with stable CAD undergoing PCI (3.02% vs 6.49%, $P=0.009$).⁴⁸ Furthermore, compared to GDMT alone, the addition of Xinyue Capsule and Fufang Chuanxiong Capsule further lowers the occurrence of cardiovascular events in patients with ACS undergoing PCI, with a reduction in the incidence of the primary endpoint (2.7% vs 6.2%, HR 0.43) and secondary endpoint (3.5% vs 8.7%, HR 0.39), without increasing the risk of major bleeding.⁴⁹ Subgroup analysis revealed that adding Compound Chuanxiong Capsule and Xinyue Capsule to GDMT for 6 months significantly reduces endpoint events at 12 months in ACS patients with mild to moderate renal insufficiency after PCI, decreasing the incidence of the primary endpoint (5.7% vs 10.86%) and the secondary endpoint (5.98% vs 10.28%) at 2 years.⁵⁰ Moreover, this combination gained an approximately 0.20% increase in survival probability as predicted by a decision-analytic Markov model^{51,52} and reduced the need for revascularization in Diabetes Mellitus patients with ACS.⁵³

Perioperative treatment with Sodium Tanshinone IIA Sulfonate, extracted from *Salvia miltiorrhiza* Bunge, further reduces the risk of major cardiovascular events at 30 days post-PCI in patients with non-ST segment elevation ACS, demonstrating a favorable safety profile.⁵⁴ Additionally, a 6-month treatment with Suxiao Jiuxin Pills (comprising Chuanxiong Rhizoma and borneol) in ACS patients post-PCI was associated with a significant reduction in 1-year MACEs ($p < 0.05$, odds ratio 1.916), alongside improvements in left ventricular ejection fraction (LVEF) and symptoms.⁵⁵

A meta-analysis involving 33,537 patients indicated that Qishen Yiqi Dripping Pill (containing Astragalus penduliflorus Lam, *Salvia miltiorrhiza* Bunge, *Panax pseudoginseng* Wall, and *Dalbergia odorifera* T.C. Chen) significantly reduces the occurrence of MACEs in PCI patients and improves prognosis.⁵⁶ Another meta-analysis showed that Tongxinluo Capsule (comprising Radix Ginseng, Scorpio, Hirudo, *Eupolyphaga seu Steleophaga*, Scolopendra, *Periostracum Cicadae*, Radix Paeoniae Rubra, and *Borneolum Syntheticum*) reduces the incidence of MI (RR 0.32), heart failure (RR 0.26), and revascularization (RR 0.26), while also improving all-cause mortality (RR 0.38) and death due to any cardiovascular event (RR 0.31) post-PCI.⁵⁷ However, it should be noted that only a few studies in these meta-analyses had sample sizes exceeding 100 individuals, and none were included in the databases searched for this paper, indicating a potential weakness in the evidence level.

RCTs in Progress

Several ongoing RCTs are currently investigating the adjunctive effects of TCM in patients undergoing PCI. Among them, one RCT is evaluating the effectiveness and safety of the Yiqi Liangxue Shengji prescription in patients with acute MI post-PCI.⁵⁸ Another trial is assessing the efficacy and safety of Danhong Injection in preventing microvascular obstruction in patients with ST-segment elevation myocardial infarction (STEMI) after PCI.⁵⁹ Additionally, a study has

been designed to determine whether Tongguan Capsule can reduce restenosis in patients following stent implantation,⁶⁰ while another trial focuses on the effectiveness of Tongxinluo in reducing clinical endpoints in STEMI patients after PCI.⁶¹

One of the largest investigations into TCM's role in PCI, the China Tongxinluo Study for Acute Myocardial Infarction (CTS-AMI), was a large-scale, randomized, double-blind, placebo-controlled trial examining the efficacy of Tongxinluo in STEMI patients.⁶¹ The study enrolled 3777 patients from 124 hospitals across China, comparing Tongxinluo to a placebo alongside standard STEMI treatments. Results demonstrated that Tongxinluo significantly reduced the 30-day and 1-year rates of major adverse cardiac and cerebrovascular events (MACCEs) compared to placebo. These findings aligned with those from smaller studies, including one that reported improved cardiac function and reduced adverse events in post-PCI STEMI patients treated with Tongxinluo.⁶² We have summarized the current clinical evidence available (Table 1) and anticipate that these ongoing RCTs will provide more high-quality evidence to further evaluate the role of TCM in PCI.

Table 1 Adjunctive Effect of Traditional Chinese Medicine in Patients Undergoing Percutaneous Coronary Intervention: the Clinical Evidences

Drugs	Time	Sample Size (Placebo: Treatment)	Classification of Disease	Duration of Treatment: Follow-Up	Outcomes
Xiongshao Capsule	2002.6–2003.12	335 (169: 166)	CHD undergoing PCI	6m: 12m	Increased minimum lumen diameter
Danhong Injection	2007.1–2018.12	846 (423: 423)	Contrast-related including CAG or PCI	~7d: 10d	Reduced contrast induced acute kidney injury
	2011.3–2012.3	120 (60: 60)	UA undergoing PCI	Peri-procedural 7d: 24h after PCI	Decreased CK-MB and cTnT, improved systolic function
Fufang Chuanxiong Capsule and Xinyue Capsule	2008.4–2009.10	808 (404: 404)	ACS undergoing PCI	6m: 12m	Reduced MACEs, gained 0.20% survival probability
	2008.4–2009.10	702 (351: 351)		6m: 24m	Reduced MACE
	2008.7–2008.12	100 (50: 50)		6m: 12m	Improved heart functions, decreased MACEs (12m)
	2008.5–2009.6	504 (245: 259)		6m: 40 Markov cycles	Improved the long-term clinical effectiveness in UA after PCI
	2008.4–2009.10	281 (145: 136)		6m: 12m	Reduced the event of revascularization and recurrent angina of ACS patients complicated with DM after PCI (12m)
	2008.4–2009.10	426 (215: 211)		6m: 12m	Deferred decline of renal function, improved clinical outcomes
Shuangshen Tongguan Capsule	2008.11–2010.11	137 (62: 67)	STEMI undergoing PCI	6m: 6m	Improved angina symptoms and heart functions in patients with CM syndrome of qi-deficiency and blood stasis
Shenzhu Guanxin Granule	2009.1–2011.1	187 (74: 113)	Non-emergent PCI	3m: 12m	Reduced angina pectoris attacks in patients with CM syndrome of qi-deficiency, turbid phlegm and blood stasis
Danhong Injection and Naoxintong Tablet	2009.2–2009.8	100 (50: 50)	ACS undergoing PCI	(Danhong Injection 2w, Naoxintong Tablets 3m): 3m	Decreased serum scd40l level and improved cardiac functions
Compound Danshen Dripping Pill	2009.1–2012.3	399 (331: 68)	AMI undergoing primary PCI	12m: 12m	Reduced no-reflow phenomenon in nondiabetes mellitus patients
Fangshuan Capsule	2010.6–2012.12	100 (50: 50)	UA undergoing PCI	2w: 12h after PCI	Improved CM syndrome and attenuated myocardial damage
Cordyceps Sinensis	2012.8–2014.7	150 (51: 99)	ACS undergoing elective PCI	6d: 6d	Dose-dependent reduced the incidence of CIN
Suxiao Jiuxin Pills	2013.3–2015.2	200 (100: 100)	ACS undergoing PCI	6m: 12m	Reduced MACEs, improved systolic function, and symptoms
Xinyue Capsule	2014.1–2016.7	1068 (534: 534)	SCAD undergoing PCI	24w: 12m	Reduced MACEs
Sodium Tanshinone IIA Sulfonate	2014.10–2016.4	372 (180: 192)	UA or NSTEMI	5d: 30d	Reduced myocardial injury and MACEs
Supplementing Qi And Hemostasis Formula	2017.5–2018.5	117 (58: 59)	CAD undergoing PCI	3m: 3m	Protecting gastrointestinal bleeding after PCI

Mechanisms Studies

Antiplatelet Effects

The addition of Tongxinluo Capsule to dual antiplatelet therapy with aspirin and clopidogrel significantly reduced the incidence of platelet hyperactivity within 30 days in ACS patients post-PCI compared to dual antiplatelet therapy alone (15.8% vs 24.8%).⁶³ Another study further supported these findings, demonstrating that adding Tongxinluo Capsule for 3 months, compared to conventional dual antiplatelet therapy, enhanced platelet inhibition and lowered the incidence of ischemic events at 1-year follow-up in CAD patients undergoing PCI.⁶⁴ Notably, the incidence of mild bleeding events was significantly lower in the Tongxinluo group compared to the group treated with aspirin and ticagrelor. The study also suggested that Tongxinluo Capsule achieved its maximum platelet inhibition effect at 3 months, which is later than ticagrelor, which reached its peak at 1 month.

In addition to Tongxinluo Capsule, other TCM drugs have demonstrated significant antiplatelet effects. For example, in ACS patients, the rate of ADP-induced platelet aggregation was significantly elevated 12 hours after PCI, but this was significantly improved after 30 days of treatment with Maixuekang Capsule.⁶⁵ This treatment also resulted in a significant reduction in the incidence of major adverse cardiovascular events (MACEs) at 12 months follow-up (6.9% vs 12.5%, $p < 0.01$). We hypothesize that the improved prognosis in ACS patients post-PCI attributed to Maixuekang Capsule may be related to its ability to inhibit platelet aggregation.

Similarly, evidence suggests that the addition of Bunchang Naoxintong Capsule for at least 3 months enhanced the antiplatelet effect of dual therapy with aspirin and clopidogrel and reduced the 1-year incidence of MACEs in CAD patients undergoing PCI who have the CYP2C19*2 polymorphism.⁶⁶ Furthermore, a 1-month treatment with Xuefu Zhuyu Decoction, which includes ingredients such as Semen Persicae and Flos Carthami, has been shown to overcome clopidogrel resistance, potentially through mechanisms related to rs2046934 polymorphism and its methylation.⁶⁷

Anti-Inflammation Effects

The addition of Salvia to GDMT was shown to further reduce plasma asymmetric dimethylarginine (ADMA) levels in patients with non-STEMI undergoing PCI. This reduction may represent a potential mechanism for improving MACEs and mortality in these patients.⁶⁸ Similarly, studies have demonstrated that Danhong Injection, when added to GDMT, significantly decreased plasma soluble P-selectin and high-sensitivity C-reactive protein (hs-CRP) levels in ACS patients undergoing PCI, indicating its potential to suppress inflammatory responses.⁶⁹

Other TCM formulations have also exhibited regulatory effects on hs-CRP. For instance, hs-CRP levels were significantly elevated in ACS patients 12 hours post-PCI. However, after 30 days of treatment with Maixuekang Capsule (Hirudin), hs-CRP levels were markedly lower, and the incidence of 12-month MACEs was significantly reduced. These findings suggest that the drug may exert vasoprotective effects, at least in part, by inhibiting inflammation. Further supporting this, postoperative treatment with Xuezhikang for 8 weeks, in addition to GDMT, reduced serum hs-CRP, MMP-9, and LDL-C levels in CAD patients who underwent elective PCI. Notably, the effect was more pronounced at higher doses, suggesting a dose-dependent relationship between the reduction in inflammatory factors and lipid-lowering efficacy.⁷⁰

In addition to hs-CRP, other inflammatory biomarkers have been shown to be regulated by TCM. In patients with STEMI complicated by cardiogenic shock (CS), Shenfu Injection (a combination of Panax ginseng C.A. Mey and Aconitum Carmichaelii Debeaux) combined with intra-aortic balloon pump (IABP) significantly shortened IABP support times compared to IABP alone (52.87 ± 28.84 vs 87.45 ± 87.31 , $p = 0.047$). Moreover, Shenfu Injection significantly reversed the CRP peak and reduced levels of tumor necrosis factor- α (TNF- α) and interleukin-1 (IL-1), indicating its ability to suppress inflammatory reactions in AMI patients undergoing IABP and emergency PCI, thereby shortening the course of treatment.⁷¹

Further evidence highlights the anti-inflammatory potential of TCM compounds. Adjunct therapy with Berberine, an active compound of *Coptis chinensis* Franch, has been shown to improve clinical outcomes by ameliorating circulating levels of MMP-9, ICAM-1, and VCAM-1 in ACS patients following PCI.⁷² Additionally, experimental studies in animal models have demonstrated that a detoxification and blood circulation-activating decoction containing Honeysuckle,

Radix Scrophularia, Radix Angelicae Sinensis, liquorice, Salvia Miltiorrhiza, and Panax Notoginseng reduced restenosis through the TLR4/NF- κ B pathway by suppressing pro-inflammatory cytokines after balloon injury.⁷³

Inhibiting Smooth Muscle Proliferation

Studies have shown that Panaxquin quefolium diolsaponins reduce Ang II-stimulated vascular smooth muscle cell (VSMC) proliferation by suppressing the expression of proto-oncogenes. This finding provides valuable insights for the development of innovative TCM approaches to prevent restenosis following PCI.⁷⁴ Another TCM-derived drug, Hydroxysafflor yellow A (the active ingredient of Carthami Flos), has demonstrated the ability to inhibit VSMC proliferation and migration. This effect is mediated, in part, by suppressing the activation of Akt signaling induced by platelet-derived growth factor-BB.⁷⁵ As a result, this agent shows promise for the prevention and treatment of cardiovascular diseases, including coronary atherosclerosis and restenosis post-PCI. Additionally, Magnolol, extracted from *Magnolia Officinalis*, has been found to reduce the risk of restenosis and vascular remodeling after PCI. This is likely achieved by inhibiting thrombin-induced connective tissue growth factor expression in VSMC through the protease-activated receptor-1/JNK-1/activator protein-1 signaling pathway.⁷⁶

Vasodilating

Early studies have demonstrated that the addition of Danhong Injection to GDMT for 2 weeks significantly reduces plasma endothelin-1 (ET-1) levels in ACS patients following PCI, suggesting a vasodilating effect as part of its pharmacological actions.⁷⁷ This vasodilatory effect was further supported by subsequent research, which found that treatment with Danhong Injection combined with Naoxintong capsules led to lower levels of endothelin-1 and von Willebrand factor, along with higher nitric oxide levels, compared to GDMT alone in ACS patients after PCI. Additionally, Shuangshen Tongguan Capsule, which contains *Salvia Miltiorrhiza Bunge*, *Radix Ginseng*, *Rhodiola Crenulatae Radix Et Rhizoma*, *Radix Notoginseng*, and *Lignum Dalbergiae Odoriferae*, was shown to regulate ET-1 levels in unstable angina (UA) patients 24 hours after PCI. This indicates that the drug may support blood supply to the ischemic heart by dilating coronary arteries.

Moreover, the vasodilatory effects of TCM may involve other signaling pathways. For instance, Tongmai Yangxin Pill, which includes *Rehmanniae Radix*, *Spatholobi Caulis*, *Ophiopogonis Radix*, *Polygoni Multiflori Radix Praeparata*, *Asini Corii Colla*, *Glycyrrhizae Radix et Rhizoma*, *Schisandrae chinensis Fructus*, and *Codonopsis Radix*, has been shown to reduce the myocardial no-reflow phenomenon through endothelium-dependent nitric oxide-cyclic guanosine monophosphate signaling. This is achieved by activating the cyclic adenosine monophosphate/protein kinase A pathway in adult male SD rat models, resulting in reduced ischemic areas, improved LVEF, and ultimately providing a protective effect for the ischemic heart.⁷⁸

Improving Microcirculation

For patients undergoing elective PCI, the administration of Qishen Yiqi Dripping Pills within one week preoperatively and one month postoperatively, in addition to GDMT, has been demonstrated to reduce myocardial injury and protect microvascular function. This effect is evidenced by a decrease in postoperative cTnI levels and the index of microcirculatory resistance.⁷⁹ Similar benefits have been observed with other TCM treatments. For instance, a one-week intravenous administration of Danhong Injection (40 mL twice daily) has been shown to effectively improve coronary microcirculation injury post-PCI, with an efficacy comparable to that of statins.⁸⁰ Additionally, Anxin granules, which contain *Ginseng Radix et Rhizoma*, *Cinnamomi Ramulus*, *Trichosanthis Pericarpium*, *Hirudo*, and *Poria*, when combined with tirofiban, have been found to enhance cardiac function by improving coronary microcirculation in AMI patients after PCI.⁸¹

Protecting the Endothelium

Research has demonstrated that a continuous infusion of Danhong Injection over a period of 3–4 days can elevate endothelial progenitor cells (EPCs) to a stable level in peripheral blood for one day. This suggests that the drug can effectively mitigate PCI-mediated endothelial injury and enhance endothelium repair by boosting the mobilization of EPCs.⁸² Further analysis identified lithospermic acid and salvianolic acid D as the primary active components in Danhong Injection. Similarly, another traditional Chinese medicine, Tongguan Capsule (comprising *Radix Astragali*, *Radix Salviae Miltiorrhizae*, *Hirudo*, and *Borneolum*),

exhibited comparable effects on EPCs.⁸³ The study indicated that the number of EPCs in peripheral blood could be increased by taking Tongguan Capsule for one month in CAD patients undergoing PCI, leading to a significant improvement in LVEF after three months of treatment. Previously mentioned, Shenzhu Guanxin Granule was known to alleviate angina symptoms, though the underlying mechanism was unclear. Subsequent research by the same team revealed that the drug dose-dependently improves cardiac hemodynamic function and reduces infarct size by promoting angiogenesis, which is facilitated through the upregulation of platelet endothelial cell adhesion molecule-1/CD31 and vascular endothelial growth factor expressions.⁸⁴

Perspectives and Suggestions

Potential Advantages of TCM for the Adjunctive Treatment of PCI

TCM has a history of clinical practice spanning thousands of years in China and continues to be used today. Primarily derived from natural sources such as plants, animals, and minerals—with plants being the most common—TCM is widely regarded for its accessibility, effectiveness, and cost-efficiency. These characteristics have ensured its widespread use and preservation over centuries. In contemporary practice, clinical experts in TCM have curated a selection of representative medicines from this vast repository, tailored to address modern diseases. These medicines have been reformulated into modern preparations and are prescribed after thorough clinical validation and mechanistic studies. Such new formulations are now extensively used in China and are gradually being introduced to the international market to benefit patients globally. For instance, Xinyue Capsules and Shenzhu Guanxin Granules, both modified forms of patented TCM, have been proven effective in treating CAD, including in patients undergoing PCI. These medicines work through multi-component, multi-target mechanisms and are widely utilized across China.⁸⁵ Additionally, a study involving 1094 AMI patients across 26 tertiary hospitals demonstrated that 86.47% of patients used TCM intravenous preparations, and 52.56% used TCM decoctions, highlighting the widespread use of TCM in clinical settings.⁸⁶

The treatment approach of TCM is characterized by its holistic regulatory effects. Through a diverse array of active ingredients, TCM exerts multi-target and multi-pathway regulation, offering a network-based, three-dimensional intervention. This approach not only focuses on treating the disease but also emphasizes protecting the normal functions of the body. Additionally, TCM treatments are often individualized, tailored to the specific symptoms and characteristics of each patient. This customization may involve adjusting the types of medicines, dosages, and preparation methods, which reflects the principle of personalized treatment. For example, Danhong Injection has been shown to be an effective supplement to GDMT in PCI, working through multiple targets and downstream signaling pathways. This contributes to various beneficial effects, such as improving vascular endothelial function, suppressing inflammation, preventing platelet coagulation, and promoting antioxidation.⁸⁷

Moreover, TCM often combines multiple drugs based on its unique theoretical framework, resulting in synergistic effects that can enhance efficacy and reduce toxicity. These combinations may also address secondary diseases or conditions, thereby improving overall therapeutic outcomes. For instance, a study found that Guanxinning Tablet, which contains Danshen and Chuanxiong, combined with aspirin did not increase the incidence of bleeding events compared to aspirin alone after one year of dual-antiplatelet therapy in patients with CAD undergoing PCI who also had heart-blood stasis syndrome as per TCM diagnosis.⁸⁸

Problems in Current Research and Suggestions

The current body of research on TCM combined with PCI is plagued by a scarcity of high-quality evidence, with few studies meeting the most rigorous standards. Many studies are limited by small sample sizes, often involving fewer than 100 cases, and only a few surpassing 1000 cases (Table 1). This issue, coupled with insufficient understanding of clinical research methodologies and statistical analysis, has led to a dearth of robust clinical studies. Even fewer studies adhere to the stringent requirements of multicenter RCTs, resulting in a general lack of strong evidence and reduced credibility in the findings. Despite being a focal point of contemporary research, investigating the mechanisms of TCM presents numerous challenges. These include the complexity of identifying active ingredients, difficulties in pinpointing multi-effective targets, and the challenge of mapping downstream signaling pathways. For TCM therapies with demonstrated clinical efficacy, it is crucial to produce both high-quality clinical evidence and thorough mechanistic studies to facilitate

the integration of TCM into modern medical practice. The complexity of TCM, such as the need for concoction and the variability introduced by different modifications in clinical applications, complicates the study of fixed-prescription mechanisms. While changes in target expression and signaling pathways can be observed in clinical studies, confirming these findings in mechanistic studies remains difficult.

To address these challenges, we propose two main strategies. First, modern research protocols and advanced techniques should be employed to generate high-quality clinical evidence for the use of TCM in PCI. Studies should adhere to the 5Rs framework: identifying the Right study population, selecting the Right TCM agents, choosing the Right formulation, setting the Right treatment course, and observing the Right endpoint indicators. Additionally, studies must fully comply with RCT requirements, including adequate sample sizes, appropriate statistical methods, and ethical clearance from the Medical Ethics Committee to ensure compliance with medical standards. Specific TCM syndromes should be a focal point in PCI research. For instance, the severity of blood stasis syndrome, a predominant TCM syndrome type in CAD, correlates with the complexity of coronary lesions and the degree of stenosis, and is a significant factor in restenosis post-PCI.⁸⁹ In AMI patients, blood stasis syndrome and stagnant phlegm syndrome are prevalent in TCM sthenia syndrome cases, while Qi deficiency syndrome is dominant in TCM asthenia syndrome cases.⁹⁰ Regarding formulations, TCM injections, which are preferred during the perioperative period, have shown potential advantages in treating CAD patients undergoing PCI.⁹¹ Commonly used herbs in TCM injections and decoctions for CAD include *Salvia*, *Poria*, *Astragalus*, *Radix Paeoniae*, and others.

Secondly, traditional techniques in modern medicine should be employed to enhance multi-target, multi-pathway, and network-based mechanism research in TCM for PCI. Concurrently, new techniques should be leveraged to deepen mechanistic research in emerging areas. For example, accumulating evidence suggests that the therapeutic efficacy of herbal medicines can be attributed to epigenetic modifications, including regulation of DNA methylation, histone modification, and noncoding RNAs.⁹² Another promising technique, Chinmedomics, integrates metabolomics and serum pharmacology based on TCM syndromes and could be instrumental in exploring TCM mechanisms.⁹³ These and other advanced methodologies have the potential to significantly advance our understanding of the targets and signaling pathways regulated by TCM in patients undergoing PCI (Figure 2).

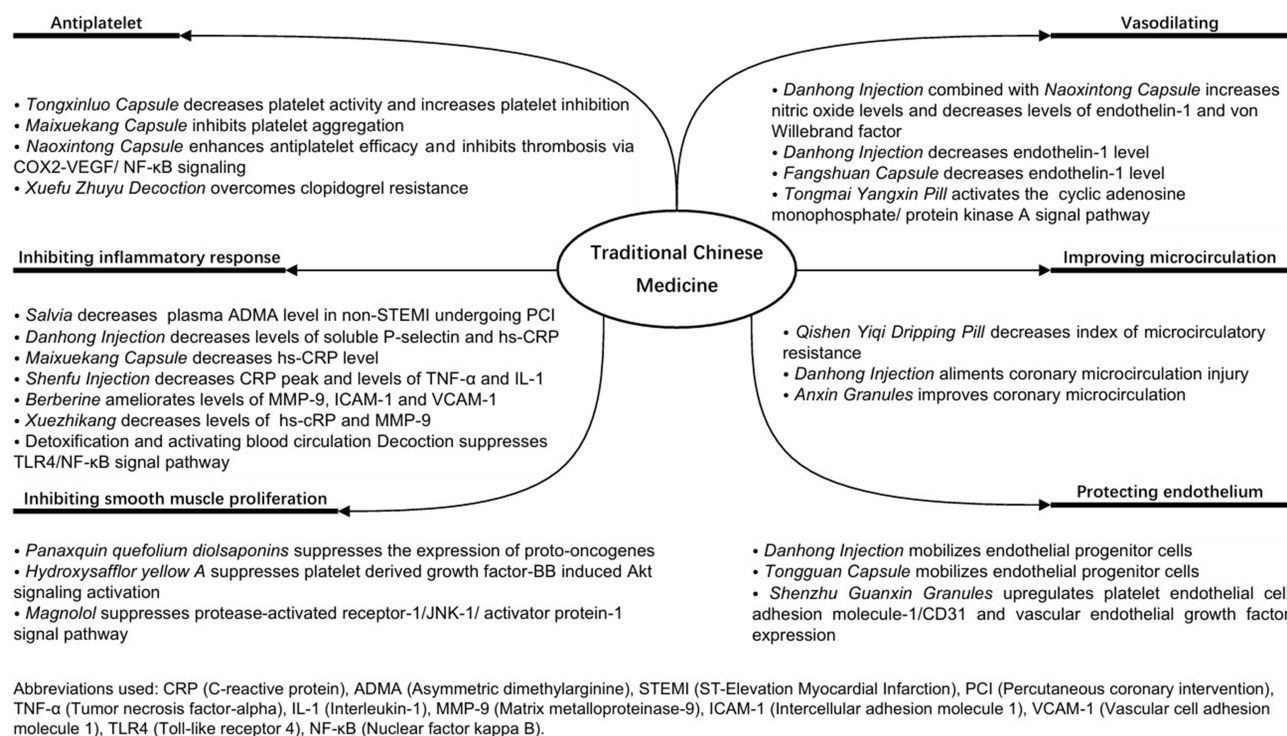


Figure 2 Adjunctive effect of traditional Chinese medicine in patients undergoing percutaneous coronary intervention: evidence of mechanism.

Conclusions

Pharmacotherapy is a cornerstone in the management of patients with CAD undergoing PCI, with GDMT being the current recommended therapeutic strategy. Despite the combined interventions of pharmacotherapy and PCI, there remain areas for improvement in the treatment of CAD, particularly in terms of clinical symptoms, complications, comorbidities, and both short- and long-term prognoses. TCM, with its unique complementary advantages, has demonstrated the following roles in the treatment of CAD patients undergoing PCI: alleviating symptoms, restoring cardiac function and biomarker levels, preventing the no-reflow/slow-flow phenomenon, inhibiting in-stent restenosis, improving prognosis, and reducing complications. These benefits are attributed to mechanisms such as antiplatelet effects, anti-inflammation, inhibition of smooth muscle proliferation, vasodilation, improvement of microcirculation, and endothelial protection.

Although current studies have limitations, advancements in research on TCM as a complementary therapy to GDMT, supported by modern research protocols and techniques, will likely enhance clinical outcomes in CAD patients undergoing PCI, providing high-quality clinical evidence and revealing precise mechanisms of action.

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Disclosure

All authors declare that there are no conflicts of interest regarding the publication of this paper.

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