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META-ANALYSIS

# Adjunctive Effect and Safety of Chinese Herbal Medicine in Patients with Coronary Artery Disease Undergoing Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis

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## ABSTRACT

**Objective** • The primary objectives of this systematic review and meta-analysis were to assess the impact of Chinese herbal medicine (CHM) as an adjunctive therapy in patients with coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI) and to evaluate its safety and efficacy.

**Methods** • Studies were obtained from multiple databases, including PubMed, Web of Science, China National Knowledge Infrastructure Database (CNKI), WanFang Data (WanFang), and Chinese Science and Technology Journal Database (VIP). Randomized controlled trials evaluating the effects of CHM intravenously or orally in patients with CAD undergoing PCI were included. The primary outcome was improvements in major adverse cardiovascular events (MACEs), and the secondary outcomes included differences in echocardiography, serum biomarkers, vascular structures and functions, clinical symptoms, and adverse drug reactions. Data synthesis was conducted using relative risk (RR), weighted mean difference (MD), and 95% confidence intervals (CI).

**Results** • Forty-seven trials, including 12,638 participants, were included in the meta-analyses. CHM significantly reduced MACEs compared with the control group(RR =0.51, 95% CI= 0.45 to 0.58)). CHM also led to improvements in left ventricular ejection fraction((MD=6.93, 95% CI = 4.03 to 8.03), ventricular end-diastolic dimension(MD=-5.01, 95% CI = -7.0 to -3.03), and cardiac troponin-I levels(MD=-0.37, 95% CI = -0.77 to 0.03]). The anti-inflammatory effects of CHM were observed through downregulation of C-reactive protein(MD=-2.13, 95% CI = -3.1 to -1.05) and high-sensitivity CRP (MD=-1.47, 95% CI= -2.47 to -0.48) when compared with the control groups. CHM also showed a protective effect on renal function and augmented platelet inhibition(7.05, 95% CI=5.91 to 8.19, $P < .00001$). The blood stasis scores of patients treated with Chinese Medicine were lower in the CHM group (MD=-4.30, 95% CI= -6.53 to -2.07). No significant difference in adverse events was found between the CHM and control groups.

**Conclusion** • The addition of CHM to conventional treatment in patients undergoing PCI for CAD improved primary and secondary endpoint events with no significant adverse drug reactions. These findings suggest that CHM has better clinical efficacy and safety. However, more high-quality studies are needed to validate these results and provide further evidence for the clinical application of CHM in CAD patients undergoing PCI. (*Altern Ther Health Med.* 2024;30(5):155-161)


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## INTRODUCTION

Coronary heart disease (CAD) is a most common and severe health problem in developed and developing regions today.[1] Reperfusion therapy is currently the first choice for treating acute coronary syndromes and severe stenotic lesions in the coronary arteries, where a percutaneous coronary intervention (PCI) treatment strategy has increasingly been used.[2,3] Along with the immediate benefits of improved blood flow, there has been an increasing focus on research and clinical measures to improve the long-term prognosis of PCI, mainly for developing and applying perioperative drugs for PCI and in-stent restenosis interventions. In addition, issues such as post-PCI symptom improvement, regulation of serum markers, and the management of complications such as contrast nephropathy are also attracting attention.

Chinese herbal Medicine (CHM) has a long and extensive clinical history in East Asia and has significantly improved health by preventing and treating diseases. The classic formulas and their modified forms still play a role in the prevention and

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treatment of diseases in clinical practice, among which cardiovascular diseases are one of the most widespread and cutting-edge areas of clinical applications. Clinical studies have shown the efficacy and safety of CHM when combined with modern treatments for managing CAD, showing improvements in the clinical prognosis, physicochemical biomarkers, and symptoms following PCI.[4] For example, CHM may have efficacy in preventing stent restenosis,[5] reducing contrast-induced renal damage,[6] and improving the psychosomatic status after PCI.[7] However, the quality of the relevant evidence is low, and no systematic analysis of CHM efficacy as an adjunct to improving PCI-related indicators has been reported, motivating us to write this article.

The primary objective of this study is to evaluate the adjunctive Effect and safety of CHM in patients with coronary artery disease undergoing PCI.

## METHODS

This protocol is based on the guidelines of PRISMA[8] and instructions from the Cochrane Reviewer Handbook.[9]

### Data Sources and Search Methods

The following databases were searched: PubMed, Web of Science, China National Knowledge Infrastructure Database (CNKI), WanFang Data (WanFang) and Chinese Science and Technology Journal Database (VIP). The search time was restricted from Jan 2011 to Sept 2021. The search terms for the English databases included (Medicine, Chinese Traditional) and (Percutaneous Coronary Intervention), while for the Chinese databases, a number of terms, such as herbal Medicine and percutaneous coronary intervention, were included. See the supplementary material for details.

### Eligibility Criteria

**Inclusion criteria.** (1) Randomized controlled trials evaluating the effects of CHM in patients with CAD undergoing PCI. (2) The experimental group was treated with CHM intravenously or orally, and the control group was treated with a placebo or blank control. The course of treatment was not limited. Both groups could receive the same conventional modern medicine treatment following the guidelines focused on CAD.

**Exclusion criteria.** (1) Non-randomized controlled trials. (2) Unrelated and duplicated documents. (3) Review articles or meta-analyses without original data. (4) Studies with fewer than 3 researchers, studies not conducted in conjunction with modern Medicine, or studies with sample sizes fewer than 150 in Chinese databases.

### Data Extraction and Quality Analysis

Two reviewers (Ma and Kong) independently screened the titles and abstracts of identified studies for initial eligibility. Screening the full-text articles according to the inclusion and exclusion criteria described above was followed, with disagreements resolved by discussion or by referral to a third reviewer (Zheng). The primary outcome was an improvement in major adverse cardiovascular events (MACEs), including cardiovascular death, recurrent myocardial infarction, heart failure, revascularization, stroke, recurrent angina pectoris, arrhythmia, and readmission due to emergency cardiovascular events and intrastent restenosis/thrombosis. The secondary outcomes included differences in echocardiography, serum biomarkers, vascular structures and functions, clinical symptoms and drug adverse reactions. When the number of studies included in the meta-analysis was 10 or greater, a funnel plot was used to analyze the publication deviation. Outcomes supported by fewer than 3 papers were not meta-analysed. The analysis software used was Revman 5.4.1 for Windows.

The risk of bias was assessed using the Cochrane Risk of Bias Tool as either low, high, or unclear for individual elements from five domains (selection, performance, attrition, reporting, and other). Two reviewers independently extracted the data and assessed the risk of bias. The discrepancies were resolved by discussion or by referral to a third reviewer.

### Data synthesis and analysis

Relative risk (RR), weighted mean difference (MD), and 95% confidence intervals (CI) were reported for the outcomes. Heterogeneity of the included studies was assessed by a chi-square test and the inconsistency index statistic ($I^2$). A fixed-effects model was used to calculate the pooled RR and MD if no heterogeneity occurred ($I^2 < 50\%$ or $P > .05$). A random-effects model was used to calculate the pooled RR and MD if substantial heterogeneity occurred ($I^2 > 50\%$ or $P < .05$).

## RESULTS

### Included studies and their characteristics

Out of 3644 articles, 2945 were excluded due to unrelated studies. Of 699 reports reviewed in full, 652 were excluded based on the eligibility criteria. Forty-seven trials, including a total of 12638 participants, contributed data to the meta-analyses (Figure 1).

**Figure 1.** Flow diagram of the screening and selection of the articles

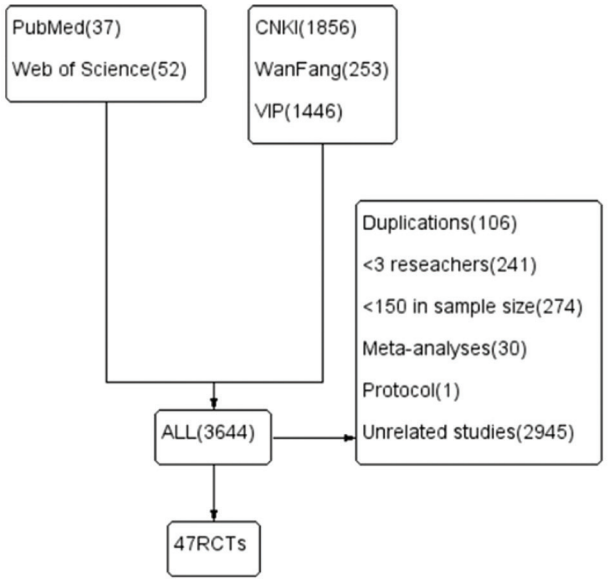

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**Table 1.** Characteristics of the randomized controlled trials of CHM for PCI

| Study | Study time | Sample size (T/C) | Gender (M/F) T | Gender (M/F) C | Age (T/C) | Classification of patient | Intervention T | Intervention C | Duration (Treatment: Follow-up) | Outcomes |
|---|---|---|---|---|---|---|---|---|---|---|
| Chen 2011[10] | 2007.7-2010.2 | 160(80/80) | 48/32 | 46/34 | 71.5±5.6/70.7±5.8 | ACS | Tongxinluo Capsule | RMT | 6m:6m | ③ |
| Li 2011[11] | 2007.10-2009.10 | 500(252/248) | 201/51 | 195/52 | 60.1±9.6/56.7±7.8 | STEMI | Compound Danshen Dripping Pill | RMT | 30d:30d | ②③④ |
| Shang 2011[12] | 2002.6–2003.12 | 152(73/79) | 50/23 | 52/27 | 67.79±4.77/66.70±4.16 | CAD | Xiongshao Capsule | RMT | 6 m:12 m | ①⑤ |
| Liu 2012[13] | 2008.7–2008.12 | 100(50/50) | 45/5 | 44/6 | 61.68±7.64/62.78±8.60 | ACS | Xiongshao Capsule | RMT | 6 m:12 m | ①②③④ |
| Meng 2012[14] | 2009.4-2009.12 | 130(61/69) | 43/18 | 56/13 | 63.07±10.41/63.28±10.03 | ACS | Berberine | RMT | 1 m:1m | ③ |
| Chen 2014[15] | 2009.7-2010.7 | 90(45/45) | 36/9 | 35/10 | 62.01±11.90/64.00±11.29 | CAD | Naoxintong Capsule | RMT | 3 m: 12 m | ①③ |
| Ge 2014[16] | 2008.7-2010.6 | 236(120/116) | 72/48 | 68/48 | 67.03±13.46/65.23±12.19 | ACS | Maixuekang Capsule | RMT | 12 m | ③ |
| He 2014[17] | 2012.1-2014.1 | 160(80/80) | 59/21 | 64/16 | 63.5±7.3/64.9±9.4 | STEMI | Anxin Granule | RMT | 4d: 6 m | ④ |
| Lu 2014[18] | 2008.2-2012.2 | 180(90/90) | 48/42 | 46/44 | 60.2±6.9/61.8±7.2 | CAD | Tongxinluo Capsule | RMT | 12 m:12 m | ① |
| Mei 2014[19] | 2011.1-2013.1 | 180(90/90) | 54/36 | 56/34 | 70±5.4/69±6.2 | CAD | Qishen Yiqi Pill | RMT | POP10d: 7d | ③ |
| Zhang 2014[20] | 2010.2-2012.10 | 177(90/87) | 47/43 | 45/42 | 75.9±4.9/76.4±4.7 | UA | Yiqi Huoxue Decoction | RMT | 14d:14d | ③ |
| Fan 2015[21] | 2011.2-2013.8 | 320(162/158) | 112/50 | 110/48 | 59.3±10.3/58.7±9.6 | ACS | Danhong Injection | RMT | 7d:7d | ③ |
| Meng 2015[22] | 2013.10-2014.10 | 160(80/80) | 43/37 | 41/39 | 57.8±2.0/57.4±2.8 | CAD | Yimai Tongluo Decoction | RMT | 1 m:1m | ①②③ |
| Xu 2015[23] | 2009.1-2011.1 | 187(113/74) | 86/27 | 51/23 | 70.35±9.61/68.08±10.38 | PCI | Shenzhu Guanxin Recipe | RMT | 3 m:6 m | ①④ |
| Zhang 2015[24,25] | 2010.5-2012.3 | 1023(514/509) | 438/71 | 441/73 | 65.6±7.9/65.6±7.8 | CAD | Shenshao Oral Lotion | RMT | 12w: 12 m | ③⑤ |
| Huang 2016[26] | 2012.6-2014.9 | 218(109/109) | 61/48 | 54/55 | 63.4±8.2/64.1±9.3 | CAD | Shenqi Decoction | RMT | 6 m:6 m | ①③④ |
| Huang 2016[27] | 2013.1-2015.12 | 240(120/120) | 79/41 | 82/38 | 54.22±110.37 | STEMI | Yiqi Huayu Decoction | RMT | POP 24 h: 24 h | ③⑤ |
| Mao 2016[28] | 2012.1-2015.12 | 88(44/44) | 28/16 | 27/17 | 67.54±8.39/68.38±10.41 | NSTEACS, IPBSS | Danlou tablets | RMT | 3 m: 6 m | ①② |
| Yang 2016[29] | 2011.3-2015.9 | 343(172/171) | 137/35 | 134/37 | 57.93±9.77/58.63±10.27 | CAD with T2DM | Tongxinluo Capsule | RMT | 12 m: 12 m | ①③ |
| Huang 2017[30] | 2014.12-2016.10 | 484(232/252) | 194/38 | 200/52 | 64.8±12.1/63.2±12.0 | AMI | Salvianolate | RMT | ≥7d: 1 m | ①③ |
| Wang 2017[31] | 2008.4–2009.10 | 701(351/350) | 284/67 | 247/10 | 60 (53.15, 67.57): 61(54.00, 69.31)[a] | ACS | Fufang Chuanxiong Capsule and Xinyue Capsule | RMT | 6 m:24 m | ① |
| Wang 2017[32] | 2012.4-2016.6 | 160(84/76) | 52/32 | 48/28 | 58.72±9.62/56.62±8.78 | CAD | Jiedu Huoxue Fang | RMT | POP 7d: 3 m | ①③ |
| Xing 2017[33] | 2011.1-2016.1 | 160(80/80) | 45/35 | 42/38 | 57.37±6.85/59.76±8.27 | STEMI, QDHTS | Huayu Paidu Decoction | RMT | 60d:60d | ③④ |
| Xue 2017[34] | 2013.8-2015.7 | 386(193/193) | 95/98 | 94/99 | 70±7.25/69±8.35 | CAD | Sofren injection | RMT | POP 6d: 3d | ③ |
| He 2018[35] | 2012.7-2013.3 | 80(40/40) | 29/11 | 32/8 | 65.3±8.8/63.9±10.1 | CAD, QDBSS | QishenYiqi Dripping Pill | RMT | POP 3-7d: 24 h | ③⑤ |
| Liu 2018[36] | 2014.6-2017.5 | 240(120/120) | 63/57 | 68/52 | 64.6±6.2/63.3±7.1 | CAD | Xuefu Zhuyu Decoction | RMT | POP 6d: 3d | ③ |
| Zhang 2018[37] | 2015.4-2016.4 | 156(78/78) | 40/38 | 42/36 | 60.37±2.58/58.14±2.45 | AMI | Buyang Huanwu Decoction | RMT | 3 m:3 m | ②③ |
| Zhu 2018[38] | 2013.2-2017.2 | 200(100/100) | 58/42 | 62/38 | 63.18±10.94/62.97±11.97 | STEMI | Huanglian Jiedu Decoction | RMT | 7d: 7d | ②③⑤ |
| Zhu 2018[39] | 2016.3-2017.6 | 160(80/80) | 63/13 | 60/18 | 53.2±7.6/54.4±9.1 | STEMI | Shexiang Tongxin Pill | RMT | 1 m:1m | ②⑤ |
| Zhang 2018[40] | 2013.11-2014.5 | 119(60/59) | 36/24 | 39/20 | 58.1±11.6/58.7±10.8 | ACS | Tongxinluo Capsule | RMT | 30d: 12 m | ①③⑥ |
| Hu 2019[41] | 2014.1-2014.1 | 42(21/21) | 14/7 | 14/7 | 60.33±11/62.05±10.67 | CAD | Danhong Injection | RMT | 7d: 7d | ③④ |
| Ma 2019[42] | 2015.10-2017.12 | 160(80/80) | 63/17 | 60/20 | 30-80[b] | CAD, QDBSS | Yiqi Liangxue Shengji Recipe | 8 W: | 8W:24 m | ①⑥ |
| Yu 2019[43] | 2016.7-2017.10 | 242(119/123) | 65/54 | 67/56 | 57.9±5.8/58.2±5.8 | CAD with T2DM | Xingqi Jieyu Decoction | RMT | 12 m:12 m | ①③④ |
| Guo 2020[44] | 2014.1-2016.7 | 1054(530/524) | 380/150 | 363/161 | 59.95±9741/60.4±9.64 | stable CAD | Xinyue Capsule | RMT | 24w:48w | ①④⑥ |
| Li 2020[45] | 2016.6-2017.12 | 186(92/94) | 58/34 | 62/32 | 65±29/65±26 | CAD | Xuemaitong II Granule | RMT | POP 8d: 5d | ①③④ |
| Lu 2020[46] | 2017.7-2018.12 | 200(100/100) | 54/46 | 55/45 | 57.00±2.86/57.50±2.74 | ACS, BSS | Xuefu Zhuyu Decoction and Xinmailong Injection | RMT | 10d:10d | ②③④ |
| Ou 2020[47] | 2016.10-2017.6 | 128(60/68) | 54/6 | 55/13 | 64.8±11/65.2±10.7 | NSTEACS | Salvianolate | RMT | POP 3 times:12 m | ① |
| Ren 2020[48] | 2013.10-2015.7 | 167(84/83) | 50/34 | 55/28 | 63.7±9.5/62.9±11.6 | CAD | Salvianolate | RMT | POP4d: 1 m | ③ |
| Shen 2020[49] | 2013.3-2015.2 | 187(92/95) | 24/68 | 23/72 | 61.04±9.42/61.28±9.23 | ACS | Suxiao Jiuxin Pill | RMT | 6 m:12 m | ①②③④⑥ |
| Su 2020[50] | 2015.6-2018.12 | 368(184/184) | 88/96 | 101/83 | 78.2±6.7/74.3±8.4 | ACS | Yiqi Huayu Lishui Decoction | RMT | 8w:8w | ②③ |
| Wang 2020[51] | 2008.4-2010.10 | 808 (404/404) | 332/82 | 281/123 | 60(31,75)/61(34,75)[c] | ACS, BSS | Fufang Chuanxiong Capsule and Xinyue Capsule | RMT | 6 m:12 m | ①④ |
| Yu 2020[52] | 2017 .9-2018.9 | 440(220/220) | 144/76 | 155/64 | 59.65±10.30/60.59±10.21 | ACS, IPBSS | Huayu Qutan Granule | RMT | 1 m:12 m | ①⑥ |
| Zhang 2020[53] | 2008.5-2009.1 | 426(211/215) | 121/94 | 152/59 | 64.66±7.49/65.23±7.68 | ACS | Fufang Chuanxiong capsule | RMT | 6 m:12 m | ①③ |
| Chen 2021[54] | 2017.10-2019.10 | 180(90/90) | 68/22 | 70/20 | 60.17±11.25/60.39±10.43 | AMI, IPBSS | Huayu Qutan Granule | RMT | 1w:3 m | ②④ |
| Li 2021[55] | 2018.1-2020.1 | 150(75/75) | 45/30 | 39/36 | 51.6±2.8/53.9±2.5 | AMI, QDBSS | Buyang Huanwu Decoction | RMT | 8w:8w | ②③④ |
| Ma 2021[56] | 2017.1-2019.3 | 410(205/205) | 125/81 | 120/85 | 62.36±5.61/62.76±5.52 | CAD, severe BSS | Xuefu Zhuyu Decoction | RMT | 4w:4w | ③④ |

[a]Median (range)
[b]Range
[c]P50 (P25, P75)

**Note**: Two articles based on the same study conducted by some researchers were regarded as one study in this meta-analysis(24,25).

**Abbreviations**: ① MACEs (cardiovascular death, recurrent myocardial infarction, heart failure, revascularization, stroke, recurrent angina pectoris, arrhythmia, in-stent restenosis/thrombosis, and readmission), ② echocardiography, ③ serum biomarkers, ④ clinical symptoms, ⑤ vascular structures and functions, and ⑥ adverse drug reactions. ACS: Acute coronary syndromes. AMI, Acute myocardial infarction; BSS, Blood stasis syndrome; NSEACS, Non-ST-elevation ACS; IPBSS, Intermingled phlegm and BSS; POP, Perioperative period; QDBSS, Qi deficiency and BSS; RMT, Routine medical treatment; STEMI, ST-Segment elevation myocardial infarction; T2DM, Type 2 diabetes mellitus; UA, Unstable angina; QDHTS, Qi deficiency and hyperactivity of toxin syndrome.

**Table 2**. Details of the effects of CHM after PCI on subgroups of MACEs.

| MACEs | Sample Size | Heterogeneity *P* value | Results of meta-analyses *P* value | Results of meta-analyses RR[95% CI] | Studies |
|---|---|---|---|---|---|
| Cardiovascular Death | 4841 | 0.69 | .07 | 0.59 [0.34, 1.03] | (10,16,23,30,31,40,44,47,49,51,52) |
| Myocardial Infarction | 4605 | 0.97 | <.00001 | 0.43 [0.3, 0.62] | (13,16,18,23,28,29,31,40,42,44,46,47,49,51, 52) |
| Stroke | 4286 | 0.31 | .02 | 0.57 [0.36, 0.90] | (13,16,30,31,40,44,46,49,51,52) |
| Revascularization | 3075 | 0.95 | .003 | 0.62 [0.45, 0.85] | (12,16,31,40,42,44,47,51) |
| Heart Failure | 4422 | 0.92 | <.0001 | 0.45 [0.31, 0.66] | (11,13,28,29,31,32,40,42,44,45,47,49,51) |
| Arrhythmia | 1332 | 0.1 | .005 | 0.75 [0.62, 0.92] | (11,13,28,30,45) |
| Angina Pectoris | 1777 | 0.93 | <.00001 | 0.46 [0.36, 0.59] | (13,16,18,22,29,32,40,42,43,45) |
| In-stent Restenosis/Thrombosis | 2180 | 0.35 | <.00001 | 0.42 [0.30, 0.60] | (11,12,26,29,30,32,40,45,47) |
| Readmission | 3530 | 0.6 | <.0001 | 0.57 [0.44, 0.73] | (18,23,30,31,40,44,51) |

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**Figure 2.** Risk of bias summary. A: Judgements about each risk of bias item for each included study. B: Judgements about each risk of bias item presented as percentages across all included studies.

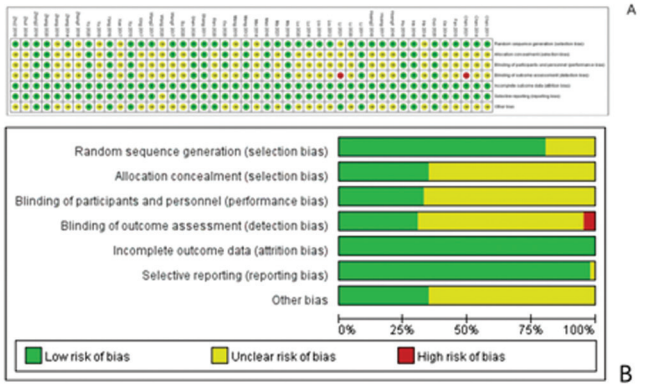



**Figure 3.** Forest plot of the overall Effect of CHM after PCI on MACEs.

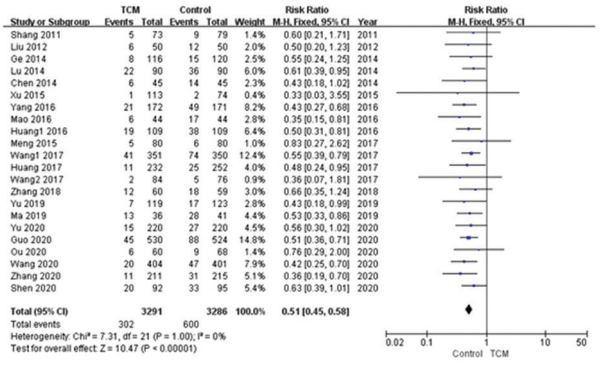
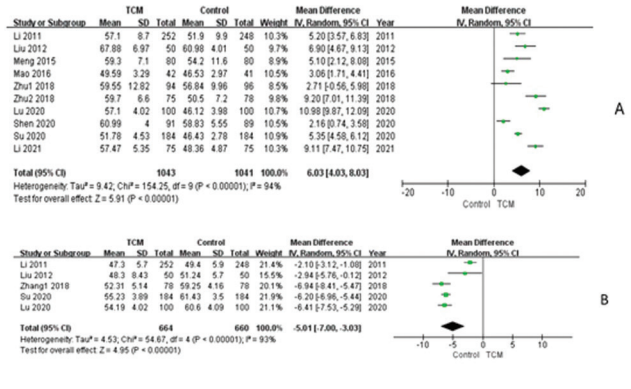



**Figure 4.** The echocardiographic effects of CHM after PCI. A: LVEF B: LVEDD




The included studies investigated 34 different CHMs, among which Tongxinluo capsule and salvianolate were reported in 3 articles: Xuefu Zhuyu decoction, Buyang Huanwu decoction, Huayu Qutan granule and Fufang Chuanxiong capsule combined with Xinyue capsule were reported in 2 articles; and others, including Xuefu Zhuyu decoction combined with Xinmailong injection, were reported in 1 article. The characteristics of the included studies are shown in Table 1.[11-56]

**Risk of bias**

Although a few studies were judged to have a high risk of bias for blinding methods, most of the included studies had a low or unclear risk of bias across all of the domains assessed (Figure 2).

## META-ANALYSIS

### Primary outcomes

Figure 3 shows the overall Effect of CHM after PCI on the primary outcome MACEs. Across 22 comparisons involving 6577 participants, CHM significantly reduced the incidence of MACEs relative to control (RR=0.51, 95%CI =0.45 to 0.58). Table 2 lists the details of the effects of CHM after PCI on the subgroups of MACEs. See the Supplementary Material for details. A fixed-effects model for all outcomes was used because there was no significant heterogeneity among the individual studies ($P$ = 1.0, $I^2$ = 0%).

### Secondary outcomes

**Echocardiography.** Figure 4 shows the echocardiographic effects of CHM after PCI. In 10 study comparisons involving 2084 participants, CHM led to a significant improvement in left ventricular ejection fraction (LVEF) compared with the control groups (MD=6.93, 95% CI= 4.03 to 8.03]). In 5 study comparisons involving 1324 participants, CHM significantly reduced the left ventricular end-diastolic dimension (LVEDD) compared with the control groups (MD=-5.01, 95% CI= -7.0 to -3.03). The random-effects model was performed with the IV test and found significant statistical heterogeneity among individual studies ($P$ < .00001, $I^2$ =94%).

**Serum Biomarkers.** Figure 5 shows the effects of CHM after PCI on regulating the serum biomarkers. In 3 study comparisons involving 400 participants, CHM led to a downregulation of cTNI compared with the control group (MD=- 0.37, 95% CI= -0.77 to 0.03]). The anti-inflammatory effects were found to be attributed to the downregulation of CRP in 3 studies (MD=-2.13, 95% CI= -3.1 to -1.05) and hs-CRP in 5 studies (MD=-1.47, 95% CI= -2.47 to -0.48) when compared with the control groups. For renal functions, CHM showed a protective effect by downregulating the SCr levels (MD=-7.46, 95% CI= -18.48 to -3.57, $P$ > .05) and upregulating eGFR (MD=6.05, 95% CI= 2.09 to 10.01, $P$ = .03). Meta-analysis showed that platelet inhibition could be augmented by CHM (MD=7.05, 95% CI=5.91 to 8.19, $P$ < .00001). The random-effects model was performed with the IV test and found significant statistical heterogeneity among the individual studies, with the exception of the platelet inhibiting effect, where a fixed-effects model was used because no significant heterogeneity (P=0.16; $I^2$=42%) was detected.

**Symptoms.** The blood stasis scores of the patients treated with Chinese Medicine were lower in the CHM group than in the control group (MD=-4.30, 95% CI= -6.53 to -2.07, Figure 6). Other tools for symptom evaluation (QOL, SF-36) were not analyzed because fewer than 3 studies that used each tool were included in this article.[11,33,41,45,55]

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**Figure 5.** The regulatory effects of CHM after PCI on serum biomarkers. A: cTNI. B: CRP. C: hs-CRP. D: SCr. E: eGFR. F: platelet inhibition rate.

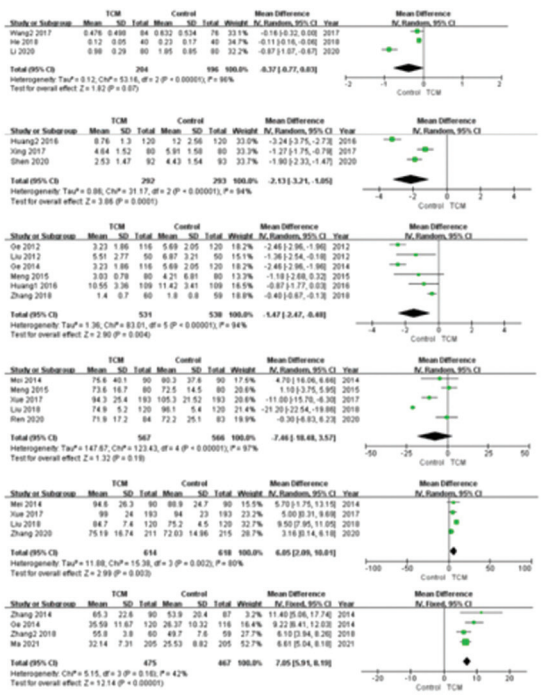


**Figure 6.** Improvement in blood stasis syndrome scores of CHM after PCI.

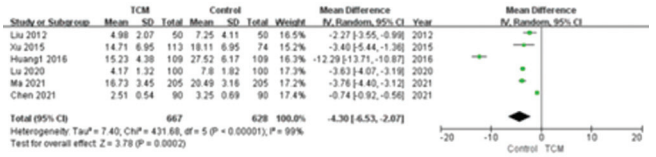
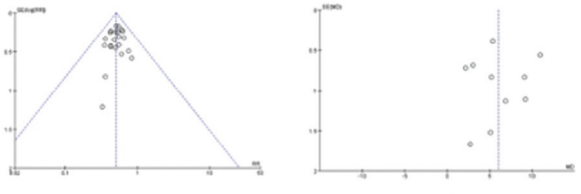


**Figure 7.** Adverse drug reactions of CHM after PCI.

**Figure 8.** The funnel plot of studies for MACEs (A) and LVEF (B)



**Adverse Drug Reactions.** Adverse events were reported in 5 trials. No difference was found between the CHM and control groups (MD=1.01, 95% CI= 0.89 to 1.16, Figure 7).

### Publication Bias

Publication bias was evaluated in a funnel plot by comparing the symmetry of the included studies for MACEs and LVEF, which were studied by at least 10 studies each. The funnel plot was symmetrical visually for clinical efficiency and LVEF (Figure 8).

## DISCUSSION

CHM has been reported as a complementary and alternative method to prevent CAD.[4] A few studies have revealed the potential use of CHM after PCI, including reducing the in-stent restenosis rate[57] and improving MACE events, heart function, and the quality of life among ACS patients with early PCI.[49] Through an analysis of the literature over the last decade, we explored the adjuvant role of CHM in PCI, including its impact on primary outcomes such as MACEs and stent restenosis and secondary outcomes such as cardiac ultrasound, serum markers, clinical symptoms and adverse drug reactions. The meta-analysis of the included literature showed improvements in both primary and secondary outcomes with no significant adverse drug reactions, demonstrating the clinical efficacy and safety of applying CHM after PCI.

### Findings in the context of the literature

**Impact on the primary outcomes.** This systematic review and meta-analysis showed that adding CHM to conventional treatment could further reduce the events of MACEs and reduce the risk of cardiovascular death, non-fatal myocardial infarction, heart failure, stroke, and renal dysfunction. CHM has also been proven to have a more pronounced inhibitory effect on in-stent restenosis, with the ability to improve the lumen area and coronary blood flow.[12,35,38,39,45]

**Impact on secondary outcomes.** CHM has an adjunctive effect on cardiac function recovery of PCI patients, which the improvement in ejection fraction could affirm. It also inhibits cardiac remodelling and reducing LVEDD, thus helping to maintain normal cardiac morphology. The effects of CHM on serum markers are mainly in the modulation of cTNI, inflammatory factors, and renal function indicators. Our analysis showed that the addition of CHM to conventional treatment could further reduce the cTNI expression levels, suggesting that CHM has an inhibitory effect on PCI-related myocardial injury and could protect cardiomyocytes. It could further reduce the CRP and hs-CRP expression levels, indicating that CHM has a regulatory effect on PCI- related inflammatory activation and can reduce vascular injury; it could also further enhance the inhibition of platelet function, which in turn reduces the occurrence of thrombotic events. With these improvements in serum creatinine and eGFR levels, CHM was demonstrated to have an ameliorative effect on PCI-related renal damage, which could reduce the risk of contrast-induced nephropathy. In addition, CHM could significantly improve the CM symptom score associated with PCI and reduce clinical symptoms.[11,33,41,45,55] Despite the ameliorative Effect on both primary and secondary endpoint events, adjuvant CHM

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treatment did not show significant adverse drug reactions, demonstrating a high clinical safety profile.

### Strengths and limitations

The inclusion criteria for our study arbitrarily added more restrictions to the Chinese literature, such as limiting the number of investigators to more than three and the sample size of the studies to no fewer than 150, to improve the quality of the included literature. However, this could exclude some of the high-quality studies from the scope of analysis in this paper, thus not providing a more comprehensive picture of the complementary therapeutic role of CHM in PCI. Nevertheless, we believe that the limited number of such excluded studies would have little impact on the results of the meta-analysis and that it is feasible to increase the inclusion criteria for the Chinese literature to include only higher-quality studies. The bias analysis showed that the included studies had a moderate to high risk of bias, mainly in the blinding management of outcomes, while the funnel plot analysis showed that most of the outcomes had a low risk of publication bias. In addition, most of the selected studies had small sample sizes, and there was a lack of high-quality studies with large, multicentre and cross-territory studies.

## CONCLUSIONS

Adding CHM to conventional treatment improved MACEs, cardiac functions ,and levels of cardiac troponin-I and CRP in patients with CAD undergoing PCI with no significant adverse drug reactions, demonstrating better clinical efficacy and safety. However, there is still a need for rigorous, high-quality studies to further corroborate the results and provide more evidence to support the clinical application of CHM after PCI.

### ETHICAL COMPLIANCE

Not applicable.

### CONFLICTS OF INTEREST

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

### AUTHOR CONTRIBUTION

Zheng contributed to the study concept, study design, and drafting of the paper; Ma and Kong contributed to the acquisition and analysis of the data; Yang contributed to study supervision.

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