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Tong-xin-luo capsule for patients with coronary heart disease after percutaneous coronary intervention (Review)

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[Intervention Review]

Tong-xin-luo capsule for patients with coronary heart disease after percutaneous coronary intervention

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ABSTRACT

Background

Percutaneous coronary intervention (PCI) is a standard treatment for coronary heart disease (CHD). Restenosis, defined as a 50% reduction in luminal diameter at six months after PCI, indicates a need for revascularisation. Restenosis has proven to be a major drawback to PCI. Tong-xin-luo is one of the prophylactic strategies for cardiovascular events in patients after PCI that is widely used in China, but its efficacy and safety have not been systematically evaluated.

Objectives

To systematically assess the efficacy and safety of Tong-xin-luo capsules in preventing cardiovascular events after PCI in patients with CHD.

Search methods

We searched the Cochrane Central Register of Controlled Trials in *The Cochrane Library*, MEDLINE (OVID), EMBASE (OVID), WanFang, Chinese Biomedical Database, Chinese Medical Current Contents, and China National Knowledge Infrastructure from their inception to June 2014. We also searched other resources, including ongoing trials and research registries. We applied no language restrictions.

Selection criteria

Randomised controlled trials of participants with CHD after PCI were included. Participants in the intervention group received Tong-xin-luo capsules for at least three months.

Data collection and analysis

Two review authors independently extracted data and assessed the risk of bias. Any disagreements were resolved by discussion with a third review author. The primary outcomes included occurrence of angiographic restenosis and adverse events; the secondary outcomes included myocardial infarction, heart failure, angina, all cause mortality, mortality due to any cardiovascular event, use of revascularisation, patient acceptability, quality of life and cost-effectiveness. Dichotomous data were measured with risk ratios (RRs) with 95% confidence intervals (CIs).

Main results

Sixteen studies involving 1063 participants were identified. The risk of bias for fifteen studies was high and along with imprecision and possible publication bias, this lowered our confidence in the results. There was low quality evidence that Tong-xi-luo reduced the rates of angiographic restenosis (RR 0.16, 95% CI 0.07 to 0.34), myocardial infarction (RR 0.32, 95% CI 0.16 to 0.66), heart failure (RR 0.26, 95% CI 0.11 to 0.62), and use of revascularisation (RR 0.26, 95% CI 0.15 to 0.45). There was very low quality evidence for the effect of Tong-xin-luo on all-cause mortality (RR 0.38, 95% CI 0.06 to 2.56), angina (RR 0.24, 95% CI 0.17 to 0.34) and death due to any cardiovascular event (RR 0.31, 95% CI 0.08 to 1.12). Adverse events were seldom reported, and included gastrointestinal reactions and nausea.

Authors' conclusions

The addition of Tong-xin-luo to conventional Western medicine may possibly prevent restenosis and recurrence of cardiovascular events in patients with CHD after PCI. However, the data are limited by publication bias and high risk of bias for included studies. Further high-quality trials are required to evaluate the potential effects of this intervention.

PLAIN LANGUAGE SUMMARY

Tong-xin-luo capsule for patients with coronary heart disease after percutaneous coronary intervention

Review question: What is the efficacy and safety of Tong-xin-luo capsules in preventing cardiovascular events after percutaneous coronary intervention, a procedure involving placing a stent to open up the heart's blood vessels, in patients with coronary heart disease?

Background: Coronary heart disease is a major cause of mortality globally. Percutaneous coronary intervention is regarded as a standard treatment for coronary heart disease to improve symptoms of heart-related chest pain. However, a major drawback of percutaneous coronary intervention is the need for a repeat procedure due to symptoms related to recurring narrowing of the heart's blood vessels. Previous studies have indicated that Tong-xin-luo capsule, a Chinese herbal medicine product, might be effective in preventing recurrence of narrowing of a blood vessel after percutaneous coronary intervention.

Study characteristics: We included sixteen randomised controlled trials (1063 participants) comparing Tong-xin-luo capsules plus conventional treatment with placebo plus/or conventional treatment (literature search date: though June 2014). All studies were undertaken in China. The sample size was from 50 to 178 and the duration of follow-up ranged from three months to two years.

Key results: We found that Tong-xin-luo may possibly reduce the risk of narrowing of a blood vessel detected by angiography, cardiovascular events (including myocardial infarction, angina and heart failure) and use of repeat procedure. Adverse events were seldom reported.

Quality of evidence: Because of high risk of bias for fifteen studies, imprecision and possible publication bias, the quality of evidence was low or very low for all study outcomes.

SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Tong-xin-luo compared with placebo/no treatment for patients with CHD after PCI

Patient or population: participants with CHD after PCI

Settings: China

Intervention: Tong-xin-luo capsules

Comparison: placebo/no treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo/no treatment	Tong-xin-luo				
Occurrence of angiographic restenosis [follow-up: 6 months]	**134 per 1000**	**21 per 1000** (9 to 46)	**RR 0.16** (0.07 to 0.34)	595 (6)	⊕⊕⊖⊖ **low**	Quality of evidence downgraded two levels due to study limitations (lack of blinding in all studies, high risk of reporting bias in one study).
Adverse event	NA	NA	NA	NA	NA	Adverse events were not evaluated as very limited information was reported from original studies.
Occurence of myocardial infarction [follow-up: 3-48 months]	**Myocardial infarction**		**RR** 0.32 (0.16 to 0.66)	1306 (13)	⊕⊕⊖⊖ **low**	Quality of evidence downgraded two levels due to study limitations (lack of blinding in all studies except Wang 2010, high risk of reporting bias in two studies).
	22 per 1000	**7 per 1000** (3 to 21)				
	Acute myocardial infarction					
	53 per 1000	**16 per 1000** (6 to 44)				
Occurrence of angina	**211 per 1000**	**51 per 1000** (36 to 72)	**RR 0.24** (0.17 to 0.34)	1210 (11)	⊕⊖⊖⊖ **very low**	Quality of evidence downgraded two levels due to study limitations (lack of blinding in all studies ex-

[follow-up: 3-48 months]						cept Wang 2010, high risk of reporting bias in one study), and one additional level due to publication bias.
Occurence of heart failure [follow-up: 3-48 months]	**88 per 1000**	**23 per 1000** (10 to 54)	**RR 0.26** (0.11 to 0.62)	529 (4)	⊕⊕⊝⊝ **low**	Quality of evidence downgraded two levels due to study limitations (lack of blinding in all studies, high risk of reporting bias in one study).
All-cause mortality [follow-up: 3-48 months]	**12 per 1000**	**5 per 1000** (1 to 31)	**RR 0.38** (0.06 to 2.56)	[419] (4)	⊕⊝⊝⊝ **very low**	Quality of evidence downgraded two levels due to study limitations (lack of blinding in all studies except Wang 2010, high risk of reporting bias in one study), and one additional level due to imprecision of the estimate.
Mortality due to any cardiovascular event [follow-up: 3-48 months]	**34 per 1000**	**11 per 1000** (3 to 39)	**RR 0.31** (0.08 to 1.12)	552 (5)	⊕⊝⊝⊝ **very low**	Quality of evidence downgraded two levels due to study limitations (lack of blinding in all studies, high risk of reporting bias in one study), and one additional level due to imprecision of the estimate.
Use of revascularisation [follow-up: 3-48 months]	**166 per 1000**	**43 per 1000** (25 to 75)	**RR 0.26** (0.15 to 0.45)	806 (8)	⊕⊕⊝⊝ **low**	Quality of evidence downgraded two levels due to study limitations (lack of blinding in all studies, high risk of reporting bias in two studies).

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
CHD: coronary heart disease; PCI: percutaneous coronary intervention; CI: confidence interval; RR: risk ratio; NA: not available.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

BACKGROUND

Description of the condition

Cardiovascular diseases (CVDs), which mainly refers to a group of disorders of the heart and blood vessels, are a major cause of death and disability globally (Lonn 2010; Lozano 2012). According to the fact sheet published by the World Health Organization (WHO) in September 2011, CVDs caused about 17.3 million deaths in 2008 and are responsible for 30% of all deaths worldwide (WHO 2011). Moreover, CVDs are expected to account for 46.6% of all deaths by 2020 and 80% of CVD deaths will occur in developing countries (WHO 2002; WHS 2010). Among all deaths attributed to CVDs, about half were due to coronary heart disease (CHD; Go 2014). CHD is a condition in which plaque builds up inside the coronary arteries and can decrease oxygen supply to the heart muscle (NHLBI 2011). According to previous studies, about one in six deaths in the United States were due to CHD in 2010 (Go 2014) and one in six men and one in seven women in the UK died from CHD in 2008 (Bhattarai 2012). Percutaneous coronary intervention (PCI), a non-surgical procedure that involves placing a stent to open up the blood vessels obstructed by plaque, is an effective treatment for CHD (Grech 2003; Singh 2011). However, restenosis has proven to be the major drawback to PCI and frequently causes a return of symptoms and the need for repeated coronary intervention (Kang 2012; Richard 2002; Testa 2009).

Restenosis is a recurrence causing significant narrowing in the treated vessel, which is generally considered as a wound healing response to trauma of the vascular wall (Agema 2001; Odell 2006). Clinically, restenosis is defined as recurrent angina pectoris that indicates a need for revascularisation of the treated vessel (Cutlip 2007). It is angiographically defined as a 50% reduction in luminal diameter at six months after PCI. So far, the mechanism of restenosis has not been fully clarified. It is thought that restenosis is due to the combined effect of early elastic recoil in vessels, mural thrombus formation, neointimal proliferation, extracellular matrix formation, and chronic geometric arterial changes (Dangas 1996). According to the study by Giglioli et al, more than 40% of patients have restenosis detected within six months after an angioplasty (Giglioli 2009). This frequently results in renewed symptoms such as angina that hamper the long-term efficacy of PCI (Fattori 2003; Rajaqopal 2003). There are many strategies aimed at preventing cardiovascular events in patients after PCI, which include using antiplatelet drugs, thrombin inhibitors, and Tong-xin-luo. However, some of these interventions have adverse effects (Dörffler 2005; Serruys 1995; Rosanio 1999).

Description of the intervention

Tong-xin-luo capsule is a drug that has been studied since 1995 based on the theory of Chinese herbal medicine.The recommended dose range is 1.14 g to 1.52 g in three to four capsules (0.38 g in each capsule) and administered three to four times a day, with a total dose of between 3.5 g and 6.0 g per day. The treatment is given as a four-week course (Wu 2001; Zhou 2011). Currently, Tong-xin-luo capsule is widely used for treating cardiac-cerebral vascular diseases in China. Its effect on prevention and treatment of restenosis among CHD patients after PCI has become an important topic in both Chinese and Western medical research areas. Previous studies indicated that Tong-xin-luo can effectively relieve angina, reduce the frequency of acute attacks of angina, and prevent restenosis of stents (Wang 2003; Zhang 2004; Zhou 2007 a; Zhu 2004). Potential interactions with other drugs are unclear. Related adverse events have been reported which include gastrointestinal tract symptoms, gingival bleeding, and increased partial thromboplastin time (Nong 2000).

How the intervention might work

The main composition of Tong-xin-luo capsules is complex and includes Hirudo, Radix Ginseng, Scorpio, Eupolyphaga Seu Steleophage, Scolopendra, Periostracum Cicadae, Lignum Dalbergiae Odoriferae, Radix Paeoniae Rubra, and Borneolum Syntheticum (Zhou 2011). Previous studies have shown the following.

- Hirudin-like materials, which are produced by Scorpio, Hirudo, Eupolyphaga Seu Steleophage, and Scolopendra (Huntington 2003; Yu 2011; Zhou 1997), can stop blood clotting by reducing the secretion of extracellular matrix (Paul 1994) and suppressing the aggregation of platelets and inflammatory cells (Chen 2007; Modi 1995).
- Radix Ginseng has cardiokinetic function as well as inhibiting the platelet adhesion reaction and thrombosis formation (Pei 1986; Xu 1988).
- Radix Paeoniae Rubra dilates coronary arteries, causes thrombolysis, improves myocardial ischemias, inhibits proliferation of vascular smooth muscle cells, and prevents onset of endothelial injury (Lu 2006; Ruan 2003; Wang 2008).
- Periostracum Cicadae is an anticonvulsive and significantly slows heart rate (Zheng 1998).
- Scolopendra extraction could increase blood vessel perfusion flow and strengthen cardiac contractility (Chen 1985).
- Eupolyphaga Seu Steleophage could improve tolerance to hypoxia and increases cardiac output (Nong 1989).

Why it is important to do this review

Due to incomplete evidence on the benefits and possible adverse effects of Tong-xin-luo capsule, a systematic review on the therapeutic efficacy and safety of Tong-xin-luo capsule use is needed. The results of our review may shed new light on the prevention of cardiovascular events for patients with coronary heart disease after PCI and may also provide new treatment methods for cardiovascular disease with reduced expense and side effects.

OBJECTIVES

To systematically assess the efficacy and safety of Tong-xin-luo capsules in preventing cardiovascular events after PCI in patients with CHD.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs). Single-arm trials, animal studies and reviews were excluded.

Types of participants

Participants were male or female of any age or ethnic origin with CHD after PCI. Participants were eligible regardless of recruitment through clinical or community settings.

Types of interventions

Tong-xin-luo capsule was regarded as the intervention in our study. Tong-xin-luo capsule used alone after PCI and with a treatment duration of no less than three months was compared with at least one valid comparator, including no intervention, placebo, or an effective Western medicine intervention supported by reasonable clinical evidence.

Types of outcome measures

We considered the following outcome measures.

Primary outcomes

- Occurrence of angiographic restenosis
- Adverse events

Secondary outcomes

- Occurrence of myocardial infarction (MI), heart failure, or angina
- All cause mortality
- Mortality (death) due to any cardiovascular event
- Use of revascularisation, including PCI and coronary artery bypass graft surgery
- Patient acceptability
- Quality of life
- Cost-effectiveness

Search methods for identification of studies

A comprehensive search strategy was formulated in an attempt to identify all relevant studies regardless of publication status. Electronic databases were searched and handsearching of journals was carried out.

Electronic searches

We searched the following main electronic databases, with no restriction in publication language.

- Cochrane Central Register of Controlled Trials (CENTRAL Issue 5, 2014; *The Cochrane Library*).
- MEDLINE (OVID, 1950 to June week 1 2014).
- EMBASE (OVID, 1947 to week 23 2014).
- WanFang (1998 to August week 2 2014).
- China National Knowledge Infrastructure (CNKI; 1993 to April week 2 2013).
- Chinese Biomedical Database (CBM; 1978 to April week 2 2013).
- Chinese Medical Current Contents (CMCC; 1994 to April week 2 2013).

The search strategies used can be found in Appendix 1. No language restrictions were applied.

Searching other resources

We searched the following clinical trial registries for ongoing and unpublished trials from 1994 to June 2013.

- Current Controlled Trials (http://www.controlled-trials.com).
- WHO International Clinical Trials Registry Platform (ICTRP; http://apps.who.int/trialsearch/).
- ClinicalTrials.gov (www.clinicaltrials.gov).
- Chinese Clinical Trial Register (www.chictr.org).
- China Master's Theses Full-text Databases (CMFD; http://oversea.cnki.net/kns55/brief/result.aspx?dbPrefix=CMFD).
- China Doctoral Dissertation Full-text Database (CDFD; http://oversea.cnki.net/kns55/brief/result.aspx?dbPrefix=CDFD).
- China Proceedings of Conference Full-text Database (CPCD).

The search strategies used can be found in Appendix 1.

Handsearching

Handsearching was not performed as the journals we would have planed to search manually (including China Journal of Chinese Materia Medica, Chinese Journal of Basic Medicine in Traditional Chinese Medicine, and Chinese Journal of Integrated Traditional and Western Medicine) were included in WanFang database.

Data collection and analysis

Two authors independently carried out selection of studies, data extraction, and quality assessment. Data analysis was conducted using Review Manager Version 5.1 (RevMan 2008) according to the statistical guidelines referenced in the current version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Selection of studies

Two authors (XF, ZY) independently scanned the titles and abstracts of every record retrieved for eligibility assessment. The full-texts of any literature with unclear information in the title or abstracts, and potential eligible studies were retrieved for clarification. All studies selected by the two authors were cross checked. Any disagreement was resolved by discussion with a third author (CM).

Data extraction and management

Two authors (XF, YQ) independently extracted data using a standard form pre-designed for this review. The data extracted were as follows: study characteristics (authors, location, title, etc.), patient characteristics (number of patients, age, gender, race, baseline disease severity, etc.), intervention, control, methodological information (randomisation, allocation concealment, blinding, loss to follow-up, selective outcome reporting),outcomes. The authors of the original studies were consulted for unclear or missing information where necessary. Any disagreement were resolved by discussion.

Assessment of risk of bias in included studies

The risk of bias in selected studies was independently assessed by two authors (YQ, VC), under the guidance of the Cochrane Heart Group and using the tool described in the *Cochrane Handbook for Systematic Review of Interventions* (Higgins 2011). Any disagreement was resolved by a third author (CM). In order to confirm and validate the methods of allocation concealment and the randomisation procedure, the original authors of all trials were contacted. Risk of bias assessments are presented in tables on the following domains (Higgins 2011).

- Sequence generation.
- Allocation concealment.
- Blinding.
- Incomplete outcome data.
- Selective outcome reporting.
- Other bias.

The risk of bias for each domain was categorized as:

- Low risk of bias;
- High risk of bias;
- Unclear risk of bias.

Measures of treatment effect

Dichotomous data (occurrence of angiographic restenosis, adverse events, myocardial infarction, heart failure, angina, all cause mortality, mortality due to any cardiovascular event, use of revascularisation) were analysed using risk ratios (RRs) with 95% confidence intervals (CIs). It has been shown that RR is more intuitive (Boissel 1999) than the odds ratio (OR) and that OR tend to be interpreted as RR by clinicians (Deeks 2000), which leads to an overestimate of the effect. We planned to analyse continuous outcomes using weighted mean differences (with 95% CI). Standardized mean differences would have been employed if different measurement scales were used. Skewed data and non-quantitative data would have been presented descriptively.

Unit of analysis issues

We did not include any cluster randomised trials or cross-over studies in this review. All included studies are two-arm trials and no control group was used more than once in the meta-analysis. When assessing event data, we avoided counting more than one outcome event for any participant. Where we were unclear about the data (for example, where a study reported numbers of myocardial infarctions, but did not report the number of people who experienced a myocardial infarctions) we asked authors for further information.

Dealing with missing data

When there were missing data, we contacted the original authors of the study to obtain the relevant missing data. If missing data could not be obtained, an imputation method was used. We used sensitivity analysis to assess the impact on the overall treatment effects of inclusion of trials which did not report an intention-to-treat analysis, had high rates of participant attrition, or had other missing data.

Assessment of heterogeneity

The clinical and methodological heterogeneity were evaluated by considering the variability in important participant factors among trials and trial factors (randomisation concealment, blinding of outcome assessment, losses to follow-up, treatment type, co-interventions), respectively. Statistical heterogeneity was tested using the Chi^2 test (significance level 0.1; Lau 1997) and I^2 statistic (0% to 40%: minimal heterogeneity; 30% to 60%: may represent moderate heterogeneity; 50% to 100%: substantial heterogeneity). We planned to explain the source of heterogeneity by subgroup analysis and meta-regression.

Assessment of reporting biases

We used funnel plots to assess potential publication bias (Egger 1997) for the meta-analyses with the outcomes MI and angina, as these analyses included 10 or more studies (Higgins 2011; Sterne 2001).

Data synthesis

Each outcome was combined and calculated using the statistical software RevMan 5.1 (RevMan 2008), according to the statistical guidelines referenced in the current version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). All the meta-analyses were performed with a fixed-effect model using the Mantel-Haenszel method as no significant heterogeneity was found ($I^2 < 50\%$ or $P > 0.1$).

Subgroup analysis and investigation of heterogeneity

We planned to perform subgroup analyses based on the following factors. However, subgroup analyses were not carried out because: there were insufficient data in the original studies allow us to classify the included studies into different subgroups according the pre-specified factors.

- Patient characteristic (age, sex).
- Types of treatment (Western medicine alone, Western medicine plus Tong-xin-luo).
- Follow-up period.
- Type of stent.

Sensitivity analysis

We planned to perform sensitivity analysis to explore the source of heterogeneity as follows, however there were insufficient numbers of studies.

- Quality components, including full-text publications versus abstracts, preliminary results versus final results, published versus unpublished data.
- Risk of bias (by omitting studies that were judged to be at high risk of bias).

RESULTS

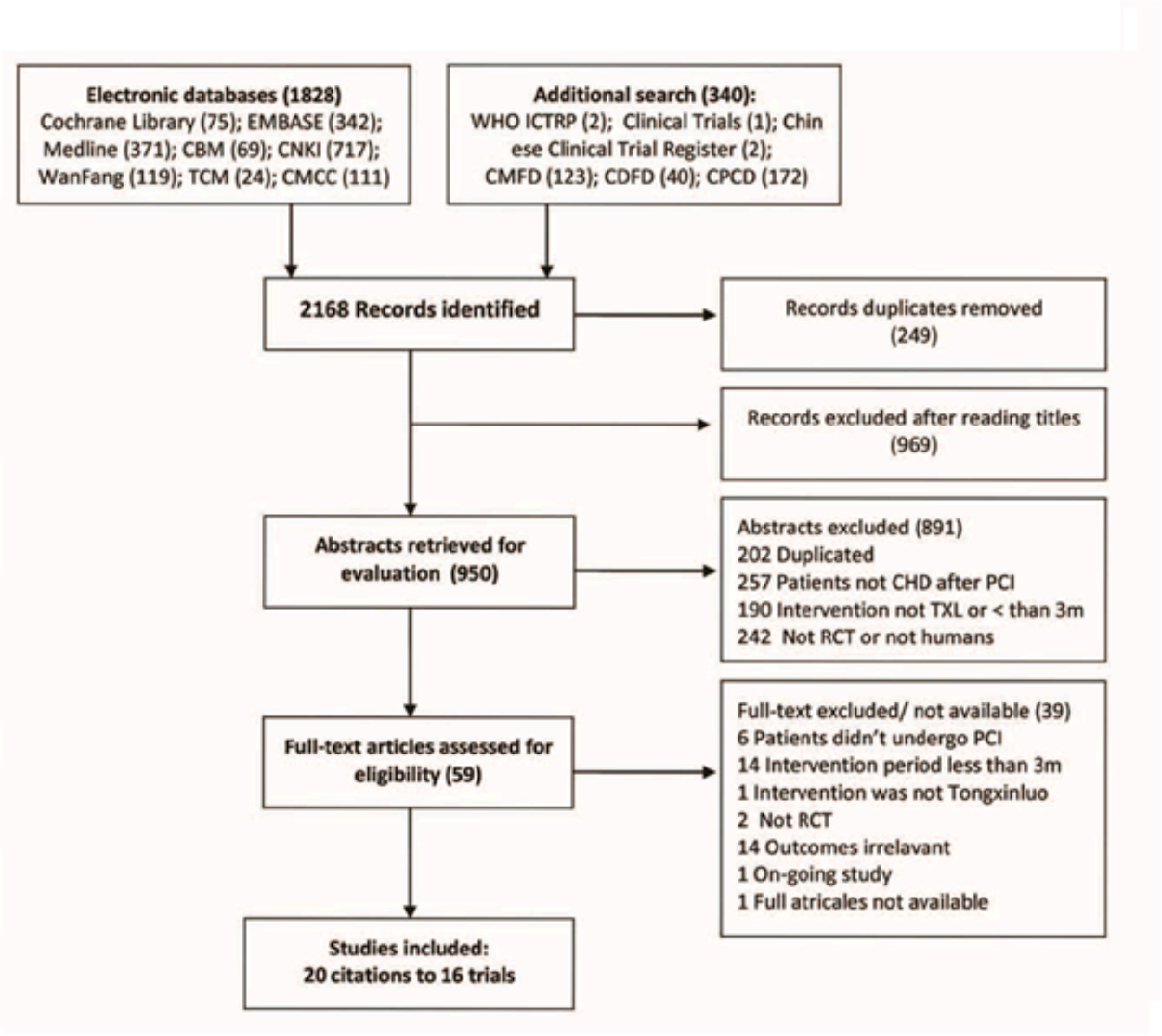
Description of studies

For a detailed description of studies, see Characteristics of included studies.

Results of the search

As shown in the flow chart (Figure 1), our search in electronic bibliographic databases yielded 2168 citations, of which 59 were classified as potentially relevant and were subjected to full text assessment. Sixteen studies with 20 citations met the defined inclusion criteria.

Figure 1. Flow chart of study selection



Included studies

Design of included studies

All the included studies were RCTs of single centre, parallel design, with a control group; one study used a randomised, double-blind, placebo-controlled design (Wang 2010). All included studies were conducted in China, and were performed in hospital settings.

Participants in included studies

A total of 1603 participants were included in the 16 trials, and the number of participants in the studies ranged from 50 (Di 2012) to 178 (Zhang 2009a). The age of participants ranged from 30 to 78 years. All participants showed objective symptoms of CHD and had received a successful PCI. The duration of follow-up ranged from three months (Dai 2011) to two years (Chen 2011) in studies where length of follow-up was provided.

Interventions in included studies

All included trials compared Tong-xin-luo capsule plus conventional treatment with the same conventional treatment alone except one study (Wang 2010), which compared Tong-xin-luo capsule plus conventional treatment with placebo plus the same conventional treatment. Participants all received aspirin, clopidogrel, and low molecular weight heparin after PCI as background therapy. Eight studies reported the use of statins as routine treatment, of which four studies prescribed atorvastatin, one prescribed pravastatin, and three studies did not report which class of statin was prescribed. Other treatments including beta-blockers, nitrates, and angiotension conversion enzyme inhibitors were selectively applied according to illness status of participants. Tong-xin-luo capsule (three to four capsules, three times per day) was initiated on the day of PCI. In one study (Wu 2010), participants in the treatment group began to take Tong-xin-luo seven days before PCI. The treatment duration and time of follow ranged from three months (Yang 2009a) to two years (Zhang 2009a).

Outcome measures of included studies

- Six studies (Chen 2011; Dai 2011; Liang 2010; Wu 2010; Xiao 2007; Zhou 2007b) reported on the incidence of restenosis.
- Three studies (Di 2012; Huang 2010; Zhang 2009a) mentioned occurrence of adverse events.
- Five studies (Dong 2012; Huang 2010; Liang 2010; Wang 2009a; Wu 2010) reported on the incidence of acute myocardial infarction (AMI), eight studies (Di 2012; Li 2004; Wang 2010; Xiao 2007; Yang 2009a; Zhang 2009a; Zheng 2010; Zhou 2007b) reported on the incidence of myocardial infarction (MI).
- Eleven studies (Chen 2011; Di 2012; Li 2004; Liang 2010; Wang 2009a; Wang 2010; Wu 2010; Xiao 2007; Yao 2006; Zhang 2009a; Zhou 2007b) assessed occurrence of angina.
- Four studies (Chen 2011; Xiao 2007; Yang 2009a; Zhang 2009a) measured occurrence of heart failure.
- Four studies (Di 2012; Wang 2010; Yang 2009a; Zhang 2009a) reported on all-cause mortality; five studies (Dong 2012; Huang 2010; Xiao 2007; Yang 2009a; Zhang 2009a) had data available for mortality due to any cardiovascular event.
- Eight studies (Di 2012; Dong 2012; Huang 2010; Wu 2010; Yang 2009a; Zhang 2009a; Zheng 2010; Zhou 2007b) assessed the use of revascularisation, including PCI and coronary artery bypass graft surgery.
- No studies reported mortality (death) due to restenosis after PCI. None of the studies mentioned patient acceptability, quality of life or cost-effectiveness.

Regarding study outcomes, all studies reported the number of patients who experienced related event, except one study (Li 2004) which reported the number of events in each group.

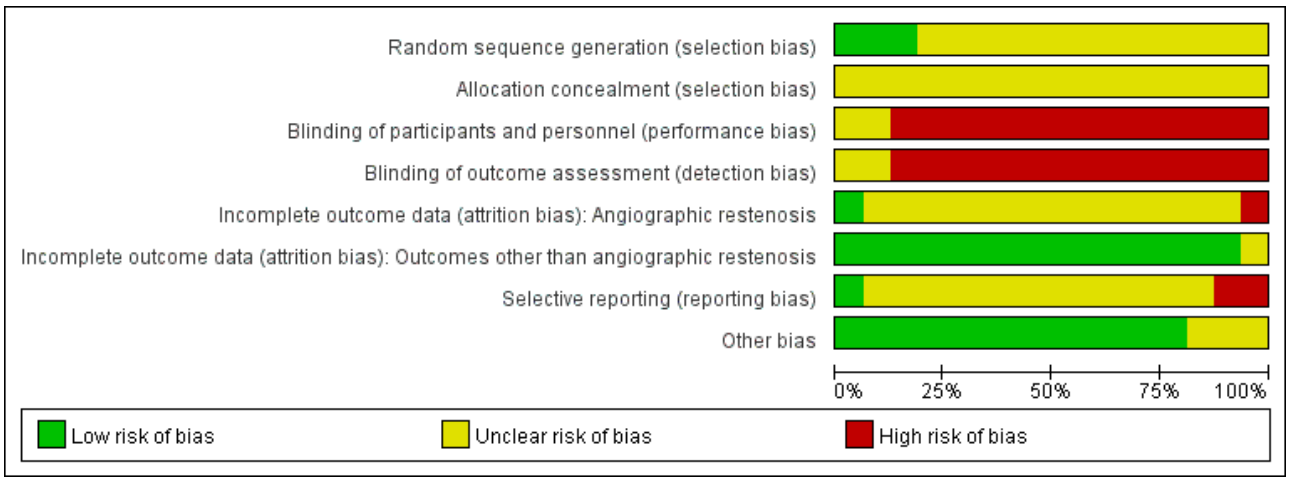
Excluded studies

In total, thirty eight articles were excluded on the basis of their full-text versions for the following reasons (Characteristics of excluded studies): six studies (Chang 2004; Qu 2011; Su 2000; Xiao 2004; Zhang 2008; Zhang 2009b) included patients who did not receive coronary stenting; one trial (Jiang 2008) did not use Tong-xin-luo as an intervention; the intervention period of Tong-xin-luo in 14 articles (Chen 2007; Fan 2008; Fu 2012; Han 2009; Han 2011; Liu 2009; Lu 2012; Wang 2009c; Xu 2007; Zhang 2007; Zhang 2006; Zhang 2005; Zhao 2010; Zhao 2011) was less than three months; two studies (Gao 2007; Xu 2008) were not RCTs; 14 studies (Guo 2012; Kuang 2011; Li 2012; Li 2008; Ma 2009; Tao 2012; Tu 2006; Wang 2007; Wang 2012; Wang 2009b; Yang 2009b; Yang 2010; Yang 2012; Zhang 2010) didn't repot relevant outcomes; and for one study (Hou 2008) only an abstract was published with no data available. We found one on-going study (Han 2012; Characteristics of ongoing studies).

Risk of bias in included studies

All included studies, except for the study by Wang et al (Wang 2010), were considered to have a high risk of bias as at least one domain of methodology was judged at high risk of bias. We tried to contact the study authors to clarify domains of unclear risk of bias but received no reply. Detailed information for the assessment of risk of bias for each included study is described in risk of bias tables under Characteristics of included studies, and authors' judgements about each risk of bias item are presented in Figure 2.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

All the included studies mentioned randomisation. However, only three studies (Chen 2011; Yang 2009a; Zhang 2009a) reported allocation sequence generated by using random number tables or drawing of lots. None of the others described the method of randomisation in details. None of the included studies mentioned allocation concealment.

Blinding

Only one study (Wang 2010) mentioned blinding, but no detailed information about the blinding method was provided. We considered other studies to be at high risk of bias because blinding was not reported and placebo was not used. Patients, doctors and other key study personnel were highly likely to know the allocation.

Incomplete outcome data

One study (Yang 2009a) reported one withdrawal before randomisation. None of the studies mentioned losses to follow-up after randomisation, except that more than half of participants in one study (Xiao 2007) did not undergo coronary angiography, so the occurrence of angiographic restenosis was not reported. There was no loss to follow-up in terms of the other outcomes in this study. None of the other studies reported withdrawals or loss to follow-up. None of the studies mentioned intention-to-treat analysis (ITT).

Selective reporting

No study protocols were available for the included studies. Therefore, most studies were considered to have an unclear risk of bias. Two studies that did not report all the outcomes listed in the methods section were judged as having high risk of bias (Yang 2009a; Zhou 2007b).

Other potential sources of bias

The included studies may have been influenced by the small study effect as none of the included studies mentioned sample size calculation and most of them were small (ranged from 50 to 178 patients). However, baseline information including sex, age, comorbidity, types of coronary pathological changes, number of stents implanted and other risk factors appeared to be balanced between Tong-xin-luo groups and control groups in 13 studies (P > 0.05), and the usage of Tong-xin-luo capsule and conventional treatment were similar, so we considered these 13 trials to be of low risk of bias from other potential sources. The other three studies (Liang 2010; Zheng 2010; Zhou 2007b) were judged as having an unclear risk of bias, because sufficient information was not provided on baseline characteristics.

Effects of interventions

See: **Summary of findings for the main comparison**

Primary outcome measures

1. Occurrence of angiographic restenosis

Six trials (Chen 2011; Dai 2011; Liang 2010; Wu 2010; Xiao 2007; Zhou 2007b) involving 595 participants had relevant data on angiographic restenosis investigated at 6 month follow-up comparingTong-xin-luo plus conventional treatment with conventional treatment alone. Tong-xin-luo plus conventional treatment was better at reducing the risk of occurrence of angiographic restenosis (6/305 vs. 41/290, RR 0.16, 95% CI 0.07 to 0.34, P < 0.00001; see Analysis 1.1).

2. Adverse events

Meta-analysis for the outcome of adverse events was not performed due to insufficient data. In one study there was one case of gastrointestinal reaction relieved without medication in the treatment group and one case of gastrointestinal reaction relieved after symptomatic treatment in the control group (Di 2012). Three patients had mild nausea and mild pain in the upper left abdomen at the beginning of Tong-xin-luo treatment in one study (Zhang 2009a); the symptoms disappeared once the patients started taking the medication between meals. No severe adverse events were reported in these two studies. One study reported no adverse events in the treatment group (Huang 2010).

Secondary outcome measures

1. Occurrence of MI

Five trials (Dong 2012; Huang 2010; Liang 2010; Wang 2009a; Wu 2010) with 453 participants reported on the outcome of AMI, and eight trials (Di 2012; Li 2004; Wang 2009a; Xiao 2007; Yang 2009a; Zhang 2009a; Zheng 2010; Zhou 2007b) with 853 patients reported MI. The pooled estimate of these 13 studies showed that the addition of Tong-xin-luo to conventional treatment reduced the risk of MI compared to conventional treatment alone (7/659 vs. 27/647, RR 0.32, 95% CI 0.16 to 0.66, P 0.002; see Analysis 1.2).

2. Occurrence of heart failure

Four studies (Chen 2011; Xiao 2007; Yang 2009a; Zhang 2009a) of 529 participants investigated occurrence of heart failure. The pooled results showed that the combined treatment of Tong-xin-luo and conventional treatment reduced the risk of heart failure (6/268 vs. 23/261 RR 0.26, 95% CI 0.11-0.62, P 0.003; See Analysis 1.3).

3. Occurrence of angina

A total of 11 RCTs involving 1210 participants (Chen 2011; Di 2012; Li 2004; Liang 2010; Wang 2009a; Wang 2010; Wu 2010; Xiao 2007; Yao 2006; Zhang 2009a; Zhou 2007b) provided data on occurrence of angina. Pooled results demonstrated a reduced incidence of angina in the Tong-xin-luo group (33/616 vs. 137/594, RR 0.24, 95% CI 0.17-0.34, P 0.00001; See Analysis 1.4).

4. All-cause mortality and mortality due to any cardiovascular event

Four studies of 419 participants reported all-cause mortality. Two studies (Di 2012; Wang 2010) reported no deaths in either treatment or control groups, so the estimate was pooled from the two other studies (Yang 2009a; Zhang 2009a). There was no evidence of a difference between the Tong-xin-luo group and the control group (1/219 vs. 3/200, RR 0.38, 95% CI 0.06-2.56, P 0.32; see Analysis 1.5)

Five studies (Dong 2012; Huang 2010; Xiao 2007; Yang 2009a; Zhang 2009a) consisting of 532 participants reported outcomes of mortality due to cardiovascular events, and there was some evidence that Tong-xin-luo plus conventional treatment reduced the risk of death due to cardiovascular events in comparison to conventional treatment alone, though the test did not reach statistic significance (1/285 vs. 7/267, RR 0.31, 95% CI 0.08-1.12, P 0.07; see Analysis 1.6).

5. Use of revascularisation

Pooled analysis of eight studies (Di 2012; Dong 2012; Huang 2010; Wu 2010; Yang 2009a; Zhang 2009a; Zheng 2010; Zhou 2007b) including 806 participants showed a significant effect in favour of the addition of Tong-xin-luo to conventional treatment (15/409 vs. 58/397, RR 0.26, 95% CI 0.15 to 0.45, P < 0.00001; see Analysis 1.7).

6. Patient acceptability, quality of life or cost-effectiveness

Meta-analyses were not done as none of the included studies reported these outcomes.

Sensitivity analysis

Sensitivity analyses by study quality were not performed because most of the included studies were considered to have high risk of

bias. There was an insufficient number of studies for meta-analysis after removing studies at high risk of bias.

Publication bias

Funnel plots were used to assess potential publication bias for the outcomes of MI and angina as more than 10 trials were included for each of them. A symmetrical funnel plot of MI indicate no risk of publication bias (see Figure 3), but an asymmetrical funnel plot of angina suggested that high risk of publication bias existed (see Figure 4).

Figure 3. Funnel plot of comparison: 1 Tong-xin-luo + Conventional treatment vs. Conventional treatment, Outcome: 1.2 Occurence of myocardial infarction.

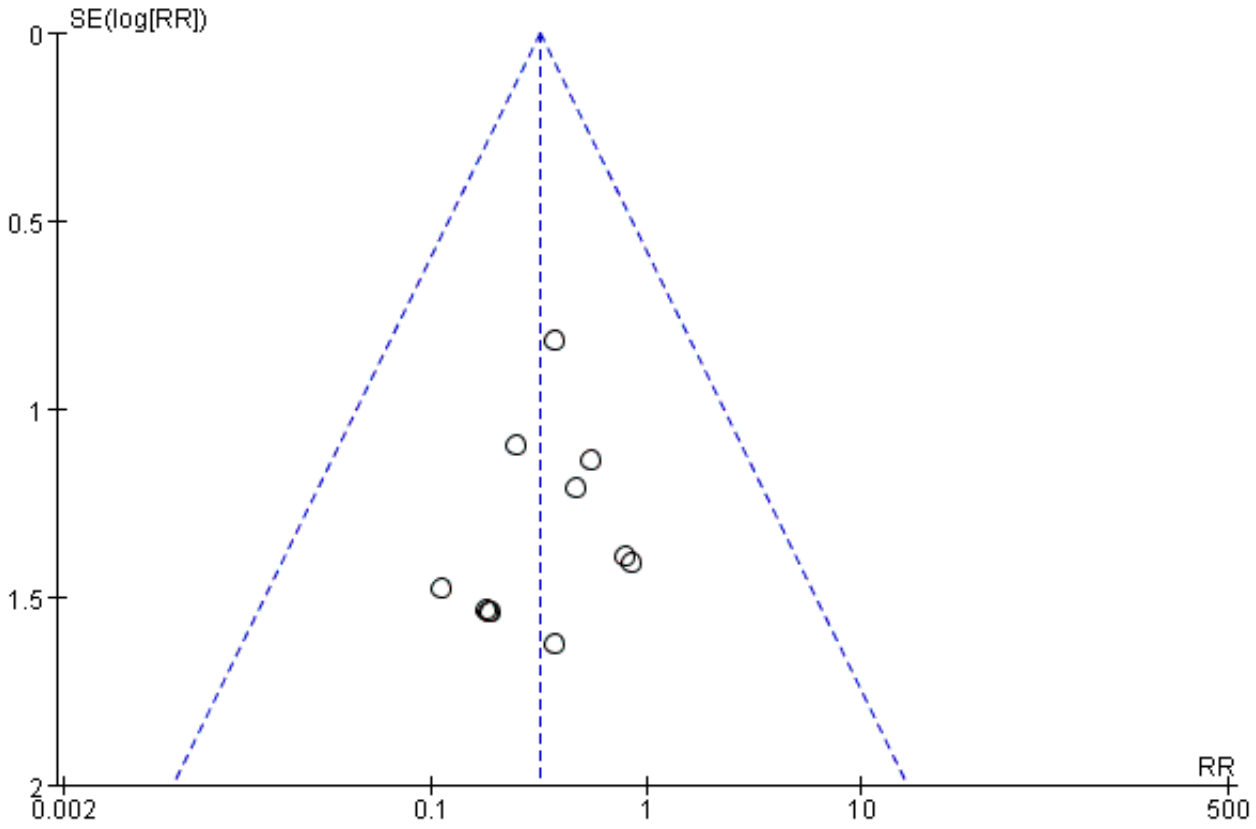
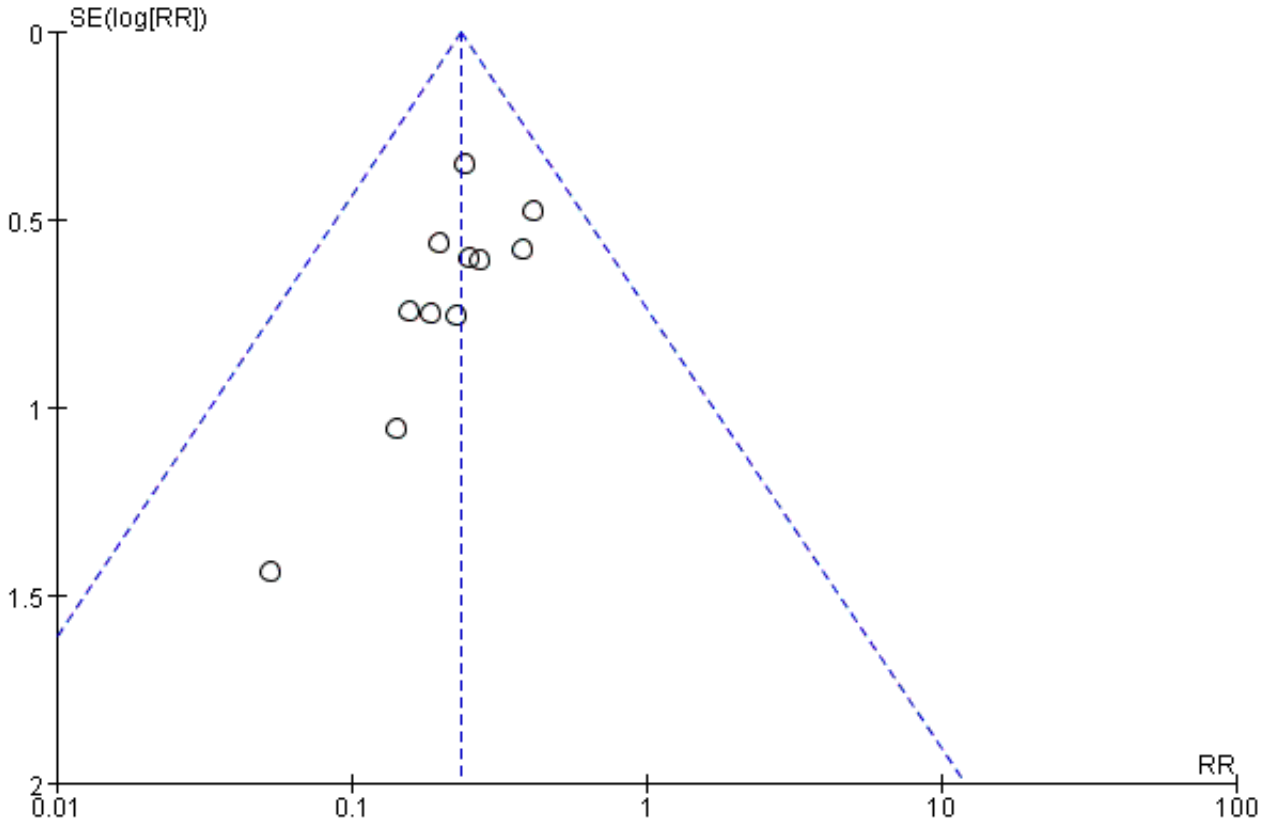


Figure 4. Funnel plot of comparison: 1 Tong-xin-luo + Conventional treatment vs. Conventional treatment, Outcome: 1.4 Occurrence of angina.



DISCUSSION

Summary of main results

This systematic review included 16 RCTs which evaluated the effects of Tong-xin-luo in addition to conventional treatment. The meta-analysis demonstrated that Tong-xin-luo capsule in combination with conventional Western medicine was significantly more effective in preventing angiographic restenosis, cardiovascular events (MI, angina and heart failure), and revascularisation, when compared with conventional Western medicine alone. There was some evidence that the addition of Tong-xin-luo to conventional treatment reduced the risk of all-cause mortality or mortality due to any cardiovascular event though the estimates failed to achieve statistical significance. This might be due to small sample size. The statistical heterogeneity was low in all meta-analyses. No severe adverse events were observed in the patients treated with Tong-xin-luo.

The effect of Tong-xin-luo was generally not obvious in included trials, but the pooled estimates from meta-analyses were significant when the sample size increased. However, the study findings should be interpreted with caution because most of the included studies were at high risk of bias.

Overall completeness and applicability of evidence

Sixteen RCTs involving 1063 patients were included in this review. This review examined the efficacy of Tong-xin-luo in patients with CHD after PCI. Although the age and gender of participants in the included trials were representative of CHD patients who undergo successful PCI operations, the sample size of the included trials was generally small. Furthermore, all participants were recruited from Chinese populations. This may limit the generalizability of the study results to patients of other ethnicities.

Quality of the evidence

Because of the limitations of the included studies, including imprecision and publication bias, the quality of evidence was considered low or very low for most study outcomes of this systematic review. Most publications provided very limited information about trial design and methodology. Only three studies described the methods of randomisation. Methods of allocation concealment or blinding were not mentioned in most of the included studies. Lack of blinding may have lead to an unbalanced prescription of other treatments such as statins, which may have influenced the results. As most of the included studies generally did not provide sufficient information for us to assess whether the prescription of other medicines were consistent and balanced, the potential influence is unclear. In addition, no included studies mentioned sample size calculation and most of the included studies consisted of small numbers of participants. As smaller studies are usually less rigorous than large scale studies and are more likely to show a large treatment effect (Pereira 2012), the treatment effects of Tong-xin-luo need to be evaluated by future large-scale RCTs. Additonal potential problems in the design and conduct of traditional Chinese medicine research (Wang

2007) should also be noted. Thus, although this review shows a potentially protective effect of Tong-xin-luo, the results should be interpreted with caution. Future research is very likely to change the estimates.

Potential biases in the review process

We attempted to minimise bias in the review process. One of the major challenges to conducting reviews across different cultural medical disciplines is the language barrier and resulting insufficient literature search (Wu 2013). A comprehensive search without language restrictions was conducted to identify all relevant studies. Study selection, assessment of risk of bias and data extraction were independently carried out by two review authors. The review was strictly conducted according to the protocol, however, potential biases might still exist. Asymmetrical funnel plots of angina suggest that publication bias may be present; this might lead to overestimates of effect size of Tong-xin-luo in reducing the risk of angina. In addition, the inclusion criteria of participants in different trials varied from each other, with some trials only including patients with AMI, while others only included patients with angina; this suggests that there may be some clinical heterogeneity among included studies. Lastly, the overall analysis did not consider the varying trial durations and drug usage as part of routine treatment. However, no significant heterogeneity was identified in the meta-analysis, which suggests the impact of trial duration and drug usage on the treatment effect was low.

Agreements and disagreements with other studies or reviews

We did not identify any other systematic reviews with a focus on Tong-xin-luo capsule for restenosis after PCI in patients with CHD. Two systematic reviews on the efficacy of Tong-xin-luo were identified. One included 18 studies and assessed the effects of Tong-xin-luo in patients with unstable angina pectoris (Wu 2006). This study's results suggested that Tong-xin-luo reduces the risk of AMI, angina and need for revascularisation, but the poor quality of included studies was of concern. The other review included only two trials assessed the efficacy for acute cerebral infarction (Zhuo 2008) and was unable to determine whether Tong-xin-luo has a favourable effect or not in acute ischaemic stroke.

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review indicated that Tong-xin-luo may possibly reduce incidence of angiographic restenosis, revascularisation, and CVDs, without causing severe adverse effects, in patients with CHD after PCI. However, these results should be considered as hypothesis generating rather than hypothesis testing due to the small sample size, high risk of bias in the included studies, publication bias and low quality of evidence.

Implications for research

This systematic review has important implications for future research. Firstly, further studies of high quality are needed. Improvement of methodological quality should be achieved, including use of placebo and clear descriptions of randomisation and allocation concealment. Secondly, future studies should report quality of life, patient acceptability and cost. Morever, most of the included studies were small. More studies with large sample sizes are needed to verify the protective effect of Tong-xin-luo. Lastly, cost-effectiveness studies of Tong-xin-luo are also needed as such evidence is lacking.

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REFERENCES

References to studies included in this review

Chen 2011 *{published data only}*

Chen ZQ. Effect of Tongxinluo capsule on platelet activity and function of vascular endothelium functions as well as prognosis at different stage in patients with acute coronary syndrome after undergoing percutaneous coronary intervention [通心络胶囊对急性冠状动脉综合征患者介入治疗不同时期血小板活化和血管内皮功能以及预后的影响]. *South China Journal of Cardiovascular Diseases* 2011;**suppl**:84.

* Chen ZQ, Hong L, Wang H, Yin Q. Effect of Tongxinluo capsule on platelet activities and vascular endothelium functions as well as prognosis in patients with acute coronary syndrome undergoing percutaneous coronary intervention [通心络胶囊对急性冠状动脉综合征患者介入治疗后血小板活化和血管内皮功能及预后的影响]. *Chinese Journal of Integrated Traditional and Western Medicine* 2011;**31**(04):487-91.

Chen ZQ, Hong L, Wang H, Yin Q, Lu LX, Lai YL. Effect of Tongxinluo capsule on platelet activities and vascular endothelium functions at different stages in patients with acute coronary syndrome undergoing percutaneous coronary intervention [通心络胶囊对急性冠状动脉综合征患者介入治疗后血小板活化血管内皮功能的影响]. *Chinese Pharmaceutical Journal* 2012;**47**(4):311-5.

Dai 2011 *{published data only}*

Dai GF, Yang SJ. Clinical observation for the effect of Tong-xin-luo capsules in preventing restenosis in patients with coronary heart disease after percutaneous coronary intervention [通心络胶囊干预冠心病PCI 术后再狭窄临床观察]. *Guangming Journal of Chinese Medicine* 2011;**26**(9):1823-4.

Di 2012 *{published data only}*

Di J. Research on the Effect of Tongxinluo capsule on the Instent Restenosis of Small Vessels and Long Affection in Coronary Artery [通心络胶囊对冠状动脉小血管长病变支架术后再狭窄的影响研究][Master's thesis]. Nanjing: Nanjing University of Chinese Medicine, 2012.

Dong 2012 *{published data only}*

Dong SQ, Dong YW. Influence of Tongxinluo on inflammatory and cytokinesendothelial function in patients with acute myocardial infarction after percutaneous coronary intervention [通心络胶囊对急性心肌梗死患者经皮冠状动脉介入治疗术后炎症因子及血管内皮功能的影响]. *Chinese Journal of Clinicians (electronic edition)* 2012;**6**(7):1865-7.

Huang 2010 *{published data only}*

Huang B. Influence of Tongxinluo on inflammation reaction and endothelial function in patients with acute myocardial infarction after percutaneous coronary intervention [通心络胶囊对急性心肌梗死介入术后炎性反应和血管内皮功能的影响]. *Journal of New Chinese Medicine* 2010;**42**(9):22-4.

Li 2004 *{published data only}*

Li YW. Research on the Effects of Tongxinluo Capsules on Local Cerebral Blood Flow in Patients with Cerebral Infarction [通心络胶囊对植入冠状动脉支架预后影响的研究]. *Journal of Bethune Military Medical College* 2004;**2**(2):75-7.

Liang 2010 *{published data only}*

Liang YM, Wang ZJ, Su XY. The effect of Tongxinluo capsules on coronary restennosis of patients with acute myocardial infarction after percutaneous coronary intervention [通心络胶囊对心肌梗死冠状动脉介入治疗患者术后再狭窄的疗效评价]. *Chinese Journal of TCM WM Critical Care* 2010;**17**(003):175-6.

Wang 2009a *{published data only}*

Wang YH, Shi HN. Effect of Tongxinluo capsules to prevent restenosis in patients after percutaneous intervention [通心络胶囊防治冠脉支架术后再狭窄疗效观察]. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2009;**18**(1):39.

Wang 2010 *{published data only}*

Wang XD, Lou B. Effect of Tongxinluo Capsule on Restenosis after Coronary Artery Stent Implantation in Patients with Type-2 Diabetes Mellitus [通心络对2型糖尿病冠状动脉小血管长病变支架术后再狭窄的影响]. *Journal of Nanjing TCM University* 2010;**26**(006):464-7.

Wu 2010 *{published data only}*

Wu ZY, Yang DC, Hou B, Chen YG. Effects of Tongxinluo Capsules on interventional therapy of patients with unstable angina. China Medical Herald, 2010, 20: 012. [通心络胶囊在不稳定型心绞痛患者介入治疗中的作用]. *China Medical Herald* 2010;**7**(20):17-20.

Xiao 2007 *{published data only}*

Xiao HB, Zhang DD, Gu J. Effects of tongxinluo on C-reactive protein and clinical prognosis in patients after coronary stenting [通心络对冠心病支架术后C 反应蛋白及预后的影响]. *Cardiac Intervention* 2007;**16**(8):520-2.

Yang 2009a *{published data only}*

* Yang W. The protective effects of Tongxinluo capsule on myocardium after reperfusion in patients with acute myocardial infarction [通心络胶囊对急性心肌梗塞急诊PCI患者心肌保护的临床研究][Master's thesis]. Shaanxi: Shaanxi University of Chinese Medicine, 2009.

Yang W, Wang S, Xu XH, Zhang CF. NA [通心络胶囊对急性心肌梗死急诊PCI术后左室重构的影响]. *Chinese Community Doctors* 2012;**30**:8.

Yang W, Xu XH, Wang S, Zhang CF. [通心络胶囊对急性心肌梗死急诊PCI术后患者血清Ⅲ型前胶原氨基端肽及左室重构的影响]. *Chinese Journal of Difficult and Complicated Cases* 2012;**11**(6):452-3.

Yao 2006 *{published data only}*

Yao FH, Liu N, Ge GY. Clinical study of reconstriction after PCI operation in patients with coronary disease intervened by Tongxinluo capsule [通心络胶囊干预冠心病患者PCI术后再狭窄的临床研究]. *Chinese Journal of Difficult and Complicated Cases* 2006;**5**(3):191-2.

Zhang 2009a *{published data only}*

Zhang XP, Zhang Y. Long-term effect of Tongxinluo in patients with acute myocardial infarction after coronary stenting [通心络对急性心肌梗死患者置入支架后远期疗效的影响]. *Chinese Remedies & Clinics* 2009;**9**(3):243-4.

Zheng 2010 *{published data only}*

Zheng H, Teng ZH, Ma LQ. The effect of Tongxinluo capsule on level of serum CRP and blood lipid in patients with ACS post PCI [通心络胶囊对急性冠状动脉综合征介入术后患者C-反应蛋白、血脂的影响]. *Chinese Journal of Difficult and Complicated Cases* 2010;**9**(7):487-8.

Zhou 2007b *{published data only}*

Zhou J, Guo JT. Clinical Study of Tongxinluo on Preventing Re-stenosis of Stents in CHD [通心络预防冠心病患者支架术后再狭窄的临床研究]. *Hebei Medicine* 2007;**13**(10):1188-91.

References to studies excluded from this review

Chang 2004 *{published data only}*

Chang SF, Zhao M. Clinical observation for Tongxinluo in the treatment of 68 cases of unstable angina pectoris [通心络胶囊治疗不稳定型心绞痛 68 例临床观察]. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2004;**13**(2):189.

Chen 2007 *{published data only}*

Chen ZQ, Lai YY, Hong L, Wang H, Qiu Y, Yin QL, et al. The effects of Tongxinluo capsule on platelet activity and vascularendothelium function in patients with ACS after PCI [通心络对急性冠状动脉综合征患者介入术后血小板活化及血管内皮功能的影响]. *Chinese Journal of Geriatric Heart Brain and Vessel Diseases* 2007;**9**(7):460-3.

Fan 2008 *{published data only}*

Fan SM. Treatment Effects of Tongxinluo capsule on acute myocardial infarction after coronary stent [通心络胶囊在急性心肌梗死支架术后的临床应用研究]. *Qinghai Medical Journal* 2008;**38**(1):8-10.

Fu 2012 *{published data only}*

Fu DH, Song XL, Feng CH. Clinical observation of Tongxinluo capsules in treating patients with angina after PCI [通心络胶囊对冠心病介入术后心绞痛的疗效观察]. *Journal of Guiyang College of Traditional Chinese Medicine* 2012;**34**(3):171-2.

Gao 2007 *{published data only}*

Gao CY, Yang L, Zhang J, Wu YL. The long-term efficacy of Tongxinluo in patients after percutaneous coronary intervention [通心络胶囊对经皮冠状动脉介入患者长期预后的影响]. *Hebei Medical Journal* 2007;**29**(10):1067-8.

Guo 2012 *{published data only}*

Guo YH, Wang Y. Evaluation of the therapeutic effect of Tongxinluo for acute myocardial infarction using $^{99}Tc^{m}$-MIBI SPECT imaging [$^{99}Tc^{m}$-MIBI心肌灌注断层显像评价通心络对急性心肌梗死后心肌无再流的影响]. *Chinese Journal of Nucleau Medicine and Molecular Imaging* 2012;**32**(2):127-30.

Han 2009 *{published data only}*

Han XT. Study of the changes of myeloperoxidase concentration in plasma and the interventional effect of Tongxinluo capsule on patients with unstable angina [不稳定型心绞痛患者介入治疗前后血浆髓过氧化物酶水平变化及通心络胶囊的干预作用]. *Journal of Emergency in Traditional Chinese Medicine* 2009;**18**(5):730-1.

Han 2011 *{published data only}*

Han XT, Cui XJ, Li YR, Chu FY. The effect of Tongxinluo on blood lipid, hs-CRP and MMP-9 in patients with unstable angina pectoris after PCI [通心络胶囊对不稳定型心绞痛患者PCI术后血脂、血浆高敏C反应蛋白、基质金属蛋白酶一9的影响]. *Journal of Emergency in Traditional Chinese Medicine* 2011;**20**(6):873-4.

Hou 2008 *{published data only}*

Hou AJ, Liu MY, Zhao HY, Zhang M, Yuan L, Jin YZ, et al. The effect of Tongxinluo on restenosis in patients with ACS [通心络对急性冠状动脉综合征患者支架术后再狭窄的影响]. *Chinese Journal of Cardiology* 2008;**36**:221-2.

Jiang 2008 *{published data only}*

Jiang XG, Yang YB, Qi HW, Yang M. Research of prevention effect of traditional Chinese medicine on restenosis after percutaneous coronary intervention [冠心病介入治疗后再狭窄的中医药防治研究]. *Heilongjiang Journal of Traditional Chinese Medicine* 2008;**37**(4):58-9.

Kuang 2011 *{published data only}*

Kuang B, Yang Y. Protection of Tongxinluo capsule against myocardial injury in patients after elective percutaneous coronary stenting posting [通心络胶囊对择期冠脉支架置入术患者的心肌保护作用]. *Modern Hospital* 2011;**11**(5):21-3.

Li 2008 *{published data only}*

Li MJ. Inflammatory reaction and change of vascular endothelial function after percutaneous coronary intervention and the effect of Tongxinluo [冠心病介入术后炎症反应和血管内皮功能变化及通心络的干预作用]. *Journal of Chinese Physician* 2008;**10**(10):1392-4.

Li 2012 *{published data only}*

Li H. The effect of drug intervention on vascular inflammatory reaction and change of vascular endothelial function after percutaneous coronary intervention [冠状动脉介入术后血管炎症反应及内皮功能改变的药物干预分析]. *China Practical Medical* 2012;**07**(13):159-60.

Liu 2009 *{published data only}*

Liu SJ. The effect of Tongxinluo on perioperative CRP patients with ACS [通心络胶囊对急性冠脉综合征患者围手术期C反应蛋白影响的研究]. *Journal of New Chinese Medicine* 2009;**41**(7):41-2.

Lu 2012 *{published data only}*

Lu Y, Zhao XJ, Liao XC. The effect of Tongxinluo capsules on the change of hemorheology in patients with CHD after PCI [通心络胶囊对冠心病患者PCI 术后血液流变学的影响]. *Inner Mongol Journal of Traditional Chinese Medicine* 2012;**14**(4):1-2.

Ma 2009 *{published data only}*

Ma QL, Zhang SD, Ning YG, Pu XQ, Yu LG, Zheng SF, et al. Effect of Tongxinluo on endothelial function and hypersensitiveC-reactive protein in acute coronary syndrome patients undergoing percutaneous coronary intervention [通心络对急性冠脉综合征介入治疗术患者内皮功能和高敏C反应蛋白的影响]. *Journal of Central South University (Medical Sciences)* 2009;**34**(06):550-4.

Qu 2011 *{published data only}*

Qu JQ, Ma JE, Bai RL. Clinical observation of Tongxinluo in treating patients with CHD [通心络胶囊治疗冠心病心绞痛疗效观察]. *Chinese and Foreign Medical Research* 2011;**9**(12):22.

Su 2000 *{published data only}*

Su XY, Huang JX, Zhao ZJ, Zhao L, Hu YL, Su HR. Clinical observation of 96 cases of variant angina pectoris treated with Tongxinluo [通心络治疗变异型心绞痛96例临床观察]. *Chinese Journal of Integrated Traditional and Western Medicine in Intensive and Cricitical Care* 2000;**7**(2):119.

Tao 2012 *{published data only}*

Tao WG, Zhu KY. Curative effect of Tongxinluo in treatment of angina after percutaneous coronary intervention (PCI) operation [通心络治疗PCI 术后心绞痛的疗效观察]. *Medical Innovation of China* 2012;**9**(5):9-10.

Tu 2006 *{published data only}*

Tu YP, Lei MJ, Zeng LF, Gong AB, Wei WR, Wang LL, et al. Influence of Tongxinluo on C-reactive Protein in patients with diabetes after percutaneous coronary intervention [通心络胶囊对糖尿病患者冠状动脉介入术后C反应蛋白的影响]. *Chinese Remedies & Clinics* 2006;**6**(3):229-30.

Wang 2007 *{published data only}*

Wang G. Clinical study Oil Lvedv and Lvef after blood flow reconstruction interfered by Tongxinluo capsule in patients with AMI after percutaneous coronary intervention [通心络胶囊对急性心肌梗死介入治疗后左室舒张末容积和射血分数的影响]. *Chinese Journal of Primary Medicine and Pharmacy* 2007;**14**(4):570-1.

Wang 2009b *{published data only}*

Wang WY, Liu YB, Sun Y. Effect of Tongxinluo on inflammatory factor in patients with ACS [通心络胶囊对急性冠脉综合症患者介入治疗后炎症因子的影响]. *Prevention and Treatment of Cardio-cerebral-vascular disease* 2009;**9**(4):308-9.

Wang 2009c *{published data only}*

Wang X, Li J. Clinical observation for Tongxinluo in the treatment of CHD [通心络胶囊治疗冠心病的临床疗效观察]. *Chinese Journal of Modern Drug Application* 2009;**22**(3):105-6.

Wang 2012 *{published data only}*

Wang L, Liu H, Hu YC. The effect of drug intervention on vascular inflammatory reaction and vascular endothelial function after percutaneous coronary intervention [冠状动脉介入术后血管炎症反应及内皮功能改变的药物干预探讨]. *China Clinical Practical Medicine* 2012;**7**(18):169-70.

Xiao 2004 *{published data only}*

Xiao YQ, Li WK. The effect of Tongxinluo in treating patients with unstable angina pectoris [通心络治疗不稳定型心绞痛的临床观察]. *Acta medicinae Sinica* 2004;**17**(2):152-3.

Xu 2007 *{published data only}*

Xu Z, Li X. Influence of Tongxinluo on inflammatory factor of acute coronary syndrome patients after interventional therapy and its early heart complication [通心络对急性冠脉综合征患者介入治疗术后炎性因子及早期心脏并发症的影响]. *Modern Journal of Integrated Traditional Chinese Western Medicine* 2007;**16**(2):156-7.

Xu 2008 *{published data only}*

Xu LD, Liu LY. The prevention of restenosis after percutaneous coronary intervention [冠状动脉支架内再狭窄的防治]. *Practical Cardio-cerebral Pulmonary Vascular Disease* 2008;**16**(4):73-6.

Yang 2009b *{published data only}*

Yang GK. Inflammatory reaction and change of vascular endothelial function after percutaneous coronary intervention and the effect of drug intervention [冠心病介入术后血管炎症反应和内皮功能变化及药物干预作用]. *Sichuan Medical Journal* 2009;**30**(11):1788-90.

Yang 2010 *{published data only}*

Yang JX, Li MJ, Yang XH. Effect of Tongxinluo on Change of Vascular Inflammation and EndothelialFunction after Percutaneous Coronary Intervention [冠状动脉介入术后血管炎症反应和内皮功能改变及药物干预作用]. *Journal of Liaoning University of TCM* 2010;**12**(2):94-6.

Yang 2012 *{published data only}*

Yang W, Xu XH, Wang S, Zhang CF. The effect of Tongxinluo on serum ⅢPNP and ventricular remodeling in patients with AMI after PCI [通心络胶囊对急性心肌梗死急诊PCI术后患者血清Ⅲ型前胶原氨基端肽及左室重构的影响]. *Chinese Journal of Difficult and Complicated Cases* 2012;**11**(6):452-3.

Zhang 2005 *{published data only}*

Zhang W. Effect of Tongxinluo Capsule on Coagulant and Fibrinolysis System andAngiotension II in Patients with CHD after Intracoronary Stenting [通心络胶囊对冠脉内支架置入术后患者凝血纤溶系统和血管紧张素II的影响]. *Hebei Medicine* 2005;**12**(1):37-9.

Zhang 2006 *{published data only}*

Zhang JW, Yang DC. The protective effects of Tongxinluo on myocardium after reperfusion in PCI patients with acute myocardium infarction [通心络对急性心肌梗死急诊PCI患者再灌注损伤的保护性研究]. *Medicine Industry Information* 2006;**3**(21):8-10.

Zhang 2007 *{published data only}*

Zhang HW. Clinical analysis of integrated traditional and western medicine in treating 62 cases of CHD [中西医结合治疗冠心病62例临床分析]. *Theory and Practice of Chinese Medicine* 2007;**17**(7):722-3.

Zhang 2008 *{published data only}*

Zhang LJ, Li HT, Guo JT, Zhou J. The Effect of Tongxinluo Capsules on the Function of BloodVessel Endothelium(BVE)on the Patientswith Coronary Heart Disease [通心络胶囊对冠状动脉粥样硬化性心脏病人血管内皮功能的影响]. *Hebei Medicine* 2008;**14**(7):761-7.

Zhang 2009b *{published data only}*

Zhang TX, Zhou JZ. The effect of Tongxinluo on inflammatory cytokins in patients with ACS [通心络胶囊对急性冠脉综合症患者炎症因子的影响]. *China Journal of Chinese Materia Medica* 2009;**34**(14):1857-8.

Zhang 2010 *{published data only}*

Zhang HT, Jia ZH, Zhang J, Ye ZK, Yang WX, Tian YQ, et al. No-reflow protection and long-term efficacy for acute myocardialinfarction with Tongxinluo: a randomized double-blind placebo—controlled multicenter clinical trial. *Chinese Medical Journal* 2010;**123**(20):2858-64.

Zhao 2010 *{published data only}*

Zhao H, Tian JH, Hao XY, Ma L. Effects of Tongxinluo on Inflammatory factors in patients with coronary heart disease after percutaneous coronary intervention [通心络对冠心病病人PCI 术后炎症因子的影响]. *Acta Academiae Mediciane Qindao Universitatis* 2010;**46**(4):349-351.

Zhao 2011 *{published data only}*

Zhao X, Song ZJ, Hou LX. Clinical observation of Tongxinluo in treating patiens after percutaneous coronary intervention [通心络治疗支架置入术后患者的临床分析]. *Medical Information* 2011;**24**(7):173.

References to studies awaiting assessment

Deng 2013 *{published data only}*

Deng X. Effect of Tongxinlou capsule on restenosis after PCI in patients with CHD [通心络胶囊干预冠心病PCI术后再狭窄临床观察]. *China Medicine and Pharmacy* 2013;**3**(12):67-8.

References to ongoing studies

Han 2012 *{published data only}*

NCT01721590. Tongxinluo improve high on Clopidogrel platelet reactivity in patients with coronary heart disease. http://clinicaltrials.gov/show/NCT01721590 (accessed November 2012).

Additional references

Agema 2001

Agema WRP, Jukema JW, Pimstone SN, Kastelein JJP. Genetic aspects of restenosis after percutaneous coronary interventions; towards more tailored therapy. *European Heart Journal* 2001;**22**(22):2058-74.

Bhattarai 2012

Bhattarai N, Charlton J, Rudisill C, Gulliford MC. Coding, recording and incidence of different forms of coronary heart disease in primary care. *PLoS ONE* 2012;**7**(1):e29776.

Boissel 1999

Boissel JP, Cucherat M, Li W, Chatellier G, Gueyffier F, Buyse M, et al. The problem of therapeutic efficacy indices. 3. Comparison of the indices and their use. *Therapie* 1999;**54**(4):405-11.

Chen 1985

Chen CY. Effect of Scolopendra extraction in the experiment of rabbit heart. *Chinese Medicine Pharmacology and Clinical Practice* 1985;**1**(1):124-5.

Chen 2007

Chen ZQ, Lai YY, Hong L, Wang H, Qiu Y, Yin QL, et al. The effects of Tongxinluo capsule on platelet activity and vascular endothelium function in patients with ACS after PCI. *Chinese Journal of Geriatric Heart Brain and Vessel Diseases* 2007;**9**(7):460-3.

Cutlip 2007

Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007;**115**(17):2344-51.

Dangas 1996

Dangas G, Fuster V. Management of restenosis after coronary intervention. *American Heart Journal* 1996;**132**(2 Pt 1):428-36.

Deeks 2000

Deeks JJ. Issues in the selection of a summary statistic for meta-analyses of binary data. Abstracts of 8th International Cochrane Colloquium. Cape Town: The Cochrane Collaboration, Oct 25-28th, 2000.

Dörffler 2005

Dörffler-Melly J, Koopman MM, Prins MH, Büller HR. Antiplatelet and anticoagulant drugs for prevention of restenosis/reocclusion following peripheral endovascular treatment. *Cochrane Database of Systematic Reviews* 2005, Issue 1. [DOI: 10.1002/14651858.CD002071.pub2]

Egger 1997

Egger M, Davey-Smith G, Schneider M, Minder CSO. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**13**(7109):629-34.

Fattori 2003

Fattori R, Piva T. Drug-eluting stents in vascular intervention. *Lancet* 2003;**361**(9353):247-9.

Giglioli 2009

Giglioli C, Valente S, Margheri M, Comeglio M, Chiostri M, Romano SM, et al. An angiographic evaluation of restenosis rate at a six-month follow-up of patients with ST-elevation myocardial infarction submitted to primary percutaneous coronary intervention. *Internation Journal of Cardiology* 2009;**131**(3):362-9.

Go 2014

Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. Heart Disease and Stroke Statistics - 2014 Update. A report from the American Health Association. *Circulation* 2014;**129**(3):e28-e292.

Grech 2003

Grech ED. ABC of interventional cardiology: percutaneous coronary intervention II: the procedure. *BMJ* 2003;**326**(24):1137-40.

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions 5.0.2 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Huntington 2003

Huntington JA, Baglin TB. Targeting thrombin – rational drug design from natural mechanisms. *Trends in Pharmacological Sciences* 2003;**24**(11):589-95.

Kang 2012

Kang Y, Lao H, Yu X, Chen J, Zhong S. Progress in genetic and epigenetic research on in-stent restenosis after percutaneous coronary interventions. *Chinese Journal of Medical Genetics* 2012;**29**(1):38-42.

Lau 1997

Lau J, Ioannidis JP, Schmid CH. Quantitative synthesis in systematic reviews. *Annals of Internal Medicine* 1997;**127**(9):820-6.

Lonn 2010

Lonn E, Bosch J, Teo KK, Pais P, Xavier D, Yusuf S. The polypill in the prevention of cardiovascular diseases: key concepts, current status, challenges, and future directions. *Circulation* 2010;**122**(20):2078-88.

Lozano 2012

Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010. *Lancet* 2012;**380**(9859):2095-128.

Lu 2006

Lu XY, Shi DZ, Xu H. Clinical study on effect of *Xiongshao* capsule on restenosis after percutaneous coronary intervention. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2006;**26**(1):13-7.

Modi 1995

Modi NB, Baughman SA, Paasch BD. Pharmacokinetics and pharmacodynamics of TP-9201, a GPIIbIIIa antagonist, in rats and dogs. *Journal of Cardiovascular Pharmacology* 1995;**25**(6):888.

NHLBI 2011

National Heart Lung and Blood Institute (NHLBI). Health Topic: Coronary heart disease. Available from http://www.nhlbi.nih.gov/health/health-topics/topics/cad/ 2011.

Nong 1989

Nong ZJ, Shen YY, Dong HC. The effect of Eupolyphaga Sinensis Walk alkaloids on rabbits cardial pump function. *Journal of Anhui Traditional Chinese Medical College* 1989;**8**(3):84-6.

Nong 2000

Nong MZ. Research on combined treatment of unstable angina pectoris with TCM and WM. *Zhong Yi Han Shou Tong Xun* 2000;**19**(4):51-2.

Odell 2006

Odell A, Grip L, Hallberg LR. Restenosis after percutaneous coronary intervention (PCI): experiences from the patients' perspective. *European Journal of Cardiovascular Nursing* 2006;**5**(2):150-7.

Paul 1994

Johnson PH. Hirudin: Clinical potential of a thrombin inhibitor. *Annual Review of Medicine* 1994;**45**:165-77.

Pei 1986

Pei YQ, Wen SR, Wang XY, Huo SP, Wei MC. Study of cardiac stimulation of Ginsenoside of upper part over grand. *Journal of Beijing Medical University* 1986;**18**(2):140-1.

Pereira 2012

Pereira TV, Horwitz RI, Ioannidis JP. Empirical evaluation of very large treatment effects of medical interventions. *JAMA* 2012;**308**(14):1676-84.

Rajaqopal 2003

Rajaqopal V, Rockson SG. A review of mechanisms and management. *American Journal of Medicine* 2003;**115**(7):547-53.

RevMan 2008 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.

Richard 2002

Holubkov R, Laskey WK, Haviland A, Slater JC, Bourassa MG, Vlachos HA, et al. Angina 1 year after percutaneous coronary intervention: a report from the NHLBI Dynamic Registry. *American Heart Journal* 2002 Nov;**144**(5):826-33.

Rosanio 1999

Rosanio S, Tocchi M, Patterson C, Runge MS. Prevention of restenosis after percutaneous coronary interventions: the medical approach. *Journal of Thrombosis and Haemostasis* 1999;**82 Suppl 1**:164-70.

Ruan 2003

Ruan JL, Zhao ZX, Zeng QZ, Qian ZM. Recent advances in study of component and pharmacological roles of Radix Paeoniae Rubra. *Chinese Pharmacological Bulletin* 2003;**19**(9):965-70.

Serruys 1995

Serruys PW, Herrman JP, Simon R, Rutsch W, Bode C, Laarman GJ, et al. A comparison of hirudin with heparin in the prevention of restenosis after coronary angioplasty. *The New England Journal of Medicine* 1995;**333**(12):757-63.

Singh 2011

Singh IM, Holmes DR Jr. Myocardial revascularization by percutaneous coronary intervention: past, present, and the future. *Current Problems in Cardiology* 2011;**36**(10):375-401.

Sterne 2001

Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. *Journal of Clinical Epidemiology* 2001;**54**(10):1046-55.

Testa 2009

Testa L, Van Gaal WJ, Biondi Zoccai GG, Agostoni P, Latini RA, Bedogni F, et al. Myocardial infarction after percutaneous coronary intervention: a meta-analysis of troponin elevation applying the new universal definition. *QJM* 2009;**102**(6):369-78.

Wang 2003

Wang HJ, Huang YW, Sun J, Zhu CH, Zhang L. Effect of Tongxinluo capsule on function of vascular endotheliumin patients with unstable angina pectoris. *Chinese Journal of Integrated Traditional Chinese and Western Medicine* 2003;**23**(8):587-9.

Wang 2007

Wang G, Mao B, Xiong ZY, Fan T, Chen XD, Wang L, et al. The quality of reporting of randomized controlled trials of traditional Chinese medicine: a survey of 13 randomly selected journals from mainland China. *Clinical Therapeutics* 2007;**29**(7):1456-67.

Wang 2008

Wang CH, Wang R, Cheng XM, He YQ, Wang ZT, Wu C, et al. Comparative pharmacokinetic study of paeoniflorin after oral administration of decoction of Radix Paeoniae Rubra and Radix Paeoniae Alba in rats. *Journal of Ethnopharmacology* 2008;**117**(3):467-72.

WHO 2002

World Health Organization. Life course perspectives on coronary heart disease, stroke and diabetes. Department of Noncommunicable Disease Prevention and Health Promotion. Noncommunicable Disease and Mental Health Cluster 2002.

WHO 2011

World Health Organization. Health topic: cardiovascular diseases (CVDs). Available from http://www.who.int/mediacentre/factsheets/fs317/en/index.html 2011.

WHS 2010

World Health Statistics. Cause-specific mortality and morbidity. Available at: http://www.who.int/whosis/whostat/EN_WHS09_Table2.pdf 2010.

Wu 2001

Wu YL. Luobing theory of Chinese medicine and cardio-cerebral antipathy. 1st Edition. Beijing: Chinese Science and Technical Publish House, 2001.

Wu 2006

Wu T, Harrison RA, Chen XY, Ni J, Zhou L, Qiao J, et al. Tongxinluo (Tong xin luo or Tong-xin-luo) capsule for unstable angina pectoris. *Cochrane Database of Systematic Reviews* 2006, Issue 4. [DOI: 10.1002/14651858.CD004474.pub2]

Wu 2013

Wu XY, Tang JL, Mao C, Yuan JQ, Qin Y, Chung VC. Systematic reviews and meta-analyses of traditional Chinese medicine must search Chinese databases to reduce language bias. *Evidence Based Complementary and Alternative Medicine* 2013:812179.

Xu 1988

Xu YJ. Effect of inhibition platelet adhesion reaction of Radix Ginseng. *Journal of Pharmacology* 1988;**23**(5):284-5.

Yu 2011

Yu M, Huang YN, Mo W. Progress and prospect of Hirudin and Its derivants research. *Pharmaceutical Biotechnology* 2011;**18**(4):351-4.

Zhang 2004

Zhang Q, Yang LH, Qiao P, Cui TX. Effects of tongxinluo capsule in the treatment of 68 patients with unstable angina pectoris. *Chinese Journal of Primary Medicine and Pharmacy* 2004;**11**(9):1080-1.

Zheng 1998

Zheng HZ, Dong ZH, Se J. Periostracum Cicadae. Modern Study of Traditional Chinese Medicine. 1st Edition. Beijing: Xue Yuan Press, 1998:5137-45.

Zhou 1997

Zhou JK, Liu C. Thrombin inhibitor—hirudin. *Chinese New Drugs Journal* 1997;**6**(3):186-7.

Zhou 2007 a

Zhou J, Guo JT. Clinical study of Tongxinluo on preventing re-stenosis of stents in CHD. *Hebei Medicine* 2007;**13**(10):1188-91.

Zhou 2011

Zhou ZR, Tang HQ, Li JH, Yang LL, Hu H. Tongxinluo capsule for coronary heart disease: a systematic review. *Chinese Journal Of Evidence-Based Medicine* 2011;**11**(9):1078-83.

Zhu 2004

Zhu QL. Study on Tongxinluo capsule in preventing and treating coronary restenosis after PTCA. Journal of Shandong University of Traditional Chinese Medicine 2004:CNKI:CDMD:2.2004.102498.

Zhuo 2008

Zhuo Q, Yang X, Wu T, Liu G, Zhou L. Tongxinluo capsule for acute stroke. *Cochrane Database of Systematic Reviews* 2008, Issue 4. [DOI: 10.1002/14651858.CD004584.pub2]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Chen 2011

Methods	Study design: randomised controlled trial. Method of randomisation: random number table. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Patients were all diagnosed as having ACS based on coronary arteriography, and in accordance with the diagnostic criteria formulated by the European Society of Cardiology in September 2000. Tong-xin-luo group: 80 patients (male/female: 48/32; age: 71.5 ± 5.6 years). Control group: 80 patients (male/female: 46/34; age: 70.7 ± 5.8 years).
Interventions	Control: conventional treatment (pre-operation: aspirin 100 mg qd, clopidogrel 75 mg qd; post-operation: aspirin, clopidogrel, nitroglycerin, low molecular weight heparin, ACEI, atorvastatin). Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (4 capsules tid; 0.26 g/capsule). Duration of intervention: 6 months.
Outcomes	Occurrence of angiographic restenosis; Occurrence of heart failure and angina.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised, random number table was used.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Low risk	Same numbers of participants randomly assigned and analysed. No missing outcome data.
Incomplete outcome data (attrition bias)	Low risk	Same numbers of participants randomly assigned and analysed. No missing outcome data.

Chen 2011 *(Continued)*

Outcomes other than angiographic restenosis		
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline characteristics (sex, age, type of angina, disease severity, disease duration, comorbidities, blood glucose, blood pressure, serum lipoid, etc.) were comparable between the two groups (P > 0.05). The study appeared to be free of other sources of bias.

Dai 2011

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Included participants were 45 to 74 years old, all diagnosed as CHD based on coronary arteriography, and successfully underwent PCI operation. Tong-xin-luo group: 31 participants (male/female: 19/12; age: 61.3 ± 7.23 years). Control group: 30 participants (male/female: 17/13; age: 63.5 ± 6.1 years).
Interventions	Control: conventional treatment (aspirin 100 mg qd, clopidogrel 75 mg qd, atorvastatin 20 mg qn; other symptomatic treatment was applied according to illness state). Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules. Duration of intervention: 6 months.
Outcomes	Occurrence of angiographic restenosis.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.

Dai 2011 *(Continued)*

Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	No missing outcome data.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Unclear risk	Outcomes were not reported.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information showed no statistical differences in sex, age, disease duration and type of PCI operation between two groups (P > 0.05). The study appeared to be free of other sources of bias.

Di 2012

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6-12 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Included participants were over 18 years of age, with evidence of coronary arteriography showing stenosis of more than 70% deduction in small vessels. Tong-xin-luo group: 25 participants (male/female: 18/7; age: 64.60 ± 8.69 years). Control group: 25 participants (male/female: 16/9; age: 63.04 ± 7.84 years).
Interventions	Control: conventional treatment (aspirin 100 mg qd, clopidogrel 75 mg qd, atorvastatin 10-20 mg qd). Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (3 capsules tid; 0.38 g/capsule). Duration of intervention: 6-12 months. Co-intervention: none.
Outcomes	Occurrence of myocardial infarction and angina; All cause mortality; Use of revascularisation, including PCI and coronary artery bypass graft surgery.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.

Di 2012 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information between groups showed no statistical differences in sex, age, smoking history, history of disease, types of CHD, levels of blood glucose and levels of blood lipoid (P > 0.05). The study appeared to be free of other sources of bias.

Dong 2012

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were those who underwent emergency PCI within 6 hours of AMI. Tong-xin-luo group: 35 participants (male/female: 21/14; age: 61.20 ± 11.47 years). Control group: 28 participants (male/female: 15/13; age: 58.80 ± 8.96 years).
Interventions	Control group: conventional treatment (low molecular weight heparin 5000 IU subcutaneous injection bid for 3 days; aspirin 100 mg qd, clopidogrel 75 mg qd, ACEI, nitroglycerin, etc). Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (4 capsules tid). Duration of intervention: 12 months.
Outcomes	Occurrence of myocardial infarction; Mortality (death) due to any cardiovascular event.
Notes	
Risk of bias	

Dong 2012 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Low risk	The study protocol is not available, but study reported same outcomes as described in the methods.
Other bias	Low risk	Baseline information between groups showed no statistical differences in sex, age, smoking, comorbidities, number of stents and length of lesion between two groups (P > 0.05). The study appears to be free of other sources of bias.

Huang 2010

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were diagnosed as acute ST segment elevation myocardial infarction based on the Acute Myocardial Infarction Diagnosis and Treatment Guidelines formulated by the Chinese Society of Cardiology of the Chinese Medical Doctors Associations in 2001, and received PCI within 12 hours after occurrence of AMI. There were 62 patients in the Tong-xin-luo group, and 58 in the control group. male/female: 68/52; age: 58.3 ± 12.6 years.
Interventions	Control group: conventional treatment (low molecular weight heparin, aspirin 100 mg qd, clopidogrel 75 mg qd). Tong-xin-luo group: conventional treatment + Tong-xin-luo capsules (4 capsules, tid). Duration of intervention: 6 months.

Huang 2010 *(Continued)*

Outcomes	Occurrence of myocardial infarction; Mortality (death) due to any cardiovascular event; Use of revascularisation.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	Same numbers of participants randomly assigned and analysed. No missing outcome data.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information showed no statistical differences in sex, age, smoking, drinking habits, comorbidities, Killip's cardiac functional classification, number and distributions of coronary pathological changes, blood pressure, levels of blood glucose and levels of blood lipoid between the two groups (P > 0.05). The study appeared to be free of other sources of bias.

Li 2004

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were those who underwent PTCA and stenting successfully.

Li 2004 *(Continued)*

	Tong-xin-luo group: 38 participants (age: 56.6 ± 11.2 years). Control group: 38 participants (age: 54.9 ± 11.8 years).
Interventions	Conventional treatment: • Pre-operation (from 3 days before operation): aspirin 300 mg qd, clopidogrel 250 mg bid. • Intra-operation: heparin 10000 IU, then 1000 IU/hour during operation. • Post-operation: aspirin 300 mg qd, then reduced to 100 mg qd after 2 weeks; clopidogrel 250 mg bid, reduced to 250 mg qd after 4 weeks and applied for 3 months. ACEI, nitroglycerin and statin, were selectively applied. Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (4 capsules, tid). Control: conventional treatment. Duration of intervention: 6 months. Co-intervention: none.
Outcomes	Occurrence of myocardial infarction and angina.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information between groups showed no statistical differences in age, number of stents implanted, types of CHD and distributions of coronary pathological changes between the two groups (P > 0.05). The study appeared to be free of other sources of bias.

Liang 2010

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were patients with AMI, with evidence of coronary arteriography showing stenosis ≥ 70%, who successfully received stent implantations. There were 42 patients in Tong-xin-luo group, and 38 in control group. male/female: 52/28; mean age: 55 years (ranging from 40 to 70).
Interventions	Control group: conventional treatment (low molecular weight heparin, aspirin, clopidogrel, beta-blockers, nitrates, statin). Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (0.52 g, tid). Duration of intervention: 6 months. Co-intervention: none.
Outcomes	Occurrence of angiographic restenosis; Occurrence of myocardial infarction and angina.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	Whether all participants were brought back for angiography was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.

Liang 2010 *(Continued)*

Other bias	Unclear risk	Insufficient information to assess whether potential risk of other bias existed.

Wang 2009a

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were those who underwent PCI successfully (residual stenosis < 20%), aging from 35 to 74. Tong-xin-luo group: 40 participants (male/female: 28/12; age: 54.2 ± 10.2 years). Control group: 40 participants (male/female: 26/14; age: 52.5 ± 11 years).
Interventions	Control group: Conventional treatment (low molecular weight heparin 6000 IU subcutaneous injection bid for 5 days; aspirin 100 mg qd, clopidogrel 75 mg qd). Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (3 capsules, tid; 0.38 g/capsule). Duration of intervention: 6 months. Co-intervention: none.
Outcomes	Occurrence of myocardial infarction and angina.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.

Wang 2009a *(Continued)*

Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information showed no statistical differences in sex, age, smoking, comorbidities, length of lesion and distributions of coronary pathological changes between the two groups (P > 0.05). The study appeared to be free of other sources of bias.

Wang 2010

Methods	Study design: randomised, double-blind, parallel, placebo-controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 12 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were diagnosed as having type II diabetes mellitus based on oral glucose tolerance test, and had evidence of coronary arteriography showing stenosis of no less than 70% reduction in small vessels with length of lesions no less than 3 mm. Tong-xin-luo group: 68 participants (male/female: 43/25; age: 65.2 ± 9.9 years). Control group: 64 participants (male/female: 45/19; age: 65.1 ± 10.4 years).
Interventions	Control group: conventional treatment (aspirin 300 mg qd, and reduced to 100 mg qd after a month; clopidogrel 75 mg qd; atorvastatin 20 mg qn) + placebo. Tong-xin-luo group: conventional treatment + Tong-xin-luo capsules (3 capsules, tid; 0.38 g/capsule). Duration of intervention: 12 months.
Outcomes	Occurrence of myocardial infarction and angina; All cause mortality.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description about blinding. No placebo.

Wang 2010 *(Continued)*

Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information showed no statistical differences in sex, age, smoking, comorbidities, number and length of stents implanted, number and distributions of coronary pathological changes and level of serum creatinine between the two groups (P > 0.05). The study appeared to be free of other sources of bias.

Wu 2010

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were patients with unstable angina based on the Unstable Angina Diagnosis and Treatment Guidelines formulated by the Chinese Society of Cardiology of the Chinese Medical Doctors Associations in 2007, and underwent PCI successfully. Tong-xin-luo group: 57 patients (male/female: 32/25; age: 71.4 ± 4.5 years). Control group: 53 patients (male/female: 31/22; age: 69.8 ± 4.3 years).
Interventions	Control: conventional treatment: • Pre-operation: aspirin 100 mg qd, clopidogrel 75 mg qd for more than 7 days. • Post-operation: aspirin, clopidogrel, nitroglycerin, low molecular weight heparin, ACEI, etc. Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (4 capsules, tid; 0.38 g/capsule) Duration of intervention: 6 months. Co-intervention: none.
Outcomes	Occurrence of angiographic restenosis; Occurrence of myocardial infarction, heart failure and angina; Use of revascularisation, including PCI and coronary artery bypass graft surgery.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Wu 2010 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	Whether all participants were brought back for angiography was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information showed no statistical differences in sex, age, comorbidities, number and distributions of coronary pathological changes, blood pressure, levels of blood glucose and levels of blood lipoid between the two groups ($P > 0.05$). The study appeared to be free of other sources of bias.

Xiao 2007

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: 37 of 62 participants in Tong-xin-luo group and 47 of 70 participants in control group did not undergo coronary arteriography, the occurrence of angiography restenosis for these participants was lost to follow-up. Intention-to-treat analysis: not mentioned.
Participants	Participants were those who successfully received bare-metal coronary stents. Tong-xin-luo group: 62 participants (male/female: 42/20; age: 53 ± 12 years). Control group: 70 participants (male/female: 49/21; age: 55 ± 10 years).
Interventions	Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (4 capsules, tid). Control group: Conventional treatment. Duration of intervention: 6 months. Co-intervention: none.

Xiao 2007 *(Continued)*

Outcomes	Occurrence of angiographic restenosis; Occurrence of myocardial infarction, heart failure, and angina; Mortality (death) due to any cardiovascular event.
Notes	There were no losses to follow-up in the outcomes measured, except angiographic restenosis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	High risk	37 of 62 participants in Tong-xin-luo group and 47 of 70 participants in control group did not undergo coronary arteriography.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information showed no statistical differences in sex, age, comorbidities, types of coronary pathological changes and average number of stents between the two groups ($P > 0.05$). The study appeared to be free of other sources of bias.

Yang 2009a

Methods	Study design: randomised controlled trial. Method of randomisation: random number table. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 3 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.

Yang 2009a *(Continued)*

Participants	Participants were diagnosed as having AMI based on the Acute Myocardial Infarction Diagnosis and Treatment Guidelines formulated by the Chinese Society of Cardiology of the Chinese Medical Doctors Associations in 2001, who successfully underwent PCI. Tong-xin-luo group: 30 participants (male/female: 22/8; age mean: 58 years). Control group: 29 participants (male/female: 25/4; age mean: 56 years).
Interventions	Control group: conventional treatment: • Pre-operation: aspirin 300 mg qd, clopidogrel 600 mg qd. • Intra-operation: heparin 1000 IU/kg, then 1000 IU/hour during operation. • Post-operation: low molecular weight heparin 5000 IU subcutaneous injection bid for 7 days; aspirin 300 mg qd. Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (3 capsules, tid). Duration of intervention: more than 24 months. Co-intervention: none.
Outcomes	Occurrence of myocardial infarction and heart failure; Mortality (death) due to any cardiovascular event; All cause mortality; Use of revascularisation.
Notes	Withdrawal of one participant before randomisation was reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised, random number table was used as randomisation method.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	Same numbers of participants randomly assigned and analysed. No missing outcome data.
Selective reporting (reporting bias)	High risk	The study protocol is not available, but some outcomes of interest described in the methods were not reported.

Yang 2009a *(Continued)*

Other bias	Low risk	Baseline information showed no statistical differences in sex, age, comorbidities, numbers of coronary pathological changes and classification of the New York Heart Function Assessment between the two groups (P > 0.05). The study appeared to be free of other sources of bias.

Yao 2006

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were patients with CHD, with evidence of coronary arteriography showing stenosis ≥ 70%, who successfully received stenting. Tong-xin-luo group: 38 participants (age: 56.6 ± 10.9 years). Control group: 38 participants (age: 50.1 ± 12.4 years).
Interventions	Control group: conventional treatment: • Pre-operation(3 days before operation): aspirin 300 mg qd, clopidogrel 75 mg qd, simvastatin 20 mg qd. • Intra-operation: heparin 10000 IU/kg, then 1000 IU/hour during operation. • Post-operation: low molecular weight heparin 600 ml subcutaneous injection bid for 5 days; aspirin 300 mg qd, clopidogrel 75 mg qd. Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (4 capsules, tid). Duration of intervention: 6 months. Co-intervention: none.
Outcomes	Occurrence of angina.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.

Yao 2006 *(Continued)*

Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	There was no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information between groups showed no statistical differences in sex, age, length of lesions, distributions of coronary pathological changes and severity of stenosis between the two groups (P > 0.05). The study appears to be free of other sources of bias.

Zhang 2009a

Methods	Study design: randomised controlled trial. Method of randomisation: drawing of lots. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 3-48 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were diagnosed as having AMI based on the diagnostic criteria formulated by the European Society of Cardiology in September, 2000, and underwent PCI successfully. Tong-xin-luo group: 96 participants (male/female: 70/26; age: 60 ± 5 years). Control group: 82 participants (male/female: 57/25; age: 58 ± 8 years).
Interventions	Conventional treatment: • Pre-operation: aspirin 100-300 mg, clopidogrel 600 mg. • Post-operation:aspirin 100 mg qd; clopidogrel 75 mg qd for 9-12 months, other symptomatic treatment (ACEI, nitroglycerin, etc.) was applied according to illness state. Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (3 capsules, tid). Duration of intervention: more than 24 months. Co-intervention: none.
Outcomes	Occurrence of myocardial infarction, angina and heart failure; Mortality (death) due to any cardiovascular event; All cause mortality; Use of revascularisation.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Zhang 2009a *(Continued)*

Random sequence generation (selection bias)	Low risk	Randomised, drawing of lots was used as randomisation method.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	Same numbers of participants randomly assigned and analysed. No missing outcome data.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Low risk	Baseline information between groups showed no statistical differences in sex, age, comorbidities, smoking, length of lesions, number of stents, types of stents and number of coronary pathological changes between the two groups (P > 0.05). The study appeared to be free of other sources of bias.

Zheng 2010

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were patients diagnosed as having ACS who underwent emergency PCI 12-24 hours after admission. Tong-xin-luo group: 34 participants (male/female: 28/6; age: 63 ± 10 years). Control group: 56 participants (male/female: 46/10; age: 61 ± 11 years).
Interventions	Control group: conventional treatment (low molecular weight heparin, aspirin, clopidogrel, beta-blockers, nitrates, statin, etc.). Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (3 capsules, tid; 0.38 g/capsule). Duration of intervention: 6 months. Co-intervention: none.

Zheng 2010 *(Continued)*

Outcomes	Occurrence of myocardial infarction; Use of revascularisation.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description about blinding. No placebo.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No description about blinding. No placebo.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	The outcome was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	Same numbers of participants randomly assigned and analysed. No missing outcome data.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Unclear risk	Insufficient information to assess whether potential risk of other bias exists.

Zhou 2007b

Methods	Study design: randomised controlled trial. Method of randomisation: no description. Concealment of allocation: no description. Exclusions post randomisation: none. Length of follow-up: 6 months. Losses to follow-up: none. Intention-to-treat analysis: not mentioned.
Participants	Participants were patients diagnosed as having CHD based on the World Health Organization diagnostic criteria, who successfully received stent implantations. There were 70 patients in the Tong-xin-luo group, and 66 in the control group. male/female: 86/50; mean age: 56.8 years (ranging from 30 to 76).

Zhou 2007b *(Continued)*

Interventions	Control group: conventional treatment (low molecular weight heparin, aspirin, clopidogrel, beta-blockers, nitrates, statin, etc.). Tong-xin-luo group: conventional treatment plus Tong-xin-luo capsules (3 capsules, tid). Duration of intervention: 6 months. Co-intervention: none.
Outcomes	Occurrence of myocardial infarction and angina; Use of revascularisation, including PCI and coronary artery bypass graft surgery.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but detailed information on the randomisation method was not provided.
Allocation concealment (selection bias)	Unclear risk	No description about the allocation procedure.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description about blinding.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description about blinding.
Incomplete outcome data (attrition bias) Angiographic restenosis	Unclear risk	Whether all participants were brought back for angiography was not reported.
Incomplete outcome data (attrition bias) Outcomes other than angiographic restenosis	Low risk	Same numbers of participants randomly assigned and analysed. No missing outcome data.
Selective reporting (reporting bias)	High risk	The study protocol is not available, but some outcomes of interest described in the methods were not reported in results.
Other bias	Unclear risk	Insufficient information to assess whether potential risk of other bias exists.

Abbreviations
ACS: acute coronary syndrome
qd: daily
ACEI: angiotensin-converting-enzyme inhibitor
CHD: coronary heart disease
qn: every night
PCI: percutaneous coronary intervention
tid: three times daily
bid: twice daily
AMI: acute myocardial infarction
PCTA: percutaneous transluminal coronary angioplasty

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Chang 2004	Patients did not undergo PCI.
Chen 2007	Intervention period was less than 3 months.
Fan 2008	Intervention period was less than 3 months.
Fu 2012	Intervention period was less than 3 months.
Gao 2007	Not RCT.
Guo 2012	Did not report outcomes listed in inclusion criteria.
Han 2009	Intervention period was less than 3 months.
Han 2011	Intervention period was less than 3 months.
Hou 2008	No full-text or data available.
Jiang 2008	Intervention was not Tong-xin-luo.
Kuang 2011	Did not report outcomes listed in inclusion criteria.
Li 2008	Did not report outcomes listed in inclusion criteria; randomisation not mentioned.
Li 2012	Did not report outcomes listed in inclusion criteria.
Liu 2009	Intervention period was less than 3 months.
Lu 2012	Intervention period was less than 3 months.
Ma 2009	Did not report outcomes listed in inclusion criteria.
Qu 2011	Patients did not undergo PCI.
Su 2000	Patients did not undergo PCI.
Tao 2012	Did not report outcomes listed in inclusion criteria.
Tu 2006	Did not report outcomes listed in inclusion criteria.
Wang 2007	Did not report outcomes listed in inclusion criteria.
Wang 2009b	Did not report outcomes listed in inclusion criteria.
Wang 2009c	Intervention period was less than 3 months.
Wang 2012	Did not report outcomes listed in inclusion criteria.
Xiao 2004	Patients did not undergo PCI.
Xu 2007	Intervention period was less than 3 months.

Study	Reason for exclusion
Xu 2008	Not RCT, a review.
Yang 2009b	Did not report outcomes listed in inclusion criteria.
Yang 2010	Did not report outcomes listed in inclusion criteria; randomisation not mentioned.
Yang 2012	Did not report outcomes listed in inclusion criteria.
Zhang 2005	Intervention period was less than 3 months.
Zhang 2006	Intervention period was less than 3 months.
Zhang 2007	Intervention period was less than 3 months.
Zhang 2008	Patients did not undergo PCI.
Zhang 2009b	Patients did not undergo PCI.
Zhang 2010	Didn't report outcomes listed in inclusion criteria.
Zhao 2010	Intervention period was less than 3 months.
Zhao 2011	Intervention period was less than 3 months.

Abbreviations
PCI: percutaneous coronary intervention
RCT: randomised controlled trial

Characteristics of studies awaiting assessment *[ordered by study ID]*

Deng 2013

Methods	RCT
Participants	Participants were patients diagnosed as having CHD based on the World Health Organization diagnostic criteria, who successfully received stent implantations. There were 31 patients in Tong-xin-luo group, and 30 in control group. male/female: 41/20; mean age: ranging from 41 to 78.
Interventions	Tong-xin-luo
Outcomes	The minimum diameter of the target vessel, degree of stenosis; The occurrence of restenosis.
Notes	

Abbreviations
RCT: randomised controlled trial
CHD: coronary heart disease

Characteristics of ongoing studies *[ordered by study ID]*

Han 2012

Trial name or title	Tongxinluo Improve High on Clopidogrel Platelet Reactivityn Patients With Coronary Heart Disease
Methods	Randomised double-blind trial
Participants	ACS (including unstable angina pectoris, non-ST-segment elevation myocardial infarction and ST-elevation myocardial infarction; at least one coronary stent; age between18 and 75; high on-treatment platelet reactivity defined as an ADP-induced platelet aggregation (by VerifyNow, PRU ≥ 236) at 24 hours after clopidogrel loading (300 - 600 mg) or 24 hours after PCI.
Interventions	Tong-xin-luo
Outcomes	Platelet aggregation rate; Inflammation Marker (hsCRP, CD62P-CD41); BT, FIB and aPTT; Major ischemic event (including MI, ischemic stroke and all-cause mortality); Bleeding event; Adverse drug reaction and withdrawal rate; Angina recurrence; Traditional Chinese medicine angina symptoms scores; Intra-stent thrombosis.
Starting date	November 1, 2012
Contact information	Yaling Han, MD Tel: +86-24-23922184 E-mail: 13998847715@qq.com
Notes	

Abbreviations
ACS: acute coronary syndrome
PRU: P2Y12 reactivity unit
PCI: percutaneous coronary intervention
aPTT: activated partial thromboplastin time
MI: miocardial infarction

DATA AND ANALYSES

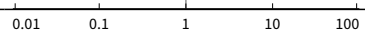
Comparison 1. Tong-xin-luo + Convetional treatment vs. Convetional treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Occurrence of angiographic restenosis	6	595	Risk Ratio (M-H, Fixed, 95% CI)	0.16 [0.07, 0.34]
2 Occurence of myocardial infarction	13	1306	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.16, 0.66]
3 Occurence of heart failure	4	529	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.11, 0.62]
4 Occurrence of angina	11	1210	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.17, 0.34]
5 All-cause mortality	4	419	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.06, 2.56]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Mortality due to any cardiovascular event	5	552	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.08, 1.12]
7 Use of revascularization	8	806	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.15, 0.45]

Analysis 1.1. Comparison 1 Tong-xin-luo + Convetional treatment vs. Convetional treatment, Outcome 1 Occurrence of angiographic restenosis.

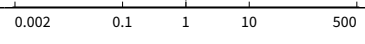
Study or subgroup	Tong-xin-luo n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Chen 2011	1/80	6/80		13.88%	0.17[0.02,1.35]
Dai 2011	1/31	2/30		4.7%	0.48[0.05,5.06]
Liang 2010	0/42	3/38		8.49%	0.13[0.01,2.43]
Wu 2010	2/57	10/53		23.97%	0.19[0.04,0.81]
Xiao 2007	2/25	6/23		14.46%	0.31[0.07,1.37]
Zhou 2007b	0/70	14/66		34.51%	0.03[0,0.53]
Total (95% CI)	**305**	**290**		**100%**	**0.16[0.07,0.34]**
Total events: 6 (Tong-xin-luo), 41 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.94, df=5(P=0.71); I^2=0%					
Test for overall effect: Z=4.64(P<0.0001)					



Favours Tong-xin-luo — Favours control

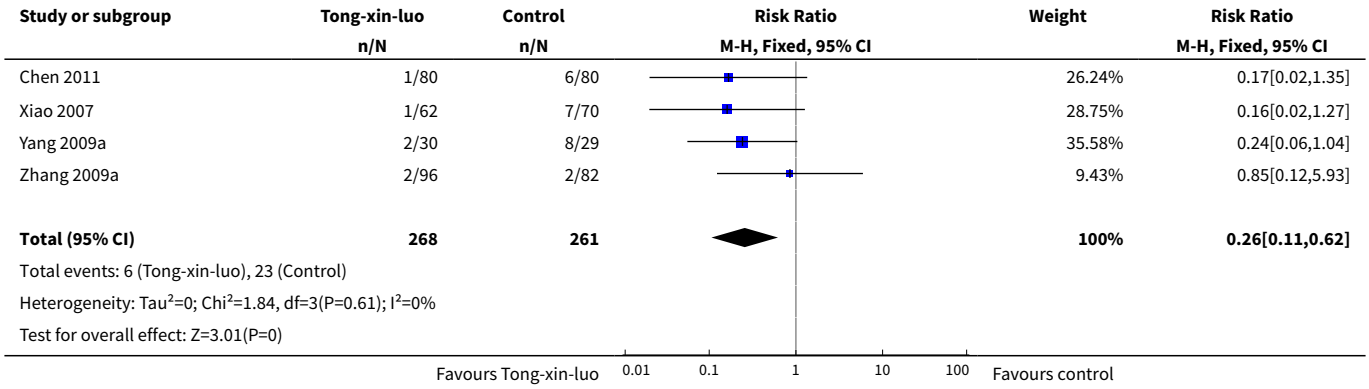
Analysis 1.2. Comparison 1 Tong-xin-luo + Convetional treatment vs. Convetional treatment, Outcome 2 Occurence of myocardial infarction.

Study or subgroup	Tong-xin-luo n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Di 2012	0/25	0/25			Not estimable
Dong 2012	1/35	1/28		3.78%	0.8[0.05,12.23]
Huang 2010	2/62	5/58		17.59%	0.37[0.08,1.85]
Li 2004	0/38	4/38		15.32%	0.11[0.01,1.99]
Liang 2010	0/42	2/38		8.92%	0.18[0.01,3.66]
Wang 2009a	1/40	4/40		13.62%	0.25[0.03,2.14]
Wang 2010	1/68	2/64		7.01%	0.47[0.04,5.06]
Wu 2010	0/57	2/53		8.81%	0.19[0.01,3.79]
Xiao 2007	0/62	1/70		4.8%	0.38[0.02,9.06]
Yang 2009a	0/30	0/29			Not estimable
Zhang 2009a	1/96	1/82		3.67%	0.85[0.05,13.44]
Zheng 2010	1/34	3/56		7.72%	0.55[0.06,5.07]
Zhou 2007b	0/70	2/66		8.76%	0.19[0.01,3.86]
Total (95% CI)	**659**	**647**		**100%**	**0.32[0.16,0.66]**
Total events: 7 (Tong-xin-luo), 27 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.24, df=10(P=0.99); I^2=0%					
Test for overall effect: Z=3.08(P=0)					

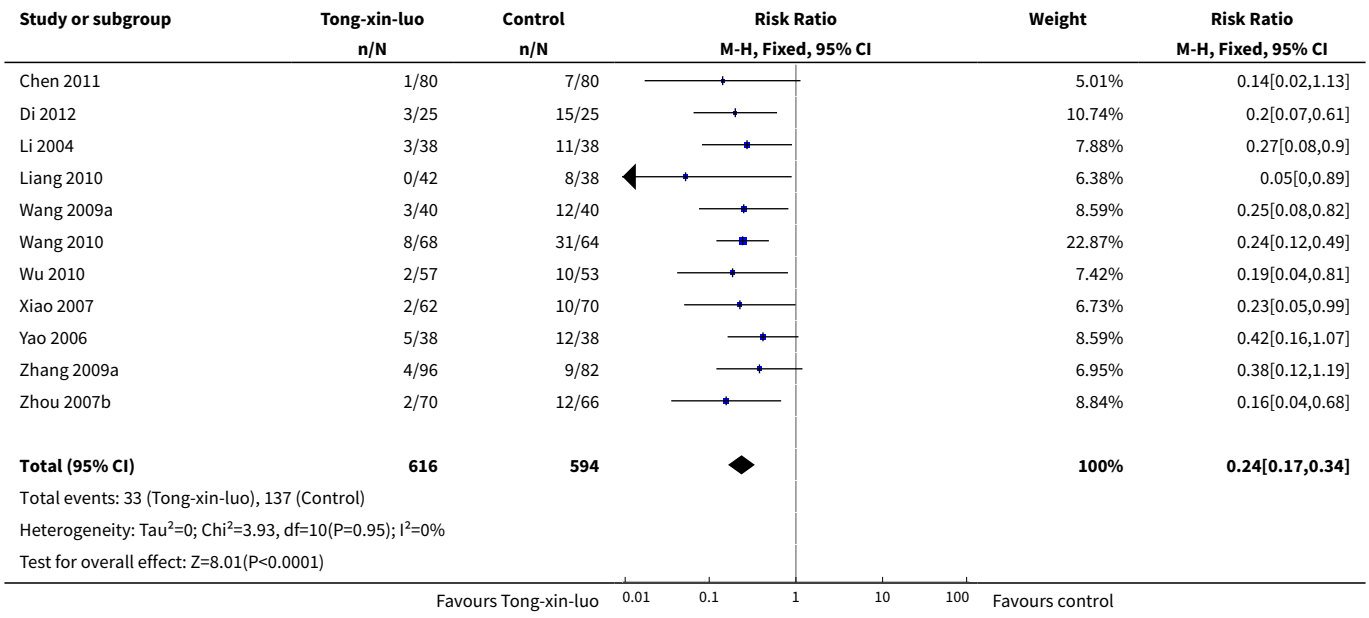


Favours Tong-xin-luo — Favours control

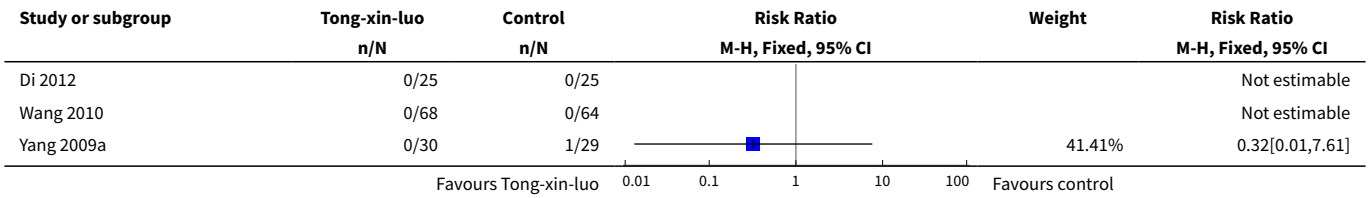
Analysis 1.3. Comparison 1 Tong-xin-luo + Convetional treatment vs. Convetional treatment, Outcome 3 Occurence of heart failure.

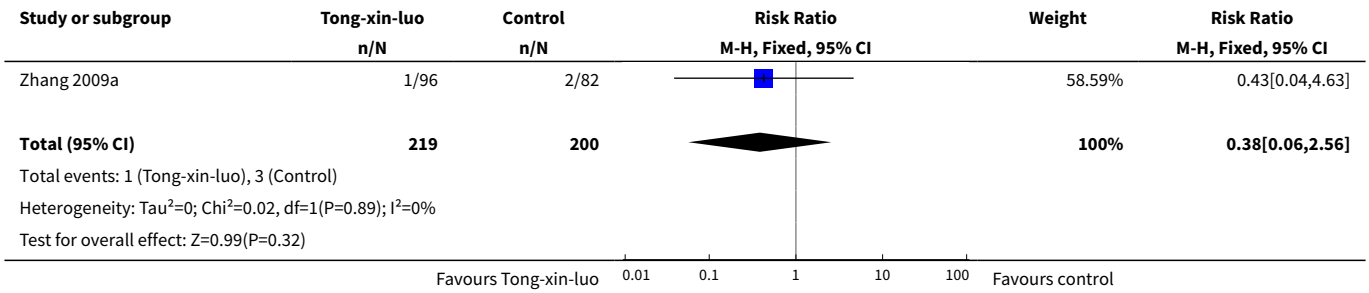


Analysis 1.4. Comparison 1 Tong-xin-luo + Convetional treatment vs. Convetional treatment, Outcome 4 Occurrence of angina.

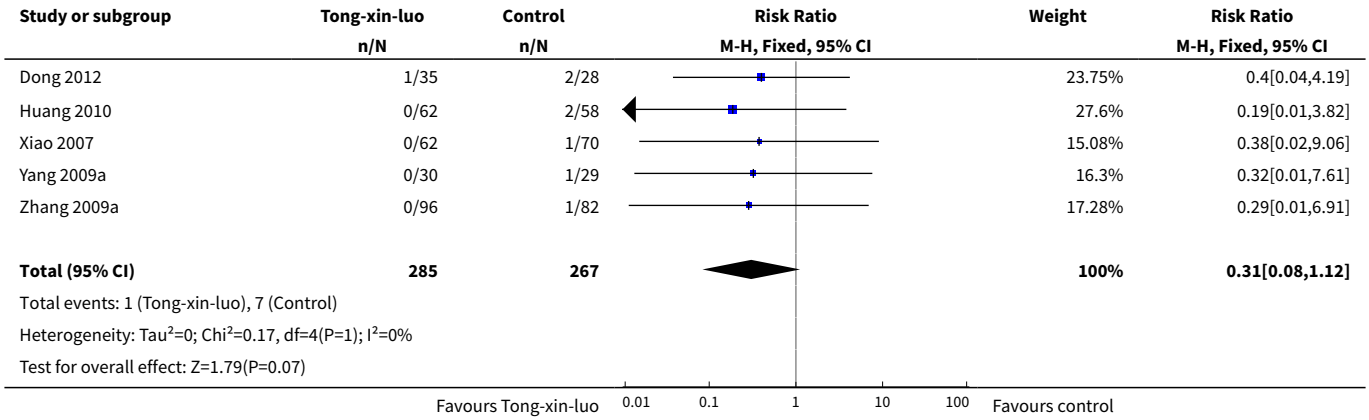


Analysis 1.5. Comparison 1 Tong-xin-luo + Convetional treatment vs. Convetional treatment, Outcome 5 All-cause mortality.

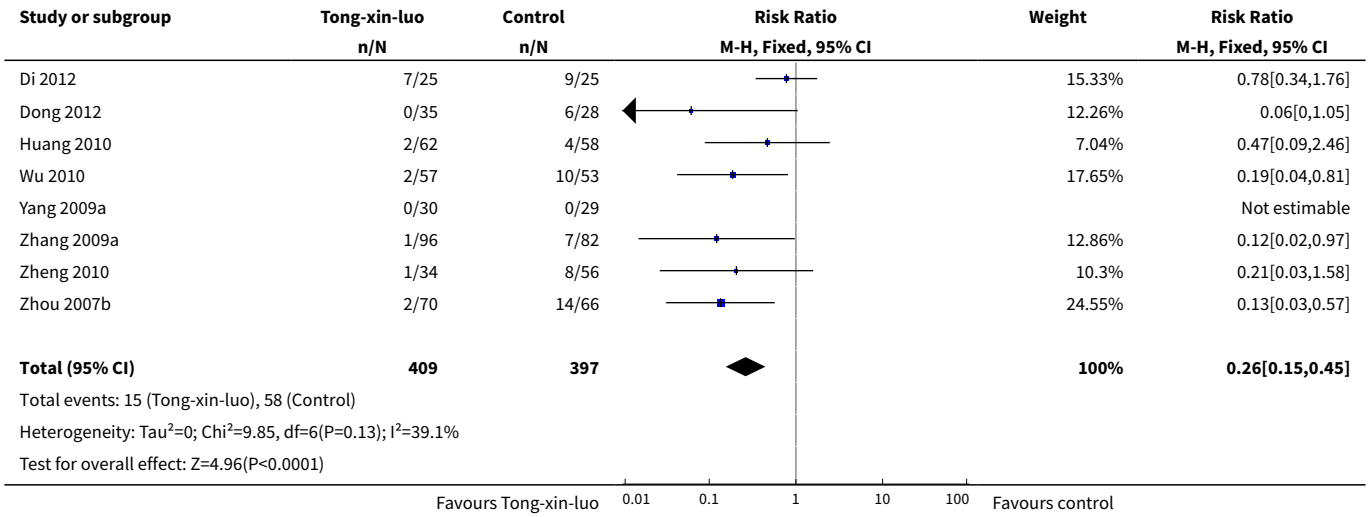




Analysis 1.6. Comparison 1 Tong-xin-luo + Convetional treatment vs. Convetional treatment, Outcome 6 Mortality due to any cardiovascular event.



Analysis 1.7. Comparison 1 Tong-xin-luo + Convetional treatment vs. Convetional treatment, Outcome 7 Use of revascularization.



APPENDICES

Appendix 1. Search strategies

Cochrane Library

#1 Tongxinluo
#2 Tong Xin Luo
#3 Tong-xin-luo
#4 TXL
#5 Tongxinluo*
#6 Enter terms for search#1 or #2 or #3 or #4 or #5

MEDLINE

1. exp Cardiovascular Diseases/
2. cardio*.tw.
3. cardia*.tw.
4. heart*.tw.
5. coronary*.tw.
6. angina*.tw.
7. ventric*.tw.
8. myocard*.tw.
9. pericard*.tw.
10. isch?em*.tw.
11. emboli*.tw.
12. arrhythmi*.tw.
13. thrombo*.tw.
14. atrial fibrillat*.tw.
15. tachycardi*.tw.
16. endocardi*.tw.
17. (sick adj sinus).tw.
18. exp Stroke/
19. (stroke or stokes).tw.
20. cerebrovasc*.tw.
21. cerebral vascular.tw.
22. apoplexy.tw.
23. (brain adj2 accident*).tw.
24. ((brain* or cerebral or lacunar) adj2 infarct*).tw.
25. exp Hypertension/
26. hypertensi*.tw.
27. peripheral arter* disease*.tw.
28. ((high or increased or elevated) adj2 blood pressure).tw.
29. exp Hyperlipidemias/
30. hyperlipid*.tw.
31. hyperlip?emia*.tw.
32. hypercholesterol*.tw.
33. hypercholester?emia*.tw.
34. hyperlipoprotein?emia*.tw.
35. hypertriglycerid?emia*.tw.
36 or/1-35
37. tongxinluo.tw.
38. Drugs, Chinese Herbal/
39. tong xin luo.tw.
40. (chinese adj3 (medic* or drug* or capsul*)).tw.
41. Medicine, Chinese Traditional/
42 or/37-41
43. randomized controlled trial.pt.
44. controlled clinical trial.pt.
45. randomized.ab.
46. placebo.ab.
47. drug therapy.fs.
48. randomly.ab.

49. trial.ab.
50. groups.ab.
51. 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
57. exp animals/ not humans.sh.
58. 51 not 57
59 36 and 42 and 58

EMBASE

#1 Tongxinluo.tw.
#2 Tong xin luo.tw.
#3 Tong-xin-luo.tw.
#4 TXL.tw.
#5 tongxinluo.mp.
#6 tongxinluo$.mp.
#7 #1 or #2 or #3 or #4 or #5 or #6

Wangfang

(通心络 or 通新络 or 通欣络 or 通心洛 or 痛心络) and (介入治疗 or 介入手术 or 经皮冠状动脉 or 冠状动脉介入 or 冠脉介入 or 冠脉成型 or 冠脉成形 or 冠状动脉成形 or 冠状动脉成型 or 经皮经管冠状动脉 or 经皮经管冠脉 or 经皮腔内冠状动脉 or 经皮腔内冠脉 or 支架 or PCI)

CMCC

((通心络 OR 通新络 OR 通欣络 OR 通心洛 OR 痛心络/fld=关键词) OR (通心络 OR 通新络 OR 通欣络 OR 通心洛 OR 痛心络/fld=摘要) OR (通心络 OR 通新络 OR 通欣络 OR 通心洛 OR 痛心络) OR (通心络 OR 通新络 OR 通欣络 OR 通心洛 OR 痛心络/fld=题名)) AND ((介入治疗 OR 介入手术 OR 经皮冠状动脉 OR 冠状动脉介入OR 冠脉介入 OR 冠脉成型 OR冠脉成形 OR 冠状动脉成形 OR 冠状动脉成型OR 经皮经管冠状动脉 OR经皮经管冠脉 OR 经皮腔内冠状动脉 OR经皮腔内冠脉 OR 支架 OR PCI/fld=题名) OR (介入治疗 OR 介入手术 OR 经皮冠状动脉 OR 冠状动脉介入OR 冠脉介入 OR 冠脉成型 OR冠脉成形 OR 冠状动脉成形 OR 冠状动脉成型OR 经皮经管冠状动脉 OR 经皮经管冠脉 OR 经皮腔内冠状动脉 OR经皮腔内冠脉 OR 支架 OR PCI/fld=关键词) OR (介入治疗 OR 介入手术 OR 经皮冠状动脉 OR 冠状动脉介入OR 冠脉介入 OR 冠脉成型 OR冠脉成形 OR 冠状动脉成形 OR 冠状动脉成型OR 经皮经管冠状动脉 OR经皮经管冠脉 OR 经皮腔内冠状动脉 OR经皮腔内冠脉 OR 支架 OR PCI/fld=摘要) OR (介入治疗 OR 介入手术 OR 经皮冠状动脉 OR 冠状动脉介入OR 冠脉介入 OR 冠脉成型 OR冠脉成形 OR 冠状动脉成形 OR 冠状动脉成型OR 经皮经管冠状动脉 OR经皮经管冠脉 OR 经皮腔内冠状动脉 OR 经皮腔内冠脉 OR 支架 OR PCI))

TCM

#1 WXTIC=通心络 OR 通新络 OR 通欣络 OR 通心洛 OR 痛心络

#2 WXMES=通心络 OR 通新络 OR 通欣络 OR 通心洛 OR 痛心络

#3 WXKW=通心络 OR 通新络 OR 通欣络 OR 通心洛 OR 痛心络

#4 %通心络 OR 通新络 OR 通欣络 OR 通心洛 OR 痛心络%

#5 #1 OR #2 OR #3 OR #4

#6 %介入治疗 or 介入手术 or 经皮冠状动脉 or 冠状动脉介入 or 冠脉介入 or 冠脉成型 or 冠脉成形 or 冠状动脉成形 or 冠状动脉成型 or 经皮经管冠状动脉 or 经皮经管冠脉 or 经皮腔内冠状动脉 or 经皮腔内冠脉 or 支架 or PCI%

#7 WXTIC=%介入治疗 or 介入手术 or 经皮冠状动脉 or 冠状动脉介入 or 冠脉介入 or 冠脉成型 or 冠脉成形 or 冠状动脉成形 or 冠状动脉成型 or 经皮经管冠状动脉 or 经皮经管冠脉 or 经皮腔内冠状动脉 or 经皮腔内冠脉 or 支架 or PCI%

#8 WXMES=介入治疗 or 介入手术 or 经皮冠状动脉 or 冠状动脉介入 or 冠脉介入 or 冠脉成型 or 冠脉成形 or 冠状动脉成形 or 冠状动脉成型 or 经皮经管冠状动脉 or 经皮经管冠脉 or 经皮腔内冠状动脉 or 经皮腔内冠脉 or 支架 or PCI

#9 WXKW=%介入治疗 or 介入手术 or 经皮冠状动脉 or 冠状动脉介入 or 冠脉介入 or 冠脉成型 or 冠脉成形 or 冠状动脉成形 or 冠状动脉成型 or 经皮经管冠状动脉 or 经皮经管冠脉 or 经皮腔内冠状动脉 or 经皮腔内冠脉 or 支架 or PCI%

#10 #6 OR #7 OR #8 OR #9

#11 #5 and #10

CNKI

(SU='通心络' OR TI='通心络' OR KY='通心络' OR AB='通心络' OR FT='通心络' OR SU='通新络' OR TI='通新络' OR KY='通新络' OR AB='通新络' OR FT='通新络' OR SU='通欣络' OR TI='通欣络' OR KY='通欣络' OR AB='通欣络' OR FT='通欣络' OR SU='痛心络' OR TI='痛心络' OR KY='痛心络' OR AB='痛心络' OR FT='痛心络' OR SU='通心洛' OR TI='通心洛' OR KY='通心洛' OR AB='通心洛' OR FT='通心洛') and (SU='介入治疗' OR AB='介入治疗' OR KY='介入治疗' OR FT='介入治疗' OR SU='介入手术' OR AB='介入手术' OR KY='介入手术' OR FT='介入手术' OR SU='经皮冠状动脉' OR AB='经皮冠状动脉' OR KY='经皮冠状动脉' OR FT='经皮冠状动脉' OR SU='冠状动脉介入' OR AB='冠状动脉介入' OR KY='冠状动脉介入' OR FT='冠状动脉介入' OR SU='冠脉介入' OR AB='冠脉介入' OR KY='冠脉介入' OR FT='冠脉介入' OR SU='冠脉成型' OR AB='冠脉成型' OR KY='冠脉成型' OR FT='冠脉成型' OR SU='冠脉成形' OR AB='冠脉成形' OR KY='冠脉成形' OR FT='冠脉成形' OR SU='冠状动脉成形' OR AB='冠状动脉成形' OR KY='冠状动脉成形' OR FT='冠状动脉成形' OR SU='冠状动脉成型' OR AB='冠状动脉成型' OR KY='冠状动脉成型' OR FT='冠状动脉成型' OR SU='经皮经管冠状动脉' OR AB='经皮经管冠状动脉' OR KY='经皮经管冠状动脉' OR FT='经皮经管冠状动脉' OR SU='经皮经管冠脉' OR AB='经皮经管冠脉' OR KY='经皮经管冠脉' OR FT='经皮经管冠脉' OR SU='经皮腔内冠状动脉' OR AB='经皮腔内冠状动脉' OR KY='经皮腔内冠状动脉' OR FT='经皮腔内冠状动脉' OR SU='经皮腔内冠脉' OR AB='经皮腔内冠脉' OR KY='经皮腔内冠脉' OR FT='经皮腔内冠脉' OR SU='支架' OR AB='支架' OR KY='支架' OR FT='支架' OR SU='PCI' OR AB='PCI' OR KY='PCI' OR FT='PCI') and (SU='临床试验' or SU='随机对照试验' or AB='随机' or AB='随机对照' or AB='临床试验' or AB='临床研究' or AB='临床观察' or AB='临床效果' or AB='临床分析' or AB='临床疗效' or AB='临床比较' or AB='对照研究' or AB='对照试验' or AB='对照治疗' or AB='对照观察' or AB='对照分析' or AB='对比研究' or AB='对比观察' or AB='对比分析' or AB='分组研究' or AB='比较研究' or AB='多中心研究' or AB='疗效观察' or AB='疗效评价' or AB='疗效分析' or AB='疗效比较' or AB='治疗研究' or AB='治疗比较' or AB='效果比较' or AB='盲法' or AB='双盲' or AB='单盲' or AB='安慰剂' OR FT='随机')

Search items for clinical trial registers

Tongxinluo, Tong Xin Luo, Tong-xin-luo, TXL, Tongxinluo, 通心络 , 通新络 , 通欣络 , 通心洛 , 痛心络 .

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Date analysis: Chen Mao, Wilson Wai San Tam and Jin-Ling Tang

Results interpretation: Chen Mao, Xiao-Hong Fu, Yafang Huang, Jin-Qiu Yuan, Vincent CH Chung, Joey SW Kwong, Wei Xie and Jin-Ling Tang

Review drafting: Chen Mao, Xiao-Hong Fu, Jin-Qiu Yuan, Yafang Huang, Zu-Yao Yang and Jin-Ling Tang

DECLARATIONS OF INTEREST

Nothing to declare.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- The Grant from the Chinese Medicine Department of Hospital Authority (MD09948), Hong Kong.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol, we planned to perform subgroup analyses based on patient characteristics, type of treatment, follow-up period and type of stent. However, in this review, type of stent was not reported in most studies and it was difficult to separate participants with different baseline characteristics from original trials, so subgroup analyses based on patient characteristics or type of stent were not performed. Intervention of treatment groups in all included trials was Tong-xin-luo plus conventional treatment, so there was no obvious difference in types of treatment. Also, the follow-up period varied among studies; for most outcomes, limited studies provided outcome data according to time of follow-up, which prevented us from analysing outcome data according to the follow-up period.

In addition, we planed to perform sensitivity analyses by excluding studies with high risk of bias. However, such sensitivity analyses were not performed because most of the included studies were considered to have high risk of bias. There were insufficient numbers of studies for meta-analysis after removing studies with high risk of bias.

Lastly, because it is very difficult to ascribe CV death due to restenosis, we did not pool the mortality due to restenosis after PCI, which was a primary outcome in the study protocol. In addition, we did not identify any study that reported this outcome.

INDEX TERMS

Medical Subject Headings (MeSH)

*Percutaneous Coronary Intervention; Angina Pectoris [prevention & control]; Capsules; Cause of Death; Coronary Disease [*drug therapy]; Coronary Restenosis [*prevention & control]; Drugs, Chinese Herbal [*therapeutic use]; Heart Failure [prevention & control]; Myocardial Infarction [prevention & control]; Randomized Controlled Trials as Topic; Secondary Prevention [*methods]; Treatment Outcome

MeSH check words

Humans