

Yangxin decoction for the treatment of angina pectoris of coronary heart disease

A systematic review of randomized controlled trial

Xiao-hong Yu, MD^a, Xi-wen Yu, MD^b, Zhe-ming Xu, MB^{c,*} , Hai-xiang Li, MM^d

Abstract

Background: This study assessed the effectiveness of Yangxin Decoction (YXD) in the treatment of coronary heart disease (CHD) patients with angina pectoris (AP).

Methods: In this study, we systematically and comprehensively searched the PUBMED, EMBASE, Cochrane Library, CNKI, WANGFANG, and VIP databases from their establishment to June 1, 2022. Clinical randomized controlled trials of YXD for the management of AP in patients with CHD were considered for inclusion. The outcomes included the response rate of AP, response rate based on electrocardiogram, and the rate of nitroglycerin use. Two authors independently performed literature selection, data extraction, and methodological quality assessment. Any differences were resolved by a third author through a discussion.

Results: Nine trials involving 819 patients were included. The meta-analysis results showed that YXD significantly improved the response rate of AP (OR = 2.98, 95% CI: 1.96–4.55, $I^2 = 0\%$, $P < .01$) and the response rate based on the electrocardiogram (OR = 1.88, 95% CI: 1.28–2.78, $I^2 = 26\%$, $P < .01$), and significantly reduced the rate of nitroglycerin use (OR = 2.04, 95% CI: 1.19–3.52, $I^2 = 0\%$, $P = .01$).

Conclusions: The results of this study showed that YXD was effective in the treatment of patients with AP of CHD. Further studies are required to confirm these results.

Abbreviations: AP = angina pectoris, CHD = coronary heart disease, CI = confidence interval, RCTs = clinical randomized controlled trials, TCM = traditional Chinese medicine, YXD = Yangxin decoction.

Keywords: angina pectoris, coronary heart disease, effectiveness, meta-analysis, randomized controlled trial, systematic review, Yangxin decoction

1. Introduction

Coronary heart disease (CHD) is one of the most common heart disorders that seriously threatens public health.^[1–4] It is also one of the leading causes of death globally.^[4–6] Its prevalence is increasing annually, accounting for over 40% of all deaths.^[6–8] Therefore, more attention should be paid to this issue in future studies.

Angina pectoris (AP) is a major CHD.^[9–11] It consists of 2 types: stable and unstable angina.^[12,13] According to theory of traditional Chinese medicine (TCM), AP belongs to the “*Xiong Bi*,” “chest arthralgia,” and “heartache.” Its major pathogenesis is explained by “heart pulse stasis” and “Qi stasis.”^[14–20] Clinical practice has proven that Yangxin Decoction (YXD) has unique advantages for the management of patients with AP of CHD.^[21–29]

Previous studies have reported that YXD can improve the AP of CHD by increasing the levels of serum 6-Keto-PGF 1 α , high-density lipoprotein cholesterol, and apolipoprotein A.^[30,31] It can also enhance myocardial function and aortic abnormalities.^[32] Another study found that YXD can protect the ischemic myocardium by regulating vascular endothelial function, improving nitric oxide and nitric oxide synthase production, and decreasing TXB2 production.^[33]

A variety of clinical studies have reported the effectiveness of YXD in the treatment of patients with AP of CHD.^[21–29] However, there is insufficient evidence-based medicine evidence to systematically and comprehensively investigate its effectiveness on patients with AP of CHD. Therefore, this study aimed to systematically evaluate the clinical effectiveness of YXD in the management of patients with AP of CHD.

X.-h.Y. and X.-w.Y. have contributed equally to this study.

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The authors have no conflicts of interest to disclose.

All authors state that they do not have any completing interests in this study.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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2. Methods

2.1. Ethical statement

This study did not involve any individual data; therefore, no ethical approval was required for this systematic review.

2.2. Eligibility criteria

2.2.1. Inclusion criteria. This study included randomized controlled trials (RCTs) of YXD in patients with AP of CHD. The patient was diagnosed with AP of CHD. Patients in the control group received routine treatment, whereas those in the treatment group were treated with YXD based on the control group. The outcomes were the response rate of AP, the response rate based on electrocardiogram, and the rate of nitroglycerin use.

2.2.2. Exclusion criteria. The exclusion criteria were as follows: repetitive publications, nonclinical trials, case reports, case series, noncontrolled trials, quasi-RCTs, wrong comparisons, non-RCTs, studies with insufficient data and unavailable data reporting, and unclear diagnosis and treatment course.

2.3. Literature retrieval

PUBMED, EMBASE, Cochrane Library, CNKI, WANGFANG, and VIP databases were searched from inception to June 1, 2022. In addition, we checked the reference lists of relevant reviews to avoid omitting potential RCTs. The search terms included “coronary heart disease,” “coronary disease,” “atherosclerosis,” “angina pectoris,” “stable angina pectoris,” “angina, stable,” “angina, unstable,” “microvascular angina,” “Yangxin decoction,” “randomized controlled trial,” “controlled trials,” “clinical trials,” “random,” and “randomly.”

2.4. Literature selection and data collection

Two authors independently selected the literature by scanning titles/abstracts and carefully reading the full-text against the eligibility criteria. Two authors independently collected data from the included trials. This included publication information (title, first author, year of publication, and published journal), methodological quality (study design type, randomization method, allocation, blinding details, and outcome report), intervention and control details (modality type, treatment course, and dose), and associated outcomes. Any divergence was resolved by discussion or consultation with a third author.

2.5. Study methodological quality assessment

Two reviewers independently evaluated the study quality using the Cochrane Risk of Bias Tool. We investigated each study using 7 domains, and each was further judged as having a high, unclear, or low risk of bias. A third author helped to resolve any differences through discussion or consultation.

2.6. Statistical analysis

RevMan 5.4 software (Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration) was used for the statistical analysis. The dichotomous data are presented as odds ratios (OR). Continuous data were calculated as mean difference and 95% confidence interval (CI). Heterogeneity across the included RCTs was checked using I^2 statistics. $I^2 \leq 50\%$ suggested acceptable heterogeneity, and a fixed-effects model was used. $I^2 > 50\%$ indicated significant heterogeneity, and a random-effects model was used. We conducted a

meta-analysis if sufficient data were collected on the same outcomes. Otherwise, we reported the associated results using a narrative and descriptive summary.

3. Results

3.1. Study selection

As shown in Figure 1, 913 records were retrieved. Of these, 447 duplicate records were excluded from the analysis. After scanning the titles, abstracts, and full papers, 9 RCTs were finally included in this study (Fig. 1).

3.2. General characteristics

All 9 included RCTs were published in China, and 819 patients diagnosed with CHD and AP were included in this study (Table 1). All control groups received routine treatment and all treatment groups received YXD and routine treatment. The treatment course lasted for 2–8 weeks. The characteristics of the 9 RCTs are listed in Table 1.

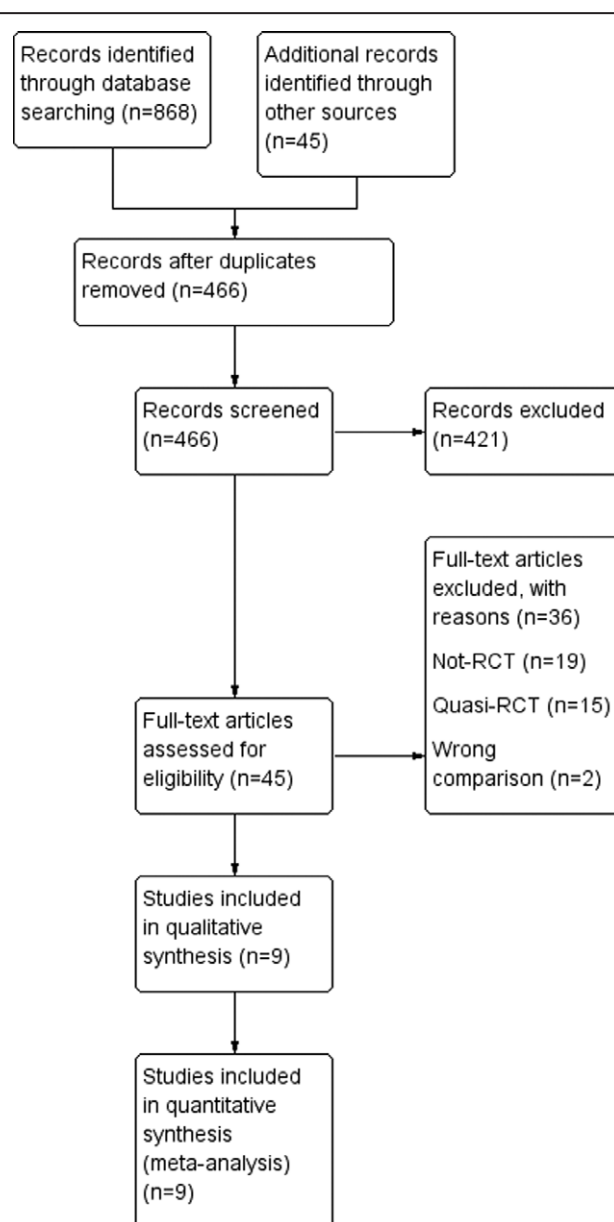


Figure 1. Flow chart of study selection.

Table 1
General characteristics of included randomized controlled trials.

Study	Sample size (T/C)	Age (yrs, T/C)	Gender (M/F)	Intervention	Control	Outcomes	Treatment course
Jia 2020 ^[21]	26/25	T:52.3±4.1 C:53.1±4.3	T:14/12 C:14/11	YXD plus Routine treatment	Routine treatment	①	4 wks
Liu 2019 ^[22]	40/35	T:64.8±7.5 C:64.5±7.7	T:23/17 C:20/14	YXD plus Routine treatment	Routine treatment	②	4 wks
Wu 2012 ^[23]	49/48	T:50.2±8.6 C:51.2±8.5	T:26/23 C:28/20	YXD plus Routine treatment	Routine treatment	①②	4 wks
Xie 2018 ^[24]	75/75	T:56.6±5.5 C:57.0±5.7	T:40/35 C:41/34	YXD plus Routine treatment	Routine treatment	①	8 wks
Yu 2011 ^[25]	53/50	T:59.7±1.4 C:60.1±1.2	T:21/32 C:20/30	YXD plus Routine treatment	Routine treatment	①②③	4 wks
Yu 2012 ^[26]	58/57	T:58.1±4.3 C:58.4±4.0	T:32/26 C:30/27	YXD plus Routine treatment	Routine treatment	①②③	4 wks
Yu 2018 ^[27]	52/48	T:55.3±5.1 C:57.2±11.7	T:32/20 C:31/17	YXD plus Routine treatment	Routine treatment	①②	4 wks
Zhai 2014 ^[28]	30/30	56.8*	27/33	YXD plus Routine treatment	Routine treatment	①②③	4 wks
Zhu 2013 ^[29]	34/34	T:59.5±6.7 C:59.9±6.1	T:19/15 C:20/14	YXD plus Routine treatment	Routine treatment	①	2 wks

①: effect rate of angina pectoris; ②: effect rate based on electrocardiogram; ③: nitroglycerin rate.

*Age reported as mean age.

C = control group, F = female, M = Male, T = treatment group, YXD = Yangxin decoction.

3.3. Study quality assessment

All 9 RCTs^[21–29] described the randomization details sufficiently (Fig. 2). Four studies reported an adequate allocation.^[23,25,26,29] All studies also provided sufficient information on incomplete outcome data, selective reporting, and other bias.^[21–29] However, none of these studies provided sufficient information regarding blindness^[21–29] (Fig. 2).

3.4. Meta-analysis of response rate of AP

Eight studies involving 744 patients reported the response rate for AP.^[21,23–29] No heterogeneity across the 8 studies was detected ($I^2 = 0\%$, $P = .46$); therefore, a fixed-effects model was utilized. The results showed that YXD combined with routine treatment was better than the control group in enhancing the response rate of AP, and the difference was statistically significant (OR = 2.98, 95% CI: 1.96–4.55, $P < .01$) (Fig. 3).

3.5. Meta-analysis of response rate based on electrocardiogram

Six studies involving 550 patients reported the response rate based on the electrocardiogram. Heterogeneity among the 6 trials was small ($I^2 = 26\%$, $P = .24$); therefore, we used a fixed-effects model to pool the data. The difference was statistically significant (OR = 1.88, 95% CI: 1.28–2.78, $P < .01$), indicating that YXD combined with routine treatment for AP in CHD was better than that in the control group (Fig. 4).

3.6. Meta-analysis of nitroglycerin rate

Three studies involving 250 patients reported the rate of nitroglycerin use. There was no heterogeneity among the studies ($I^2 = 0\%$, $P = .58$), a fixed-effects model was used. This difference was statistically significant (OR = 2.04, 95% CI: 1.19–3.52, $P = .01$) (Fig. 5).

4. Discussion

AP in CHD is a clinical manifestation of myocardial ischemia, hypoxia, or necrosis due to an insufficient coronary blood supply. When it attacks, patients often experience retrosternal crushing pain that radiates to the shoulder and back. Studies have shown that AP of CHD tends to occur in middle-aged or older people. TCM has been reported to be effective in managing AP in CHD patients.

Previous similar studies have reported that YXD can effectively relieve the symptoms of patients with AP of CHD.^[34–36] However, the overall methodological quality of the included trials was very poor, which may have affected the robustness and reliability of these studies.^[34–36] Thus, it is necessary to conduct an updated study with a higher quality of the included studies.

The results of this study are partly consistent with those of previous studies.^[34–36] This systematic review of RCTs included a total of 9 trials involving 819 patients with AP of CHD. This study investigated the effectiveness of YXD in combination with routine treatment compared with routine treatment for the management of patients with AP of CHD. The results showed that YXD had better outcomes in improving the response rate of AP, response rate based on an electrocardiogram, and reduction of the rate of nitroglycerin use.

This systematic review has several limitations: (1) according to the evaluation of the Cochrane Risk of Bias Tool, the quality of included trials is still not too high, although it is higher than that in previous studies.^[34–36] Five studies did not report allocation concealment and none of the included studies reported blinding procedures. (2) No placebo or sham intervention was applied to the control group in any of the included trials, which may have affected the efficacy evaluation in this study. (3) All the included studies were conducted and published in China, which may have affected the risk of publication bias. Future studies should address these limitations in the future.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Jia 2020	+	?	?	?	+	+	+
Liu 2019	+	?	?	?	+	+	+
Wu 2012	+	+	?	?	+	+	+
Xie 2018	+	?	?	?	+	+	+
Yu 2011	+	+	?	?	+	+	+
Yu 2012	+	+	?	?	+	+	+
Yu 2018	+	?	?	?	+	+	+
Zhai 2014	+	?	?	?	+	+	+
Zhu 2013	+	+	?	?	+	+	+

Figure 2. Risk of bias summary.

5. Conclusion

The results of this study showed that the application of YXD can benefit CHD patients with AP. Future studies with more high quality trials are needed to warrant the present findings.

Author contributions

Conceptualization: Xiao-hong Yu and Zhe-ming Xu.
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 Methodology: Xiao-hong Yu, Xi-wen Yu, and Hai-xiang Li.
 Supervision: Zhe-ming Xu.
 Validation: Xi-wen Yu and Hai-xiang Li.
 Writing—original draft: Xiao-hong Yu and Zhe-ming Xu.
 Writing—review & editing: Xiao-hong Yu and Zhe-ming Xu.

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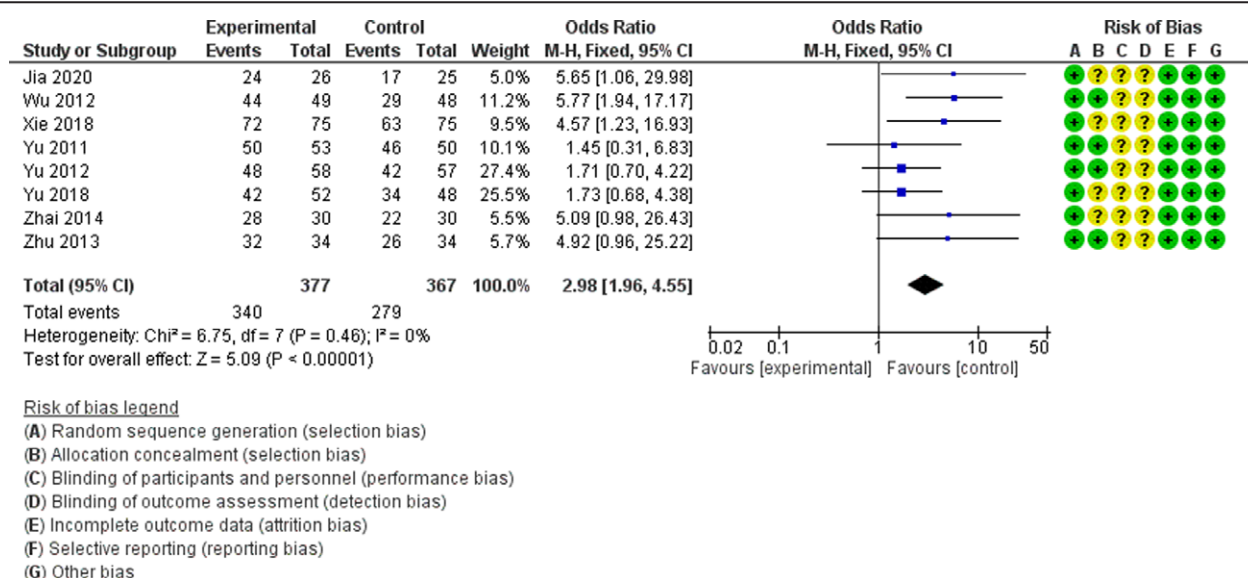


Figure 3. Meta-analysis of response rate of AP of CHD. CHD = coronary heart disease.

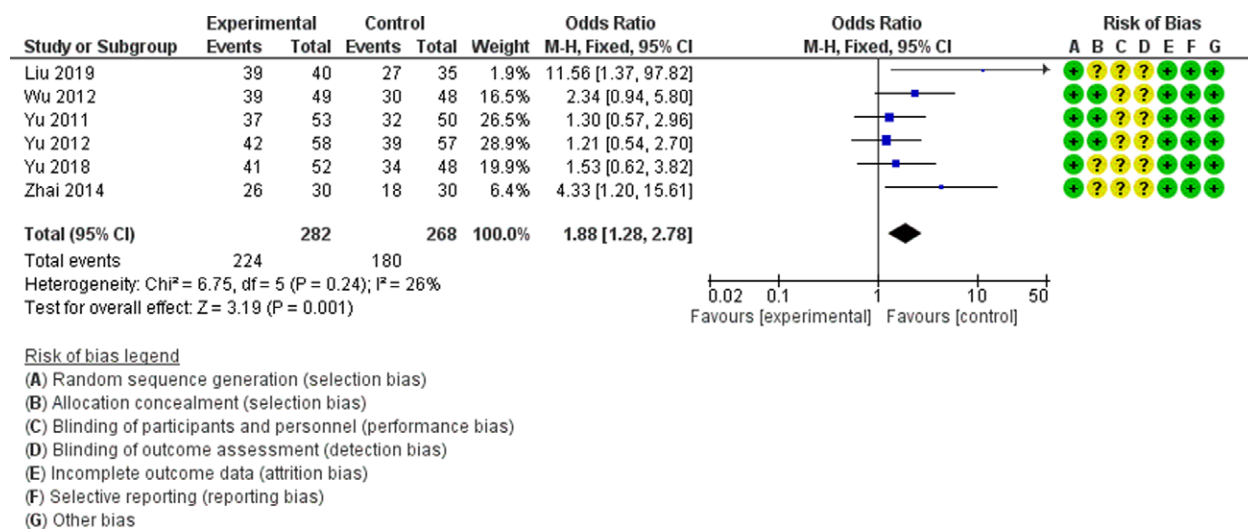
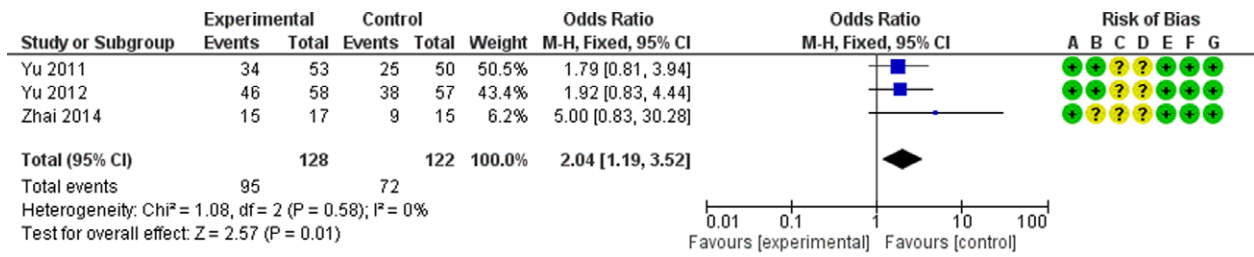


Figure 4. Meta-analysis of response rate based on electrocardiogram.



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure 5. Meta-analysis of rate of nitroglycerin use.