Acupuncture therapy for angina pectoris: a systematic review

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Abstract

OBJECTIVE: To assess the effectiveness and safety of acupuncture therapy for angina pectoris.

METHODS: Randomized controlled trials (RCTs) concerned with acupuncture treatment of angina pectoris were identified by searching Academic Source Premier, MEDLINE, Science Citation Index Expanded, and three Chinese databases (China biology medicine database, China national knowledge infrastructure, and VIP database for Chinese technical periodicals). The valid data were extracted in accordance with our inclusion and exclusion criteria. The main outcomes of the included studies were synthesized using Revman 5.1.

RESULTS: Twenty-one articles on 16 individual studies were included and evaluated as having high or moderate risk of bias according to the standards of the Cochrane Collaboration. Meta-analysis indicated that acupuncture combined with conventional drugs (ACCD) was superior to conventional drugs alone in reducing the incidence of acute myocardial infarction (AMI) [OR=0.18, 95% CI (0.04, 0.84), P=0.03]. Moreover, ACCD was superior to conventional drugs in the relief of angina symptoms [OR=4.23, 95% CI (2.73, 6.56), P<0.00001], and improvement of electrocardiography (ECG) [OR=2.61, 95% CI (1.83, 3.73), P<0.00001]. Acupuncture by itself was also superior to conventional drugs for angina symptoms [OR=3.59, 95% CI (1.76, 7.92), P=0.0004] and ECG improvement [OR=3.07, 95% CI (1.54, 6.10), P=0.001]. ACCD was superior to conventional drugs in shortening the time to onset of angina relief [WMD=-1.40, 95% CI (-1.65, -1.15), P<0.00001]. However, the time to onset was significantly longer for acupuncture treatment than for conventional treatment alone [WMD=2.43, 95% CI (1.63, 3.23), P<0.00001].

CONCLUSION: ACCD reduced the occurrence of AMI, and both acupuncture and ACCD relieved angina symptoms and improved ECG. However, compared with conventional treatment, acupuncture showed a longer delay before its onset of action. This indicates that acupuncture is not suitable for emergency treatment of heart attack. Owing to the poor quality of the current evidence, the findings of this systematic review need to be verified by more RCTs to enhance statistical power.

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Key words: Acupuncture therapy; Randomized controlled trial; Efficacy; Review; Meta-analysis

INTRODUCTION

Coronary artery disease (CAD) commonly results from atherosclerotic obstruction of coronary arteries and mostly manifests as angina pectoris and acute myocardial infarction (AMI). Acupuncture therapy has been widely used as a complementary and alternative medicine for the treatment of angina pectoris. However, the efficacy and safety of acupuncture therapy for angina pectoris have not been fully evaluated. Therefore, a systematic review of the existing literature on acupuncture therapy for angina pectoris is necessary to provide evidence-based guidance for clinical practice.
dial infarction. An ischemic heart disease, it is likely to attack people over 40 years of age. It has been reported that the incidence of angina pectoris is 0.1%-1% in European women aged 40%-54% years, and 2%-5% in men of the same age group. The incidence is 10%-15% in females and 10%-20% in males in people aged 65 to 74 years. With the rapid development of the Chinese economy, ischemic heart disease has become increasingly common in recent years. According to a survey of a community in Beijing, the incidence of angina pectoris and myocardial infarction is 30.7% (male 26.2%, female 33.7%) and 2.9% (male 4.8%, female 1.7%), respectively. It has been estimated that the global mortality of CAD will rise from 6.3 million in 1990 to 11 million by the end of 2020, and that the mortality will increase to 74.6% in the coming thirty years. Modern treatments to reduce ischemic symptoms and improve prognosis of angina pectoris include nitrates, beta blockers, calcium antagonists, aspirin, and ACE inhibitors. These drugs can have undesirable effects. For instance, nitrate treatment carries the risks of tolerance and rebound, and can cause headaches, flushed cheeks and other adverse reactions.\textsuperscript{4,5}\n\nAcupuncture was recorded in \textit{Huang Di Nei Jing\textsuperscript{6}} over two thousand years ago to work well in the treatment of chest \textit{Bi} syndrome (precordial pain). In more recent years, acupuncture therapy for angina has occasionally been reported outside China. A non-randomized controlled trial in Denmark indicated that integrated rehabilitation dominated by acupuncture reduced the risk of death in patients with coronary heart disease and decreased their economic burden.\textsuperscript{7,8}\n\nCurrently available randomized controlled trials (RCTs) have had small sample sizes and shown diverse outcomes. The assessment and integration of these trials using an evidence-based approach to guide clinical treatment are of global priority. Therefore, in this systematic review we synthesize the results of available RCTs to assess the effectiveness and safety of acupuncture therapy for angina pectoris.\n\n**METHODS**

**Inclusion criteria for studies**

All RCTs, except those containing inaccurate or incomplete data, were included.

**Inclusion criteria for participants**

Participants had been diagnosed with angina pectoris since at least three months. Participants were excluded if they had acute myocardial infarction, severe arrhythmia, heart failure, hepatic failure or renal failure.

**Inclusion criteria for the interventions**

This review included trials that made a comparison between an acupuncture-dominated therapy and nitrates. The acupuncture-dominated treatments included acupuncture combined with conventional drugs (ACCD) and acupuncture itself. ACCD or acupuncture therapy consisted of manipulations such as stimulation with filiform needles, and cupping after needling, and the duration of treatment was >10 days. We included studies that predominantly used nitrates as the conventional treatment. If they used other antianginal drugs, such as beta-blockers or calcium antagonists, we included the trial as long as the drugs were used equally across the control and experimental groups.

**Primary and secondary outcomes**

Primary outcome: incidence of myocardial infarction. Secondary outcomes: 1) improvement of angina symptoms; 2) time to onset of angina relief in response to treatment; and 3) electrocardiography (ECG) improvement.

**Search methods**

We searched the following databases: Academic Source Premier (1975 to August 2011), MEDLINE (1993 to August 2011), Science Citation Index Expanded (1973 to August 2011) and the three Chinese databases China biology medicine (1978 to August 2011), China national knowledge infrastructure (1979 to August 2011) and VIP database for Chinese technical periodicals (1989 to August 2011). Studies published in both English and Chinese were retrieved. Further, studies included in reference lists of relevant trials and reviews were also identified. The following key words were used in the search: angina, angina pectoris, coronary heart disease, acupuncture, and electroacupuncture. A sample retrieval strategy for MEDLINE is shown below.

1) acupuncture therapy.mp. or exp Acupuncture Therapy
2) electroacupuncture. mp. or exp Electroacupuncture
3) electric acupuncture. mp. or exp Electric Acupuncture
4) electric stimulat$.tw.
5) transcutaneous electrical nerve stimulation
6) tens.mp
7) or/1)-6)
8) angina pectoris.mp. or exp Angina Pectoris
9) angina.mp.
10) stable angina.mp.
11) unstable angina.mp.
12) or/8)-11)
13) 7) and 12)
14) randomized controlled trial.pt.
15) controlled clinical trial.pt.
16) randomized controlled trials.sh.
17) random allocation.sh.
18) double blind method.sh.
19) single-blind method.sh.
20) or/14)-19)
21) (animals not human).sh.
22) 20 not 21
23) clinical trial.pt.
24) exp clinical trials
26) ((sing$ or doubl$ or trebl$ or tripl$) adj25 (blind $ or mask$)).ti,ab.

**Primary and secondary outcomes**

Primary outcome: incidence of myocardial infarction. Secondary outcomes: 1) improvement of angina symptoms; 2) time to onset of angina relief in response to treatment; and 3) electrocardiography (ECG) improvement.
Data collection and extraction
RCTs evaluating the efficacy of acupuncture-dominanted therapy for angina pectoris were included. Titles and abstracts of searched studies were screened for further review. Those that appeared eligible were determined eligible by review of the full text. The inclusion criteria were applied by two authors independently. Disagreements were resolved by discussion and by consultation with other authors of our group, and a judgment was made based on consensus.

Data were collected independently by two authors using a piloted data extraction form. The following characteristics of the trials were recorded on the form: design, methods, participants, interventions, and outcomes. Any disagreements were resolved by referring to the trial report and by discussion. The standards advised by the Cochrane handbook in terms of randomization, allocation concealment, binding, complete data and selective reporting were employed to evaluate the quality of the RCTs. "Yes", "No" or "not-reported" were used to determine the standards mentioned above. The quality of each study was assessed as low risk of bias (one or more criteria not met), as moderate risk of bias (one or more criteria partly met), or as high risk of bias (all of the criteria met). For dichotomous outcomes, the number of participants experiencing the event in each group was recorded. For continuous outcomes, the means and standard deviations for each group were extracted. Data entries in RevMan 5.1 (free software downloadable from http://ims.cochrane.org/revman/download) were double-checked.

Statistical analysis
Data were used for a meta-analysis if they were available, of sufficient quality and sufficiently similar. Dichotomous data were expressed as relative risks (OR). Continuous data were expressed as weighted mean differences (WMD). Overall results were calculated based on the fixed effects model when no heterogeneity was found among pooled studies. Where heterogeneity existed, the random effects model was used. Heterogeneity was tested using the Z score and the Chi-square statistics with significance set at P<0.1. Possible sources of heterogeneity were assessed by sensitivity and subgroup analyses as described below.

RESULTS

Description of included studies
We selected 21 studies out of the 296 relevant references by screening titles and reviewing full texts. The data of the included studies were extracted using a form that included study design, sample size, intervention and outcome measure (Figure 1).

General data of included studies
Sixteen independent studies were reported in the 21 included articles. The treatment groups received either ACCD or acupuncture therapy, while the control groups were treated with conventional drugs. The number of participants varied from 49 to 200 and the duration of treatment was between 10 days and 6 weeks (Table 1).

Quality assessment of included studies
Six of the included articles reported their method of randomization, whereas none mentioned allocation concealment, blinding, loss of follow-up or drop-out, or selective report. All studies were assessed as having a low or moderate risk of bias (Table 2).

Effect of ACCD on the incidence of myocardial infarction
Two papers reported their follow-up of participants with myocardial infarction. In those trials, the patients received ACCD together with the same conventional drugs as the control group, and there was little heterogeneity between the two studies (P=1.00, I²=0%). Meta-analysis was conducted using the fixed effect model. The result indicated that ACCD was better than conventional treatment for preventing acute myocardial infarction [OR=0.18, 95%CI (0.04, 0.84), P=0.03] (Figure 2).

Effects of ACCD and acupuncture on angina symptoms
Ten studies reported the effective rate of angina relief by ACCD. There was little heterogeneity among these studies (P=0.95, I²=0%), so meta-analysis was conducted using the fixed effect model. The result indicated that ACCD was superior for improvement of angina symptoms compared to the conventional treatment [OR=4.23, 95%CI (2.73, 6.56), P<0.00001] (Figure 3). Two studies reported the effective rate of angina relief by acupuncture. There was little heterogeneity between the two studies (P=0.35, I²=0%), so meta-analysis was conducted using the fixed effect model. The result indicated that acupuncture was superior compared
Table 1 Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Intervention</th>
<th>Drugs employed as conventional treatment</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yuan ZJ</td>
<td>30</td>
<td>CT</td>
<td>isosorbide 5-mononitrate</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Wang X</td>
<td>28</td>
<td>CT</td>
<td>isosorbide 5-mononitrate, betaloc, aspirin</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Cao JP</td>
<td>30</td>
<td>CT</td>
<td>isosorbide dinitrate, aspirin</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Liu WP</td>
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<td>CT</td>
<td>isosorbide dinitrate</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Liu WP</td>
<td>32</td>
<td>CT</td>
<td>isosorbide 5-mononitrate, diltiazem hydrochloride, aspirin</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Liu WP</td>
<td>32</td>
<td>CT</td>
<td>isosorbide 5-mononitrate, diltiazem hydrochloride, aspirin</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Chang PF</td>
<td>30</td>
<td>CT</td>
<td>nitrates, betaloc</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Tong YH</td>
<td>120</td>
<td>CT</td>
<td>isosorbide 5-mononitrate, betaloc, simvastatin, aspirin</td>
<td>6 weeks</td>
</tr>
<tr>
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<td>CT</td>
<td>isosorbide 5-mononitrate, betaloc, simvastatin, aspirin</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Tong YH</td>
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<td>CT</td>
<td>isosorbide 5-mononitrate, betaloc, simvastatin, aspirin</td>
<td>6 weeks</td>
</tr>
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<td>Huang FQ</td>
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<td>isosorbide 5-mononitrate, betaloc, simvastatin, aspirin</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Xu FH</td>
<td>35</td>
<td>CT</td>
<td>nitrates, beta-blocker, calcium antagonist, aspirin</td>
<td>10 days</td>
</tr>
<tr>
<td>Yu SH</td>
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<td>CT</td>
<td>Nitrates</td>
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<tr>
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<tr>
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<tr>
<td>Lin Z</td>
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<td>CT</td>
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<td>4 weeks</td>
</tr>
</tbody>
</table>

Notes: A: acupuncture; CT: conventional treatment; T: treatment group; C: control group.

Figure 1 Flow diagram of the search method and selection process
ASP: academic source premier; SCI-E: science citation index expanded; CBM: China biology medicine; CNKI: China national knowledge infrastructure; VIP: VIP database for Chinese technical periodicals.
with the conventional treatment in reducing angina symptoms \[ \text{OR}=3.59, \text{95\% CI}(1.76, 7.92), P=0.0004 \] (Figure 4).

### Effect of ACCD and acupuncture on the time to onset of angina relief

Two studies reported the time to onset of angina relief provided by ACCD.\(^{11,22}\) There was little heterogeneity between the two studies \((P=1.00, I^2=0\%)\), so meta-analysis was conducted using the fixed effect model. The result indicated that ACCD shortened the time to onset of angina relief compared with conventional treatment \[ \text{WMD}=-1.40, \text{95\% CI}(-1.65, -1.15), P<0.00001 \] (Figure 5). Only one study reported the effect of acupuncture on the time to onset of angina relief.\(^{27}\) The fixed effect model was employed to conduct meta-analysis in which no combined effect was applied. The result showed that acupuncture had a slower onset of action

<table>
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<th>Study</th>
<th>Method of randomization</th>
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<th>blinding</th>
<th>Loss of follow-up or drop-out</th>
<th>Selective report</th>
<th>Quality assessment</th>
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<td>not reported</td>
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<td>non</td>
<td>high risk</td>
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<tr>
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<tr>
<td>Liu WP(^{14})</td>
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<td>non</td>
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<tr>
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<td>non</td>
<td>moderate risk</td>
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<td>Yin LH(^{28})</td>
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<td>Zhang L(^{30})</td>
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<td>non</td>
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<td>high risk</td>
</tr>
</tbody>
</table>

**Table 2:** Methodological quality assessment of included studies

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\[^{11}\] Chen J *et al.* Acupuncture therapy for angina pectoris: a systematic review

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Chen J et al. Acupuncture therapy for angina pectoris: a systematic review

Figure 3 Forest plot of ACCD for effective improvement of angina symptoms
ACCD: acupuncture combined with conventional drugs.

Figure 4 Forest plot of acupuncture for effective improvement of angina symptoms

Figure 5 Forest plot of the effect of ACCD in reducing the time to onset of angina relief
ACCD: acupuncture combined with conventional drugs.

Figure 6 Forest plot of the effect of acupuncture on the time to onset of angina relief

Figure 7 Forest plot of the efficacy of ACCD in improving ECG
ACCD: acupuncture combined with conventional drugs; ECG: electrocardiography.
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Experimental vs. Control

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI Year</th>
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<tbody>
<tr>
<td>Zhou W 2007</td>
<td>60</td>
<td>72</td>
<td>35</td>
<td>56</td>
<td>68.9%</td>
<td>3.00 [1.32, 6.83] 2007</td>
</tr>
<tr>
<td>Yin LH 2009</td>
<td>36</td>
<td>40</td>
<td>28</td>
<td>38</td>
<td>30.4%</td>
<td>3.21 [0.91, 11.34] 2009</td>
</tr>
</tbody>
</table>

Total (95% CI) 112 94 100.0%

Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%

Test for overall effect: Z = 3.19 (P = 0.001)

Figure 8 Forest plot of the effect of acupuncture on ECG improvement.

ECG: Electrocardiography compared to nitrates [WMD=2.43, 95% CI (1.63, 3.23), \( P<0.000\ 01 \)] (Figure 6).

**Effects of ACCD and acupuncture on ECG improvement**

Ten studies reported the efficacy of ACCD on ECG improvement. There was little heterogeneity among these studies (\( P=0.36, I=8\% \)), so meta-analysis was conducted using the fixed effect model. The result indicated that ACCD was superior compared to the conventional treatment for the improvement of ST segment ischemia [\( OR=2.61, 95\% CI (1.83, 3.73), P<0.000\ 01 \)] (Figure 7).

Two studies reported the efficacy of acupuncture in ECG improvement. There was little heterogeneity among these studies (\( P=0.93, I=0\% \)), so meta-analysis was conducted using the fixed effect model. The result indicated that acupuncture was superior compared with the conventional treatment for the improvement of ST segment ischemia [\( OR=3.07, 95\% CI (1.54, 6.10), P=0.001 \)] (Figure 8).

**Assessment of publication bias**

Judging from the symmetry of the funnel plot, no apparent publication bias was found in the meta-analysis, indicating that the results are reliable (Figure 9).

**Adverse effect**

None of the studies reported any adverse effects associated with acupuncture therapy.

**DISCUSSION**

All current randomized controlled trials were conducted in China, and all patients were Chinese. The articles were all published in Chinese journals. Nitrates treatment was given to all control groups. This typical and popular vasodilator has been proven to be effective in the treatment of angina pectoris, as reported by a systematic review abroad. Based on our analysis, acupuncture-dominated therapy appears beneficial for treating angina pectoris, as it relieves symptoms, provides pain relief, and promotes ECG restoration. However, acupuncture shows a slower time to onset than conventional treatment and is therefore not advised for the emergency treatment of ischemic disease.

The main shortcoming of the conclusions of our study is the poor quality of the original studies, as this is likely to influence the reliability of our results. It also suggests that there is a need for medical staff in China to implement further improvements in terms of the design and methodology of clinical studies. Moreover, more RCTs with larger samples are needed to validate the use of acupuncture in angina treatment.

Our study indicates that ACCD can play an active role in preventing acute myocardial infarction, which would lead to improvements in the life quality of patients. In addition, when compared to the control group, ACCD or acupuncture treatment increased the overall efficacy in terms of symptom relief and ECG improvement. When the time to onset of angina relief was used as an outcome measure, ACCD was superior to the conventional treatment alone, whereas acupuncture showed a slower onset of action. In conclusion, acupuncture therapy is indicated for treating stable angina pectoris, but it is unsuitable for the treatment of patients with an acute ischemic heart event.

**REFERENCES**

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