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Review Article

Effectiveness and safety of acupuncture for angina pectoris: An overview of systematic reviews

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ABSTRACT

Background: The number of systematic reviews meta-analyses (SRs/MAs) on the effectiveness of acupuncture for angina pectoris (AP) is increasing. Due to the inconsistent conclusions and unknown quality of these SRs/MAs, this overview aimed to systematically evaluate and synthesize the existing SRs/MAs, attempting to provide more reliable evidence for the effectiveness and safety of acupuncture in the treatment of AP.

Methods: SRs/MAs were searched via eight databases from inception to March 14, 2022. The risk of bias was evaluated using the Risk of Bias in Systematic reviews (ROBIS) tool. The quality of the methodology, reporting, and evidence were assessed by the Assess Systematic Reviews 2 (AMSTAR-2), the Preferred Reporting Item for Systematic Review and Meta-analysis for Acupuncture (PRISMA-A), and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system, respectively.

Results: Sixteen SRs/MAs were included and fifteen SRs/MAs were considered being of critically low quality according to AMSTAR-2. Only three SRs/MAs were rated at low risk of bias. No study reported all the items listed in the PRISMA-A checklist. No high-quality evidence with GRADE assessment was found. With the low-quality evidence, acupuncture combined with other interventions was superior to monotherapy (medications or Chinese medicine) in the angina symptom and electrocardiogram recovery. No adverse effects owing to acupuncture were reported.

Conclusions: Owing to the lack of high-quality evidence provided by the current SRs/MAs, the effectiveness of acupuncture for AP still warrants further proof. Further researches with more critical design and methodology are needed for providing more convincing evidence.

Registration: This review was registered at PROSPERO (www.crd.york.ac.uk/prospero/): CRD42021219367.

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1. Introduction

Angina pectoris (AP) refers to chest pain or discomfort caused by a lack of oxygen-rich blood in the heart muscle, and 54 million people live with angina pectoris globally.[1] With the growth and aging of the global population, the healthcare burden and medical costs of heart disease have gained increasing significance.[2] Angina has been shown to exert major effects on health-related quality of life by affecting individuals' working ability and longevity.[3,4]

The National Institute for Health and Care Excellence (NICE) guidance suggests that the current aim of pharmacologic management is to prevent myocardial ischemic episodes, control symptoms, improve the quality of life, and prevent cardiovascular events.[5] However, the management of AP remains unsatisfactory. Acupuncture has shown benefits in alleviating angina symptoms, preventing recurrence, and improving quality of life.[6–8] In recent years, the number of systematic reviews/meta-analyses (SRs/MAs) targeting acupuncture for AP has been increasing. Some of them concluded that acupuncture might be an effective adjunct therapy to conventional treatment[9–13] however, others have doubted the efficacy and safety of acupuncture. These published SRs/MAs have reported contradictory outcomes. Furthermore, the quality of

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these SRs/MAs is unknown, which may make the conclusions more controversial. Therefore, it is necessary to systematically evaluate and synthesize the existing evidence and to determine the clinical effectiveness and safety of acupuncture in the treatment of AP.

Overview is an approach for synthesizing the outcomes from multiple SRs/MAs, evaluating the quality and attempting to address any inconsistent outcomes.[14] The objective of this overview was to comprehensively summarize the evidence of acupuncture for AP and also to identify the limitations, thereby providing recommendations for achieving high-quality SRs/MAs.

2. Methods

This study was conducted according to the methods outlined in the Cochrane Handbook for Systematic Reviews and registered in the International Prospective Register of Systematic Reviews (PROSPERO) (no. CRD42021219367).

2.1. Search strategy

We searched four English databases (PubMed, Embase, Cochrane, and Web of Science), and four Chinese databases (Chinese National Knowledge Infrastructure [CNKI], Chinese Biological Medicine [CBM], the Chongqing VIP Chinese Science and Technology Periodical Database [VIP], and the Wan Fang database) from inception to March 14, 2022, with no language restrictions. PROSPERO, an international prospective register of systematic reviews, was searched to identify ongoing researches. The following combined text and MeSH terms were used to screen potential studies: "acupuncture," "electroacupuncture," "angina pectoris," "stable angina," and "systematic review." Examples of the search strategy are provided in Supplementary Table 1. The reference lists of the identified original or review articles were checked to identify additional studies.

2.2. Selection criteria

2.2.1. Types of studies
We included SRs or MAs of randomized controlled trials (RCTs) evaluating the effect of acupuncture in AP.

2.2.2. Types of participants
According to the existing diagnostic criteria, patients who were diagnosed with either stable or unstable AP would be included with no restrictions on age, race, and gender.

2.2.3. Types of interventions
Acupuncture (e.g., manual acupuncture, electroacupuncture, auricular acupuncture, or scalp acupuncture) or acupuncture plus conventional therapy (e.g., medications, or Chinese medicine) as an intervention for AP were included.

2.2.4. Types of comparators
The following interventions were considered as in the control group: medication, Chinese medicine, placebo (e.g., sham acupuncture), or no treatment (e.g., waiting list).

2.2.5. Types of outcome measures
The primary outcomes were effectiveness, which was assessed by the rate of efficacy, decrease of the angina attack frequency, and improvement of the symptom of angina. Secondary outcomes included the six-minute walking test (6-MWT) and electrocardiogram (ECG) recovery. The criteria of the effective rate are followed in the previous reference.[11]
We excluded SRs that met one of the following criteria: SRs including non-RCTs or with network meta-analysis; interventions of

stimulating acupuncture points without needle insertion (e.g., acupressure, moxibustion, or transcutaneous electrical nerve stimulation); control groups were treated with different types of acupuncture or needle insertion at different points; SRs without the outcomes mentioned above.

2.3. Selection of studies

Two independent investigators (W.C.Qi and H.J.Fu) assessed the eligibility of each record by using Endnote X8. They checked the study titles and abstracts for the initial screening to exclude studies that did not refer to acupuncture and angina pectoris. Eligible studies were retrieved for full-text assessment. Any disagreements were resolved by a third reviewer (D.J.Cai).

2.4. Data extraction

Data were extracted using a predefined data-extraction form (Excel software) that assessed SR information (author, publication year, included study design, number of studies, number of patients, diagnostic criteria, interventions, comparators, outcomes), reported outcomes (effect size with 95% confidence interval [95% CI], total number of patients in the intervention group/control group/both groups, and the number of studies), and information on methodology. Two independent reviewers (W.C.Qi and H.J.Fu) extracted the data in duplicate. Any disagreements were arbitrated by a third reviewer (C.Wang).

2.5. Assessment of the methodological, reporting, and evidence quality of the included SRs/MAs

Two trained reviewers (R.R.Sun and X.Li) independently assessed the included SRs to evaluate the following aspects: the methodological quality, the reporting quality, the level of risk of bias, and the quality of the primary outcomes. (1) The AMSTAR-2 checklist,[15] which contains 16 items, including 7 critical items, was used to assess the methodological quality of the included SRs, which was rated as high, moderate, low, or critically low. (2) The PRISMA-A checklist,[16] which consists of 27 items, was used to assess the reporting quality of SRs on acupuncture. The completion of each item was presented as a ratio. (3) The ROBIS tool is a new tool to assess risk of bias in SRs rather than in primary studies.[17] This tool is completed in three phases: assessment of relevance, identification of concerns with the review process, and judgment of the risk of bias. Risk of bias was rated as "low", "high," or "unclear." (4) The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for assessments of the quality of primary outcomes.[18] Any disagreements were arbitrated by a third reviewer (F.R.Liang).

3. Results

3.1. Literature search

We retrieved 453 studies, of which 16 were included in our overview (Fig. 1). Two reviewers independently excluded 143 duplicates. A total of 271 irrelevant papers were then excluded by screening the titles and abstracts. 39 full-text papers were retrieved, and 23 records (14 SRs and 9 non-SRs) were excluded because of the specific reasons outlined in Supplementary Table. 2.

3.2. Characteristics of SRs

Data extracted from the included 16 SRs/MAs published have been summarized in Table1. Among the 16 SRs/Mas, ten were reported in Chinese,[19–28] and the remaining six were reported in En-

3

Table 1
Characteristics of included SRs

Author, year (country)	Trials (subjects)	Patient diagnosis	Intervention	Comparator	Outcomes	Main results	Quality assessment	Meta-analysis	AMSTAR2	ROBIS
Chen (2012) (China)	21(1961)	AP	MA, MA + M	M	Angina symptoms relief; ECG improvement; Adverse effect	Bothe acupuncture and acupuncture combined with conventional drugs relieved angina symptoms and improved ECG.	Cochrane ROB	Yes	CL	🙁
Wang (2012) (China)	6(386)	AP	MA + CM + M, MA + M, EA + CM	CM + M, CM	Angina symptoms relief; ECG improvement; Adverse effect	Acupuncture combined with TCM group was significantly better than TCM group in improving angina pectoris symptoms and ECG.	Cochrane ROB	Yes	CL	🙂
Yu (2015) (China)	25(2058)	AP, SAP, UAP	MA, MA + M, MA + CM, EA, EA + M, EA + CM	SA; M; CM	Angina relief; ECG improvement; Adverse effect	The number of patients with ineffectiveness of angina relief and ECG improvement was less in the combined acupuncture group than in the anti-angina medicines alone group.	Cochrane ROB	Yes	CL	🙁
Li (2015) (China)	3(244)	AP	MA	CM	Effective rate	Acupuncture is an effective therapy in treating angina pectoris	Jadad scale	Yes	CL	🙂
Zhang (2015) (China)	8(640)	SAP	MA, EA, ATCM	M; CM	Angina symptoms relief; ECG improvement; Effective rate; Nitroglycerin use; Adverse effect	acupuncture significantly increased the clinical curative effects in the relief of angina symptoms and improved the ECG	Unclear	Yes	CL	🙁
Zhang (2015) (China)	11(1232)	AP	A + M	M, SA + M	Angina symptoms relief; ECG improvement; Nitroglycerin use; Ischemia time of Holter	Based on regular western medicine, acupuncture can further improve symptoms of angina and ECG, and reduce the dosage of nitroglycerin	Cochrane criteria	Yes	CL	🙂
Shao (2016) (China)	12(1006)	CHD	EA + M	M	Angina symptoms relief; ECG improvement; Effective rate; Nitroglycerin use; Adverse effect	Electroacupuncture can effectively improve the clinical symptoms and ECG, decrease the dosage of nitroglycerin	Cochrane criteria	Yes	CL	🙁
Li (2017) (China)	7(465)	UAP	MA + M	M	Angina symptoms relief; ECG improvement; Ischemia time of Holter	Acupuncture combined with routine medicine is better in relieving angina syndrome, improving ECG, and reducing the duration of myocardial ischemia in Holter.	Jadad scale	Yes	CL	🙁
Zhou (2018) (China)	4(245)	SAP	MA + M	M	Angina attack frequency; ECG improvement; Effective rate; Nitroglycerin use; 6MWT	Acupuncture combined medicine can improve the treatment efficiency, the ECG, reduce the frequency of angina and nitroglycerin consumption. There were no significant changes between two groups in 6-MWT.	Cochrane criteria	Yes	CL	🙁

Table 1 (continued)

Author, year (country)	Trials (subjects)	Patient diagnosis	Intervention	Comparator	Outcomes	Main results	Quality assessment	Meta-analysis	AMSTAR2	ROBIS
Bu (2018) (China)	21(1774)	AP	MA + M, EA + M	M	Angina symptoms relief; ECG improvement; 6MWT Ischemia time of Holter; Angina attack time; Angina intensity; Adverse effect	Acupuncture combined with medicine can reduce the symptoms of angina pectoris, reduce the number of episodes of angina pectoris	Cochrane criteria	Yes	CL	☹
Sun (2019) (China)	7(621)	AP	MA, MA + M, MA + CM	M, CM	Effective rate	Acupuncture can improve the clinical symptoms in patients with CHD	Unclear	Yes	CL	☹
Yang (2019) (China)	17(1516)	SAP	MA, EA, MA + CM	SA, M, CM	Angina attack frequency; ECG improvement; 6MWT; Angina pain intensity; Adverse effect; Effective rate	Acupuncture was associated with reduced angina attack frequency. No significant improvement was shown in nitro-glycerin use or angina intensity.	Cochrane criteria	Yes	L	☹
Huang (2019) (China)	24(1916)	AP	MA + M, MA + CM	M, CM	Markedly effective rate; Moderately effective rate	Patients who received adjunctive acupuncture treatment had a significantly increased markedly effective rate.	Jadad scale	Yes	CL	☹
Ma (2020) (China)	7(846)	SAP	MA + M	M	Angina attack frequency; Angina pain intensity;	The number of attacks in patients with angina and the degree of pain in acupuncture group were reduced more than that in the control group.	Cochrane criteria	Yes	CL	☹
Tu (2021) (China)	7(893)	CSAP	MA, EA	SA, SC	Angina attack frequency; Angina pain intensity; Adverse effect	Acupuncture combined with standard care was more effective in reducing angina attack frequency and angina pain intensity than sham acupuncture with standard care and standard care alone.	Cochrane criteria	Yes	CL	☹
Song (2021) (China)	13(1708)	CSAP	EA	Waiting treatment	Angina attack frequency; angina pain intensity; Adverse effect; Nitroglycerin use	Acupuncture group was superior to the waiting treatment group in reducing the attack frequency and alleviating pain of angina.	Cochrane criteria	Yes	CL	☹

AMSTAR2: A Measurement Tool to Assess systematic Reviews 2; AP: angina pectoris; ATCM: Acupuncture-based Traditional Chinese Medicine; CHD: coronary heart disease; CL: critically low; CM: Chinese medicines; CSAP: chronic stable angina pectoris; EA: electroacupuncture; L: Low; M: Medications; MA: manual acupuncture; ROBIS: Risk of Bias in Systematic reviews; SA: Sham acupuncture; SAP: stable angina pectoris; SC: standard care group; UAP: unstable angina pectoris; VAS: Visual Analogue Scale; 6MWT: 6cminute walk test;

☹ = Low risk; ☺ = High risk;

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                    ┌─────────────────────────────┐
                    │ Records identified through   │
                    │ database searching: Embase   │        ┌──────────────────────────┐
   Identification   │ (n = 160), Web of science (n │        │ Additional records       │
                    │ = 88), Cochrane (n = 19),    │        │ identified through other  │
                    │ PubMed (n = 18), CNKI (n =   │        │ sources PROSPERO (n = 5)  │
                    │ 44), CBM (n = 35), Wanfang   │        └──────────────────────────┘
                    │ (n = 78), VIP (n = 6)        │
                    └─────────────────────────────┘
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Identification

Records identified through database searching: Embase (n = 160), Web of science (n = 88), Cochrane (n = 19), PubMed (n = 18), CNKI (n = 44), CBM (n = 35), Wanfang (n = 78), VIP (n = 6)

Additional records identified through other sources PROSPERO (n = 5)

Screening

Duplicates records (n = 143)

Records after duplicates removed (n = 310)

Titles and abstracts excluded (n = 271)
irrelevance (n = 271)

Eligibility

Full-text articles assessed for eligibility (n = 39)

Full-text articles excluded, with reasons (n = 23)
acupuncture was not main intervention (n = 5)
angina was not the main research object (n = 7)
conference abstract/letter (n = 2)
no outcome data (n = 1)
non-SRs (n = 4)
study protocol (n = 3)
Incorrect full text format (n = 1)

Included

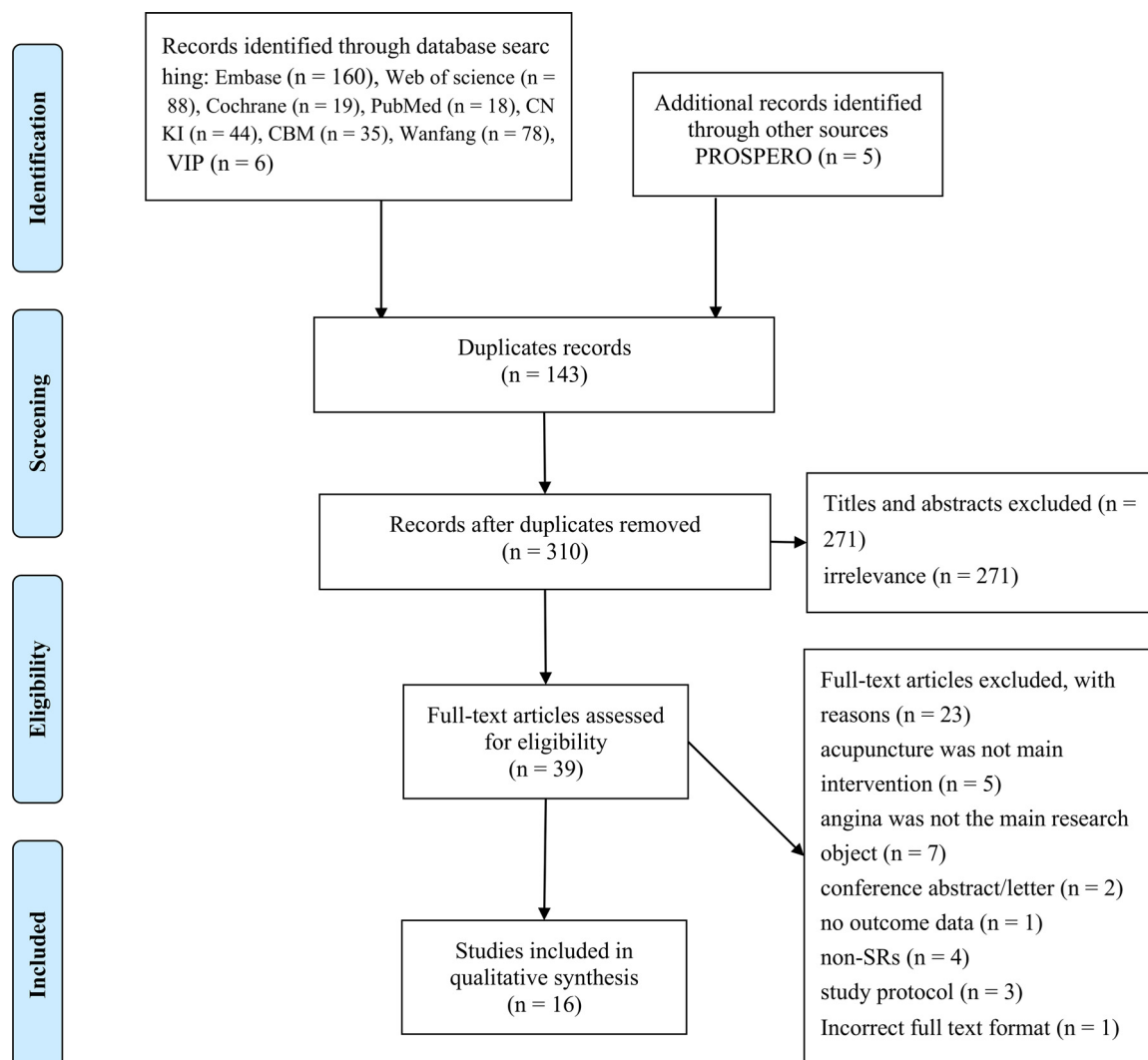Studies included in qualitative synthesis (n = 16)

Fig. 1. Flowchart of the selection process of included SRs/MAs.

glish.[9–13,29] All of them were conducted by authors from the main-land China. The number of trials included in the SRs/MAs ranged from 3 to 25, and the sample size calculated for the SRs/MAs ranged from 244 to 2058. Six SRs/MAs focused on patients diag-nosed with stable AP (SAP),[12,13,22,24,28,29] one study focused on patients with unstable AP (UAP),[20] one study included patients with coronary heart disease,[21] and the remaining eight did not identify the subtype of AP. Interventions in the experimental group were acupuncture, acupuncture plus medications, or acupuncture plus Chinese medicine, while medications, sham acupuncture, or Chinese medicine were used in the control group. In terms of the assessment of methodological quality, eleven SRs/MAs used the Cochrane criteria,[10–12,19,21–24,27–29] three used Jadad,[9,20,25] and the rest were unclear.[13,26] The conclusions from the 16 included studies differed: 14 MAs supported a positive treatment effect for acupuncture used as adjunctive therapy in patients with angina, one MA showed very low evidence to support the use of acupunc-ture for improving angina symptoms and ECG of angina patients.[11]

3.3. Results of the methodological quality

In the AMSTAR-2 assessment, seven domains can critically af-fect the validity of a review and its conclusions. The review that has more than one critical flaw would be judged as critically

low.[15] All the included SRs/MAs had more than one critical item, which were unmet, and were thus classified as critically low qual-ity (Table 1). The methodological limitations derived from three critical domains: item 2 (only two SRs/MAs registered the proto-col), item 4 (only seven SRs/MAs reviewed the reference list from the studies found), and item 7 (none of the SRs/MAs provided a list of excluded studies and justified the exclusions). Other details are showed in Supplement Table. 3.

3.4. Results of ROBIS evaluation

In the first phase, the relevance of the research topic was as-sessed and all the SRs/MAs were rated as having a low risk of bias. Table 1 presented the summary of ROBIS assessment. The sec-ond phase involves the assessment of the four domains to identify the concerns with the review process. Domain 1 intended to as-sess study eligibility criteria and five SRs/MAs were rated at a high risk of bias.[10,11,25–27] Domain 2 aimed to estimate the identifica-tion and selection studies, and nine SRs/MAs were rated at a high risk of bias.[10,20,22–28] Domain 3 proposed to evaluate the data col-lection and study appraisal, and seven SRs/MAs were at a high risk of bias.[10,11,19,20,22,25,26] Domain 4 assessed the synthesis and find-ings, and 13 SRs were rated at a high risk of bias. Phase 3 reviewed the overall risk of bias in the SRs/MAs, and only three SRs/MAs

were rated at a low risk of bias.[9,12,29] More details are presented in Supplementary Tables 4–5.

3.5. Results of the reporting quality

The overview of the PRISMA for the acupuncture (PRISMA-A) checklist is presented in Supplement Table 6. No study reported all the items of the PRISMA-A. The items of title, abstract, and introduction were all well reported. In the section of the methods, only two study[12,29] reported the protocol and registration; 13 out of 16 SRs/MAs described the types of acupuncture (81.25%). The topic of search strategy (37.5%), risk of bias across the studies (43.75%), and additional analyses (50%) were inadequately reported. In the section of the results, no research stated details of the "de-qi," and additional analyses were reported in only 50%; One study[27] did not report the limitations, and half of the studies (50%) reported funding-related information. In general, the topic of protocol registration, search strategy, and additional analysis were inadequately reported.

3.6. Evidence quality of the included SRs/MAs

Fifty-seven outcomes extracted from the included SRs/MAs were evaluated by the GRADE system. According to the GRADE assessment, the quality of evidence ranged from very low to moderate. Specifically, no high-quality evidence was found, and only seven outcomes showed moderate-quality evidence (Table 2). The risk of bias, inconsistency, and imprecision were the main reasons for downgrading. Randomization, allocation concealment, and blinding are extremely important in the assessments of the risk of bias. However, many primary RCTs included in the SRs/MAs did not report allocation concealment, blinding, or selective reporting. Heterogeneity within studies downgraded the inconsistency. Imprecision was downgraded owing to the wide confidence intervals or small number of participants (< 400). The details of GRADE assessment are provided in Supplementary Table 7.

3.7. Efficacy evaluation

Efficacy of acupuncture for SAP
The outcomes extracted from the included SRs/MAs are presented in Table 2. Six SRs/MAs reported the effectiveness of acupuncture for SAP.[12,13,22,24,28,29] Two studies revealed a significantly greater increase in the improvement of the symptom of angina and ECG recovery in the group of acupuncture plus medication or Chinese medicine than in the control group (only medication or Chinese medicine).[12,13] Three SRs/MAs reported that for the effective rate, the combined treatment (acupuncture plus medication or Chinese medicine) was superior to the medication or Chinese medicine only.[12,13,22] Four SRs/MAs found significant reduction of the frequency of the angina attack and the pain intensity in the group of acupuncture plus medication than in the medication group.[12,24,28,29] For nitroglycerin use, two reviews[13,28] revealed a significant decrease in the acupuncture combined group compared with the control group. However, the other study showed that acupuncture combined with medications showed no significant difference in nitroglycerin use compared with medications alone.[12] One review[12] showed that electro-acupuncture was superior to sham acupuncture in decreasing the frequency of angina attack [MD = −4.47, 95% CI (−6.69, −2.27), $p < 0.01$] and 6-MWT [MD = 17.50, 95% CI (17.10, 17.90), $p < 0.01$].

Efficacy of acupuncture for UAP
Two SRs/MAs reported the effectiveness of acupuncture for UAP.[11,20] The ECG recovery was reported in the two SRs/MAs, and the results showed that acupuncture plus medication or Chinese medicine were superior to medication or Chinese medicine alone.

One review[20] found significant reduction of time for the Myocardial ischemia recorded by Holter in the acupuncture plus medication group compared to the medication group [MD = −13.13, 95% CI (−15.35, 10.90), $p < 0.01$].

Efficacy of acupuncture for AP
In this overview, eight out of fourteen SRs/MAs did not report the subtype of AP clearly.[9,10,19,21,23,25–27] We also conducted GRADE evaluation on the outcomes of these eight studies (Table 2). Only one review[10] compared the effects of acupuncture plus medication with medication alone on the incidence of myocardial infarction, and the results showed that combined treatment had a greater effect than medication alone [OR = 0.18, 95% CI (0.04, 0.84), $p = 0.03$]. Compared to medication, acupuncture was more effective in improving the angina symptoms [OR = 3.59, 95% CI (1.76, 7.92), $p = 0.04$] and ECG recovery [OR = 3.07, 95% CI (1.54,6.10), $p = 0.001$]. The ECG recovery was reported in six SRs/MAs,[10,11,19,21,23,27] and the results showed that combined treatment was superior to medication or Chinese medicine alone. For the angina symptom, four studies revealed a significant increase in the group combining acupuncture with other interventions compared with the control group (that intervention only).[10,21,23,27] Three SRs/MAs[19,25,26] found significant increase in the effective rate in the combined intervention group than in the control group; however, the other one study showed no significant difference between these two groups.[21]

3.8. Safety of acupuncture for angina pectoris

Ten of the 16 SRs mentioned the adverse events of acupuncture for treating angina pectoris.[10–13,19,21,23,26,28,29] Seven SRs reported no adverse effects associated with acupuncture therapy.[10,11,13,19,21,28,29] Two SRs found no significant difference in adverse events between the acupuncture and control groups.[12,23] One SR concluded that acupuncture involved fewer adverse events in the treatment of angina.[26] Therefore, acupuncture may be a safe therapy for angina pectoris.

4. Discussion

4.1. Summary of the main findings

In the evaluation of AMSTAR-2, only one MA[12] were rated to have low quality, and the remain included SRs/MAs were rated to have critically low quality. The methodological limitations derived from the failure to provide detailed search strategies, a list of excluded studies with justification of the exclusions, as well as registration of the protocol. For the reporting quality, no study reported all the items of the PRISMA-A. Inadequate reporting topics focused on protocol registration, search strategy, and additional analysis. The ROBIS tool rated 13 out of 16 SRs/MAs to have a high risk of bias, which would result in a consequent increase in the risk of bias and in a consequent decrease in the transparency of the SRs/MAs. Limitations in the methods used by the reviewers to identify the studies, select the studies, and synthesize increased the risk of bias and affected the rigor of the SRs. For GRADE assessment, no high-quality evidence was found. The risk of bias, inconsistency, and imprecision were the main downgrading factors in the included studies. Unexplained heterogeneity resulted in inconsistencies, and small sample sizes or large confidence intervals resulted in imprecisions.

Based on the results, no definite conclusion can be drawn on whether it is recommended to use acupuncture as a complementary alternative therapy for AP. However, it is confirmed that the methodology of the SR/MAs included in this study has significant deficiencies. The poor quality of evidence from the SR/MAs may be

Table 2
Evidence quality of included studies

Patients	Outcomes	Interventions vs comparisons	Author (year)	Relative effect (95% CI)	P-value	Quality
AP	Incidence of myocardial infarction	MA + M vs M	Chen (2012)	OR 0.18 (0.04, 0.84)	0.03	L
	Angina symptom relief	MA + M vs M	Chen (2012)	OR 4.23 (2.73, 6.56)	<0.01	L
		MA vs M	Chen (2012)	OR 3.59 (1.76, 7.92)	0.04	VL
		A + M/CM vs M/CM	Wang (2012)	OR 5.68 (2.59, 12.43)	<0.01	VL
		EA + M/CM vs M/CM	Shao (2016)	OR 1.18 (1.08, 1.29)	0.002	L
		A + M/CM vs M/CM	Bu (2018)	OR 3.61 (2.42, 5.37)	<0.01	Mo
	ECG recovery	MA + M vs M	Chen (2012)	OR 2.61 (1.83, 3.73)	<0.01	Mo
		MA vs M	Chen (2012)	OR 3.07 (1.54, 6.10)	0.001	VL
		A + M/CM vs M/CM	Wang (2012)	OR 2.65 (1.59, 4.41)	0.0002	VL
		A + M/CM vs M/CM	Yu (2015)	RR 0.48 (0.36, 0.63)	<0.01	L
		A + M/CM vs M/CM	Zhang (2015)	RR 1.28 (1.17, 1.39)	<0.01	L
		EA + M/CM vs M/CM	Shao (2016)	OR 1.99 (1.29, 3.07)	0.002	L
		A + M/CM vs M/CM	Bu (2018)	OR 3.02 (1.99, 4.59)	<0.01	L
	Ineffectiveness of angina relief	MA + M/CM vs M/CM	Yu (2015)	RR 0.33 (0.21, 0.51)	<0.01	L
	Nitroglycerin use	A + CM vs CM	Yu (2015)	MD -0.41 (-0.69, -0.14)	0.0003	L
	Reduce nitroglycerin use	EA + M/CM vs M/CM	Shao (2016)	OR 3,40 (1.56, 7.41)	0.002	VL
	Effect rate	A + CM vs CM	Li (2015)	OR 0.12 (0.04, 0.35)	<0.01	VL
		A + M/CM vs M/CM	Zhang (2015)	RR 1.25 (1.17, 1.33)	<0.01	Mo
		EA + M/CM vs M/CM	Shao (2016)	OR 1.27 (0.64, 2.52)	0.49	L
		A + M/CM vs M/CM	Sun (2019)	OR 3.76 (2.44, 5.80)	<0.01	L
	Myocardial ischemia time of Holter	A + M/CM vs M/CM	Zhang (2015)	WMD -16.94 (-37.54, 3.66)	0.11	VL
		A + M/CM vs M/CM	Bu (2018)	MD -16.93 (-34.46, 0.60)	0.06	L
	6-MWT	A + M/CM vs M/CM	Bu (2018)	MD 31.63 (29.18, 34.08)	<0.01	VL
	Angina attack frequency	A + M/CM vs M/CM	Bu (2018)	MD -5.37 (-5.53, -5.21)	<0.01	L
	Angina pain intensity	A + M/CM vs M/CM	Bu (2018)	MD -0.47 (-0.52, -0.43)	<0.01	L
	Markedly effective rate	A + M/CM vs M/CM	Huang (2019)	OR 2.10 (1.62, 2.72)	<0.01	Mo
	Moderately effective rate	A + M/CM vs M/CM	Huang (2019)	OR 0.98 (0.80, 1.21)	0.876	Mo
SAP	Angina symptom relief	A + M/CM vs M/CM	Zhang (2015)	OR 2.89 (1.87, 4.47)	<0.01	L
		A + M/CM vs M/CM	Yang (2019)	RR 1.25 (1.11, 1.39)	0.01	L
	ECG recovery	A + M/CM vs M/CM	Zhang (2015)	OR 1.81 (1.23, 2.71)	0.03	L
		A + M/CM vs M/CM	Yang (2019)	RR 1.25 (1.13, 1.37)	<0.01	L
	Effect rate	MA + M/CM vs M/CM	Zhang (2015)	OR 2.13 (0.90, 5.07)	0.09	VL
		MA + M vs M	Zhou (2018)	OR 6.01 (1.94, 18.66)	0.002	VL
		A + M/CM vs M/CM	Yang (2019)	RR 1.25 (1.14, 1.37)	<0.01	VL
	Nitroglycerin use	A + CM vs CM	Zhang (2015)	MD -0.44 (-0.64, -0.24)	<0.01	L
		EA + M vs M	Yang (2019)	MD -3.21 (-7.00, -0.59)	0.1	VL
		A vs SA	Yang (2019)	MD -2.92 (-10.45, -4.62)	0.45	VL
		A vs WT	Song (2021)	MD -1.56 (-2.56, -0.32)	0.002	L
	Angina attack frequency	EA + M vs M	Yang (2019)	MD -5.30 (-6.37, -4.22)	<0.01	L
		A vs SA	Yang (2019)	MD -4.47 (-6.69, -2.27)	<0.01	VL
		MA + M vs M	Ma (2020)	MD -4.93 (-5.08, -4.77)	<0.01	Mo
		A vs SA	Tu (2021)	MD -4.00 (-5.06, -2.94)	<0.01	L
		A vs SC	Tu (2021)	MD -5.10 (-5.25, -4.94)	<0.01	L
		A vs WT	Song (2021)	MD -5.38 (-5.54, -5.22)	<0.01	L
	Angina pain intensity	EA + M vs M	Yang (2019)	MD -0.90 (-1.34, -0.47)	<0.01	L
		EA vs SA	Yang (2019)	MD -0.94 (-2.20, 0.32)	0.14	L
		MA + M vs M	Ma (2020)	MD -0.48 (-0.53, -0.44)	<0.01	Mo
		A vs SA	Tu (2021)	MD -0.46 (-0.81, -0.11)	0.01	L
		A vs SC	Tu (2021)	MD -0.72 (-0.96, -0.48)	<0.01	L
		A vs WT	Song (2021)	MD -0.47 (-0.52, -0.43)	<0.01	L
	6-MWT	A + M vs M	Yang (2019)	MD 36.98 (-18.56, 92.52)	<0.19	VL
		EA vs SA	Yang (2019)	MD 17.50 (17.10, 17.90)	<0.01	L
		A vs WT	Song (2021)	MD 30.65 (28.18, 33.12)	<0.01	L
UAP	Effective rate	MA + M vs M	Li (2017)	OR 6.31 (0.91,10.87)	<0.01	VL
	ECG recovery	MA + M vs M	Li (2017)	OR 1.98 (1.18, 3.33)	0.01	L
		A + M/CM vs M/CM	Yu (2015)	RR 0.62 (0.42, 0.90)	0.01	L
	Myocardial ischemia time of Holter	MA + M vs M	Li (2017)	MD -13.13 (-15.35, 10.90)	<0.01	VL

A: acupuncture; AP: angina pectoris; CHD: coronary heart disease; CI, confidence interval; CM: Chinese medicines; EA: electroacupuncture; ECG: electrocardiogram; L, low; M: Medications; MA: manual acupuncture; MD, mean difference; Mo, moderate; OR, odds ratio; RR, relative risk; SA: Sham acupuncture; SAP: stable angina pectoris; SC: Standard care; SMD, standardized mean difference; UAP: unstable angina pectoris; VL, very low; WT: Waiting treatment; 6-MWT: six-minutes walking test;
Values of the included SR were expressed with the second decimal places in P values, although some values have more than 2 decimal places, such as p<0.00001;
①Included RCTs did not report randomization, allocation concealment, blinding, loss of drop-out or selective report; ②Small sample size or large confidence interval; ③Unexplained heterogeneity; ④Suspicion of publishing bias.

due to irregularities in the practices of reviewers or methodological limitations of the original RCTS included.

4.2. Overall completeness and applicability of the evidence

This overview systematically evaluated the methodological quality and reporting quality of SR/MAs in acupuncture for angina.

This study included all published SR/MAs of acupuncture for angina pectoris (SAP and UAP) and used the most comprehensive assessment tools to provide more convinced evidence for clinical work. The findings from this overview represent the most comprehensive currently available evidence base to guide the choice about acupuncture for AP. Thus, the completeness of the evidence in this overview is high. However, all the SRs/MAs included in

this overview were conducted in the mainland China, and included original RCTs performed in only two countries (China and Denmark). In addition, the evidence quality of acupuncture for AP ranged from very low to moderate. The findings showed that rigorously designed SR/MAs are needed to confirm the potential benefit of acupuncture in the treatment of AP.

4.3. Certainty of evidence

In this overview, half of SRs/MAs did not report the subtype of AP clearly, which will affect the interpretation of the results. The results of five SR/MAs [12,13,24,28,29] suggested that acupuncture is effectively improve angina symptom, ECG, attack frequency and pain intensity in patients with stable angina pectoris. Two SR/MAs indicated that acupuncture is effectively improve ECG in patients with unstable angina pectoris.[11,20] However, the methodology quality of the included SRs/MAs were poor, which would increase the risk of bias and reduce the credibility of the evidence. Furthermore, the original RCTs with small sample size included in the SRs/MAs were of high risk of bias and judged as poor quality. The above reasons lead to the poor credibility of research evidence in acupuncture for AP.

4.4. Potential bias in the review process

The review methods were established prior to conduct of the review, and we also pre-registered the study protocol on PROSPERO. Throughout the evaluation process, we performed study selection and data extraction in duplicate to avoid the risk of bias. In this overview, we retrieved only Chinese and English databases, which may give rise to bias.

4.5. Implication for clinical practice

For clinicians, this overview showed very low evidence to support the use of acupuncture for improving angina symptoms and ECG of angina patients. In this overview, it is worth noting that there are no objective criteria for evaluating the efficacy of acupuncture in treating angina. The following outcomes were used to assess the efficacy of acupuncture: effective rate, angina symptom relief, angina attack frequency, angina pain intensity, 6-MWT, ECG recovery, myocardial ischemia time of Holter, and nitroglycerin use. The criteria for effectiveness were inconsistent among the included studies. Some studies used effective rate (calculated based on the frequency and duration of angina attacks), while others used angina attack frequency or intensity as indicators of treatment effect. Moreover, the scales used to assess angina symptoms were inconsistent. Therefore, we recommend that researchers in the original RCTs use pain, angina attack frequency, duration, and intensity as outcomes, rather than calculated effective rate. Furthermore, the myocardial infarction size, the level of ST segment elevation, myocardial enzymes, and cardiac troponin are also recommended.

4.6. Implication for research

This overview identified several challenges. Only two SRs was registered under PROSPERO with a published protocol.[12,29] Researchers are now being encouraged to pre-register their protocols for improving the quality of secondary research. Only four studies developed a comprehensive search protocol. Incomplete searches can lead to bias, and the different article pools on the same topic are more likely to draw inconsistent conclusions. A SR[28] published in 2021 did not include a multicenter high-quality RCT of acupuncture for stable angina pectoris (published in 2019), which would have had a large impact. Most SRs/MAs did not report the detailed

characteristics of the original RCTs, which limited the ability to extrapolate the results. Six SRs did not identify all the important potential sources of bias in the included studies with an appropriate assessment tool.[9,13,19,20,25,26] There were errors in the description of the effect indicators (the method described in the paper did not match the forest plots display).[23,24] The PRISMA-A tool has been developed for acupuncture SRs and MAs based on the PRISMA statement. However, most included studies did not report on these areas in detail. Half of SRs/MAs included different types of patients with angina, and when the reviewers did not conduct subgroup analyses, it would be difficult to draw credible conclusions. Furthermore, most of the included original RCTs do not provide a random sequence generation method and state whether the allocation is concealed; only a few trials referred to blinding, and most of the participant and doctors were not blinded. All the above reasons may cause the quality of evidence to be downgraded. In order to facilitate more convincing evidence-based medical research, we encourage future systematic reviewers to strictly implement and report SRs/MAs in accordance with the relevant standards.

4.7. Limitations

Several limitations should be noted. First, most of the SRs/MAs were conducted with low quality and high risk of bias in methodology. Thus, the results should be interpreted with caution. Second, owing to the complexity of acupuncture therapy and limitations of synthesis methods, definitive conclusions could not be drawn. Third, more important key outcomes, such as cardiac enzymes, need to be included for assessing the clinical effectiveness of acupuncture for angina. Fourth, AMSTAR-2 is a tool published in 2017, and it may be impractical to use it to strictly evaluate SRs/MAs published before 2017. However, we believe that this tool will promote reviewers to report their research to the highest possible standard. Finally, all the SRs/MAs included in this overview were conducted in the mainland China, and included original RCTs performed in only two countries (China and Denmark), which may lead to a risk of publication bias.

4.8. Conclusions

Owing to the lack of high-quality evidence provided by the current SRs/MAs, the effectiveness and safety of acupuncture for AP still warrants further proof. Further randomized controlled trials with more critical design and methodology are still needed for providing more convincing evidence.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Ethical statement

Since no private patient data was contained in the reporting, there are no ethical considerations associated with this review.

Data availability

All data from this study are included in this article. No additional data are available.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imr.2022.100864.

CRediT authorship contribution statement

Wen-Chuan Qi: Conceptualization, Formal analysis, Writing – original draft. **Hong-Juan Fu:** Conceptualization, Writing – original draft, Formal analysis. **Rui-Rui Sun:** Formal analysis, Writing – review & editing. **Xiang Li:** Formal analysis, Writing – review & editing. **Ding-Jun Cai:** Methodology, Data curation, Writing – review & editing. **Chao Wang:** Methodology, Data curation, Writing – review & editing. **Fan-Rong Liang:** Conceptualization, Formal analysis, Data curation, Writing – review & editing.

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