

Analgesic effect of acupuncture in patients with stable angina: integrative review

Efeito analgésico da acupuntura em pacientes com angina estável: revisão integrativa

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ABSTRACT

BACKGROUND AND OBJECTIVES: Angina is a clinical syndrome characterized by pain or discomfort, considered stable when it occurs for several weeks without progressing to an acute coronary event. Anginal pain management can be performed with pharmacological and non-pharmacological treatments, among which acupuncture is a non-pharmacological option. The aim of this study was to carry out an integrative review of the analgesic effect of acupuncture in patients with stable angina. **CONTENTS:** An integrative review was carried out in April 2021 in databases: Pubmed, Scopus, Cinahl and Bireme. Controlled descriptors “angina pectoris”, “angina stable”, “acupuncture”, “acupuncture therapy”, “acupuncture analgesia” were used. After screening and analyzing the manuscripts, seven experimental studies of the randomized controlled trial type were selected. The results suggest that acupuncture in patients with stable angina can promote an analgesic effect with clinical improvement of symptoms.

CONCLUSION: Acupuncture can be an adjuvant therapeutic alternative for the treatment of patients with stable angina, since it can promote an analgesic effect with clinical improvement of symptoms.

Keywords: Acupuncture analgesia, Acupuncture therapy, Angina pectoris, Angina stable, Pain management.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A angina é uma síndrome clínica caracterizada por dor ou desconforto, considerada estável quando ocorre por várias semanas sem evoluir para um evento coronariano agudo. O manejo da dor anginosa pode ser realizado por meio de tratamentos farmacológicos e não farmacológicos, incluindo a acupuntura como uma opção não farmacológica complementar. O objetivo deste estudo foi realizar uma revisão integrativa sobre o efeito analgésico da acupuntura em pacientes com angina estável.

CONTEÚDO: Foi realizada uma revisão integrativa no mês de abril de 2021 nas bases de dados: Pubmed, Scopus, Cinahl e Bireme. Foram utilizados os descritores controlados “angina pectoris”, “angina stable”, “acupuncture”, “acupuncture therapy”, “acupuncture analgesia”. Após triagem e análise dos manuscritos, foram selecionados sete estudos experimentais do tipo ensaio controlado randomizado. Os resultados sugerem que a acupuntura pode promover efeito analgésico com melhora clínica dos sintomas em pacientes com angina estável.

CONCLUSÃO: A acupuntura pode ser uma alternativa terapêutica complementar para tratamento de pacientes com angina estável, uma vez que pode promover efeito analgésico com melhora clínica dos sintomas.

Descritores: Analgesia por acupuntura, Angina estável, Angina pectoris, Manejo da dor, Terapia por acupuntura

INTRODUCTION

Angina is a clinical syndrome that features pain or discomfort in any of the following areas: chest, epigastrium, jaw, shoulder, back, or upper limbs. It is typically triggered or aggravated by physical activity or emotional stress and mitigated using nitroglycerin and its derivatives. Angina usually affects people with coronary artery disease (CAD), but it can also occur in cases of valvular heart disease, hypertrophic cardiomyopathy, uncontrolled hypertension, and in patients with spasm and coronary endothelial dysfunction¹.

An anginal condition is considered stable if it occurs for several weeks and doesn't develop into an acute coronary event. Seizures typically appear in conditions in which there is increased myocardial oxygen demand in a patient with more than 70% light obstruction of one or more coronary arteries. Additionally, the extension, quantity, location and morphology of the stenoses, the presence of collateral circulation and the vasomotor reactivity of the coronary bed are related to the resulting degree of ischemia².

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Pharmacological and non-pharmacological treatments are used for relief of anginal pain. Pharmacological treatments include nitrates, calcium channel antagonists, and trimetazidine, which reduce symptoms and episodes of myocardial ischemia¹. Acupuncture is a complementary non-pharmacological therapy option for patients with stable angina³. In China, complementary therapies of Traditional Chinese Medicine (TCM), such as acupuncture, have been used to treat the symptoms of CAD⁴. The mechanisms of pain reduction and cardiovascular dysfunction by acupuncture may be related to the release in the central nervous system of excitatory and inhibitory neurotransmitters that alter the processing of sensory information and, ultimately, the autonomic flow and, therefore, cardiovascular function⁵. There is a gap in the literature regarding the use of non-pharmacological therapies, especially acupuncture, as adjuvant methods for the relief of pain related to stable angina. This study's objective was to perform an integrative review on the analgesic effect of acupuncture in patients with stable angina.

CONTENTS

Integrative review including experimental studies for a better understanding of the subject⁶, carried out with the following steps: formulation of the problem, data collection, data assessment, analysis and interpretation and presentation of results⁷.

The study was guided by the following question: is acupuncture an effective complementary non-pharmacological method for the relief of pain related to stable angina?

Searches were performed in the following databases: Pubmed, Scopus, Cinahl, and Bireme, using the controlled descriptors "angina pectoris", "angina stable", "acupuncture", "acupuncture therapy", "acupuncture analgesia", with the addition of the Boolean operators AND and OR, during the month of April 2021. Original primary studies, with no restrictions for language and publication year, that investigated the analgesic effect of acupuncture in patients with stable angina were included. The following were excluded: studies that used animal models, systematic

reviews, integrative, narrative, and scoping reviews, editorials, letters to the editor, commentaries, experience reports, research involving pediatric population or with other types of unstable, refractory and variant, or Prinzmetal angina, and those which did not have the full text available.

The studies found were screened by reading the titles and abstracts. Then, they were read in their entirety so that the eligibility criteria could be analyzed (Figure 1). The data from the included studies were compiled in an electronic spreadsheet prepared by the authors. The main characteristics of the studies were summarized in a table: authors, study design, level of evidence, sample size, and objectives (Table 1). The articles were classified according to the

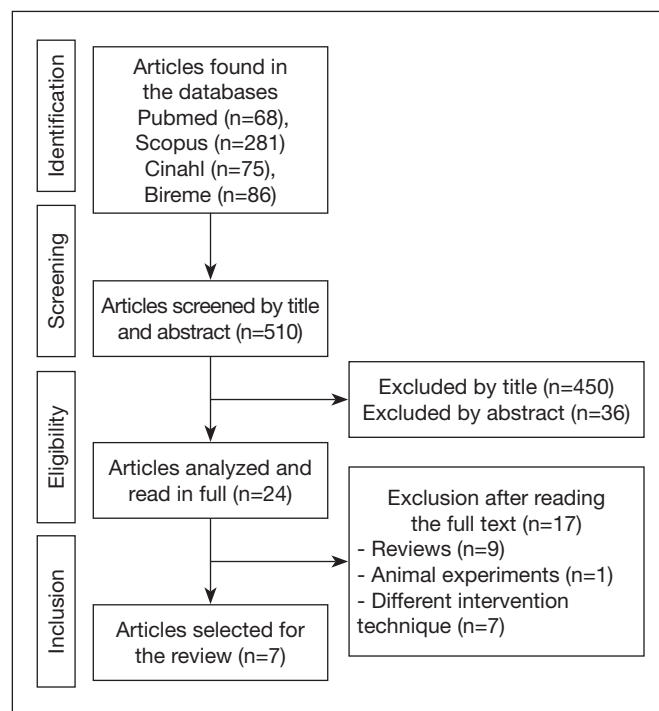


Figure 1. Flowchart of articles identification and selection

Table 1. Description of articles included in the study

Authors	Design	LE	Sample size	Objectives
Zhao et al. ⁹	RCT	2	398 patients (AAMG: 99, AUMG: 99, SAG: 101, NAG: 99)	Investigate the efficacy and safety of acupuncture as an adjunct therapy to antianginal treatments in reducing the frequency of angina attacks in patients with chronic stable angina.
Wang et al. ¹⁰	RCT	2	45 patients (IG: 15; ACG: 15; e HPG: 15)	Observe the clinical effect of acupuncture at the <i>Neiguan</i> point in patients with stable angina and to evaluate the proportion of neutrophils and lymphocytes in peripheral blood.
Ballegaard et al. ¹¹	RCT	3	49 patients received acupuncture	Elucidate the effect of acupuncture in patients with stable angina, discuss the methodological problems of the studies, research the relationships of the psychosocial factors, changes in skin temperature and pain thresholds.
Richter, Herlitz and Hjalmarsen ¹²	RCT	2	21 patients received acupuncture	Evaluate the effect of acupuncture in patients with stable angina.
Ballegaard, Meyer and Trojaborg ¹³	RCT	2	33 patients (IG=17; CG=16)	Evaluate the effect of acupuncture in patients with stable angina and methodological problems of the studies.
Ballegaard et al. ¹⁴	RCT	2	49 patients (IG: 24; CG: 25)	Evaluate the effect of acupuncture in patients with mild stable angina.
Ballegaard et al. ¹⁵	RCT	2	26 patients (IG:13; CG: 13)	Evaluate the effect of acupuncture in patients with severe stable angina.

LE = level of evidence; RCT = randomized controlled trial; AAMG = acupuncture on the affected meridian group; AUMG = acupuncture in the unaffected meridian group; SAG = sham acupuncture group; NAG = no acupuncture group; IG = intervention group; CG = control group; ACG = active control group; HPG = healthy patient group.

level of evidence proposed in the Oxford Center for Evidence-Based Medicine (OCEBM) tool, which classifies evidence from level one to five, the first level being the most relevant⁸.

A scarcity of studies on the subject was evidenced, a wide variation in the publication period (1986 to 2019), and a large temporal gap for the development of new research. The studies included in the final analysis had experimental design, but most (6; 85.7%) had a small sample size, which increases the probability of random errors and decreases the statistical power of their inferences. The main results of the articles are described in table 2.

Although few studies on the use of acupuncture in patients with stable angina were found, literature shows that the application of acupuncture has shown therapeutic effects in other diseases, such as fibromyalgia, providing pain relief and improved quality of life¹⁷, as well as in patients with temporomandibular dysfunction for the control of facial pain¹⁸.

Acupuncture provided an analgesic effect, with a decrease in the frequency of angina episodes and reduction of nitroglycerin consumption, evidenced in six of the seven articles included in the study⁹⁻¹⁴. The decrease in anginal episodes was strongly evi-

Table 2. Results of articles included in the study.

Authors	Protocol	Results
Zhao et al. ⁹	The acupuncture treatment consisted of 12 sessions, during four weeks, three times a week. The points used in the group that received acupuncture on the affected meridians were PC6 and HT5 bilaterally. In the group that received acupuncture on the unaffected meridians, the points applied were LU6 and LU9.	Acupuncture on the disease-affected meridian points significantly reduced the frequency of angina attacks compared with acupuncture on the unaffected meridian points, in the sham acupuncture group and in the group of patients who didn't receive acupuncture. Adjunct therapy with acupuncture had a significant effect on angina relief within 16 weeks compared to pharmacological therapy alone. In addition, it resulted in better regulation of anxiety and depression at 12 weeks after acupuncture treatment.
Wang et al. ¹⁰	Treatment with acupuncture was performed at the <i>Neiguan</i> point (Pericardium 6) every two days for four weeks. The group that received only antianginal drugs did not receive acupuncture and there was no intervention in the healthy group.	Acupuncture may improve the stability of chronic effects in patients with angina, possibly reducing the number of anginal episodes, nitroglycerin dosage, and the degree of angina in these patients.
Ballegaard et al. ¹¹	Acupuncture treatment was performed according to TCM, and each patient went through ten sessions in the supine position for three weeks. Diaries were filled out for evaluation of well-being and a global assessment was performed after the treatment. Exercise tests were performed on an exercise bike.	Acupuncture promoted greater exercise tolerance and cardiac work capacity. Improved daily well-being, reduced anginal attack rates, and reduced nitroglycerin consumption were observed.
Richter, Herlitz and Hjalmarson ¹²	The treatment was performed three times a week, for four weeks. The following main points were used: <i>Neiguan</i> (Pericardium 6), <i>Tongli</i> (Heart 5), <i>Xinshu</i> (Urinary bladder 15), <i>Pishu</i> (Urinary bladder 20), and <i>Zusanli</i> (Stomach 36). The additional points were <i>Shenmen</i> (Heart 7), <i>Hegu</i> (Large intestine 4), <i>Quchi</i> (Large intestine 11), and <i>Taichong</i> (Liver 3). Patients were given questionnaires for self-assessment of pain and angina attacks. Exercise tests were performed on an exercise bike.	Patients who received acupuncture had fewer angina attacks per week (mean reduction of 4.5 attacks) and chest pain during exercise appeared at higher workloads (an increase of 10 W), pain intensity was decreased (1.4 to 0.8), and ST-segment depression was reduced (average of 0.32 mm).
Ballegaard, Meyer e Trojaborg ¹³	Acupuncture tests were performed in the supine position, and were applied to the left hallux and index finger. There was a rest period of 30 minutes before insertion at point <i>Hegu</i> 4 (large intestine) bilaterally, located between the first and second metacarpal. Exercise tests were performed on an exercise bike.	A minimal antianginal benefit was observed, defined as a 15% increase in tolerance to exercise and/or dPRP, with a 30% reduction in angina attack rate and nitroglycerin consumption. The 19 patients who had angina pectoris <4 years exhibited a significant increase in exercise tolerance, compared to 14 patients with a longer duration of disease. The effect of acupuncture was shown to be more pronounced in patients with fewer years of angina diagnosis.
Ballegaard et al. ¹⁴	Acupuncture was administered in ten treatments in the supine position for three weeks. Exercise tests were performed on an exercise bike. Journals were filled out every day and a subjective global assessment was done at the end of the trial.	The study shows that there is no difference in the effect of genuine and sham acupuncture in patients with mild angina. In both groups, a significant beneficial effect was observed on nitroglycerin consumption, angina attack rate, and overall well-being. Exercise tolerance and time of pain onset were slightly improved by genuine acupuncture, but again with no significant difference between the groups.
Ballegaard et al. ¹⁵	The active treatment used acupuncture at points Pericardium 6 (<i>Neiguan</i>), Stomach 36 (<i>Zusanli</i>) and Urinary Bladder 14 (<i>Jueyinshu</i>) bilaterally. In the sham treatment, the needles were inserted in the same segments as in the active treatment, but outside the Chinese meridian system and were not trigger points. Exercise tests were performed on an exercise bike.	Patients who received the active acupuncture treatment had a significant improvement in exercise test variables regarding the dPRP and maximal PRP, which can be interpreted as an increase in cardiac work capacity. No significant difference was detected regarding the other exercise test variables, anginal attack rate, or nitroglycerin consumption.

TCM = Traditional Chinese Medicine; PRP = maximal pressure rate; dPRP = difference of pressure rate between rest and maximal exercise.

denced in the largest multicenter clinical trial investigating the adjuvant effects of acupuncture in patients with stable angina⁹. Furthermore, other effects of acupuncture corroborate the clinical improvement of symptoms, evidenced by improved exercise tolerance, which is expressed by the difference in pressure rate between rest and maximal exercise (dPRP) and increased cardiac work capacity¹¹⁻¹⁵. This increase in exercise endurance consequently delays the onset of anginal pain¹².

Additionally, in one study, electrocardiographic analysis revealed decreased ST-segment depression, which is usually increased in angina attacks¹². The belief is that the vasodilation resulting from sympathetic inhibition promoted by acupuncture is responsible for the clinical improvement in patients with stable angina¹³.

The time and severity of the disease seem to modify the effect of acupuncture in patients with stable angina, since the benefit was greater in mild cases and those with less time of disease¹³. Improvements in well-being, anxiety and depression were other secondary outcomes reported^{9,14}.

As for the studies' methodology, there was homogeneity among some of the inclusion and exclusion criteria of the studied populations. The diagnosis of stable angina and anginal manifestation in the last six months were pre-requisites for eligibility in the studies. Among the exclusion criteria, previous cardiac surgery, previous acute myocardial infarction (AMI), valvular heart disease, severe heart failure, severe arrhythmias, hypertension, previous treatment with acupuncture, and chest pain of non-cardiac origin were some of the criteria established so that there would be no influence or compromise of the results. Only one of the studies did not consider as an exclusion factor the history of AMI and previous coronary artery bypass graft surgery¹².

On the other hand, there was heterogeneity among the acupuncture techniques employed in the studies, with the following points and meridians used: pericardium 6 (*Neiguan*), heart 5 (*Tongli*), heart 7 (*Shenmen*), urinary bladder 14 (*Jueyinshu*), urinary bladder 15 (*Xinshu*), urinary bladder 20 (*Pishu*), stomach 36 (*Zusanli*), large intestine 4 (*Hegu*), large intestine 11 (*Quchi*), and liver 3 (*Taichong*).

A meta-analysis investigating acupuncture prescription for treatment of chronic stable angina through association rule mining, network analysis, and underlying mechanisms revealed that PC6, LU9, and ST36 were the top three acupuncture points used for treatment, and the top three meridians reported were the pericardium meridian, lung meridian, and heart meridian¹⁸. The present review has the limitation of not including searches on eastern databases and the gray literature. However, the main international databases were included without language and time restrictions. Therefore, taking into account the present findings, it is suggested that acupuncture may be a complementary therapeutic alternative for pain management of patients with stable angina. Nonetheless, additional clinical trials with greater methodological rigor are needed to provide more solid evidence for its implementation in clinical practice, since there is significant heterogeneity between the intervention protocols of the published studies.

CONCLUSION

Acupuncture can promote analgesic effects with clinical improvement of symptoms in patients with stable angina, resulting in the main outcomes: reduced anginal attack rate, decreased nitroglycerin consumption, improved tolerance to exercise, increased cardiac work capacity, decreased ST-segment depression, and improvements in general well-being.

AUTHORS' CONTRIBUTIONS

João Paulo Aragão Silva

Data Collection, Research, Writing - Preparation of the original

Caique Jordan Nunes Ribeiro

Writing - Review and Editing

Mariangela da Silva Nunes

Writing - Review and Editing

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