



Review Article

Acupuncture for the Treatment of Cardiovascular Diseases: A Systematic Review

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Abstract

Acupuncture, for the western countries, is an innovative and low-cost therapy for treatment and prevention of cardiovascular diseases (CVDs). However, most of its effects and mechanisms are poorly understood. Thus, the objective of this work was to systematically review the literature regarding the clinical effects of acupuncture for the treatment and prevention of CVDs. A search for papers published in English or Portuguese in the past 20 years was conducted at PubMed, SciELO, and PEDro databases. Clinical trials conducted on the effects of acupuncture were included in this review. Two reviewers extracted the data independently from the remaining 17 articles after screening. The most used acupoint was PC6 (10 studies, 64.7%), followed by ST36 (6 studies, 35.3%) and auricular acupoints (4 studies, 23.5%). Among the clinical applications, hypertension was the most studied CVD, with acupuncture being the most reported method among the studies (70.6%). Only three articles reported no benefit in the treatment of CVDs for the methodology used. We conclude that although several studies indicated an improvement in the response of the cardiovascular system in CVDs by acupuncture, electroacupuncture, or electrostimulation treatment, the heterogeneity of the studies does not allow a standardization of its application for each specific disease, making further studies necessary for its use to become a reality.

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1. Introduction

The World Health Organization estimates that 17.5 million people died of cardiovascular diseases (CVDs) in 2012, representing 31% of all deaths worldwide [1]. The coronary artery disease (CAD) is the leading cause of death, followed by cerebral vascular disease. Together, both are responsible for 7.4 and 6.7 million of deaths, respectively [2]. The global number of deaths caused by CVDs increased by 12.5% during the last decade [3]; in the last 2 decades, the prevalence of CVDs has been particularly high in low and middle-income countries, which account for 80% of the deaths caused by CVDs [4]. The estimated annual cost of interventions for prevention and treatment of CVDs in those countries is just over US\$8 billion [5]. In Brazil, it is estimated that approximately US\$ 3.2 billion was spent in the health sector with direct costs for cases of severe CVDs in 2004; combined with the indirect cost of retirements and incapacity benefits incurred by CVDs, the effect on the economy was around US\$12 billion [6].

The scenario described above favors the applying of innovative and low-cost therapies, such as most alternative and complementary therapies, for treatment and prevention of CVDs. Traditional medicine methods, including acupuncture, electroacupuncture (EA), and transcutaneous electrical acupoint stimulation (TEAS), have been increasingly adopted by health-care professionals despite the lack of evidences on its effects on CVDs [7].

Acupuncture is a traditional therapeutic method from East Asia, dating back more than 2000 years [8]. It is based on peripheral neural stimulation by the introduction of needles into specific regions of the body surface, called acupuncture points or acupoints, with the intention of promoting organic and functional changes for therapeutic purposes or simple neuromodulation [9]. The occidental scientific community has been studying acupuncture effectiveness and its physiological mechanisms of action on the relief of pain, revealing it to be a powerful mode of sensorial stimulation. Recently, the number of studies publishing about acupuncture effects on a wide spectrum of pathologies and etiologies, such as infection, inflammation, dysfunction of the autonomic, peripheral, and central nervous system, metabolic disorders, and CVDs has increased [10,11].

EA is an acupuncture method in which acupoints are stimulated by a pulsating electric current applied through metallic needles from an electrostimulation device [12]. One of the main advantages of EA, from a clinical or research perspective, is its capacity to define the intensity objectively and quantifiably by altering the amplitude of wave and frequency [13].

Transcutaneous electrical acupoints stimulation (TEAS) is another acupuncture method [12]. It is based on the application of a pulsating electric current to the surface of the skin, above the regions corresponding to acupoints, using electrodes. Studies performed with rats have demonstrated that the efficacy and mechanisms of the analgesic response induced by TEAS are similar to those induced by EA and acupuncture. In addition, it has been demonstrated that electrical stimulation at an acupoint with the use of electrodes can reach deeper tissues and

induce the intended effects without the need for needles [12,14], thereby, reducing interurrences caused by needles such as discomfort by perforation, risk of future infections [15], and localized argyria [16].

Currently, the effects of acupuncture, EA, and TEAS for the treatment of CVDs remains poorly understood, and most of its mechanisms have not yet been completely elucidated. So, the purpose of the current study was to review the literature on the effects of acupuncture, EA, and TEAS in CVDs.

2. Methods

This systematic review followed the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [17] as well as the tutorial for writing systematic reviews [18].

We performed literature searches with the PubMed, SciELO, and PEDro databases, using concomitant and alternating combinations of the following English descriptors: "acupuncture," "electrostimulation," and "electroacupuncture" with "hypertension," "cardiovascular disease," "coronary artery" and "heart" as Medical Subject Headings (MeSH, <http://www.nlm.nih.gov/mesh/meshhome.html>); and the following are Portuguese descriptors: "acupuntura", "eletroestimulação" and "eletroacupuntura" with "hipertensão", "doenças cardiovasculares", "doença coronariana," and "válvula cardíaca." Two reviewers extracted the data independently.

Clinical trials published between January 1997 and September 2017, in English or Portuguese, which provided the full text in the aforementioned databases and indicated results regarding the association of one of the relevant techniques for treatment and/or prevention of CVDs, were included in this study. Reviews, observational, and experimental studies using animal models were excluded from the study.

The methodological quality of the studies was analyzed based on the score on the Physiotherapy Evidence Database scale provided in the PEDro database (Table 1). This analysis was performed independently by two evaluators, and disagreements were resolved by discussion and consensus. If a selected study was not scored in this database, the authors ranked it using the Portuguese (Brazilian) version of the scale [19].

3. Results

A total of 506 articles were selected, of which 120 were excluded based on the date of publication, 316 were excluded because they were not clinical trials, 37 were excluded because they were not available in English or Portuguese (29 in Chinese, 2 in Spanish, 2 in German, 1 in Russian, 1 in Japanese, 1 in Korean, and 1 in Persian), and 16 were excluded for not directly associating one of the techniques with at least one CVD. Finally, 17 studies were included in the present review (Fig. 1) and are summarized in Table 2.

4. Discussion

In the studies analyzed in this review, the most used acupoint among the different techniques was the PC6

Table 1 Methodological quality assessment by the Physiotherapy Evidence Database (PEDro) Scale.

PEDro scale items												
Author, date	1	2	3	4	5	6	7	8	9	10	11	Score
Abdi et al, 2017	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	7/10
Carpenter et al, 2010	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	8/10
Ho et al, 1999	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	5/10
Jiang, 2003	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	4/10
Kim et al, 2012	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8/10
Kurono et al, 2002	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10
Li et al, 2015	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	8/10
Liu et al, 2015	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9/10
Lomuscio et al, 2011	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
Park et al, 2010	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9/10
Severcan et al, 2012	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	No	4/10
Wang et al, 2015	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
Yang et al, 2010	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	8/10
Yeh et al, 2015	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10
Yilmaz et al, 2017	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7/10
Yin et al, 2007	Yes	Yes	No	Yes	9/10							
Zamotrinsky et al, 1997	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10

1 = eligibility criteria; 2 = random allocation; 3 = concealed allocation; 4 = baseline comparability; 5 = blind patients; 6 = blind therapists; 7 = blind assessors; 8 = adequate follow-up; 9 = "intention-to-treat" analysis; 10 = between-group comparisons; 11 = point estimates and variability.

Eligibility criteria item does not contribute to total score.

(*Neiguan*) acupoint (10 studies, 64.7%), followed by ST36 (Zu San Li) acupoint (6 studies, 35.3%) and auricular acupoints (4 studies, 23.5%). The simultaneous use of acupoints PC6 and ST36 was also observed in five clinical studies for the treatment of hypertension [20–24]. Anatomically, the heart is innervated by lower thoracic and upper cervical nerve segments, which also innervate the somatic area around PC6 acupoint. Moreover, the PC6 acupoint is located on the forearm surface in a region corresponding to the anatomical path of the median nerve [25,26], which may corroborate the relationship between the point stimulus and the physiological changes observed in the cardiovascular system.

Among the CVDs, to which the analyzed techniques were clinically applied, the most common was hypertension, totaling 10 studies. Of these, nine were related to acupuncture and only one to EA, with 80% reporting positive results in the modulation of the disease through the reduction of blood pressure (BP). Abdi et al [27] performed a double-blind randomized controlled clinical trial in which obese and hypertensive patients (not receiving drug therapy) were submitted to auricular acupuncture or abdominal EA, at Tianshu (ST25), Weidao (GB28), Zhongwan (RN12), Shuifen (RN9), Guanyuan (RN4), and Sanyinjiao (SP6) acupoints, during 6 weeks, showing a more expressive decrease in systolic blood pressure (SBP) and diastolic blood pressure (DBP) by abdominal EA compared to auricular acupuncture. In a randomized clinical trial, blinded for assessors and for statistician, conducted by Liu et al [21], 15 primary moderate hypertensive patients were submitted to acupuncture at LI11, SP4, ST36, LT3, and PC6 acupoints twice a week for 8 weeks; a reduction was observed in DBP but not in SBP, despite the improvement observed in parasympathetic tonus. Yin et al [24], in another double-blind randomized

controlled clinical trial, submitted 21 hypertensive or pre-hypertensive patients for 8 weeks treatment with acupuncture in several acupoints, including ST36 and PC6, observing a decrease in SBP and DBP at the end of 17 treatment sessions compared to sham acupuncture group. Interestingly, in a study, blinded for participants and for statisticians, conducted by Li et al. [22], 65 moderate hypertensive patients (not receiving antihypertensive medication) were treated with EA at PC5, PC6, ST36, and ST37 once a week for 8 weeks, evidencing a reduction in SBP and DBP, accompanied by a significant reduction in plasma norepinephrine and renin levels at the end of the follow-up, suggesting a physiological modulation by EA. Severcan et al [28] reported an increase on plasma nitric oxide (NO) concentration with a decrease in SBP and DBP observed after 10 weeks of treatment of hypertensive patients with acupuncture at EX-HN3 (Yintang), KI3, LIV3, SP9, LI4, HT7, ST36, and SP6 acupoint. NO is a potent vasodilator produced in vascular endothelial cells by the conversion of the amino acid arginine into citrulline, by enzymatic action of NO synthase, and plays a critical antihypertensive role in the homeostasis of BP [29]. EA, also, inhibits sympathetic stimulus by regulating the expression of NO synthase in the central nervous system [30, 31]. The depressant effect of EA on BP occurs mainly through vasodilation of mesenteric vessels caused by the inhibition of sympathetic tonus, which is responsible for vasoconstriction [29].

Unlike the aforementioned studies, Yeh et al [32], in a randomized clinical trial, observed no effects on BP and sympathovagal balance after 10 weeks of auricular acupuncture for the treatment of patients with primary hypertension. Also, Jiang [9], in a randomized controlled trial with 60 hypertensive patients, treated the intervention group daily with acupuncture at the LI11 (*Quchi*), ST40

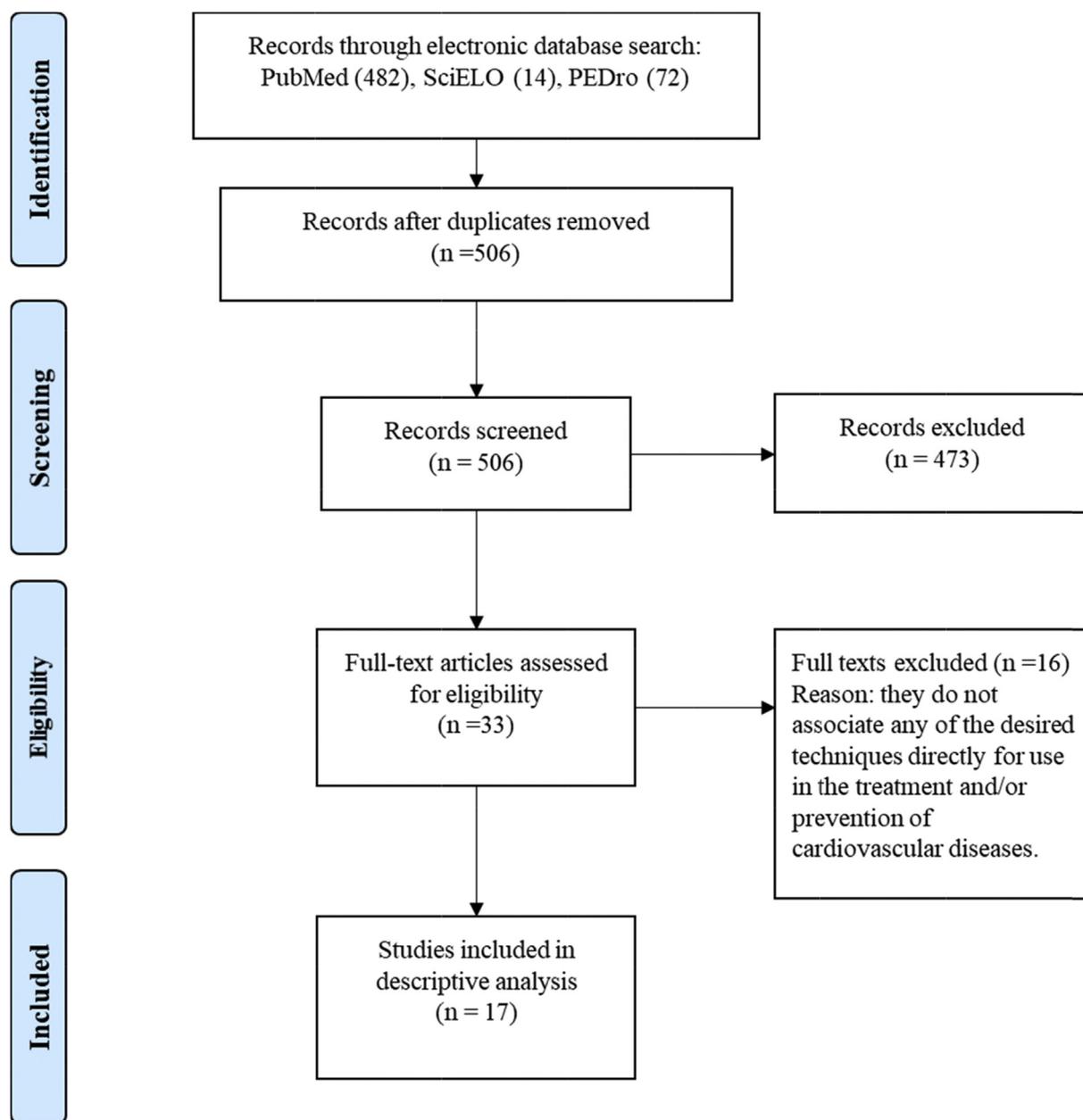


Figure 1 PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

(Fenglong), and LR3 (Taichong) acupoints for 30 minutes, during 6 days, observing no differences in BP between intervention and control groups after the follow-up. This may be explained by the fact that some patients are usually low-respondents to acupuncture for BP reduction [22], evidencing the necessity for understanding those involved mechanisms for a more precise prescription of acupuncture with this objective.

The CAD was another important application of acupuncture among CVDs, observed in five studies. Zamotrinsky et al [33], in a randomized controlled trial, submitted 10 patients with CAD with inability to perform any activity without angina or angina at rest to auricular EA. After 10 procedures, the EA exerted a vagotonic/sympatholytic effect with a decrease of angina threshold, with

patients' no longer developing angina either at rest or after a moderate physical load. Moreover, their dependence on treatment with vasodilators had decreased considerably. Also, EA improved stress-induced proteins, such as the thermal shock protein (HSP70i), which participates in the elimination of damaged or defective proteins [34] directly inhibiting apoptosis [35].

Interestingly, Wang et al [36] showed, in a randomized controlled trial with 60 patients, that 30 minutes of EA administered at PC6 acupoint prior to heart valve replacement surgery leads to cardioprotection, evidenced by post operative reduced serum levels of cardiac troponin I, a critical marker of myocardial injury [37], a lower usage of inotropic drugs and a shortened intensive care unit stay time. The cardioprotective action of EA was also studied by

Table 2 Study characteristics.

Author, year	Technique	Application points	Study type	Sampling (number of individuals)	Duration	Related cardiovascular disease	Main results
Abdi et al, 2017 [27]	Acupuncture	Abdominal (ST25, GB28, RN12, RN9, RN4, and SP6). Auricular (TF4, CO1, CO4, CO17, and HX1)	Controlled; randomized	Auricular: 204 (102C 102T); Abdominal: 196 (98C 98T)	2 times per week for 6 weeks	Hypertension	Significant time-dependent improvement in systolic blood pressure (SBP) measurements in the abdominal intervention group, a significant increase in SBP level in the auricular intervention group.
Carpenter et al, 2010 [43]	Acupuncture	Back Shu, PC6, EX12, urinary bladder (15, 17, 18, 20, 23), and auricular.	Cross-over; single-blind	12T	1 time	Vasovagal syncope and Hypertension	Significant decrease in sympathetic balance (<i>low frequency: high SBP at rest</i>).
Ho et al, 1999 [38]	Acupuncture	PC6	Controlled	22C, 22T	1 time	Coronary disease	Mean values of left ventricular ejection fraction increased significantly at baseline, during, and after 15 minutes of acupuncture but became insignificant at one week.
Jiang, 2003 [9]	Acupuncture	LI11, ST40, and LR3	Controlled; randomized	30T, 30C	1 time per day; 6 days	Hypertension	There was no difference in BP and plasma levels of ET-1 between the treated group and the control group.
Kim et al, 2012 [23]	Acupuncture	ST36 and PC6	Placebo-controlled; randomized; double-blind	12T, 16P	2 times per week, 8 weeks	Hypertension	Increased diastolic blood pressure (DBP) at night and increased number of dippers.

(continued on next page)

Table 2 (continued)

Author, year	Technique	Application points	Study type	Sampling (number of individuals)	Duration	Related cardiovascular disease	Main results
Kurono et al, 2002 [39]	Acupuncture	PC6	Randomized	16T (10 LN, 6 SPM)	1 time	Coronary disease	There was an increase in the diameter of the coronary artery in some patients after acupuncture but coronary narrowing in other patients.
Li et al, 2015 [22]	Electroacupuncture	PC5, PC 6, ST36, and ST37	Two-arm parallel randomized; blinded for participants and for researcher	65T (33 in points PC5-6 + ST 36 + 37/in LI 6-7 + GB 37-39)	1 time per week; 8 weeks	Hypertension	Peak decrease and median SBP and DBP; decreased plasma concentrations of norepinephrine, renin and aldosterone.
Liu et al, 2015 [21]	Acupuncture	LI11, SP4, ST36, LT3, and PC6	Controlled; randomized; blinded for assessors and for statistician	48T, 13C	8 weeks	Hypertension	Decrease only of DBP and reduction of heart rate variability (HRV) of HF in the 4th and 8th week of treatment of the treated group.
Lomuscio et al, 2011 [40]	Acupuncture	PC6, C7, and BL15	Controlled; randomized; single-blind	17T, 13P, 24C, 26R	1 time per week; 10 weeks	Atrial fibrillation	Decreased recurrence rate of arrhythmias in the intervention group.
Park et al, 2010 [20]	Acupuncture	ST36 and PC6	Placebo-controlled; randomized; double-blind; cross-over	15T, 15P	7 times; 1 week	Hypertension	Significant improvement of flow-mediated dilatation of the brachial artery in acupuncture ST 36 and ST 36 + PC6.
Severcan et al, 2012 [28]	Acupuncture	EX-HN3, KI3, LIV3, SP9, LI4, HT7, ST36, and SP6	Randomized	32T	1 time per week, 10 weeks	Hypertension	Reduction of SBP and DBP values and increase of nitric oxide concentration during the 10 sessions.

Wang et al, 2015 [36]	Electroacupuncture	PC6 and PC4	Controlled; randomized	102T, 102C	1 time	Coronary disease	Significant improvement in cardiac function and reduction of adverse cardiovascular and cerebrovascular events in the treated group.
Yang et al, 2010 [37]	Electroacupuncture	PC6, LU7, and LU2	Controlled; randomized	30T, 30C	1 time per day; 5 days	Heart valve disease	Pretreatment with electroacupuncture resulted in a cardioprotective effect in patients undergoing valve replacement heart surgery.
Yeh et al, 2015 [32]	Acupuncture	Auricular	Controlled; randomized	63T, 60C	10 weeks	Hypertension	There were no significant differences in HRV parameters, heart rate, BP, and quality of life.
Yilmaz et al, 2017 [42]	Electrostimulation	Peroneal nerve	Controlled; randomized	11T, 11C	1 time	Critical ischemia	No significant difference was observed between the treated group and the control group.
Yin et al, 2007 [24]	Acupuncture	ST36, LI11, BL25, SP3, LU9, BL13, KI7, KI2, CV4, LI1, GV14, GB20, HT7, and PC6	Placebo-controlled; randomized; double-blind	15T, 15P	17 times; 8 weeks	Hypertension	Decreased mean BP after 8 weeks of intervention.
Zamotrinsky et al, 1997 [33]	Electroacupuncture	Auricular	Controlled; randomized	10T, 10C	1 time	Coronary disease	Relief of angina symptoms; decrease in certain biochemical signs of myocardial damage, and increase in heart tolerance to operative reperfusion injury.

C = individuals in the control group; P = individuals in the placebo group; T = individuals in the treated group; R = individuals in the reference group; LN = leaving needle method; SPM = sparrow pecking method.

In the analysis of the heart rate variability, the HF has a great correlation with the parasympathetic modulation of heart rate while LF is related to the sympathetic modulation.

Wang et al [36] in a randomized controlled trial with 204 patients. The EA was performed 30-minute at Antiguan (PC6) and Ximen (PC4) acupoints 1 to 2 hours prior to percutaneous coronary intervention, resulting in a lower incidence of acute myocardial infarction, improvement in cardiac function, and fewer adverse events such as sudden death, arrhythmias, heart failure, acute thrombosis, myocardial infarction, and stroke after percutaneous coronary intervention. Ho et al [38] stimulated the EH6 acupoint of 22 patients who had angiographically proven CAD (>50% diameter stenosis) for 30 minutes, demonstrating that acupuncture improved cardiac function in these but not on control patients. Although the previously described, Kurono et al [39] demonstrated that in patients with vasospastic angina, the acupuncture at EH6 acupoint could be deleterious, leading to vasospasm of coronary artery.

According to Lomuscio et al [40], acupuncture treatment at PC6, HT7, and BL 15 acupoints leads to similar benefits as amiodarone, an antiarrhythmic agent which is the most effective drug used worldwide for treatment of atrial fibrillation [41], reducing the recurrence of atrial fibrillation after electrical cardioversion therapy. Transcutaneous electrostimulation for peripheral limb ischemia was studied by Yilmaz et al [42]. Electrostimulation of the peroneal nerve produced a substantial increase in blood velocity in anterior tibialis artery, associated with better clinical outcomes, in terms of longer walking distance. The two last studies did not suggest any mechanism for the observed effects.

In conclusion, this review demonstrates that acupuncture may be a viable alternative as a complementary therapy for CVD, particularly for hypertension and CAD. However, the heterogeneity of the studies does not allow a standardization of its application for each specific disease, making further studies necessary for its use to become a reality.

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Disclosure statement

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jams.2018.07.005>.

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