

## REVIEW

## Massage therapy for essential hypertension: a systematic review

XJ Xiong<sup>1</sup>, SJ Li<sup>2</sup> and YQ Zhang<sup>3</sup>

Massage, an ancient Chinese healing art, is widely practiced for symptom relief in hypertensive patients with anxiety, depression, headache, vertigo, chronic pain in neck, shoulder and back. A large number of case series and clinical trials have been published. However, it is still unclear whether massage can be recommended as an effective therapy for essential hypertension (EH). We estimated the current clinical evidence of massage for EH. Articles published before 10 December 2013 were searched using Cochrane Library, PubMed, EMBASE, Chinese Scientific Journal Database (VIP), Chinese Biomedical Literature Database, Wanfang data and Chinese National Knowledge Infrastructure. Randomized controlled trials comparing massage with any type of control intervention were included. Trials testing massage combined with antihypertensive drugs versus antihypertensive drugs were included as well. Meta-analysis was performed on the effects on blood pressure (BP). Twenty-four articles involving 1962 patients with EH were selected. Methodological quality of most trials was evaluated as generally low. Meta-analyses demonstrated that massage combined with antihypertensive drugs may be more effective than antihypertensive drugs alone in lowering both systolic BP (SBP; mean difference (MD):  $-6.92$  ( $-10.05$ ,  $-3.80$ );  $P < 0.0001$ ) and diastolic BP (MD:  $-3.63$  ( $-6.18$ ,  $-1.09$ );  $P = 0.005$ ); massage appears beneficial for reducing SBP (MD:  $-3.47$  ( $-5.39$ ,  $-1.56$ );  $P = 0.0004$ ) for hypertensive patients as compared with antihypertensive drugs. Safety of massage is still unclear. There is some encouraging evidence of massage for EH. However, because of poor methodological quality, the evidence remains weak. Rigorously designed trials are needed to validate the use of massage in future.

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## INTRODUCTION

Hypertension is one of the most important preventable causes of death worldwide.<sup>1,2</sup> It has been ranked as the leading global risk factor for mortality and as the third leading risk factor for disease burden by the comparative Risk Assessment Collaborating Group.<sup>3,4</sup> It affects approximately 1 billion individuals worldwide both in developed and developing countries.<sup>5</sup> In 1914, Fisher discovered a relationship between high blood pressure (BP) and mortality among life-insurance applicants.<sup>6</sup> Recent researches also verified that BP level is highly related to vascular outcomes.<sup>7</sup> There is robust evidence from randomized trials showing that even a small reduction of BP could contribute to the prevention of cardiovascular events (especially stroke).<sup>8</sup> Prevention and effective treatment of essential hypertension (EH) is of utmost importance worldwide. Unfortunately, despite the availability of efficient pharmacological and nonpharmacological therapies, both BP control rates and improvements of patients' quality of life still remain unsatisfactory.<sup>9,10</sup> Effective treatment of EH is mostly limited by not only underdiagnosis and undertreatment, but also availability, cost and adverse effects of antihypertensive medications, given the increasing of absolute numbers of patients affected by EH.<sup>2</sup> Therefore, in the western countries, the scientific community has progressively become more aware of the physiologic and remedial effects of alternative medical treatments,<sup>11–13</sup> including traditional Chinese medicine (TCM),<sup>14,15</sup> in searching for a certain therapy with potential efficacy and few adverse effects.<sup>16,17</sup> They hope that beneficial effect could be obtained from nonpharmacological approaches such as yoga,<sup>18</sup> qigong,<sup>19</sup> Tai Chi,<sup>20</sup> acupuncture,<sup>21</sup> moxibustion<sup>22</sup> and massage,<sup>23,24</sup> which might complement western medicine to a certain extent. This situation is also partially supported by recently

published studies.<sup>25–27</sup> As a result, some of these approaches and treatments are now being integrated into the medical school curriculum and reimbursed by health insurance companies.

Massage therapy, an ancient traditional healing art, has first been described in TCM dating back as far as 5000 years ago.<sup>28</sup> It is defined as the systematic manipulation of soft tissues of the whole body areas to bring about generalized improvements in health, such as relaxation or improved sleep, or specific physical benefits, such as relief of muscular aches and pains by trained therapists.<sup>29</sup> As a commonly used form of treatment in almost all cultures, it is widely accepted by patients from America, European countries and elsewhere.<sup>30</sup> According to the studies conducted by Eisenberg *et al.*,<sup>31</sup> almost half of all visitors to complementary and health-care providers selected massage therapy. These findings were also verified by surveys commissioned by American Massage Therapy Association and others, which ranked massage therapy the highest among alternative and complementary practices that are perceived as always or usually effective, both in the United States and the United Kingdom.<sup>32–34</sup> According to TCM theory, a possible explanation for how massage works is that it could promote circulation of qi, blood and fluid throughout the body, dredge meridians and collaterals to relieve pain, and regulate yin and yang.<sup>35</sup> It has been widely used to improve health care, prevent disease and prolong life for a wide range of conditions, symptoms and situations including hypertension,<sup>36,37</sup> rehabilitation after cardiac surgery,<sup>38,39</sup> type 2 diabetes,<sup>40</sup> headache,<sup>41</sup> dementia,<sup>42</sup> advanced cancer,<sup>43,44</sup> preterm/low birth-weight infants,<sup>45</sup> stress,<sup>46</sup> fibromyalgia,<sup>47</sup> osteoarthritis,<sup>48</sup> neck pain,<sup>49</sup> low back pain,<sup>50,51</sup> fatigue,<sup>52</sup> recovery from exercise,<sup>53</sup> injury prevention<sup>54</sup> and for enhancing the quality of life of patients with other chronic diseases.<sup>55</sup> Until

<sup>1</sup>Department of Cardiology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China; <sup>2</sup>Department of Biological Science and Technology, School of Life Sciences, Tsinghua University, Beijing, China and <sup>3</sup>Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada. Correspondence: Dr XJ Xiong, Department of Cardiology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beixiangye 5, Beijing 100053, China.

E-mail: xiongxingjiangtcm@163.com or 5administration@163.com

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now, more and more scientific researches are now being conducted toward studying the efficacy of massage therapy as many aspects have strong physiologic and even pharmacodynamic effects.<sup>56</sup> It is increasingly used for symptom relief in hypertensive patients with anxiety, depression, headache, vertigo, chronic pain in neck, shoulder and back. As a result of the relaxation response and through the increase in blood flow throughout the body, an overall decrease in BP for pre-hypertension and hypertension is thought to occur, which had been confirmed by several studies.<sup>32,57–62</sup>

In more recent years, a large number of case series and randomized controlled trials (RCTs) have occasionally been reported to be effective in treating EH as adjunctive method outside China. However, currently available RCTs had small sample sizes and shown diverse outcomes. Few studies have systematically examined the effectiveness of massage therapy according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses compliant statement.<sup>63</sup> The assessment and integration of these trials using an evidence-based approach to guide clinical treatment are of global priority. Therefore, the purpose of the present study was to synthesize the results of available RCTs to assess the effectiveness and safety of massage therapy for EH.

## MATERIALS AND METHODS

### Database and search strategies

We conducted literature searches in the following databases: Cochrane Library (December, 2013), PubMed (1959–2013), EMBASE (1980–2013), Chinese Scientific Journal Database (VIP; 1989–2013), Chinese Biomedical Literature Database (1978–2013), Chinese National Knowledge Infrastructure (1979–2013) and Wanfang data (1998–2013). Studies published in both English and Chinese were retrieved. Further, studies included in reference lists of relevant trials and reviews were also identified. Literature searches were ended on 10 December 2013. Ongoing registered clinical trials were searched in the website of Chinese clinical trial registry (<http://www.chictr.org/>) and international clinical trial registry by US National Institutes of Health (<http://clinicaltrials.gov/>). The following keywords were used individually or combined in the search: 'blood pressure', 'high blood pressure', 'hypertension', 'essential hypertension', 'primary hypertension', 'massage', 'manipulation', 'tuina', 'tui na', 'an mo', 'clinical trial' and 'randomized controlled trial'. Bibliographies of included trials were hand searched for further relevant articles.

### Inclusion criteria

Participants had been diagnosed with EH could be included in this study.<sup>2</sup> Participants were excluded if they had secondary hypertension, acute myocardial infarction, severe arrhythmia, heart failure, hepatic failure or renal failure. This study included trials that made a comparison between a massage-dominated therapy and antihypertensive drugs. The massage-dominated treatments included massage combined with antihypertensive drugs and massage itself. The duration of treatment should be more than 10 days. No restrictions on population characteristics were imposed. Duplicated publications reporting the same groups of participants were excluded. The main outcome measure was BP.

### Data extraction and quality assessment

RCTs evaluating the efficacy of massage-dominated therapy for EH were included. Titles and abstracts of searched studies of references for potentially relevant RCTs were screened for further review. Two authors (Xiong and Li) independently read the titles and abstracts according to the inclusion and exclusion criteria that established above. Full articles were retrieved for further identification. Then a final decision for selection or not was made.

Disagreements were resolved by discussion and by consultation with a third party (Zhang), and a judgment was made based on consensus.

Data were collected independently by two authors (Xiong and Li) using a standardized data extraction form. The following detailed characteristics of the trials were recorded: authors, title, year of publication, study size, age and sex of the participants, diagnosis standard, details of methodological information, treatment process, courses, details of the control interventions, outcomes and adverse effects. Reasons for the exclusion of trials were recorded accordingly. Missing information about the trials was obtained from the original authors whenever possible. Any disagreements were resolved by referring to the trial report and by discussion.

Two authors (Xiong and Li) evaluated the methodological quality of each RCT independently according to the standards advised by the Cochrane handbook.<sup>64</sup> Seven items about 'risk of bias' were included as below: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias. Each domain was rated as low/unclear/high risk of bias. Then trials were categorized into three levels: low risk of bias (all the items were in low risk of bias), high risk of bias (at least one item was in high risk of bias), unclear risk of bias (at least one item was in unclear).

### Data synthesis

Revman 5.1 (free software downloadable from <http://ims.cochrane.org/revman/download>) provided by the Cochrane Collaboration was used for data analyses. For dichotomous outcomes, the number of patients experiencing BP reduction in each group was recorded. For continuous outcomes, the means and s.d. for each group were extracted. The recorded data were double-checked. Dichotomous data were expressed as relative risks. Continuous data were expressed as mean differences (MDs). Heterogeneity was tested using the Z-score and the  $\chi^2$  ( $I^2$ ) statistics with significance set at  $P < 0.1$ . Overall results were calculated based on the fixed effects model when no heterogeneity existed among pooled studies. Random effects model was used if significant heterogeneity existed. Possible sources of heterogeneity were assessed by sensitivity if sufficient studies were found and subgroup analyses as described below.

## RESULTS

### Description of included trials

As shown in Figure 1, we selected 24 studies<sup>65–88</sup> out of the 596 relevant references after conducting a strict search process and study selection. They were conducted in four countries (the United States,  $n = 3$ ; Malaysia,  $n = 1$ ; Republic of Korea,  $n = 1$ ; China,  $n = 19$ ) and were published between 1992 and 2013. All the included studies were single-center and parallel-design study.

A total of 1962 patients with EH were included. The treatment group included either massage used alone<sup>65–78</sup> or combined with antihypertensive drugs,<sup>77,79–88</sup> whereas the control group received no intervention,<sup>65–68</sup> progressive muscle relaxation<sup>69</sup> and antihypertensive drugs.<sup>70–88</sup> Duration of treatment ranged from 10 days to 1 year. All trials used BP or BP reduction as outcome measure. Adverse effect was also described in details. The characteristics of included studies were presented in Table 1.

### Methodological quality of included trials

According to the quality assessment criteria in Cochrane standards, most of the included trials were assessed to be of general poor methodological quality. Five of the included articles

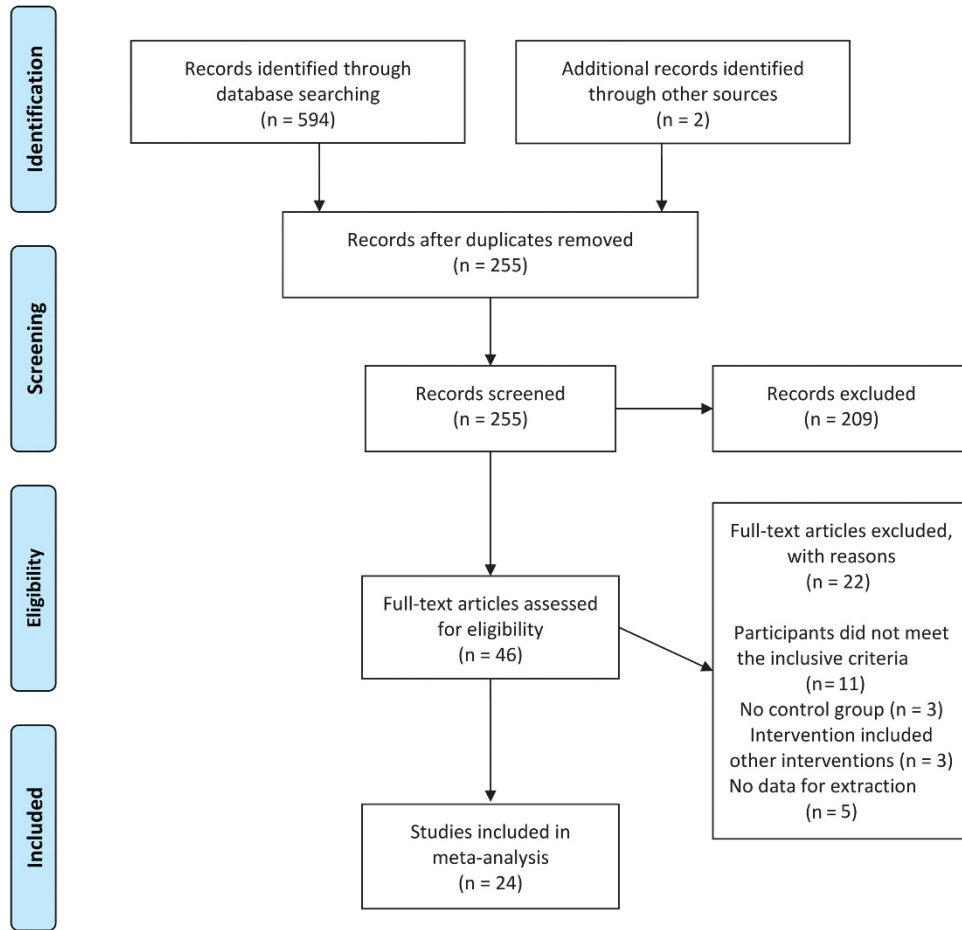


Figure 1. PRISMA 2009 flow diagram.

Table 1. Basic characteristics of the included studies

Study ID	Sample size (randomized/ analyzed) M/F	Age (years)	Diagnosis standard	Intervention	Control	Course	Main outcomes	Adverse effects report
Supa'at <i>et al.</i> <sup>65</sup>	23/16 T: 8 C: 8 F/M: NR	T: 51.00 ± 10.00; C: 51.13 ± 11.00	NR	Swedish massage (1 h/week)	No intervention	4 Weeks	(1) SBP and DBP: NSD; (2) HR: NSD	N
Ju <i>et al.</i> <sup>66</sup>	55/55 T: 28 C: 27 F/M: NR	T: 52.50 ± 4.60; C: 53.30 ± 4.60	NR	Aroma massage (1 h/week)	No intervention	4 Weeks	SBP: <i>P</i> < 0.05; DBP: NSD	N
Olney <sup>67</sup>	37/14 T: 8 C: 6 F/M: NR	T: 52.38 ± 14.04; C: 57.33 ± 11.41	NR	Back massage (10 min/day, 3 times/week)	No intervention	10 Weeks	SBP: <i>P</i> = 0.003; DBP: <i>P</i> = 0.033	N
Plaughner <i>et al.</i> <sup>68</sup>	86/14 T: 8 C: 6 F/M: NR	T: 38.60 ± 7.70; C: 36.3 ± 9.6	NR	Brief massage (10 min/day, 3 times/week)	No intervention	2 Months	SBP and DBP: comparison between them NR	N
Hernandez <i>et al.</i> <sup>69</sup>	30/30 T: 6/9 C: 8/7 F/M: NR	T: 52; C: 50	NR	Massage (30 min/day, 10 times)	Progressive muscle relaxation	5 Weeks	SBP: NSD; DBP: <i>P</i> < 0.05	N
Ji <sup>70</sup>	60/60 T: 20/15 C: 14/11	T: 53.80 ± 12.58; C: 51.90 ± 11.60	WHO-ISH GMH-1999	Massage (1 time/ day)	Nifedipine (10 mg b.i.d.)	1 Month	(1) SBP and DBP: NSD; (2) HR: NSD	Y
Hao <sup>71</sup>	60/60 T: 15/15 C: 17/13	T/C: NR	WHO-ISH GMH-1999	Massage (20 min/day)	Captopril (25 mg b.i.d.)	10 Days	SBP: <i>P</i> < 0.05; DBP: NSD	N
Wang <i>et al.</i> <sup>72</sup>	60/57 T: 29 C: 28 F/M: NR	T: 50.40 ± 10.50; C: 51.30 ± 11.4	WHO-ISH GMH-1999	Massage (no detailed information)	Hydrochlorothiazide (12.5 mg q.d.)	3 Months	SBP and DBP: comparison between them NR	N

**Table 1.** (Continued)

Study ID	Sample size (randomized/ analyzed) M/F	Age (years)	Diagnosis standard	Intervention	Control	Course	Main outcomes	Adverse effects report
Li <i>et al.</i> <sup>73</sup>	58/58 T: 31 C: 27 F/M: NR	T: 61.55 ± 3.70; C: 61.48 ± 4.11;	NR	Massage (2 times/day)	Nifedipine (5–60 mg/ day) or nitrendipine (10–60 mg/day)	3 Months	SBP and DBP: NSD	Y
Luo and Xue <sup>74</sup>	89/75 T: 36 C: 39 F/M: NR	NR	CGMH-1999	Massage (1 time/ day)	Nifedipine sustained release tablets (10 mg b.i.d.), and/or enalapril maleate (12.5–25 mg b.i.d.), hydrochlorothiazide (6.25–12.5 mg bid)	6 Months	(1) SBP and DBP: $P < 0.05$ ; (2) symptom improvement: $P < 0.05$	N
Luo and Xu <sup>75</sup>	100/100 T: 50 C: 50 F/M: NR	NR	JNC-VI	Massage (1 time/ day)	Benazepril hydrochloride (10– 21 mg q.d.)	1 Month	(1) SBP and DBP: $P < 0.05$ ; (2) symptom improvement: $P < 0.01$ BP: $P < 0.01$	N
Li <sup>76</sup>	72/72 T: 28/18 C: 18/8 330/330	T: 31–68; C: 34–65	NR	Massage (1 time/day)	Captopril (12.5–50 mg b.i.d.-b.i.d.)	1 Month	SBP and DBP: NSD	N
Liu and Xi <sup>77</sup>	T: 58/52 C1: 56/54 C2: 59/51 60/60	T: 49.50 ± 20.70; C1: 48.30 ± 19.30; C2: 49.60 ± 19.70	CGMH-2010	Massage (10 min/day, 3 times/day)	C1: nifedipine (10 mg t.i.d.) C2: T + C1	1 Month	SBP and DBP: NSD	N
Qu <sup>78</sup>	T: 13/17 C: 14/16	T: 41.66 ± 9.26; C: 40.86 ± 8.46	WHO-ISH GMH-1999	Massage (20 min/day)	Felodipine sustained release tablets (5 mg q.d.)	20 Days	BP: $P < 0.05$	N
Liu <i>et al.</i> <sup>79</sup>	80/80 T: 40 C: 40 F/M: NR	71.95 ± 12.19 (T/ C: NR)	WHO-ISH GMH-1999	Massage (1 time/ day) + C	Antihypertensive drugs (no detailed information)	1 Year	(1) SBP and DBP: $P < 0.05$ ; (2) QOL: $P < 0.05$	N
Xue and Liao <sup>80</sup>	64/58 T: 9/19 C: 14/16	T: 57.80 ± 8.70; C: 56.10 ± 9.10	CGMH	Massage (20 min/day, 2 time/day) + C	Nifedipine sustained release tablets (5– 10 mg b.i.d.)	4 Weeks	(1) SBP and DBP: $P < 0.05$ ; (2) symptom improvement: $P < 0.01$	Y
Yu <sup>81</sup>	240/240 T: 68/52 C: 72/48	T: 54.75 ± 7.10; C: 51.72 ± 10.30	CGMH-2005	Massage (1 time/ day) + C	Antihypertensive drugs (no detailed information)	20 Days	(1) SBP and DBP: $P < 0.05$ ; (2) symptom improvement: $P < 0.01$	N
Meng <i>et al.</i> <sup>82</sup>	80/80 T: 23/17 C: 19/21	T: 55.48 ± 5.28; C: 54.12 ± 6.41	CGMH-2005	Massage (1 time/ day, 5 times/ week) + C	Nifedipine controlled release tablets (30 mg q.d.)	4 Weeks	(1) SBP and DBP: $P < 0.05$ ; (2) symptom improvement: $P < 0.05$ SBP: $P < 0.05$	Y
Xu <sup>83</sup>	80/80 T: 22/20 C: 20/18 48/48	T: 59.40 ± 5.70; C: 60.80 ± 5.50	NR	Massage (15 min/day, 2 time/day) + C	Antihypertensive drugs (no detailed information)	16 Weeks	SBP and DBP: $P < 0.05$	Y
Zhou <i>et al.</i> <sup>84</sup>	T: 24 C: 24 F/M: NR	42–83 (T/C: NR)	WHO-ISH GMH-1999	Massage (30 min/day, 5 time/week) + C	Captopril (12.5–25 mg q.d.-t.i.d.)	3 Weeks	SBP and DBP: $P < 0.05$	N
Chen <i>et al.</i> <sup>85</sup>	140/128 T: 74 (F/M: NR) C: 41/13	T: 42–70; C: 41–66	NR	Massage (30 min/day, 1–2 times/ day) + C	Antihypertensive drugs (no detailed information)	3 Months	(1) SBP and DBP: NSD; (2) symptom improvement: NSD	N
Yao <sup>86</sup>	60/60 T: 30 C: 30 F/M: NR	45–76 (T/C: NR)	CGMH-2004	Massage (1 time/ day) + C	Metoprolol (100 mg q.d.)	1 Month	BP: $P < 0.05$	N
Deng <sup>87</sup>	127/127 T: 32/35 C: 29/31	T: 62.05 ± 6.73; C: 63.55 ± 7.26	NR	Massage (1 time/ day) + C	Nifedipine sustained release tablets (10 mg b.i.d.), captopril (12.5 mg q.d.)/ enalapril (10 mg q.d.)	10 Days	BP: $P < 0.05$	N
Chen and Li <sup>88</sup>	60/60 T: 14/16 C: 17/13	T: 48.23 ± 7.21; C: 50.54 ± 8.43	CGMH-2004	Massage (45 min/day, 1 time/day) + C	Ramipril (2.5 mg b.i.d.)	15 Days	BP: $P < 0.05$	N

Abbreviations: BP, blood pressure; C, control group; CGMH, Chinese Guidelines for the Management of Hypertension; DBP, diastolic blood pressure; F, female; JNC-VI, Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure; M, male; N, no; NR, not reported; NSD, no significant difference; QOL, quality of life; SBP, systolic blood pressure; T, treatment group; Y, yes; WHO-ISH GMH, World Health Organization-International Society of Hypertension guidelines for the management of hypertension.

reported their method of randomization, whereas only one mentioned allocation concealment. None mentioned double blinding. Detailed information about drop-outs and withdrawals

were reported in seven trials. Two studies reported a pre-trial estimation of sample size. Follow-up was reported only in three trials (Table 2).



# Effect of massage on BP

**Massage versus no treatment.** Four trials compared massage with no intervention.<sup>65–68</sup> One trial compared massage with progressive muscle relaxation.<sup>69</sup> We grouped both ‘no intervention’ and ‘progressive muscle relaxation’ together as ‘no

treatment’ for further analysis. Effect of massage on BP was reported in all studies, whereas two trials used figures to represent the efficacy instead of specific BP values.<sup>65,67</sup> Therefore, meta-analysis was performed based on the rest three trials.<sup>66,68,69</sup> There was significant heterogeneity among these studies, so meta-analysis was conducted using the random effects model. The result indicated that there is no difference between massage and no treatment group in lowering systolic BP (SBP; MD:  $-3.26$  ( $-10.02, 3.49$ );  $P=0.34$ ; Figure 2a) and diastolic BP (DBP; MD:  $-2.41$  ( $-8.75, 3.93$ );  $P=0.46$ ; Figure 2b).

**Massage versus antihypertensive drugs.** Nine trials compared massage with antihypertensive drugs.<sup>70–78</sup> Among them, six trials used BP values to evaluate the effect of massage.<sup>70–75</sup> Meta-analysis indicated that massage is better than antihypertensive drugs for lowering SBP (MD:  $-3.47$  ( $-5.39, -1.56$ );  $P=0.0004$ ; Figure 3a), whereas there is no difference in DBP (MD:  $-0.98$  ( $-2.28, 0.32$ );  $P=0.14$ ) was found (Figure 3b).

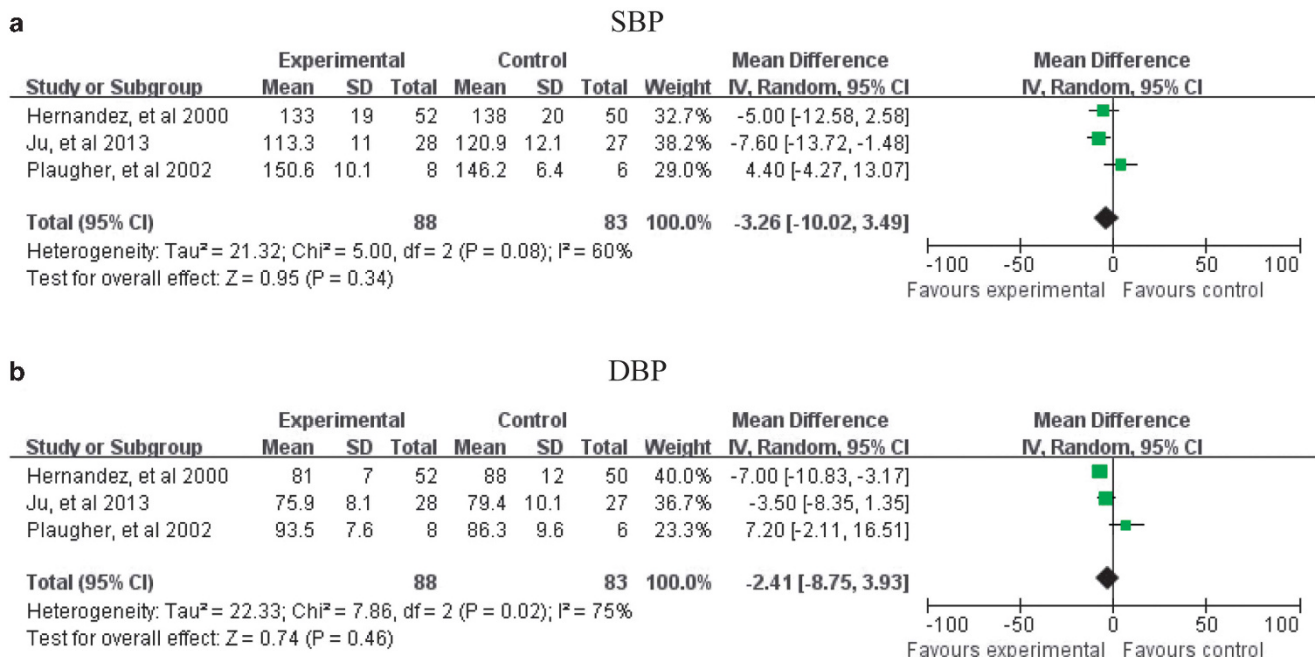
Three trials<sup>76–78</sup> summarized the effect of massage on BP into three grades named significant improvement, improvement and no improvement, rather than BP values (National Committee on Screening, and Prevention of Coronary Heart Disease and High Blood Pressure in China, 1974).<sup>89</sup> It classified BP into: ‘significant improvement’ (DBP decreased by 10 mm Hg reaching the normal range or DBP has not yet returned to normal, but has been reduced 20 mm Hg or more), ‘improvement’ (DBP decreased to less than 10 mm Hg reaching the normal range or DBP decreased by 10–19 mm Hg, but did not reach the normal range or SBP decreased 30 mm Hg or more) and ‘no improvement’ (not to reach the above standards). To permit overall synthesis of these enumeration data, we grouped them into dichotomous data, that is, ‘significant improvement’ and ‘improvement’ as ‘effective’, and ‘no improvement’ as ‘ineffective’. Meta-analysis suggested no difference in BP favoring massage (relative risk: 1.02 (0.88, 1.18);  $P=0.77$ ; Figure 3c).

**Massage combined with antihypertensive drugs versus antihypertensive drugs.** Eleven trials compared massage combined with antihypertensive drugs with antihypertensive

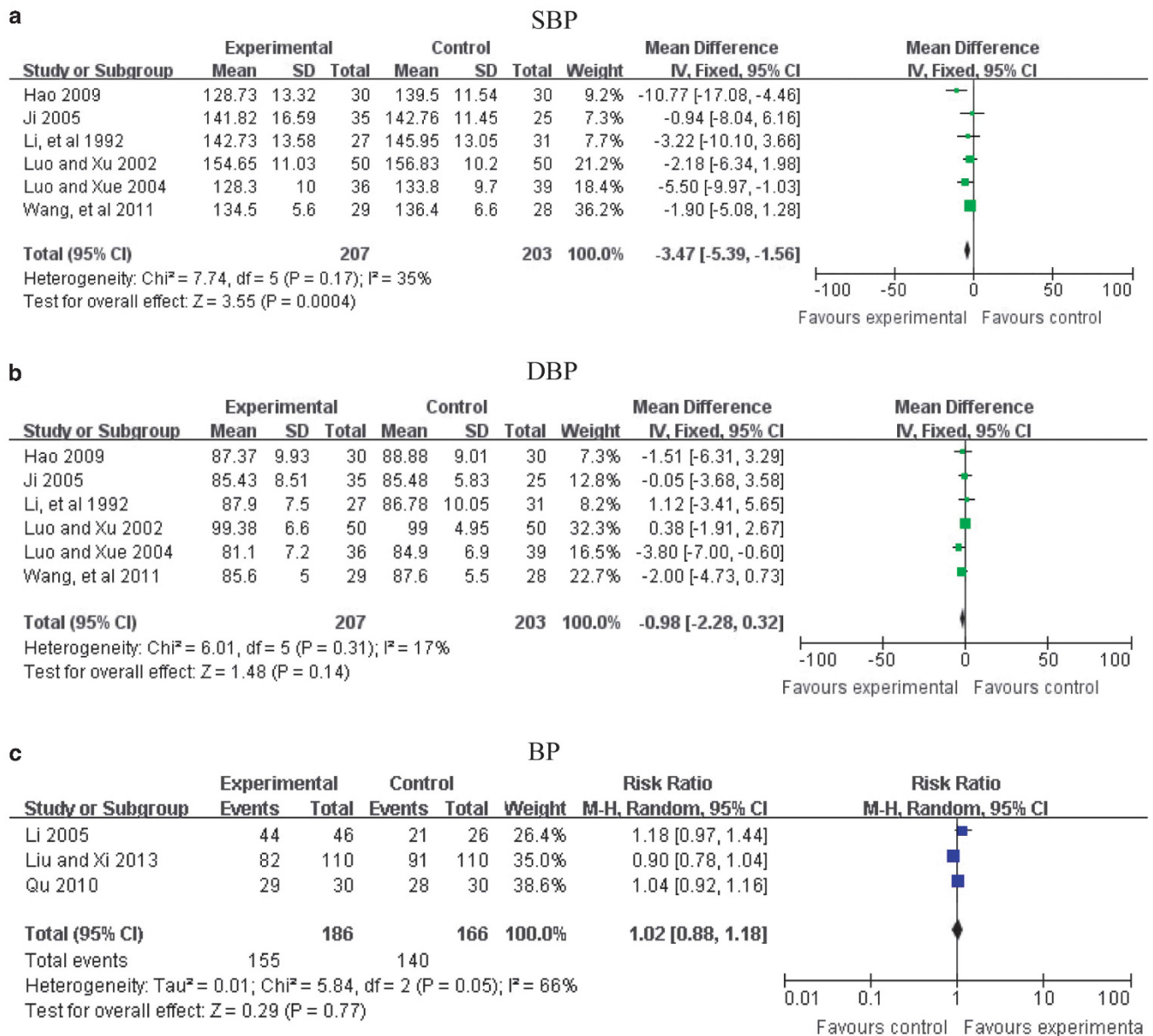
**Table 2.** Methodological quality of included studies based on the Cochrane handbook

Included trials	A	B	C	D	E	F	G
Supa'at <sup>65</sup>	?	?	?	?	+	?	–
Ju <i>et al.</i> <sup>66</sup>	?	?	?	?	?	?	?
Olney <sup>67</sup>	?	?	?	?	+	?	–
Plaughner <i>et al.</i> <sup>68</sup>	?	+	?	?	+	?	?
Hernandez <i>et al.</i> <sup>69</sup>	?	?	?	?	?	?	?
Ji <sup>70</sup>	?	?	?	?	?	+	?
Hao <sup>71</sup>	?	?	?	?	?	?	?
Wang <i>et al.</i> <sup>72</sup>	?	?	?	?	+	?	?
Li <i>et al.</i> <sup>73</sup>	?	?	?	?	?	+	?
Luo and Xue <sup>74</sup>	?	?	?	?	+	?	?
Luo and Xu <sup>75</sup>	?	?	?	?	?	?	?
Li <sup>76</sup>	?	?	?	?	?	?	?
Liu and Xi <sup>77</sup>	?	?	?	?	?	?	?
Qu <sup>78</sup>	?	?	?	?	?	?	?
Liu <i>et al.</i> <sup>79</sup>	?	?	?	?	?	?	–
Xue and Liao <sup>80</sup>	+	?	?	?	+	+	?
Yu <sup>81</sup>	+	?	?	?	?	?	?
Meng <i>et al.</i> <sup>82</sup>	+	?	?	?	?	+	?
Xu <sup>83</sup>	?	?	?	?	?	+	?
Zhou <i>et al.</i> <sup>84</sup>	?	?	?	?	?	?	?
Chen <i>et al.</i> <sup>85</sup>	?	?	?	?	+	?	?
Yao <sup>86</sup>	+	?	?	?	?	?	?
Deng <sup>87</sup>	+	?	?	?	?	?	?
Chen and Li <sup>88</sup>	?	?	?	?	?	?	?

Abbreviations: A, adequate sequence generation; B, Concealment of allocation; C, blinding (participants and personnel); D, blinding (assessor); E, incomplete outcome data addressed (ITT analysis); F, free of selective reporting; G, other potential threat to validity; +, low risk; –, high risk; ?, unclear.



**Figure 2.** Forest plot of comparison of massage versus no treatment for the outcome of BP: (a) SBP and (b) DBP.



**Figure 3.** Forest plot of comparison of massage versus antihypertensive drugs for the outcome of BP: (a) SBP, (b) DBP and (c) BP.

drugs.<sup>77,79–88</sup> Among them, seven trials used BP values to evaluate the effect of massage.<sup>79–85</sup> Although one trial showed significant reduction in both SBP and DBP, it cannot be included for further analysis.<sup>79</sup> Thus, meta-analysis was conducted according to the rest six studies.<sup>80–85</sup> The result indicated that massage combined with antihypertensive drugs was superior compared with the antihypertensive drugs in reducing SBP (MD:  $-6.92$  ( $-10.05$ ,  $-3.80$ );  $P < 0.0001$ ; Figure 4a) and DBP (MD:  $-3.63$  ( $-6.18$ ,  $-1.09$ );  $P = 0.005$ ; Figure 4b).

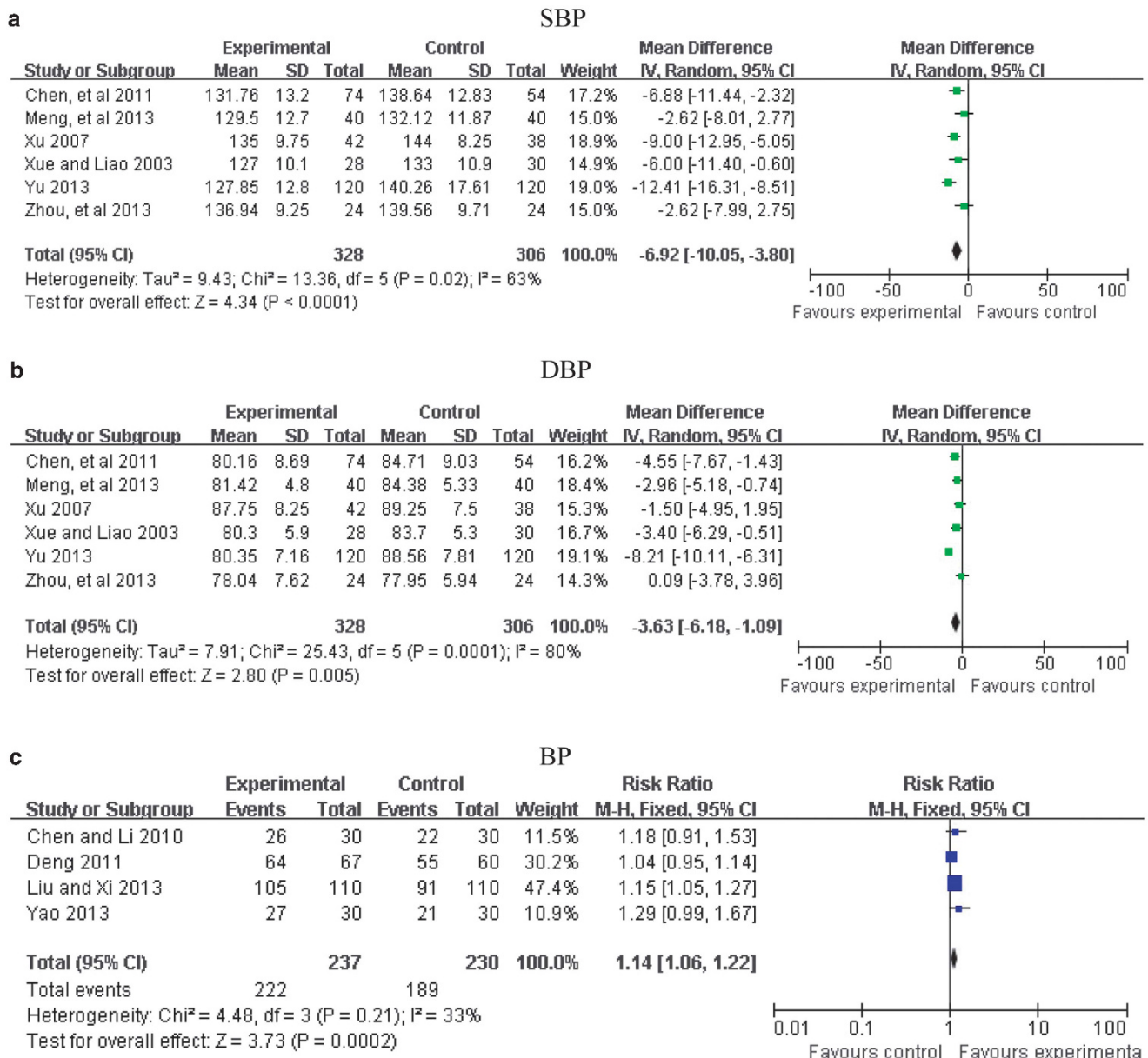
Four trials<sup>77,86–88</sup> summarized the effect of massage on BP into three grades using the efficacy standards introduced above. Meta-analysis also indicated that massage combined with antihypertensive drugs was better than antihypertensive drugs in lowering BP (relative risk: 1.14 (1.06, 1.22);  $P = 0.0002$ ; Figure 4c).

#### Assessment of publication bias

The number of trials in each subgroup was too small to conduct any sufficient additional analysis of publication bias.

#### Adverse effect

All adverse effects were not serious and relieved without special treatment. Nineteen trials (79.17%, 19/24) did not report information about adverse events. Five trials (20.83%, 5/24) reported adverse events, including flushing, fatigue, headache, dizziness, palpitations and ankle edema.<sup>70,73,80,82,83</sup> One trial reported adverse effects in nifedipine group including headache, dizziness, palpitations and ankle edema.<sup>70</sup> One trial reported adverse effects in nifedipine/nitrendipine group with flushing, dizziness, palpitations and fatigue.<sup>73</sup> One trial reported adverse effects in both massage and nifedipine sustained release tablets groups with palpitations, headache and flushing.<sup>80</sup> One trial reported three patients with headache.<sup>82</sup> No adverse effect was found in another trial.<sup>83</sup> Two trials (8.33%, 2/24) reported the number of participants who experienced adverse events.<sup>70,73</sup> Meta-analysis comparing massage with antihypertensive drugs showed massage was potentially safer than antihypertensive drugs based on the incidence of adverse events (relative risk: 0.06 (0.01, 0.28);  $P = 0.0004$ ).



**Figure 4.** Forest plot of comparison of massage combined with antihypertensive drugs versus antihypertensive drugs for the outcome of BP: (a) SBP, (b) DBP and (c) BP.

## DISCUSSION

This study has several important strengths. Massage is a commonly used non-pharmacological therapy for the management of hypertension worldwide. It is the first systematic review of randomized clinical trials on an important topic of massage for hypertensive patients in primary health care. The search for eligible trials was comprehensive. As massage was mainly practiced and researched in China, systematic reviews and meta-analyses should search not only international biomedical databases but also Chinese databases to reduce language bias and selection bias.<sup>90</sup> In our review, four main databases in Chinese were included to retrieve the maximum possible number of RCTs. All current RCTs were conducted in the United States, China and other Asian countries. These articles were published in English and Chinese. Based on our analysis, 15 trials showed that massage combined with antihypertensive drugs may be more effective than antihypertensive drugs alone in lowering both SBP and DBP; 9

trials showed that massage appears beneficial for reducing SBP for hypertensive patients as compared with antihypertensive drugs.

In addition, we rigorously assessed the methodological quality of included trials. The main limitation of the conclusions of our study is the poor quality of the original studies, as this is likely to weaken the reliability of our results. Most of the included trials did not report randomization procedures, allocation concealment, drop-outs, pre-trial estimation of sample size and follow-up. Moreover, double blinding was not applied. Inadequate reporting on the adverse effects of massage was also found in most trials. However, most of them only demonstrated that there is no adverse effect about massage in the 'Introduction' or 'Discussion' section. The safety of massage is still unclear.<sup>91</sup> We failed to perform a funnel plot analysis because of insufficient number of included trials in meta-analysis, so there may be potential publication bias. Therefore, a definite conclusion of massage for EH cannot be drawn based on the available data.



Another critical issue we need to concern is 'Exactly how effective is massage?'. Five trials published in English compared massage with no treatment.<sup>65–69</sup> Meta-analysis showed no more additional beneficial effect for EH. Frequency is one of the most important factors contributing to the positive effects of massage. It was found that massage is practiced by 0.5–1 h per week in these trials. According to TCM theory, it should be conducted every day for relieving uncomfortable symptoms,<sup>28,29,92</sup> which is supported by all other trials published in Chinese.<sup>70–88</sup> However, no trial comparing massage with no treatment conducted by Chinese researchers could be retrieved, which might make the conclusion biased and weaken the credibility. The present meta-analysis may provide an unclear answer and is therefore advised for the further rigorous evaluation under the guidance of TCM theory with the participation of TCM practitioners.<sup>93,94</sup>

## CONCLUSION

In summary, our study indicates that massage has an important role in the management of EH as complementary therapy. That is, massage combined with antihypertensive drugs may be more effective than antihypertensive drugs alone in lowering BP. However, the evidence remains weak because of poor methodological quality. More randomized trials with well design and larger sample size are warranted to validate the use of massage in future. In addition, all clinical trials must be carried out and reported according to the CONSORT Statement.<sup>95,96</sup>

## CONFLICT OF INTEREST

The authors declare no conflict of interests.

## AUTHOR CONTRIBUTIONS

XJX conceived and designed the experiments, performed the experiments, analyzed the data and wrote the manuscript. SJL and YQZ performed the experiments and analyzed the data.

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