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Pelvic Pain

Acupuncture for Chronic Prostatitis/Chronic Pelvic Pain Syndrome: A GRADE-assessed Systematic Review and Meta-analysis

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Abstract

Context: Acupuncture is a promising therapy for relieving symptoms in chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), which affects 9–16% of adult men worldwide.**Objective:** This study aims to explore the efficacy and safety of acupuncture for CP/CPPS.**Evidence acquisition:** Nine electronic databases were searched. Only randomized controlled trials were included. Two reviewers extracted data and assessed the risk of bias of trials using the revised Cochrane risk-of-bias (RoB 2.0) tool. Stata 17.0 was used to analyze the data.**Evidence synthesis:** Twelve trials were included. The results of a meta-analysis showed that acupuncture had larger effect sizes (standardized mean difference [SMD] = -1.20, confidence interval or CI [-1.69, -0.71], acupuncture compared with sham acupuncture; SMD = -1.01, CI [-1.63, -0.38], acupuncture compared with medication; SMD = -0.91, CI [-1.29, -0.54], acupuncture plus medication compared with medication) in reducing the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) total score. In decreasing NIH-CPSI pain domain score, acupuncture also led to larger effect sizes (SMD = -0.94, CI [-1.18, -0.70], acupuncture compared with sham acupuncture; SMD = -1.04, CI [-1.29, -0.79], acupuncture compared with medication; SMD = -0.85, CI [-1.23, -0.48], acupuncture plus medication compared with medication), whereas the effect sizes in the reduction of NIH-CPSI urinary domain and quality of life domain scores were medium. Compared with sham acupuncture and medication, acupuncture appears to be more effective in improving the global response rate. Results from four trials indicated that acupuncture was better than sham acupuncture in decreasing the International Prostate Symptom Score. No serious adverse effects were found in the acupuncture treatment.

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Conclusions: Current evidence supports acupuncture as an effective treatment for CP/CPPS-induced symptoms, particularly in relieving pain. Comprehensive acupuncture treatment according to individual symptoms should be considered in future clinical practice and trials for CP/CPPS.

Patient summary: In this study, we further verified the efficacy of acupuncture in patients with chronic prostatitis/chronic pelvic pain syndrome, especially in reducing pain.

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1. Introduction

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is one of the most common urological diseases in male [1,2]. According to the National Institutes of Health (NIH) consensus classification of prostatitis, CP/CPPS is classified into four categories based on its clinical manifestation and etiology characteristics: category I, acute bacterial prostatitis; category II, chronic bacterial prostatitis; category III, CP/CPPS; and category IV, asymptomatic inflammatory prostatitis [1]. The CP/CPPS (category III prostatitis) is the most common prostatitis syndrome, comprising 90–95% of prostatitis cases [3], with the symptoms of chronic and repeated pain or discomfort in the pelvic region, and possibly urinary or ejaculatory symptoms such as the frequent urinary, dysuria, and incomplete emptying, or the ejaculatory pain [4]. Some patients will also present dizziness, fatigue, memory loss, or even mental symptoms such as depression and anxiety [5].

The pathophysiology of CP/CPPS is still unclear; therefore, the effective treatment remains challenging. The current treatment aims mainly to relieve the clinical symptoms and improve the quality of life (QoL) of CP/CPPS patients [6,7]. Conventional oral medications include experiential antibiotics, α -blockers, anti-inflammatories, phytotherapy, 5- α reductase inhibitors, allopurinol, etc. [8,9]. Nevertheless, the related side effects resulting from these medications such as orthostatic hypotension, gastrointestinal reaction, etc. limit their long-term use, leading to poor adherence of patients; thus, the symptoms of CP/CPPS cannot be controlled effectively and the therapeutic effect cannot be maintained. Current data indicate that there is no ideal treatment for CP/CPPS [9,10].

Acupuncture has widely been used for a variety of urinary diseases and symptoms, including chronic prostatitis. A review indicated that acupuncture might play a role in the treatment of CP/CPPS by regulating the immune system [11], and another systematic review focusing on nonpharmacological interventions manifested that acupuncture or electroacupuncture can improve prostatitis symptoms with less adverse events [12]. Our previous studies found that current evidence supports acupuncture as an effective treatment for releasing the symptom of CP/CPPS with long-term effects, especially in relieving pain; nonetheless, the evidence was limited due to the high risk of bias among included trials and the potential heterogeneity [13,14]. Therefore, considering the newly published clinical studies

of acupuncture for CP/CPPS recently, we aim to update the previous meta-analysis to reassess the efficacy and safety of acupuncture for CP/CPPS to provide further guidance for clinical practice.

2. Evidence acquisition

2.1. Search strategy and selection criteria

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement was followed in this systematic review and meta-analysis (Supplementary Table 1: PRISMA checklist) [15]. The protocol of this review was registered in PROSPERO (CRD42015027522). MEDLINE, CENTRAL, Web of Science, EMBASE, CBM, CNKI, Wanfang database, J-stage, and CINII database were searched before November 11, 2021, dating back to literature when each database was established. MeSH subject words and free search words were used in combination, and the representative search words were “chronic prostatitis/chronic pelvic pain syndrome,” “random,” and “control” (Supplementary Table 2: specific search strategy of PubMed database).

Only randomized controlled trials (RCTs) were included before the retrieval date without restriction for language or publication status before the retrieval date; nonstandard RCTs (without sufficient randomization methods, qualified diagnosis, qualified result reports, and statistical methods), observational studies, case reports, reviews, comments, clinical experience, guidelines, research protocols, animal experiments, mechanism studies, literature analyses, repeatedly published studies, etc. were excluded.

Participants diagnosed with CP/CPPS (category III by the NIH; urogenital pain without any urinary tract infection, lower urinary tract symptoms with or without psychological problems, and sexual dysfunction for at least 3 mo in the past 6 mo) were considered; participants suffering from benign prostatic hypertrophy, acute bacterial prostatitis, prostate cancer, severe heart disease, liver and kidney dysfunction, severe mental illness, or other serious diseases were excluded.

The following eligible comparisons were included: (1) acupuncture compared with medicine, (2) acupuncture supplementing medicine compared with the same medicine, and (3) acupuncture compared with sham acupuncture. The type of acupuncture was any type of needle that was punctured into the skin (acupuncture, electroacupuncture, warm needle, abdominal acupuncture, ear acupuncture,

ture, etc.). Nonpenetrating acupuncture (laser acupuncture, acupoint pressing, and percutaneous or transcutaneous nerve electrical stimulation), acupoint injection, needle knife, and acupuncture combined with Chinese medicine were excluded.

The primary outcome was the change from baseline in the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) [16,17] total score after treatment, secondary outcomes included changes in NIH-CPSI subscale scores (pain, urinary, and QoL domain), International Prostate Symptom Score (IPSS) [18], changes in global response rate, and adverse events. The global response rate was defined as the proportion of patients with a decrease of ≥ 6 points in the total NIH-CPSI score after treatment according to the included trials.

2.2. Study selection

Two reviewers (Z.Q. and J.G.) respectively imported the preliminarily retrieved studies into EndNote X7 software for screening according to the eligibility criteria. First, the repetitive studies were screened out, followed by the review according to the title or/and abstract, and then the full-text review of the studies that were uncertain to be included was carried out to finally determine the studies eligible for inclusion. If the inclusion results were inconsistent between the two reviewers, these should be discussed with the third reviewer (J.W.).

2.3. Data extraction

The data extracted in this study were as follows: the first author, country, published year, diagnosis, sample size, patients' age, intervention information of treatment group and control group, treatment period, follow-up period, and outcomes, in which the change values of means and standard deviations were used as the scoring indicators. When the data in the trial's report are insufficient, we tried to contact the author. After two reviewers (Z.Q. and J.G.) extracted the data independently, the third reviewer (J.W.) checked and resolved the differences.

2.4. Risk of bias assessment

The revised Cochrane risk-of-bias (RoB 2) tool was used to assess the risk of bias [19] by two researchers (J.G. and Z. Q.) to evaluate each of the included RCTs in six aspects: randomization process, deviations from the intended interventions, missing data, outcome measurements, selection of the reported results, and overall bias. The evaluation criteria were "low risk," "high risk," and "some concern," and the results were collated by a third researcher (J.W.).

2.5. Statistical analysis

Stata 17.0 software (Stata Corp., College Station, TX, USA) was used for the following analysis: (1) a random-effect model was adopted for data syntheses; (2) standardized mean difference (SMD) and odds ratio (OR) were utilized as the effect values of continuous variables and dichoto-

mous variables, respectively, and 95% confidence interval (CI) was applied by both variables; (3) p values of < 0.05 were considered statistically significant; (4) as two parameters to evaluate heterogeneity, the Q statistic with $p < 0.05$ or $I^2 > 50\%$ was considered to have high heterogeneity, and otherwise considered low heterogeneity; and (5) a sensitivity analysis or subgroup analysis was used in the case of high heterogeneity or different intervention methods in the combined analysis.

2.6. GRADE assessment

As a transparent and structured quality rating system, Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) was used in this study to evaluate and grade each combined analysis, which was divided into four evaluation grades: high, moderate, low, and very low.

3. Evidence synthesis

3.1. Literature search and study selection

A total of 2577 articles were collected through the initial search, and 1576 were obtained after screening out the repeatedly published or same data. After screening out the nonconforming literature by title or abstract, 15 studies remained. Finally, three articles were screened out and 12 articles were included [20–31]. The detailed screening flow chart is shown in Figure 1.

In the 12 studies included, patients from four countries were involved. Six studies were published in English and six were published in Chinese, with a total of 1188 patients. The published years ranged from 2008 to 2021. The shortest research period was 24 d and the longest was 10 wk. The sample size ranged from 24 to 440 cases. Table 1 summarizes the characteristics of included studies, and Supplementary Table 3 presents the details of eligibility criteria, severity of disease, and previous treatment.

In the evaluation of risk of bias, all the included RCTs did not cause different risks in deviations from intended interventions, so these were rated to be of low risk. In the process of randomization, six studies were rated to have "some concerns" because these did not elaborate the allocation and concealment strategy of the intervention process, so five of them were rated to have some concerns in the overall risk evaluation. In addition, six studies were rated to be of a high risk because these did not provide blind information. Five trials were rated to have a high risk in terms of selective reporting of results or data integrity due to the lack of subscores or adverse event reports of NIH-CPSI, resulting in a high risk in the overall evaluation. Supplementary Table 4 presents the risk of bias judgments for included RCTs. Table 2 summarizes the GRADE results.

3.2. NIH-CPSI total score

The total score of NIH-CPSI was reported in all 12 RCTs, and a subgroup analysis was carried out according to different intervention methods (Fig. 2A). The results showed that in

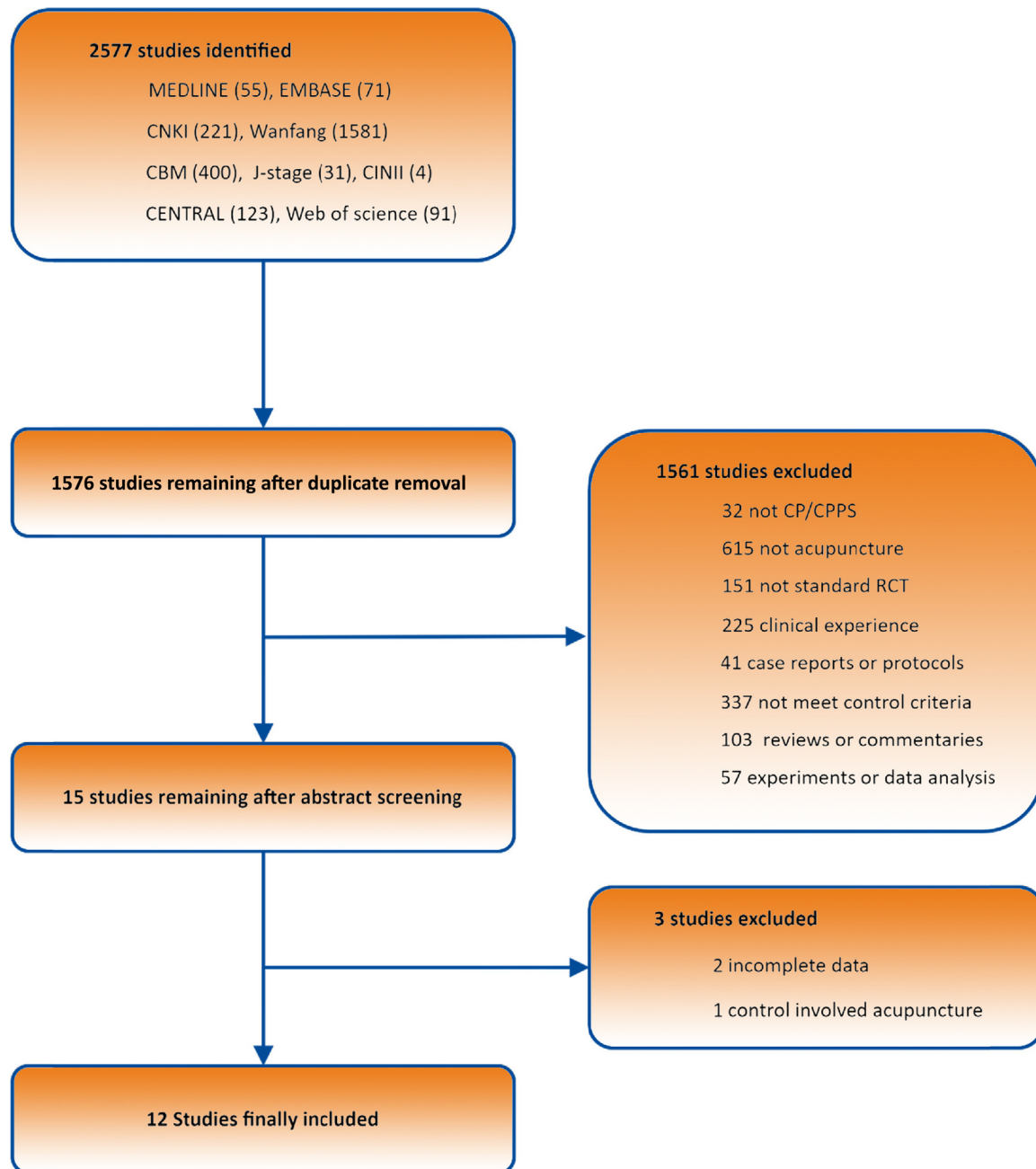


Fig. 1 – Flowchart of trial selection process for this systematic review. MEDLINE, CENTRAL, Web of Science, and EMBASE are English databases. CBM, CNKI, and Wanfang database are Chinese databases. J-stage and CINII database are Japanese databases. CP/CPPS = chronic prostatitis/chronic pelvic pain syndrome; RCT = randomized controlled trial.

the NIH-CPSI total score, acupuncture combined with medication was significantly better than single medication (SMD = -0.91 , 95% CI $[-1.29, -0.54]$, $p < 0.05$; $Q [1] < 0.001$, $p = 0.99$, $I^2 = 0$), and the heterogeneity between studies was low. Acupuncture alone was significantly more effective than medication, but the heterogeneity between studies was higher (SMD = -1.01 , 95% CI $[-1.63, -0.38]$, $p < 0.05$; $Q [5] = 36.49$, $p < 0.001$, $I^2 = 86.90\%$). The efficacy of acupuncture alone was also significantly better than that of sham acupuncture alone (SMD = -1.20 , 95% CI $[-1.69, -0.71]$, $p < 0.05$; $Q [5] = 36.09$, $p < 0.001$, $I^2 = 85.91\%$) with

high heterogeneity. The sensitivity analysis speculated that the heterogeneity may be due to the differences in treatment time and acupuncture methods between studies.

3.3. NIH-CPSI pain domain score

A total of 11 RCTs reported the NIH-CPSI pain domain score (Fig. 2B). The subgroup analysis results showed that acupuncture combined with medication were significantly better than single medication (SMD = -0.85 , 95% CI $[-1.23,$

Table 1 – Characteristics of the included randomized controlled trials

Study ID	Location (published language)	Sample size (T/C)	Patient age (yr)	Diagnosis	Intervention	Needle parameter/depth/acupoints	Comparison	Duration of treatment (acupuncture treatment time)	Outcomes	Adverse events
Lee (2008) [20]	Malaysia (English)	89 (44/45)	T: 40.9 ± 11.0 C: 42.8 ± 9.4	CP/CPPS	Acupuncture	0.3 mm stainless needles/40–60 mm/ CV1, CV4, SP6, SP9	Sham acupuncture	10 wk (30 min, twice a week)	NIH-CPSI, IPSS, IIEF, response rate	T: 8 C: 5
Lee (2009) [21]	Korea (English)	24 (12/12)	T: 39.8 ± 5.8 C: 36.4 ± 5.8	CP/CPPS (category III)	Acupuncture	0.25 mm stainless needles/30 mm/ BL32, BL33, GB30	Sham acupuncture	6 wk (20 min, twice a week)	NIH-CPSI, IPSS, response rate	T: 0 C: 1
Sahin (2015) [22]	Turkey (English)	91 (45/46)	T: 32.1 ± 7.2 C: 32.8 ± 7.0	CP/CPPS (category IIIB)	Acupuncture	0.3 mm stainless needles/25–30 mm/ BL33, BL34, BL54, CV1, CV4, SP6, SP9	Sham acupuncture	6 wk (20 min, once a week)	NIH-CPSI, response rate	NR
Qin (2018) [23]	China (English)	68 (34/34)	T: 33.8 ± 6.8 C: 35.1 ± 9.6	CP/CPPS	Acupuncture	0.3 mm stainless needles/50–60 mm/ BL33, BL35, BL23, SP6	Sham acupuncture	8 wk (30 min, three times a week)	NIH-CPSI, IPSS, response rate	T: 4 C: 1
Zhao (2014) [31]	China (Chinese)	58 (29/29)	T: 32 ± 6.91 C: 33 ± 7.39	CP/CPPS (category IIIB)	Acupuncture	NR/NR/LU7, SI3, SP4	Sham acupuncture	4 wk (20 min, twice a week)	NIH-CPSI	T: 1 C: 0
Sun (2021) [24]	China (English)	440 (220/ 220)	T: 35.5 ± 8.0 C: 36.1 ± 7.9	CP/CPPS	Acupuncture	0.3 mm stainless needles/50–60 mm/ BL33, BL35, BL23, SP6	Sham acupuncture	8 wk (30 min, three times a week from the 1st to 4th week, twice a week from the 5th to 8th week)	NIH-CPSI, IPSS, response rate	T: 20 C: 14
Zhao (2014) [31] ^a	China (Chinese)	58 (29/29)	T: 32 ± 6.91 C: 31 ± 6.78	CP/CPPS (category IIIB)	Acupuncture	NR/NR/LU7, SI3, SP4	Tamsulosin 0.2 mg daily	4 wk (20 min, twice a week)	NIH-CPSI	T: 1 C: 1
Liu (2012) [25]	China (Chinese)	65 (33/32)	T: 33.2 ± 10.6 C: 31.8 ± 8.8	CP/CPPS	Acupuncture	0.3 mm stainless needles/100 mm for CV54, 30 mm for others/CV54, CV4, ST28, SP6, LIV3, EX-HN1	Prostate 70 mg twice a day and fluoxetine 20 mg daily	4 wk (20 min, three times a week)	NIH-CPSI, response rate	NR
Qi (2012) [26]	China (Chinese)	60 (30/30)	T: 32.60 ± 7.04 C: 34.77 ± 10.88	CP/CPPS (category III)	Acupuncture plus medication	NR/25–50 mm/CV1, CV3, CV4, SP9, SP10	Medication	4 wk (30 min, twice a week)	NIH-CPSI	NR
Ma (2014) [27]	China (Chinese)	66 (37/29)	T: 31 ± 8.0 C: 33 ± 7.0	CP/CPPS (category IIIB)	Acupuncture	NR/NR/SP6, RN2, RN1, ST36, RN3, BL23	Medication	8 wk (NR, once every 2 wk)	NIH-CPSI	NR
Kucuk (2015) [28]	Turkey (English)	54 (26/28)	T: 33.3 ± 7.84 C: 33.3 ± 7.84	CP/CPPS (category IIIB)	Acupuncture	0.25 mm/40 mm/BL32, GB41, LR3, SP6, SP8, LI4	Medication	7 wk (NR, twice a week)	NIH-CPSI, response rate	T: 0 C: 0
Chen (2016) [29]	China (Chinese)	59 (30/29)	T: 34 ± 6 C: 34 ± 7	CP/CPPS	Acupuncture plus medication	0.3 mm/25–35 mm/DU24, DU22, DU21, DU20, BL6, BL7, BL8, DU18, DU17, BL9, BL10, RN3, RN4, ST29, K112, ST31, BL28, BL32, BL54, GB30	Medication	24 days (30 min, once a day)	NIH-CPSI, Response rate	NR
Chen (2016) [29] ^a	China (Chinese)	58 (29/29)	T: 33 ± 7 C: 34 ± 7	CP/CPPS	Acupuncture	0.3 mm/25–35 mm/DU24, DU22, DU21, DU20, BL6, BL7, BL8, DU18, DU17, BL9, BL10, RN3, RN4, ST29, K112, ST31, BL28, BL32, BL54, GB30	Medication	24 d (30 min, once a day)	NIH-CPSI	NR
Geng (2016) [30]	China (Chinese)	56 (28/28)	T: 29.13 ± 13.56 C: 28.84 ± 14.63	CP/CPPS (category IIIB)	Acupuncture	NR/NR/EX-HN1, DU20, RN3, RN4, RN6, SP9, GB34, SP6, ST36	Medication	4 wk (30 min, once every 2 d)	NIH-CPSI, response rate	NR

C = control group; CP/CPPS = chronic prostatitis/chronic pelvic pain syndrome; IIEF = International Index of Erectile Function; IPSS = International Prostate Symptom Score; NIH = National Institutes of Health; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; NR = not reported; T = treatment group.

^a Different groups in the same study.

Table 2 – GRADE summary

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE) ^a
	Assumed risk: control	Corresponding risk: treatment			
NIH-CPSI total score (Acu plus Med vs Med)	The mean medication in the control groups was –7.41	The mean 0.91 lower (1.29 lower to 0.54 lower)	–	119 (2)	⊕⊕○○ Low
NIH-CPSI total score (Acu vs Med)	The mean medication in the control groups was –6.53	The mean 1.01 lower (1.63 lower to 0.38 lower)	–	357 (6)	⊕⊕○○ Low
NIH-CPSI total score (Acu vs sham Acu)	The mean sham acupuncture in the control groups was –5.05	The mean 1.20 lower (1.69 lower to 0.71 lower)	–	769 (6)	⊕⊕○○ Moderate
NIH-CPSI pain domain score (Acu plus Med vs Med)	The mean medication in the control groups was –3.39	The mean 0.85 lower (1.23 lower to 0.48 lower)	–	119 (2)	⊕⊕○○ Low
NIH-CPSI pain domain score (Acu vs Med)	The mean medication in the control groups was –3.14	The mean 1.04 lower (1.29 lower to 0.79 lower)	–	292 (5)	⊕⊕○○ Low
NIH-CPSI pain domain score (Acu vs sham Acu)	The mean sham acupuncture in the control groups was –2.43	The mean 0.93 lower (1.43 lower to 0.44 lower)	–	769 (6)	⊕⊕⊕○ Moderate
NIH-CPSI urinary domain score (Acu vs Med)	The mean medication in the control groups was –2.22	The mean 0.35 higher (0.57 lower to 1.28 higher)	–	168 (3)	⊕⊕○○ Low
NIH-CPSI urinary domain score (Acu vs sham Acu)	The mean sham acupuncture in the control groups was –1.14	The mean 0.76 lower (1.06 lower to 0.45 lower)	–	769 (6)	⊕⊕⊕○ Moderate
NIH-CPSI QoL domain score (Acu vs Med)	The mean medication in the control groups was –1.94	The mean 0.68 lower (1.27 lower to 0.09 lower)	–	168 (3)	⊕⊕○○ Low
NIH-CPSI QoL domain score (Acu vs sham Acu)	The mean sham acupuncture in the control groups was –1.77	The mean 0.75 lower (1.03 lower to 0.47 lower)	–	769 (6)	⊕⊕⊕○ Moderate
Global Response rate (Acu vs Med)	698 per 1000	907 per 1000 (852–943)	OR 3.55 (1.70–7.40)	246 (4)	⊕⊕○○ Low
Global Response rate (Acu vs sham Acu)	366 per 1000	694 per 1000 (440–867)	OR 5.15 (2.21–12.01)	708 (5)	⊕⊕⊕○ Moderate
IPSS (Acu vs sham Acu)	The mean sham acupuncture in the control groups was –4.10	The mean 0.40 lower (0.56 lower to 0.24 lower)	–	620 (6)	⊕⊕⊕○ Moderate
Adverse events (Acu vs sham Acu)	62 per 1000	240 per 1000 (127–408)	OR 1.60 (0.90–2.84)	678 (5)	⊕⊕⊕○ Moderate

Acu = acupuncture; CI = confidence interval; GRADE = Grades of Recommendation, Assessment, Development, and Evaluation; IPSS = International Prostate Symptom Score; Med = medication; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; OR = odds ratio; QoL = quality of life; sham Acu = sham acupuncture.

^a Low (low certainty): our confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect. Moderate (moderate certainty): we are moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

–0.48], $p < 0.05$; $Q [1] = 0.01$, $p = 0.93$, $I^2 = 0$), and the heterogeneity between studies was low; acupuncture alone was significantly more effective than drug therapy. Similarly, the heterogeneity between studies was also low (SMD = –1.04, 95% CI [–1.29, –0.79], $p < 0.05$; $Q [4] = 3.93$, $p = 0.42$, $I^2 = 1.27\%$). The effect of simple acupuncture is also significantly better than that of simple sham acupuncture (SMD = –0.93, 95% CI [–1.43, –0.44], $p < 0.05$), but the heterogeneity between studies is high ($Q [5] = 31.96$, $p < 0.001$, $I^2 = 87.17\%$); the sensitivity analysis speculates that the heterogeneity may come from the difference of sham acupuncture methods.

3.4. NIH-CPSI urinary domain score

Among the included studies, seven RCTs reported the NIH-CPSI urinary domain score, and a subgroup analysis was carried out according to different intervention methods (Fig. 2C). The results showed that acupuncture alone was significantly more effective than sham acupuncture (SMD = –0.76, 95% CI [–1.06, –0.45], $p < 0.05$; $Q [5] = 16.24$, $p = 0.01$, $I^2 = 65.79\%$), but not superior to medication (SMD = 0.35, 95% CI [–0.57, 1.28], $p > 0.05$; $Q [2] = 17.12$, $p < 0.001$, $I^2 = 88.53\%$). There was high heterogeneity in both groups.

3.5. NIH-CPSI QoL domain score

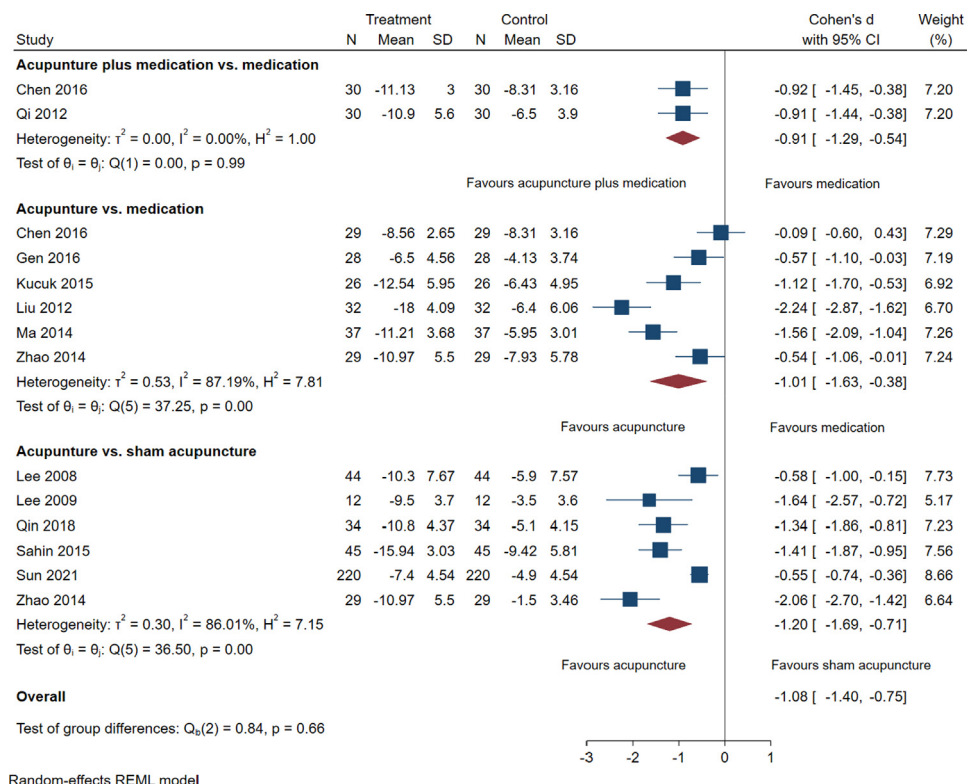
Eight RCTs reported the NIH-CPSI QoL domain score (Fig. 2D). A subgroup analysis showed that in the score results, acupuncture alone was more effective than medication (SMD = –0.68, 95% CI [–1.27, –0.09], $p < 0.05$; $Q [2] = 6.99$, $p = 0.03$, $I^2 = 71.98\%$) and sham acupuncture (SMD = –0.75, 95% CI [–1.03, –0.47], $p < 0.05$; $Q [5] = 14.04$, $p = 0.02$, $I^2 = 59.94\%$), but both had high heterogeneity.

3.6. Global response rate

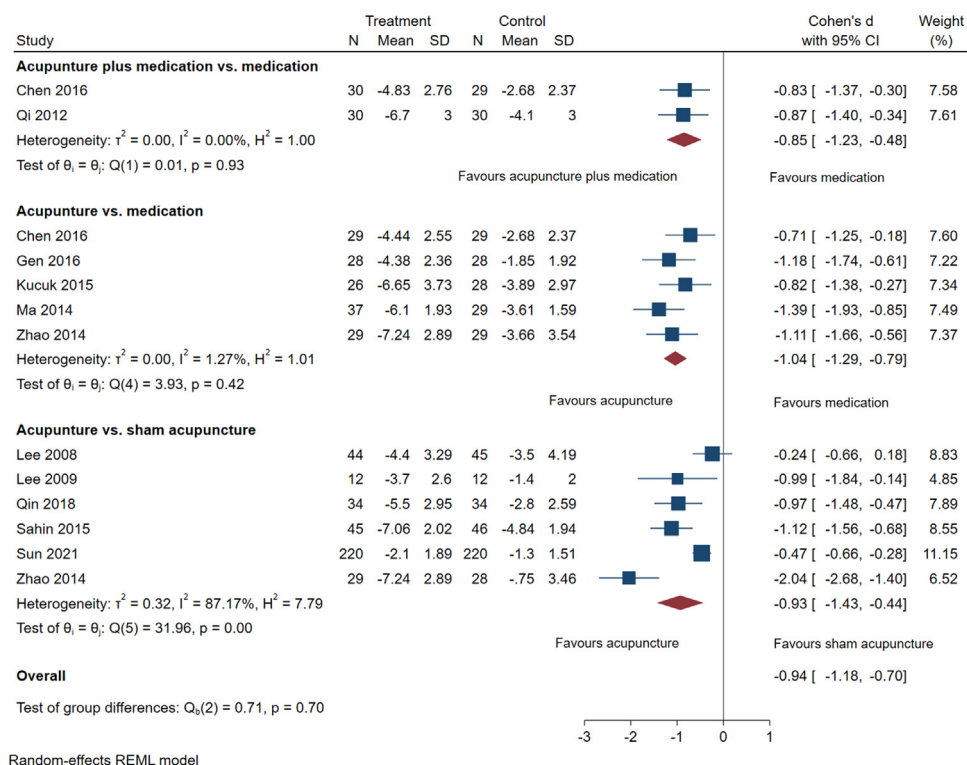
Nine RCTs reported the global response rate (Fig. 3A). A subgroup analysis showed that the results of acupuncture were significantly better than those of medication (OR = 3.55, 95% CI [1.70, 7.40], $p < 0.05$; $Q [3] = 3.07$, $p = 0.38$, $I^2 = 0$) and sham acupuncture (OR = 5.15, 95% CI [2.21, 12.01], $p < 0.05$; $Q [4] = 8.98$, $p = 0.06$, $I^2 = 62.31\%$), but the latter had high heterogeneity.

3.7. International Prostate Symptom Score

Four studies reported IPSS results (Fig. 3B), the treatment of acupuncture was significantly better than that of sham acupuncture (SMD = –0.40, 95% CI [–0.56, –0.24],

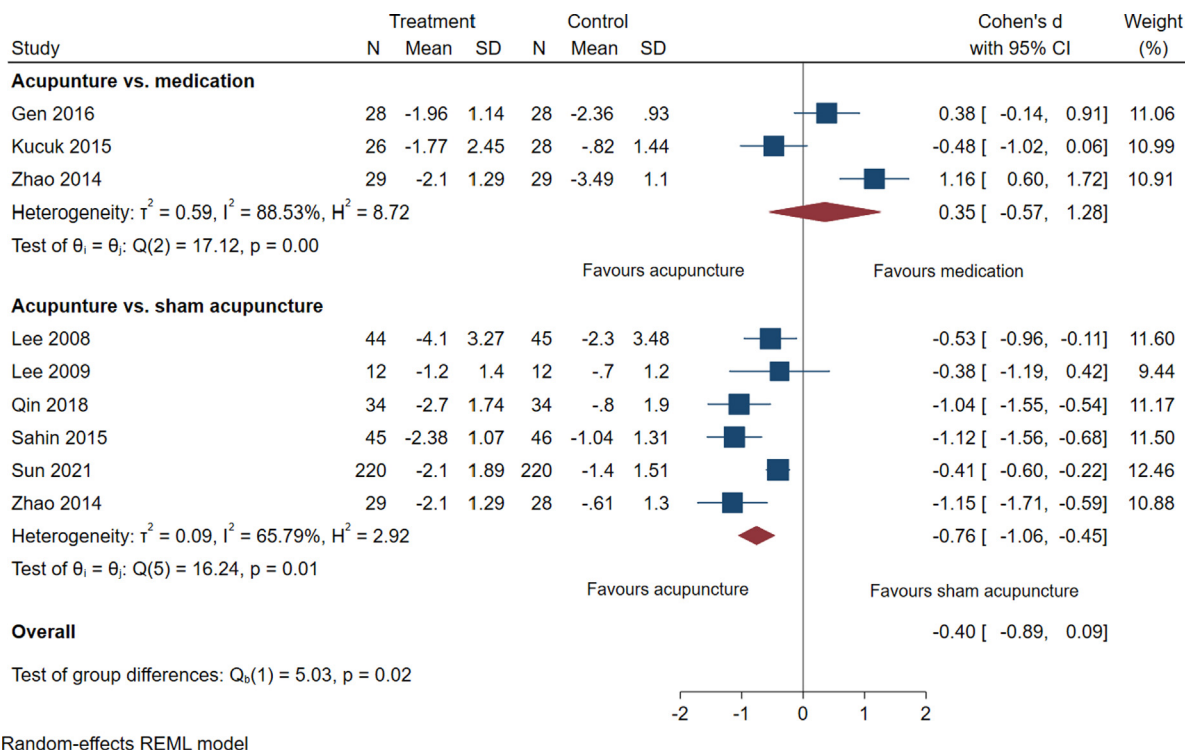


(a)



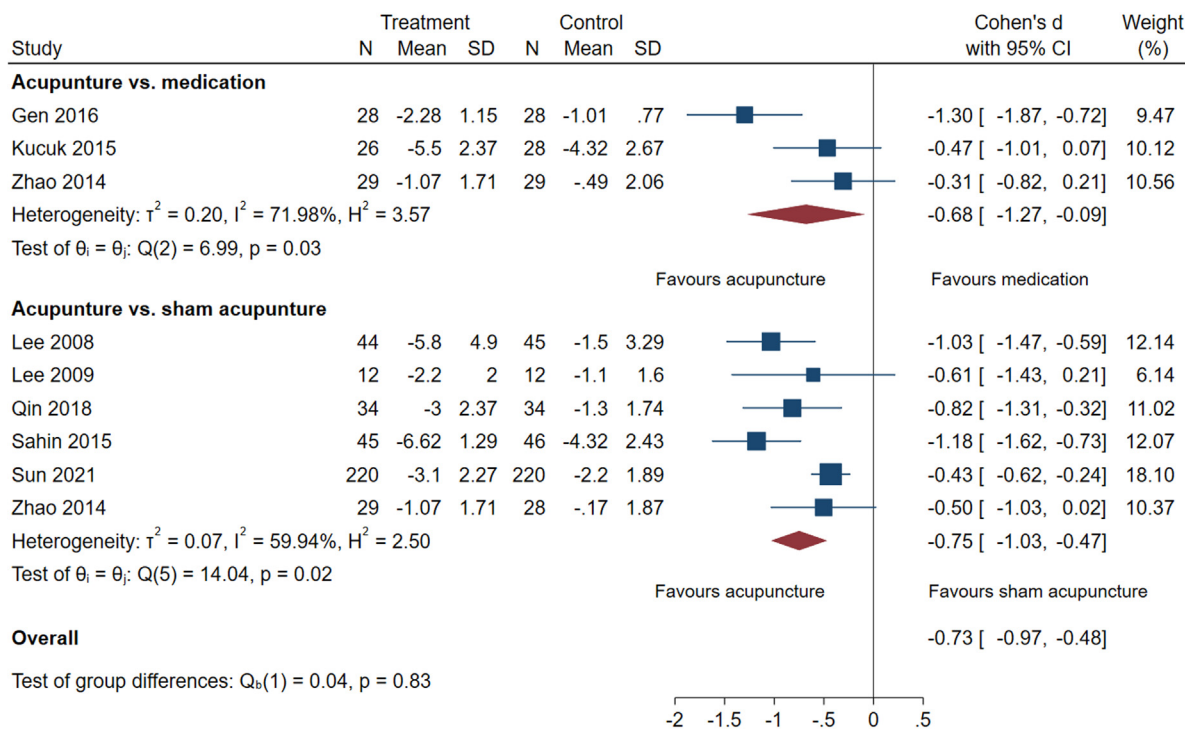
(b)

Fig. 2 – Forest plots of subgroup analysis on the (A) NIH-CPSI total score, (B) NIH-CPSI pain domain score, (C) NIH-CPSI urinary domain score, and (D) NIH-CPSI QoL domain score. CI = confidence interval; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index; QoL = quality of life; SD = standard deviation.



Random-effects REML model

(c)



Random-effects REML model

(d)

Fig. 2 (continued)

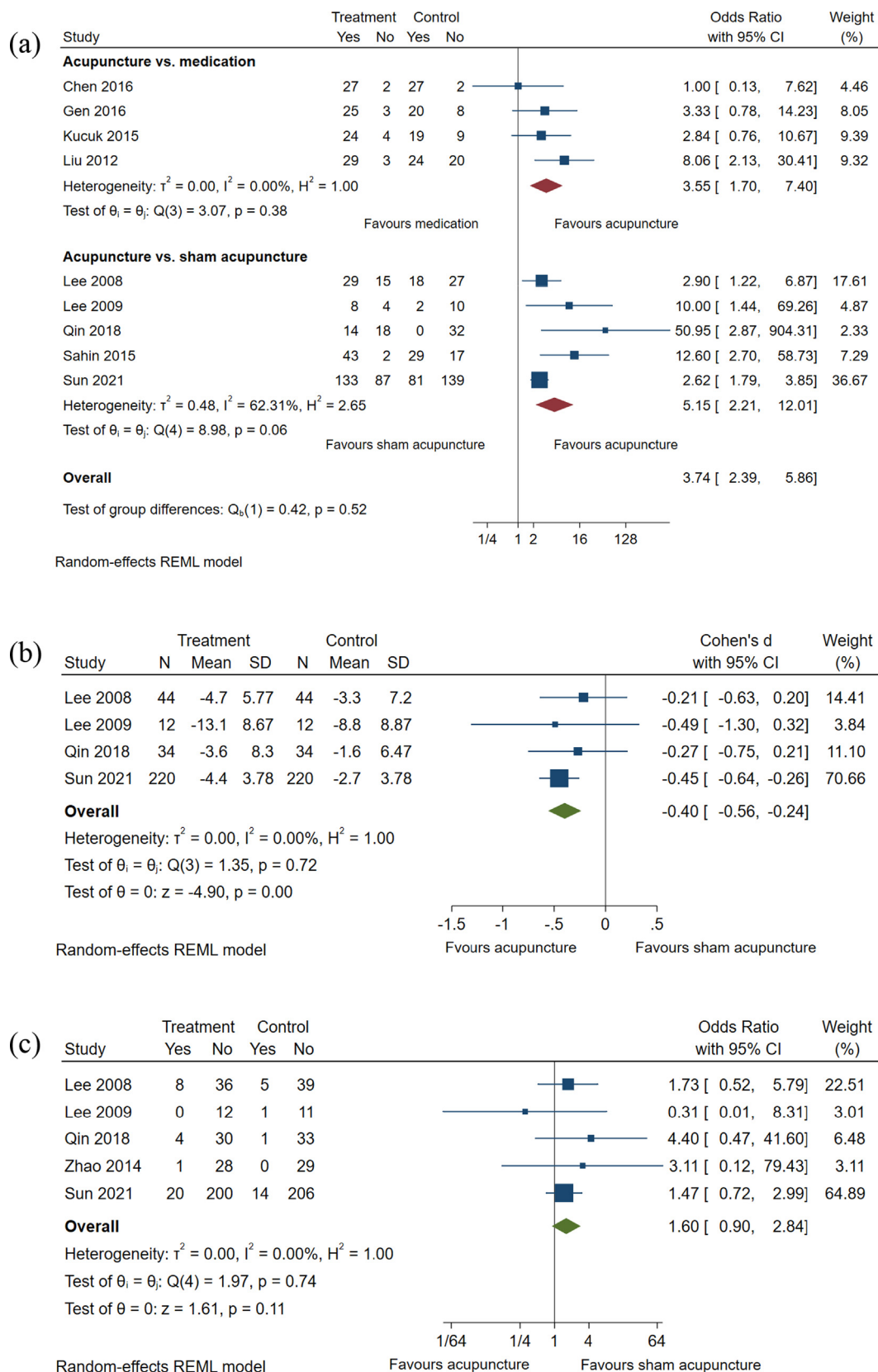


Fig. 3 – Forest plots of subgroup analysis on the (A) global response rate, (B) IPSS, and (C) adverse events. CI = confidence interval; IPSS = International Prostate Symptom Score.

$p < 0.001$; $Q(3) = 1.35$, $p = 0.72$, $I^2 = 0$), and the heterogeneity between studies was low.

3.8. Adverse events

Five studies reported adverse events (Fig. 3C), most of which were mild subcutaneous hematoma. The results showed that there was no significant difference between the adverse events caused by acupuncture and sham acupuncture, and the heterogeneity was low (OR = 1.60, 95% CI [0.90, 2.84], $p = 0.11$; $Q(4) = 1.97$, $p = 0.74$, $I^2 = 0$).

3.9. Discussion

This systematic review was an update to a previous review of acupuncture for CP/CPPS [13], and the results suggested that acupuncture might be beneficial in the treatment of CP/CPPS, especially in reducing the NIH-CPSI total and pain scores. Acupuncture has widely been used for patients with CP/CPPS in relieving symptoms, which has been recommended by the 2022 European Association of Urology guidelines on chronic pelvic pain. The guidelines state that the use of acupuncture is recommended to improve patients' symptoms and QoL, although no conclusions have been given about the durability of acupuncture's efficacy [7]. Until now, the etiology and pathological factors of CP/CPPS are still unknown; therefore, symptom control is the main goal in the treatment of patients with CP/CPPS through evaluating the NIH-CPSI score [32]. Research shows that many current medications for CP/CPPS are largely ineffective, including experiential antibiotics, α -blockers, and anti-inflammatories [9,10]; thus, the results of this review provide a promising therapy for patients with CP/CPPS. However, there is still room to improve the quality of clinical evidence. In this review, we included RCTs comparing acupuncture with sham acupuncture/medication or comparing acupuncture and medication with the same medication. Of the 12 trials included in the overall ROB, seven were rated to have a "high risk of bias" [25–31] and five to have "some concerns" [20–24] with low to moderate GRADE certainty.

The effect size evaluating the NIH-CPSI score is also known as Cohen's d , with measures of the small, medium, and large defined as 0.2, 0.5, and 0.8, respectively [33]. In trials comparing acupuncture and sham acupuncture (acupuncture vs sham acupuncture) or comparing acupuncture plus medication with medication alone (acupuncture plus medication vs medication), the effect size of Cohen's d in the NIH-CPSI total score was -1.20 (95% CI $[-1.69, -0.71]$) and -0.91 (95% CI $[-1.29, -0.54]$), separately, which were both >0.8 and signified a large difference between groups. Besides, the effect size is large in reducing the NIH-CPSI pain domain score (acupuncture plus medication vs medication: -0.85 , 95% CI $[-1.23, -0.48]$; acupuncture vs sham acupuncture: -0.93 , 95% CI $[-1.43, -0.44]$) and medium in reducing the NIH-CPSI urinary domain and QoL domain scores ($0.5 < \text{effect size} < 0.8$). The current level of evidence supports the benefits of acupuncture for relieving the symptoms of CP/CPPS, especially in pain relief. The data of acupuncture versus sham acupuncture were observed to have high heterogeneity, which might be corre-

lated with the different degrees of severity of disease of the included population, different choices of acupoints, and different frequencies and treatment periods of acupuncture. A recent study with 440 participants has added robust evidence to support the effect of acupuncture on CP/CPPS.

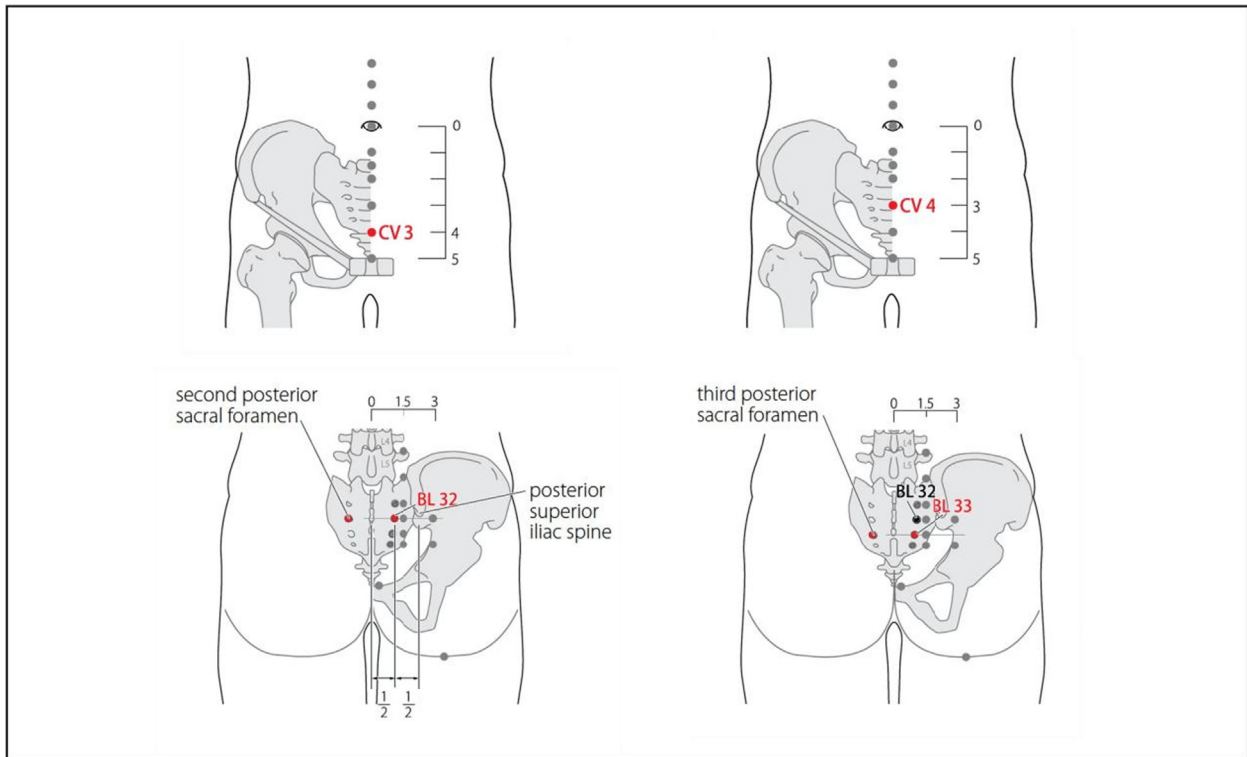
In positive controlled trials, acupuncture leads to a greater decrease in the total NIH-CPSI and pain domain scores (effect size >0.8); in terms of urinary symptoms and QoL improvement, the effect size of acupuncture was medium. The combining data showed relatively significant heterogeneity, which might be correlated to the different sorts of medicine (nonsteroidal anti-inflammatory drugs, α -blockers, or antibiotics); besides, all the five trials included, which used acupuncture versus medication, were evaluated as having a high risk of bias. Thus, due to the current evidence, conclusions on the results of acupuncture compared with medications are limited. More studies comparing acupuncture with medications should be carried out, and the factorial design is encouraged to use for better blinding and interpretation of the effect of acupuncture and medication.

There are distinct clinical symptoms of chronic prostatitis, and the main manifestations of each patient are also different, such as pain, urgent urination, and obvious mental disorders. Therefore, the urinary, psychosocial, organ-specific, infection, neurological/systemic and tenderness (UPOINT) treatment system was advocated to treat the patient with multimodal therapy based on their clinical phenotype and symptoms [34]. The UPOINT system classifies patients into urinary, psychological, organ-specific, infection, neurological/systemic, and tenderness domains [35]. The concept of individualized therapy is highly consistent with the idea of individualized therapy in traditional Chinese medicine. In future clinical practice or clinical trial by using acupuncture, the choice of the acupoints should be according to different clinical manifestations of patients. For patients with urinary frequency and urgency, GV3

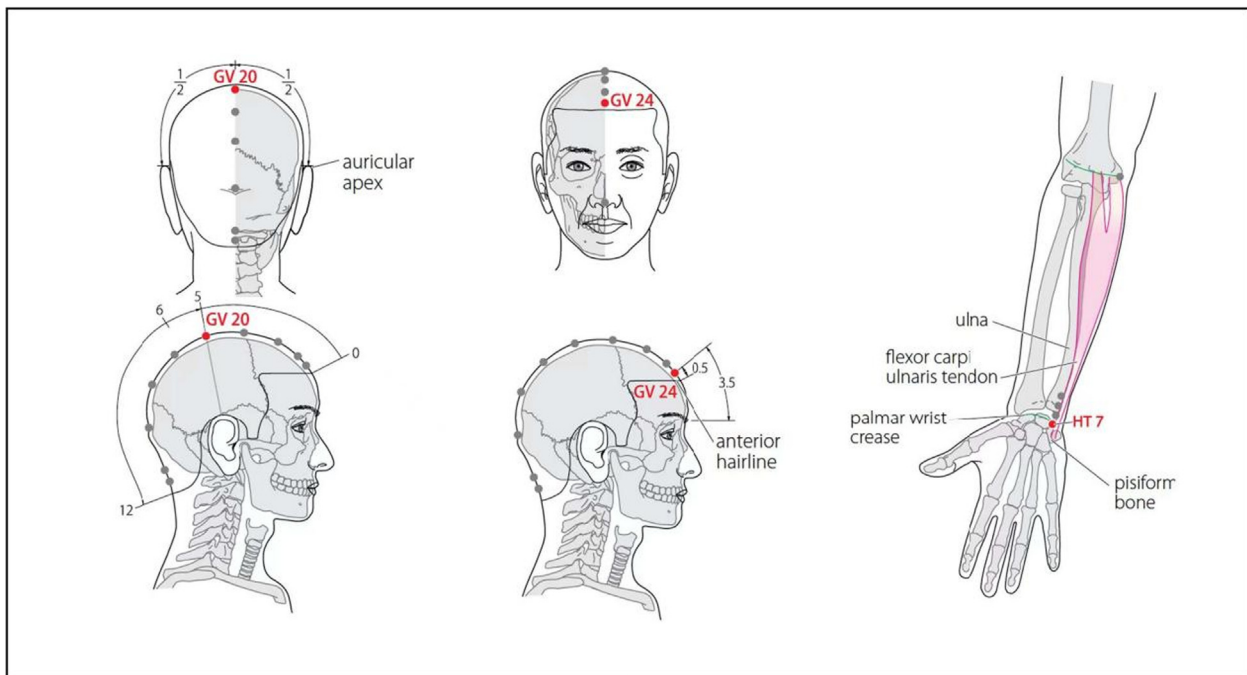
Table 3 – Elements of the UPOINT classification system and acupoint selection

Domain	Diagnostic criteria	Potential acupuncture therapies
Urinary	Associated lower urinary tract symptoms	BL32 (Ciliao), BL33 (Zhongliao), BL35 (Huiyang)
Psychological	Clinical depression with a catastrophic attitude about CP/CPPS symptoms	EX-HN3 (Yingtang), DU20 (Baihui), GV24 (Shenting)
Organ specific	Pain associated with the voiding cycle or prostate-specific tenderness	BL32 (Ciliao), BL33 (Zhongliao), BL35 (Huiyang)
Infection	Positive culture of either urine or expressed prostatic secretions	ST36 (Zusanli)
Neurological/systemic	Pain outside the pelvis or other pain disorders	GV3 (Zhongji), GV4 (Guanyuan), BL23 (Shenshu)
Tenderness	Pain or tenderness in the lower abdominal or pelvic musculature as palpated on physical exam	Electroacupuncture, warm needle moxibustion

CP/CPPS = chronic prostatitis/chronic pelvic pain syndrome; UPOINT = urinary, psychosocial, organ-specific, infection, neurological/systemic and tenderness.



(a)



(b)

Fig. 4 – (A) Acupoint location for patients with urinary frequency and urgency. CV3: Zhongji, on the lower abdomen, 4 B-cun inferior to the center of the umbilicus, on the anterior median line; CV4: Guanyuan, on the lower abdomen, 3 B-cun inferior to the center of the umbilicus, on the anterior median line; BL32: Ciliao, in the sacral region, in the second posterior sacral foramen; BL33: Zhongliao, in the sacral region, in the third posterior sacral foramen. (B) Acupoint location for patients with mental disorder such as anxiety and depression. GV20: Baihui, on the head, 5 B-cun superior to the anterior hairline, on the anterior median line; GV24: Shenting, on the head, 0.5 B-cun superior to the anterior hairline, on the anterior median line; HT7: Shenmen, on the anteromedial aspect of the wrist, radial to the flexor carpi ulnaris tendon, on the palmar wrist crease. The pictures of acupoints location are arising from WHO standard acupuncture point locations in the Western Pacific region [36].

(Zhongji), GV4 (Guanyuan), BL32 (Ciliao), and BL33 (Zhongliao) could be considered to deal with the lower urinary tract symptoms; for patients with mental disorders such as anxiety and depression, GV20 (Baihui), GV24 (Shenting), and HT7 (Shenmen) could be taken in account to regulate the mind (Table 3 and Fig. 4A and 4B [36]).

In recent findings, extracorporeal shock wave therapy has also shown good efficacy in patients with CP/CPPS, and the results of a network meta-analysis indicated that it was superior to acupuncture in short-term efficacy [37,38]. Owing to the insufficient number of patients included in these studies, we cannot recommend between extracorporeal shock wave therapy and acupuncture, but this is a direction of research that deserves more attention in the future. The limitations of this study should be noted. First, many of the trials lacked the details of concealment. Second, due to the characteristic of acupuncture, it is difficult to conduct blinding in patients and acupuncturists, especially in the trial using the medication as the control.

4. Conclusions

The evidence supported acupuncture as an effective treatment to improve symptoms of CP/CPPS, especially in pain relief. Compared with sham acupuncture, acupuncture leads to significant reductions in the pain domain of NIH-CPSI and brings a medium relief in urinary symptoms and QoL domains of the NIH-CPSI. Compared with medication, acupuncture might be more effective in reducing the NIH-CPSI total and pain scores. Nonetheless, current existing evidence allows limited conclusions to be reached through comparing acupuncture and medicine, and additional trials are needed, especially a factorial design. In terms of adverse events, there is not much difference between acupuncture and sham acupuncture. Moreover, comprehensive acupuncture treatment according to individual symptoms for patients with CP/CPPS should be considered.

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Study concept and design: Qin, Wu.

Acquisition of data: Qin, Guo, Chen, Wu.

Analysis and interpretation of data: Qin, Guo, Chen, Wu.

Drafting of the manuscript: Qin, Guo.

Critical revision of the manuscript for important intellectual content: Chen, Wu.

Statistical analysis: Qin.

Obtaining funding: Wu.

Administrative, technical, or material support: Wu, Chen.

Supervision: Wu.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.euros.2022.10.005>.

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