Acupuncture Therapy for Vascular Cognitive Impairment management: A Systematic Review and Network Meta-Analysis

Liao, YL1; Hsu, PS2; Shen, YY3; Lee, CT4; Lan, CC5; Tzeng, IS6; Liu, GT7; Hsieh, PC8.

Review question / Objective: P-Diagnosis of VCI based on any established and validated diagnostic definitions (eg. DSM-IV). I-Acupuncture, MA, EA, SA, auricular acupuncture, fire needling, and warm needling. C-Sham acupuncture, western medicine (WM), usual care (UC), or cognitive rehabilitation. O-Primary outcomes: 1) Cognitive function: MMSE, HDS, MoCA and ADAS-cog. 2) Activities of daily living: ADLS, BI and FAQ. Secondary outcomes: Risk ratio of the presence of severe adverse effect. S-RCTs regardless of publication language restrictions. (allocation of participants by random sequence).

Study designs to be included: Only randomized controlled trials (RCTs) were included in the analysis. The population included are patients diagnosed with VCI and related diagnosis (including multi-infarct dementia [MID], post-stroke cognitive impairment [PSCI], vascular cognitive impairment with non-dementia [VCIND], and vascular dementia [VD]) based on established and validated diagnostic definitions (eg. DSM-IV).

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 May 2023 and was last updated on 31 May 2023 (registration number INPLASY202350114).
(allocation of participants by random sequence).

**Rationale:** In the past, systematic reviews mostly considered acupuncture treatments as a whole to study its effectiveness. There was also a lack of studies comparing between different types of acupuncture treatments toward VCI patients. Meanwhile, selections of different types of acupuncture treatments depend largely on the preference of practitioners and patients, which lack evidence-based provements. Therefore, a strong necessity to conduct an updated systematic review and network meta-analysis study for the results of diverse acupuncture treatments is in need.

**Condition being studied:** Vascular cognitive impairment (VCI) refers to to any dementia that is mainly caused by cerebrovascular disease or impaired cerebral blood flow, ranging from subjective cognitive decline to dementia. VCI is a chronic progressive disorder manifested by reduction or disappearance of memory, cognition and language, along with a degree of change in disposition, behavior, judgement, attention and logic inference.

**METHODS**

**Search strategy:** We searched five electro-databases, including PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), China National Knowledge Infrastructure (CNKI) and Airiti Library. Relevant articles were searched from inception to April 30, 2023 without language restriction. The following keywords were used in search of English databases: ‘vascular cognitive impairment’ OR ‘acupuncture’ OR ‘manual acupuncture’ OR ‘scalp acupuncture’ OR ‘electroacupuncture’ OR ‘auricular acupuncture’ OR ‘fire needling’ OR ‘warm needling’. We also used keywords in Chinese synonyms to search Chinese databases.

**Participant or population:** The final quantitative analysis included 32 RCTs with 2443 VCI patients with diverse treatment strategies. In these studies, the patients were diagnosed as: VD (71.8%), VCIND (12.5%), PSCI (9.4%), VCI (3.1%) and MID (3.1%). The proportion of male patients varied from 40 to 73% with a mean age ranged from 58.0 ± 4.2 to 71.8 ± 3.9 years old. The included studies had similar inclusion and exclusion criteria. Patients treated with herbal medicine were excluded. All of the retrieved studies were parallel RCTs comparing the benefits of acupuncture therapy on cognition status or ADL. The patients received the different duration of the treatments for four to twelve weeks.

**Intervention:** The intervention groups are at least a type of acupuncture therapy, such as manual acupuncture [MA], scalp acupuncture [SA], electroacupuncture [EA], and auricular acupuncture[AA].

**Comparator:** The comparative interventions are conventional treatments, including western medicine [WM] and cognitive rehabilitation [CR].

**Study designs to be included:** Only randomized controlled trials (RCTs) were included in the analysis. The population included are patients diagnosed with VCI and related diagnosis (including multi-infarct dementia [MID], post-stroke cognitive impairment [PSCI], vascular cognitive impairment with non-dementia [VCIND], and vascular dementia [VD]) based on established and validated diagnostic definitions (eg. DSM-IV).

**Eligibility criteria:** We excluded studies that are not RCTs and studies in animal experiments without clinical trials. We also excluded studies using herbal medicine. Studies with no specific acupuncture points were excluded as well.

**Information sources:** We searched five electro-databases, including PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), China National Knowledge Infrastructure (CNKI) and Airiti Library.

**Main outcome(s):** The primary outcomes included: (1) cognition status (measured by
the Mini-Mental Status Examination [MMSE], Hasegama's Dementia Scale [HDS], Montreal Cognitive Assessment [MoCA], and Alzheimer's Disease Assessment Scale-cognitive subscale [ADAS-cog]; (2) activities of daily living (ADL; measured by Activities of Daily Living Scale [ADLS], Barthel Index [BI] and Functional Activities Questionnaire [FAQ]). We recorded the outcome values before and after the intervention. The mean differences represent the cognition and ADL improvement after the intervention.

Additional outcome(s): The secondary outcome was the risk ratio (RR) of the presence of severe adverse effect.

Data management: To compare the effects of different acupuncture treatments on cognitive function and ADL in treating patients with VCI, network meta-analyses were conducted using the packages netmeta, ggplot2, and reshape2. A random-effects network meta-analysis was performed using a consistency model. All graph generation and statistical analyses were performed using the statistical software RStudio (Version 1.4.1106) 15. The scatter plot was generated using GraphPad Prism 9 for macOS (Version 9.5.1, GraphPad Software, San Diego, CA, USA, http://www.graphpad.com).

Subgroup analysis: We had not conduct a subgroup analysis.

Sensitivity analysis: The inconsistency assumption was assessed using a node‐splitting model and design‐by‐treatment interaction model.

Language restriction: No language limits will be imposed on the search.

Country(ies) involved: Taiwan.

Keywords: vascular cognitive impairment; acupuncture therapy; systematic review; network meta-analysis.

Quality assessment / Risk of bias analysis: Among the 32 RCTs included, 7 RCTs were determined to have “Good” quality, and the other 25 RCTs were rated as “Fair”. There were several reasons that ranked down the quality of the articles including: (1) unable to know whether the method of randomization adequate (Q2); (2) treatments unable to reach allocation concealed (Q3); (3) unable to blind the study participants and providers to treatment group assignments (Q4); (4) no reports concerning whether the people assessing the outcomes blinded to the participants’ group assignments (Q5); and (5) no descriptions reported that the sample size being sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power (Q12).

Strategy of data synthesis: To compare the effects of different acupuncture treatments on cognitive function and ADL in treating patients with VCI, network meta-analyses were conducted using the packages netmeta, ggplot2, and reshape2. A random-effects network meta-analysis was performed using a consistency model. All graph generation and statistical analyses were performed using the statistical software RStudio (Version 1.4.1106) 15. The scatter plot was generated using GraphPad Prism 9 for macOS (Version 9.5.1, GraphPad Software, San Diego, CA, USA, http://www.graphpad.com).

Contributions of each author:
Author 1 - Yuan-Ling Liao: study conception and design, data collection, interpretation of results, drafting manuscript.
Email: yyliao.tcm@gmail.com
Author 2 - Pei-Shan Hsu: study conception and design, data collection, interpretation of results.
Email: irisacid37@gmail.com
Author 3 - Yi-Ying Shen: study conception and design, interpretation of results.
Email: eshen956@gmail.com
Author 4 - Chang-Ti Lee: study conception and design, interpretation of results.
Email: sunfish2002@gmail.com
Author 5 - Chou-Chin Lan: study conception and design, interpretation of results.
Email: bluescopy@yahoo.com.tw
Author 6 - I-Shiang Tzeng: statistical analysis, interpretation of results.
Email: stzeng@gmail.com

Author 7 - Guan-Ting Liu: statistical analysis, interpretation of results.
Email: mochabear19@gmail.com

Author 8 - Po-Chun Hsieh: study conception and design, data collection, statistical analysis, interpretation of results, drafting manuscript, supervision, project administration.
Email: pchsieh.tcm@gmail.com