Original Articles

Acupuncture and Herbal Medicine

Evaluating acupuncture as a therapeutic intervention for post-COVID-19 olfactory dysfunction: a systematic review and pilot study

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Abstract

Objective: Olfactory dysfunction (OD) is a common and persistent symptom of coronavirus disease 2019 (COVID-19) for which effective treatments remain limited. Acupuncture, widely used in Chinese medicine for olfactory disorders has uncertain efficacy in post-COVID-19 OD. Therefore, in this study, we aimed to explore the feasibility and preliminary efficacy of acupuncture in patients with post-COVID-19 OD.

Methods: This study was a dual-phased study. Phase I involved a systematic review conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, encompassing eight databases. Phase II consisted of a pilot randomized controlled trial (RCT) enrolling 25 patients with moderate to severe post-COVID-19 OD. Participants were randomly assigned to receive either real (group A) or sham (group B) acupuncture. The intervention included eight sessions over 4 weeks, with assessments at baseline, post-cycle 1, 2-week washout, post-cycle-2 treatment, and 2-week follow-up. The primary outcome was the change in scores on the 12-item Assessment of Self-Reported Olfactory Functioning and Quality of Life (ASOF). Secondary outcomes included the short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) and the traditional Chinese version of the University of Pennsylvania Smell Identification Test (UPSIT-TC).

Results: The systematic review identified 22 studies (15 case reports, seven RCTs) suggesting that acupuncture may positively influence olfactory function. In the pilot RCT, no significant baseline differences were observed between groups. Group A showed steady improvement across all ASOF domains during Cycle 1 (SOC, mean = 5.86; SRP, mean = 3.26; ORQ, mean = 3.98), with slight declines during cycle 2 and 2-week follow-up, though scores remained above baseline. Post-cycle 1, group A showed higher mean SOC and ORQ scores compared with group B (7.00 *vs.* 4.67; 3.98 *vs.* 3.39). Improvements in secondary outcomes were also more pronounced in group A, whereas group B showed minimal changes.

Conclusion: Acupuncture appears to be a safe and potentially effective treatment for post-COVID-19 OD, warranting validation through larger clinical trials.

Keywords: Acupuncture, COVID-19, Olfactory dysfunction, Pilot study, Systematic literature review

Graphical abstract: https://links.lww.com/AHM/A214

Introduction

Olfactory dysfunction (OD) is one of the most prevalent symptoms of coronavirus disease 2019 (COVID-19), affecting approximately 53.56% of patients[1]. A meta-analysis of 32,142 patients published in January 2021 reported a global pooled prevalence of 38.2% (95% confidence interval [CI]: 36.5%–47.2%)[2]. Anosmia prevalence varies by ethnicity and region, being three to six times more common in Caucasians than in Asians or African Americans[3–5]. An international multicenter study reported OD prevalence of 32% in China, 49% in France, and 69% in Germany[6]. Similarly, a cross-sectional cohort study of 120 patients in Hong Kong found that 46.7% experienced OD[7]. Consequently, the Hong Kong Centre for Health Protection officially

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recognized olfactory and gustatory dysfunction as clinical symptoms of COVID-19 on 25 May 2020[8].

The pathophysiology of COVID-19–induced OD is multifactorial, involving both peripheral and central mechanisms. The angiotensin-converting enzyme 2 (ACE2) receptor, in association with transmembrane protease serine 2 (TMPRSS2), facilitates severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cell entry[9]. ACE2 is widely expressed in respiratory, cardiovascular, and gastrointestinal tissues, explaining the multiple-organ involvement of SARS-CoV-2 infection[10–11]. The exact mechanism of COVID-19–induced OD remains uncertain; however, the peripheral nervous system (PNS) and central nervous system (CNS) are believed to play major roles.

PNS involvement

The olfactory system detects odors through the olfactory epithelium (OE), which contains olfactory receptor neurons (ORNs) that transmit odor signals to the brain, and sustentacular cells (SUS) that provide structural and metabolic support. Damage to either cell type can result in OD. Postmortem studies of patients with COVID-19 and anosmia have demonstrated focal atrophy of the OE[12], whereas animal studies have shown that SARS-CoV-2 infection causes cellular injury within the OE of hamsters, leading to anosmia following intranasal inoculation[13]. Both SUS and basal cells of OE exhibit high ACE2 and TMPRSS2 expression, rendering them susceptible to viral invasion[14–15]. Collectively, these findings suggest that SARS-CoV-2–induced OD results from direct viral infection and subsequent damage to OE structures, reducing sensory function and ciliary activity.

CNS involvement

The olfactory bulb (OB) plays a central role in olfactory processing and expresses ACE2 receptors abundantly[16–17]. One hypothesis proposes that SARS-CoV-2 invades the brain *via* olfactory sensory neurons (OSNs) in the OE, crossing the cribriform plate to reach the OB[18–19]. Experimental models using SARS-CoV-1 demonstrated rapid CNS invasion through the OB in ACE2-transgenic mice[20–21]. In humans, neuroimaging studies have revealed OB abnormalities—including microbleeding, inflammation, and edema—in patients with COVID-19 presenting with anosmia[12,19]. Resolution of OB edema on follow-up MRI was associated with clinical recovery of olfactory function[22].

The exact mechanism of COVID-related OD is not fully understood; however, its persistence after infection can significantly impair quality of life. To date, few studies have explored effective treatments. Current guidelines recommend olfactory training (OT) as the first-line therapy for post-viral OD (PVOD)[23–24]. Other options, such as topical corticosteroids, sodium citrate, and oral vitamins A and B[25–27], have shown limited efficacy and may carry adverse effects, particularly with prolonged steroid use[26,28–30]. Therefore, safe and effective treatment options are crucial for the management of OD. Traditional Chinese medicine (TCM) is an ancient Chinese therapeutic method dating back thousands of years and offers a long history and efficacy in treating olfactory disorders.

In this study, we aimed to evaluate the therapeutic potential of acupuncture for post-COVID-19 OD. To achieve this, we first conducted a systematic review of existing evidence on acupuncture for PVOD to establish a robust knowledge base and identify commonly used acupoints for clinical reference. Subsequently, we performed a pilot randomized controlled trial (RCT) to assess the feasibility of acupuncture for post-COVID-19 OD and to generate preliminary data to inform larger future studies. Through the pilot study, we also aimed to evaluate participant adherence, data loss rate, and logistical considerations relevant to subsequent large-scale trials.

Material and methods

Evidence of acupuncture for OD: a systematic literature review

Theoretical foundation

According to TCM theory, the olfactory system is closely related to the lung and large intestine meridians, which regulate the flow of *qi* and blood throughout the body. COVID-19, classified as an epidemic disease[31], disrupts this balance, leading to olfactory impairment due to *qi* stagnation or disharmony caused by SARS-CoV-2 infection.

Improvement in PVOD by following acupuncture treatment has been reported[32–33]. A case series of two post-COVID-19 OD patients demonstrated restoration of olfactory function after acupuncture, including a 38-year-old male who achieved complete recovery after three sessions targeting the Ying Xiang (LI20) point[34]. Additionally, during the COVID-19 pandemic, acupuncture was incorporated into emergency treatment guidelines in China. A study inform the Shanghai Public Health Clinical Center combined acupuncture and Chinese herbal medicine in 22 patients with COVID-19 and olfactory disturbances, reporting significant improvement in olfactory recovery[35].

While acupuncture treatment for COVID-induced OD has seldom been reported, we hypothesized that acupuncture can positively affect SARS-CoV-2–induced OD. Therefore, we conducted a comprehensive review of the literature to summarize existing evidence on acupuncture for PVOD, including study characteristics, acupoint selection, treatment modalities, and outcomes.

Literature search

A systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journal Database (VIP), and Chinese Biomedical Literature Database (CBM) from inception to March 9, 2023, and identified RCTs or case reports of acupuncture in patients with PVOD. Complete manuscripts of all relevant studies published in English and Chinese were retrieved. A complete search formula for each database is provided

in Supplementary Appendix 1, https://links.lww.com/AHM/A215.

Study selection

We included studies that investigated the effects of different forms of acupuncture on olfaction in patients with PVOD using the PICOS framework (populations, interventions, comparisons, outcomes, and study design) (Table 1). The following studies were excluded: (1) animal experiments, (2) patient populations composed exclusively of those with OD secondary to etiologies other than PVOD (eg, idiopathic or trauma), (3) studies without explicit interventions, and (4) letters to the editor, abstracts, and book chapters.

Two reviewers (DW and YW) reviewed the title and abstract of each article and individually selected studies for full-text review based on the inclusion and exclusion criteria. Conflicts were resolved by discussion and a third researcher (LLZ) was available to resolve disputes.

Data extraction

One reviewer (DW) extracted data from the selected studies using a standardized data extraction form. We extracted the following information from each included article: first author, year of publication, study design, number of participants, characteristics of the acupuncture and control groups, treatment details, acupoints, outcome data, duration of follow-up, and results. Studies were graded for quality according to the 2011 Oxford Center for Evidence-Based Medicine (OCEBM) criteria[36] (Table 2), with Level 1 and 2 evidence studies subsequently assessed for risk of bias using the modified Cochrane Collaboration Tool for Assessing Risk of Bias.

Concept of the pilot project

Ethical approval

The study was approved by the Hong Kong Baptist University Human Research Ethics (Clinical) Committee (Hong Kong, China) on the Use of Human Subjects for Teaching and Research (REC/20e21/0508) and the Hospital Authority Kowloon Central/Kowloon East Research Ethics Committee (KC/KE-21-0054/FR-3). This trial was registered at ClinicalTrials.gov (NCT04959747).

Study design

A single-blind, randomized, sham-controlled, crossover clinical trial was conducted to evaluate the efficacy of real *versus* sham acupuncture. Our methodology strongly emphasizes systematic data collection and employs a linear mixed model for rigorous statistical analysis. This choice allowed us to effectively model repeated measurements over time, providing us with the statistical power to accurately discern the effects of our interventions. This is a suitable choice for longitudinal studies such as ours.

The study was conducted in three departments of Tseung Kwan O Hospital (TKOH), Hong Kong, China, comprising the Department of Medicine, Department of Ear, Nose, and Throat (ENT), and Department of Chinese Medicine: Haven of Hope, Chinese University of Hong Kong, and Chinese Medicine Clinic cum Training and Research Centre (CMCTR). Eligible patients were randomly assigned to groups A and B. During the 4-week cycle-1 treatment period, group A, the treatment group, received real acupuncture, whereas group B, the control group, received sham acupuncture. After cycle-1 treatment, a 2-week washout period was conducted for all patients. Group B underwent real acupuncture treatment for another 4-week cycle-2 treatment, whereas group A underwent a 4-week sham acupuncture treatment. Thereafter, all patients were followed for another 2 weeks. All patients completed outcome assessments at each time point.

Participants

Patients with post-COVID-19 presenting with persistent smell loss or distortions were recruited from the

Table 1

Search strategy—PICOS approach

Population	Included	Patients with post-viral olfactory dysfunction
	Excluded	Patient populations composed exclusively of those with OD secondary to etiologies other than PVOD (eg, idiopathic, trauma)
Intervention	Included	Different forms of acupuncture
	Excluded	Non-penetrating techniques (laser acupuncture, acupressure) Studies without explicit interventions
Comparator (for RCT)	Included	Patients without treatment (no intervention/sham acupuncture/standard care (olfactory training))
Outcomes	Included	Subjective olfactory measurements Objective olfactory scores
	Excluded	Non-validated scales (self-made questionnaires)
Studies	Included	English/Chinese Randomized clinical trial/case series ≥5 subjects/well-designed controlled trial without randomization Intervention for olfactory dysfunction
	Excluded	Animal experiments Letters to the editor/abstracts/protocols without results/book chapters

OD: Olfactory dysfunction; PICOS: Population, intervention, comparator, outcomes, study design; PVOD: Post-viral OD.

Table 2

Quality rating according to Oxford Center for Evidence-Based Medicine

Level	Study design
1	High-quality RCT with clear randomization, pre-specified outcomes, and adequate power; systematic review with meta-analysis
2	Prospective non-randomized controlled trial; prospective cohort study with comparator
3	Retrospective cohort study; case-control study
4	Case series; single-arm before–after study; cross-sectional study
5	Case reports; expert opinion; mechanism-based reasoning

RCT: Randomized controlled trial.

Department of Medicine to the Department of ENT at TKOH for a baseline assessment and the Traditional Chinese version of the University of Pennsylvania Smell Identification Test (UPSIT-TC).

Patients were recruited from August 24, 2021, to June 30, 2022. A total of 25 patients completed the informed consent form and on-line baseline questionnaire. Inclusion criteria were as follows: (1) the presence of post-COVID-19 OD of moderate or severe grade (based on UPSIT-TC scores; the cutoff scores were set at 29.5 for men and 30.5 for women)[37]; (2) age 18 to 80 years; and (3) ability to read and write Chinese.

Exclusion criteria included: (1) presence of olfactory or gustatory dysfunctions before the COVID-19 epidemic; (2) history of chronic rhinosinusitis or nasal polyposis; (3) history of nasal surgery (including rhino/septoplasty with or without functional endoscopic sinus surgery); (4) pregnancy or breastfeeding; (5) medical history of cancer, conditions of the nervous system such as Parkinson disease or Alzheimer disease, or any other serious diseases; (6) unstable medical conditions; (7) acupuncture treatment received within 1 month; (8) alcoholism or drug abuse in the past year; (9) presence of needle phobia; (10) known history of developing acupuncture-related severe adverse reactions; (11) treatment for post-COVID-19 OD; (12) history of trauma, injury, or surgery to head or nose, or any bleeding from the nose.

Randomization and blinding

The remaining 13 qualified patients were randomly assigned to either the acupuncture group (AC) or sham acupuncture group (SAC) in a 1:1 ratio. The randomization sequence was computer-generated using Random Allocation Software 2.0.0 (Isfahan University of Medical Sciences, Isfahan, Iran). Allocation codes were placed in sequentially numbered, opaque, tamper-evident envelopes and stored in a locked cabinet with sole key custody maintained by the Principal Investigator (PI), who was not involved in patient recruitment or treatment. All participants, outcome assessors, statisticians, and research staff involved in patient contact, except for the acupuncturists delivering the treatments, remained blinded to treatment assignment. Group assignments were revealed to the acupuncturist immediately before each session. The success of blinding was informally assessed *via* patient feedback at the end of the trial. Emergency unblinding was allowed if serious adverse events arose, and immediate measures were required to ensure patient safety. Any request for emergency unblinding must be submitted to the PI by a coinvestigator. Appropriate medical interventions will be promptly provided, and the reasons for unblinding will be documented in detail, including the date and signature of the responsible investigator. The participant will be withdrawn from the study.

Intervention

All patients received eight sessions of acupuncture treatment lasting 30 minutes per session, twice per week, over the course of 4 weeks. The acupuncturists were Chinese Medicine Practitioners (CMPs) at the CMCTR who had received acupuncture training, had at least 3 years of clinical experience in performing acupuncture, and had experience in treating OD. Eight needles for eight acupuncture points were used for each acupuncture treatment session. The acupoint selection was based on the findings of the systematic review presented in this paper and followed the TCM principle of "Tongqiaofuxiu" (restoring nasal patency and olfaction). This regimen emphasizes points on the Hand-Yangming (Large Intestine) meridian and Governing Vessel, combining local (nasal) points with distal supportive points. The acupuncture points selected for treatment are listed in Supplementary Appendix 2, https://links.lww.com/AHM/A216.

Patients in the acupuncture (AC) group (group A) received electro-acupuncture treatment. Disposable acupuncture needles (0.25 mm in diameter and 25–30 mm in length) were inserted at a depth of 10–25 mm obliquely into the scalp acupuncture points, including Shangxing (GV 23) and Yintang (EX-HN 3), and straight into the face/body acupuncture points including Yingxiang (LI 20), Bitong (EX-HN 18), and Hegu (LI 4). Electroacupuncture was applied to the face acupoints Yingxiang (LI 20), Bitong (EX-HN 18), and Yintang (EX-HN 3) in fast and dispersed waves using an electric needle stimulator provided by CMCTR (Hwato, Electronic Acupuncture Treatment Instrument, Suzhou Medical Appliance Factory, Suzhou, China) for 30 minutes.

To account for the placebo effect of AC, patients in sham acupuncture (SAC) group (group B) received non-insertion sham acupuncture treatment with Streitberger's noninvasive acupuncture needles at the same acupoints with the same stimulation modality as the AC group. The needles were adhered to the skin using a small plastic ring instead of being inserted into the skin, and pseudo-stimulation was performed by connecting the needle to an incorrect output socket of the electrical acupuncture

stimulation instrument. The treatment duration and other procedures were the same as those in the AC group.

Outcome measures

The primary outcome measure was the Assessment of Self-reported Olfactory Function and Olfactory-Related Quality of Life (ASOF), a 12-item validated questionnaire that can be subdivided into three domains: one-item subjective olfactory capability (SOC) scale, 5-item self-reported capability of perceiving specific odors (SRP) scale, and 6-item olfactory-related quality of life (ORQ) scale. The Short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) and UPSIT-TC scores were used as secondary outcomes. The sQOD-NS consists of seven questions on social behavior, eating, annoyance, and anxiety, which are assessed using a 4-point Likert scale (0–3). The UPSIT-TC is a 40-item "scratch and sniff" multiple-choice test to assess how well participants can identify different odors. Assessments were performed at baseline, cycle-1 treatment and after 2 weeks of washout, cycle-2 treatment, and after 2 weeks of follow-up.

Statistical analysis

All efficacy and safety analyses were conducted in accordance with intention-to-treat (ITT) principles. Missing values were replaced with the last observation carried forward. Continuous variables were expressed as mean (standard deviation [SD]), and categorical variables were described using frequencies and percentages. Between-group comparisons were performed using independent sample *t* tests and Fisher exact tests. Sensitivity analyses employing Mann-Whitney *U* tests confirmed the robustness of findings to distributional assumptions. Linear mixed models were used to test for changes in diffusion data across each assessment point using the lme function in R. For each diffusion outcome, we tested for interactions between group (A or B) and time (TP1, TP2, TP3, TP4, TP5). To fit the model, we scaled each variable and entered time and group as fixed effects. Participant ID was entered as a random effect. The model equations are given in Eq. (1).

$$Outcome_{i,j} \sim B_0 + B_1\,(Time) + B_2\,(Group) + B_3\,(Time \times Group) + b_j + e_{i,j}, \quad (1)$$

where $Outcome_{i,j}$ is the mean diffusion outcome value for participant *i* at TP *j;* Time is the TPs; Group is Group A or B; Time × Group is the interaction between groups and time terms. $B_{0,1,2,3}$ are the fixed effect coefficients: B_0 is the intercept; B_1 is the linear slope for TP, B_2 is the linear slope for Group, B_3 is the coefficient of the interaction term (Time × Group). b_j is the random effect coefficient for participant *i* and $e_{i,j}$ is the error for participant *i* at TP *j*.

Visual inspection of residual plots did not reveal any conspicuous deviations from homoscedasticity or normality. To test the robustness of the findings, sensitivity analyses were performed using robust linear mixed models *via* the rlmer function in R, which is less sensitive to outliers and distribution violations. Significance level was set at a two-tailed value of $P < 0.05$. Statistical analyses were performed using R software (version 4.1.0).

Results

Systematic literature review

After duplicates were removed, 390 articles were identified. Fifty-three articles were then assessed in full after screening the titles and abstracts, and the study selection process was assessed (Figure 1). After full-text screening, 32 articles were included for data extraction, which contained 16 Case Reports (Lin 1963; Michael 2003; Zhong et al. 2008; Liu 2011; Wang and Chen 2017; Hunter et al. 2021; Bhat et al. 2022; Morita et al. 2022; Ye and Chen 2022; Li et al. 2025; Wang et al. 2025; Zhu et al. 2023; Wang et al. 2024; Li et al. 2022; Nan et al. 2025; Cheng et al. 2024)[34,38–52], seven Case Series (Shen 2001; Liu et al. 2011; Niu et al. 2008, 2009; Chen et al. 2021; Li 2002; Jiang et al. 2025)[35,53–58], and nine RCTs (Vent et al. 2010; Dai et al. 2016; Pang et al. 2016; Ma and Feng 2020; Zheng et al. 2021; Drews et al. 2022; Ding et al. 2023; Mohebbi et al. 2024; Armstrong et al. 2025)[32–33,59–65].

In total, 32 studies published between 1963 and 2025 were included. The sample sizes ranged from 1 to 116, with the overall treatment duration varying from 1 day to 4 months. The total sample size across the included studies was 865 participants, with 551 participants in RCTs, 293 in case series, and 21 in case reports. Six RCT studies were rated at OCEBM levels 1–2, whereas all case reports were rated at level 5 and case series at level 4. Risk of bias was assessed for each of the level 1 and 2 evidence studies (Figure 2). The bias risk evaluation revealed a "high risk" in two studies and "some concerns" in two studies, primarily due to issues with blinding procedures (common methodological challenges in acupuncture research), unclear allocation concealment methods, and participant dropout. Detailed characteristics of the included studies are presented in sTables 1–3 [Supplementary Appendix 3, https://links.lww.com/AHM/A217].

Despite some heterogeneity in treatment protocols across different study types, the results displayed a consistent trend. Several RCTs demonstrated that acupuncture intervention significantly outperformed control groups (such as OT, pharmacological controls, or sham acupuncture) in improving subjective olfactory function (eg, UPSIT, Sniffin' Sticks) and quality of life (QOD). Some studies also documented improvements in objective indicators. For instance, Ding et al.[63] reported that in an intranasal acupuncture group, P2 wave latency and amplitude in olfactory event-related potentials (OERPs) improved significantly compared with the intranasal steroid group. Similarly, Ma and Feng[60] observed a significantly greater increase in fibroblast growth factor (FGF) levels in the acupuncture group compared to the control group, providing preliminary evidence for the physiological effects of acupuncture. Case series further confirmed the clinical efficacy of acupuncture. Case reports provided more personalized therapeutic observations, especially for refractory cases and long-term outcomes. Multiple

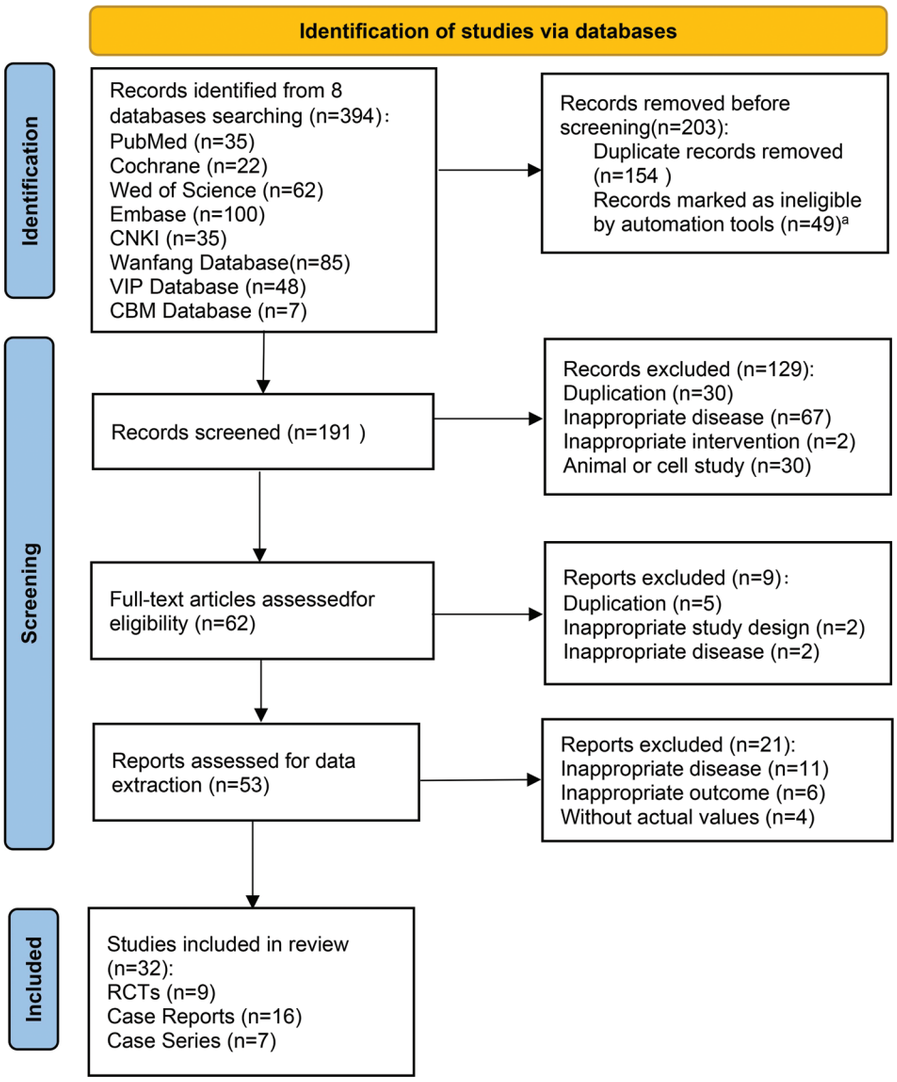

Figure 1. Flow diagram of the study selection process. [a]Includes protocol, no full-text available, conference abstract, etc. CBM: Chinese Biomedical Literature Database; CNKI: China National Knowledge Infrastructure; RCT: Randomized controlled trial; VIP: Chinese Scientific Journal Database.

reports showed symptom improvement immediately after the first treatment, with Bhat et al.[44] describing a typical case of complete restoration of olfactory function from total anosmia and Hunter et al.[43] reporting long-term efficacy lasting up to 2 years. These reports also documented innovative techniques such as fire needling and deep pterygopalatine ganglion needling, offering new avenues for future combination intervention designs. Adverse events were rare and mild, with no serious complications reported, suggesting that acupuncture is a relatively safe intervention. Through a systematic review of multi-level evidence, we identified potentially effective and reproducible treatment parameters: core acupuncture points included Shangxing (GV 23), Yintang (EX-HN 3), Yingxiang (LI 20), Bitong (EX-HN 18), and Hegu (LI 4). The treatment duration ranged from 8 to 12 weeks, with a treatment frequency of 2 to 3 sessions per week.

The statistical evidence provided by large-sample, multicenter RCTs corroborates the clinical observations from case series and case reports, forming a complete evidence chain that suggests acupuncture intervention has potential clinical value in improving olfactory function with good safety. This provides a solid theoretical foundation for subsequent pilot studies and offers a clear direction for optimizing future study protocols, particularly for standardizing treatment parameters, implementing blinding strategies, and evaluating long-term efficacy. Existing evidence provides significant reference points for the smooth progression of the next research phase.

Pilot study evaluating reliability and external validation

Characteristics of participants

Of 25 patients with post-COVID-19 OD screened, 18 (72.0%) completed the baseline assessment and 13 (52.0%) were included and randomized (Figure 3). The demographic variables of the patients are presented in Table 3. The mean age of patients was 42.15 (SD 14.05; range 18–64) years. Among the patients, eight (61.5%) were admitted to the hospital for COVID-19, and most

patients were women 10 (76.9%). None reported smoking. The mean onset of OD was 2 days (SD 1.85) after COVID-19 infection. No significant differences were observed between the groups.

Feasibility—treatment adherence and adverse events

In group B, one participant withdrew immediately, two discontinued after cycle 1, and one declined cycle 2. In

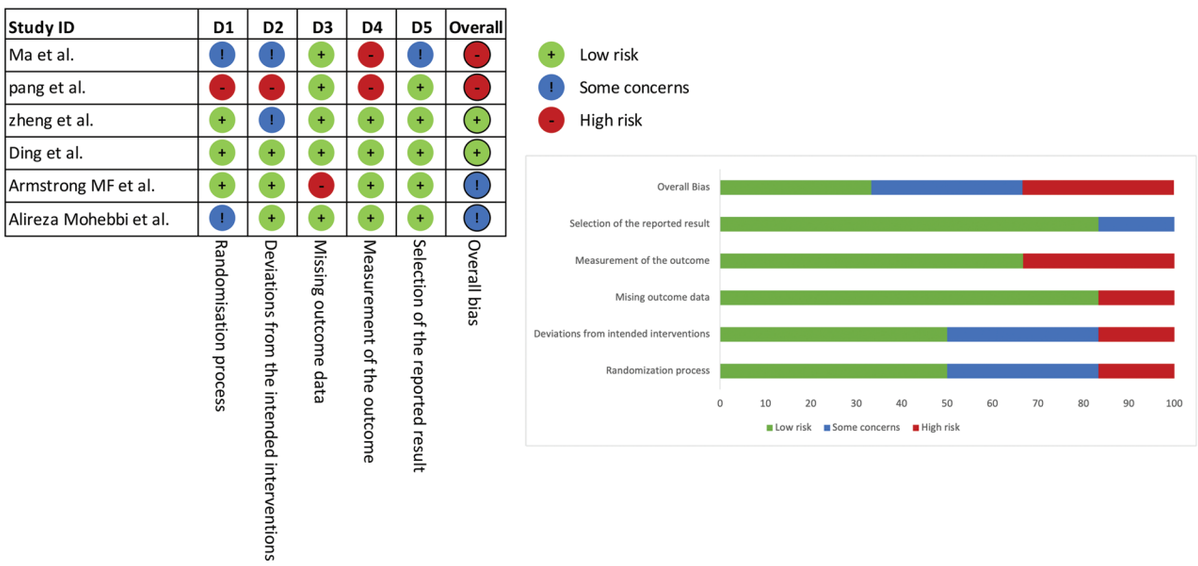

Figure 2. Risk of bias in Level 1 and 2 evidence studies.

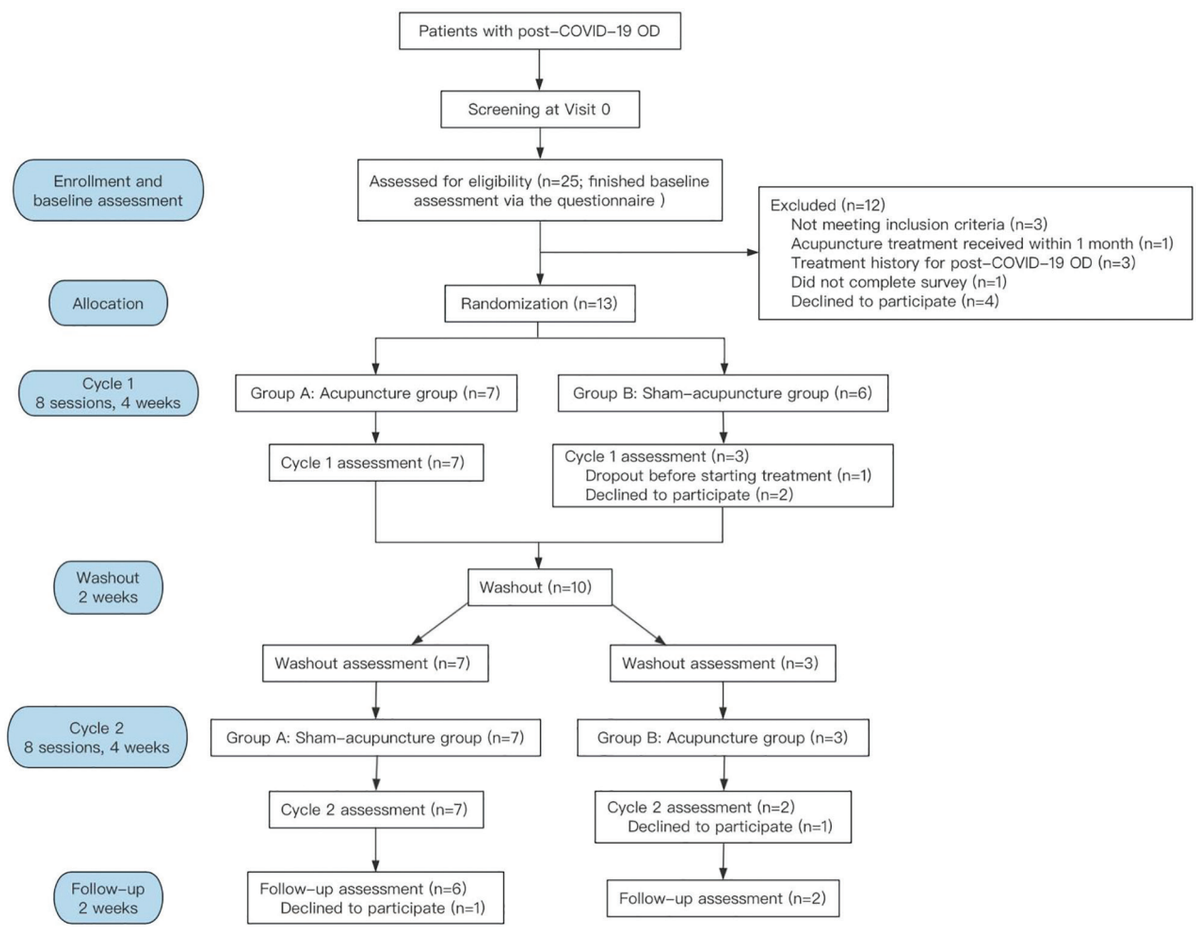

Figure 3. Participants flow through the study. COVID-19: Coronavirus disease 2019; OD: Olfactory dysfunction.

Table 3

Baseline characteristics

Patient characteristics	Total (n = 13)	Group A (n = 7)	Group B (n = 6)	P value
Female, *n* (%)	10 (76.9)	5 (71.4)	5 (83.3)	0.230
Age, years, mean (SD)	42.15 (14.05)	39.00 (14.49)	45.83 (13.83)	0.405
Hospitalization, *n* (%)	8 (61.5)	5 (71.4)	3 (50.0)	0.826
Duration of COVID-19 illness, mean (SD), days	17.92 (17.07)	21.57 (22.40)	13.67 (7.53)	0.429
Time to OD after the diagnosis of COVID-19, mean (SD), days	2.00 (1.85)	2.60 (1.82)	1.00 (1.73)	0.267

COVID-19: Coronavirus disease 2019; OD, olfactory dysfunction; SD, standard deviation.

group A, one participant withdrew before the 2-week follow-up.

None of the patients in either group experienced any negative effects of treatment in cycles 1 or 2.

Primary outcomes

The descriptive results for the three domains SOC, SRP, and ORQ of ASOF at each time point are shown in Table 4 and Figure 4. At baseline, no significant difference was observed in any domain of ASOF between groups A and B ($P > 0.05$). Group A showed a steady increase in ASOF and had significantly higher levels of these domains in cycle-1 treatment (SOC, mean = 5.86; SRP, mean = 3.26; ORQ, mean = 3.98) compared with the baseline. The ASOF level showed a slight decline with cycle-2 treatment and at 2-week follow-up but was still higher than that at baseline in group A. When comparing ASOF domains at each time point with baseline, group B did not show a significant increase.

After cycle-1 treatment, the mean SOC and ORQ values in group A were significantly higher than those in group B (7.00 *vs*. 4.67, 3.98 *vs*. 3.39, respectively). However, no significant differences were observed between groups A and B concerning ASOF at any other assessment point. Sensitivity analyses using Mann-Whitney *U* tests confirmed the robustness of these primary findings, showing consistent results (Table 5).

Secondary outcomes

The descriptive results for sQOD-NS and UPSIT at each measurement time point are presented in Table 4 and Figure 4. The mean level of secondary outcomes showed a continuous increase in group A compared with the baseline. No significant differences were found in sQOD-NS and UPSIT scores within group B (baseline *vs*. any other measurement time point). Group comparisons at all five time points did not reveal any overall significant differences in any of the secondary outcomes, except for the UPSIT measure at the 2-week follow-up ($P < 0.012$). The results of sensitivity analyses using Mann-Whitney *U* test remained consistent with the secondary findings (Table 5).

Effect of acupuncture on primary and secondary outcomes

Results from the linear mixed model revealed significant main effects of time on SOC, SRP, and ORQ, but not sQOD-NS or UPSIT-TC (Table 6). Furthermore, there were significant group × time interaction effects in ORQ from TP1 to TP2 and from TP1 to TP3, but not in SOC, SRP, sQOD-NS, or UPSIT-TC. Robust linear mixed model sensitivity analyses confirmed the consistency of these effects (Table 7).

Discussion

In this study, we combined a systematic review and a pilot RCT to examine, the efficacy of acupuncture for OD, integrating current evidence with preliminary clinical data. The review included nine RCTs, 16 case reports, and seven case series. While the included studies displayed heterogeneity and varying degrees of methodological limitations in areas such as randomization, blinding, and sample size, the body of evidence across study levels showed a consistent, predominantly positive signal, suggesting that acupuncture may be an effective and safe intervention for PVOD.

Direct comparison with established treatment modalities clarifies acupuncture's potential clinical role. OT, currently supported by Level 1A evidence[66,67], promotes neuroplastic recovery through repetitive, structured olfactory stimulation. However, OT outcomes vary widely, and its efficacy is often limited in patients with chronic, refractory, or age-related PVOD[68]. In one study, Ma and Feng[60] compared OT combined with acupuncture *versus* OT alone and found significantly greater improvements across all QOD subscales (quality of life, psychosocial function, visual analog scores) and objective biomarkers (FGF levels) in the combined group, suggesting an adjuvant effect of acupuncture. Other trials comparing acupuncture with pharmacological interventions, such as vitamin B or Ginkgo biloba extracts also reported larger improvements in TDI/UPSIT scores in the acupuncture groups (eg, Vent, Dai)[32]. Moreover, several studies indicated a faster onset of symptomatic relief following acupuncture. Collectively, these findings support a conceptual model in which acupuncture, as a multitarget, non-pharmacological intervention, complements the single-mechanism neuroplasticity effects of OT and may, in some cases, offer superior clinical benefits.

Despite these encouraging findings, the current evidence base remains limited and should be interpreted cautiously. Major sources of bias include incomplete blinding, unclear allocation concealment, and differential attrition. Furthermore, significant heterogeneity

Table 4

Mean scores and standard deviations observed for within- and between-group differences in primary and secondary outcome measures

	Group A (*n* = 7)				Group B (*n* = 6)				Between-group
	n	Mean	SD	*P* value	*n*	Mean	SD	*P* value	*P* value
SOC									
Baseline	7	3.86	2.19	Ref.	6	3.67	1.75	Ref.	0.867
Cycle-1 treatment	7	7.00	0.58	0.003*	3	4.67	1.53	0.430	0.006*
2-Week washout	7	5.86	1.35	0.062	3	4.67	1.53	0.430	0.251
Cycle-2 treatment	7	6.71	1.70	0.019*	2	4.50	0.71	0.553	0.128
2-Week follow-up	6	6.67	2.07	0.038*	2	5.50	0.71	0.216	0.482
SRP									
Baseline	7	2.09	0.45	Ref.	6	2.67	0.53	Ref.	0.055
Cycle-1 treatment	7	3.26	0.43	<0.001*	3	3.20	0.20	0.146	0.834
2-Week-washout	7	3.34	0.51	<0.001*	3	3.27	0.23	0.111	0.816
Cycle-2 treatment	7	3.09	0.49	0.002*	2	3.20	0.28	0.238	0.768
2-Week follow-up	6	3.23	0.74	0.005*	2	3.40	0.28	0.122	0.776
ORQ									
Baseline	7	2.45	0.68	Ref.	6	2.89	0.72	Ref.	0.285
Cycle-1 treatment	7	3.98	0.33	<0.001*	3	3.39	0.25	0.294	0.025*
2-Week-washout	7	4.12	0.42	<0.001*	3	3.61	0.42	0.159	0.116
Cycle-2 treatment	7	3.95	0.33	<0.001*	2	3.42	0.35	0.374	0.085
2-Week follow-up	6	4.14	0.68	0.001*	2	3.67	0.47	0.214	0.407
sQOD-NS									
Baseline	7	10.71	4.92	Ref.	6	10.83	6.24	Ref.	0.970
Cycle-1 treatment	7	13.14	3.39	0.303	3	11.00	2.00	0.966	0.346
2-week-washout	7	14.86	4.53	0.127	3	11.67	4.04	0.842	0.325
Cycle-2 treatment	7	15.00	3.96	0.098	2	11.50	0.71	0.891	0.274
2-Week follow-up	6	15.50	2.07	0.049*	2	12.00	7.07	0.830	0.261
UPSIT-TC†									
Baseline	7	21.14	7.17	Ref.	6	19.33	9.61	Ref.	0.705
Cycle-1 treatment	7	25.29	7.67	0.317	3	16.67	5.13	0.673	0.118
2-Week-follow-up	7	27.43	4.16	0.068	3	18.67	3.21	0.913	0.012*

ORQ: Olfactory-related quality of life; SD: Standard deviation; SOC: Subjective olfactory capability; sQOD-NS: Short version of the Questionnaire of Olfactory Disorders-Negative Statements; SRP: Self-reported capability of perceiving specific odors; UPSIT-TC: Traditional Chinese version of the University of Pennsylvania smell identification test.

*$P < 0.05$.

†UPSIT-TC was checked only in cycle 1.

across studies—in terms of acupoint selection, needle type, treatment frequency, duration, and outcome measures—complicates meta-analytic synthesis and weakens confidence in pooled effect estimates. However, the consistent positive trend across studies justifies continued investigation through more rigorous research designs, forming the rationale for the present pilot trial.

Acupoint prescriptions across studies reflected a coherent theoretical framework consistent with TCM principles. The core points identified in this review: Yingxiang (LI20), Yintang (EX-HN3), Shangxing (GV23), Hegu (LI4), and Bitong (EX-HN18), were not selected arbitrarily but were chosen in accordance with the TCM treatment principle of "Tongqiaofuxiu" (restoring nasal patency and olfaction). This combination integrates local and distal points along meridian pathways to harmonize systemic and local *qi* flow. In TCM, the nose is considered the orifice of the Lung; OD is believed to result from obstruction of Lung orifices, failure of clear yang to ascend, or retention of dampness or turbid phlegm. Accordingly, local point such as Yingxiang (LI20), a key point of the Hand Yangming Large Intestine Meridian located near the nose, dispels wind and heat, and promotes nasal circulation, combining an extra point Bitong (EX-HN18) adjacent to the nose, strengthens the nasal unblocking effect; Yintang (EX-HN3), located on the midline of the head between the eyebrows, is needled to guide *qi* to the affected region; Shangxing (GV23), located on the Governor Vessel (the sea of Yang meridians), are used to calm the mind, lift clear yang and promote opening of the upper orifices;

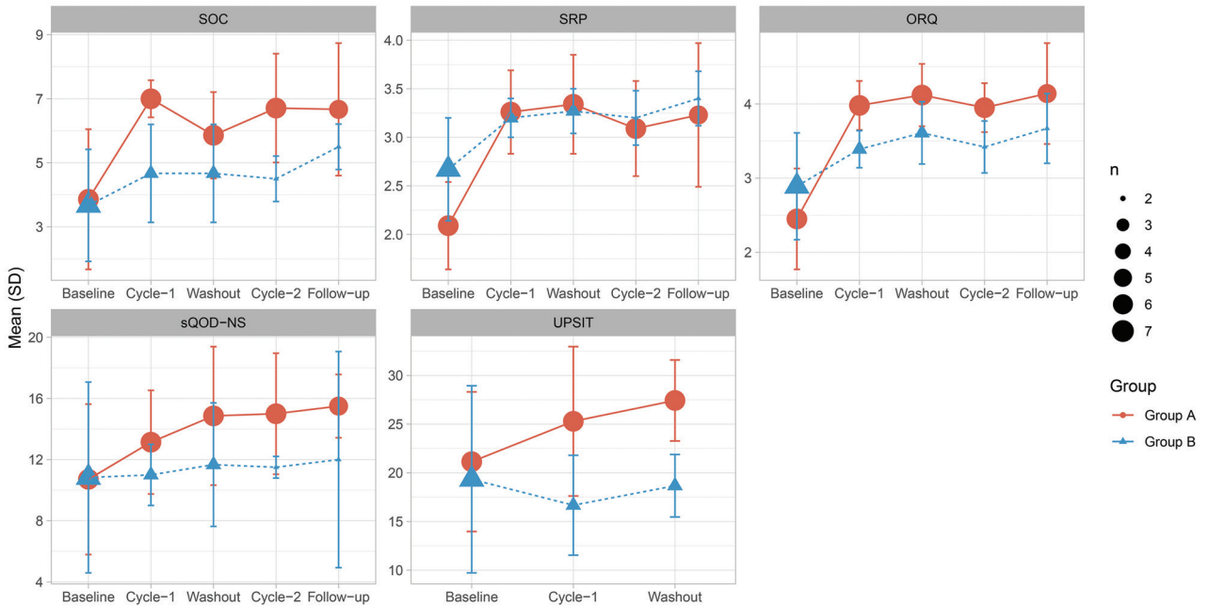

Figure 4. Olfactory dysfunction-related outcome measures in groups A and B over time. ORQ: Olfactory-related quality of life; SD: Standard deviation; SOC: Subjective olfactory capability; sQOD-NS: Short version of the Questionnaire of Olfactory Disorders-Negative Statements; SRP: Self-reported capability of perceiving specific odors; UPSIT: University of Pennsylvania Smell Identification Test.

distal point such as Hegu (LI4), the Yuan-source point of the Hand-Yangming (Large Intestine) channel, serve to regulate the meridian network affecting the face and nasal region and to support systemic *qi* circulation. Together, these acupoints act synergistically to disperse Lung *qi*, open orifices, and promote nasal circulation—an approach consistent with the observed therapeutic effects across diverse studies. Based on this theoretical coherence, our review-derived treatment parameters (2–3 sessions/wk) and validated outcome measures (eg, UPSIT) provided a transparent and reproducible foundation for our pilot study design.

The pilot trial's findings were consistent with the literature. Participants receiving true acupuncture (group A) demonstrated steady increases in ASOF scores, with significant improvements after cycle 1. While performance slightly declined after cycle 2, scores remained above baseline. Improvements were particularly notable in the SOC and UPSIT assessments, indicating enhanced olfactory function. These findings suggest that acupuncture exerts a positive, albeit time-dependent, therapeutic effect on post-COVID-19 OD. Disease duration is usually a prognostic factor; however, there is a disagreement regarding the recovery rates of olfactory disorders. One common belief is that olfactory disorders have the possibility of self-healing and that the duration of olfactory disorders is negatively correlated with changes in olfactory function scores[69]. For example, Hendriks[70] reported a 35% recovery rate for olfactory impairment within 12 months. Similarly, Heilmann et al.[71] showed a significant improvement in olfactory function in 35% of patients after an average duration of 4 months. However, another contrasting belief is that, as the duration of olfactory loss increases, the potential for recovery decreases[72,73]. This finding was also observed in the present study. Hence, future research is needed to confirm both beliefs; however, a consensus remains that patients with olfactory impairment have a better prognosis than those with olfactory loss.

To address limitations noted in prior studies—such as lack of control groups, heterogeneous samples, and subjective assessments[33,74,75]—this study employed a sham-controlled design and standardized, validated instruments to minimize bias. The absence of adverse effects further supports the safety of acupuncture in this population.

Nonetheless, this study has some limitations. First, collaboration with the ENT departments extended treatment timelines and reduced participant compliance, resulting in a smaller sample size and several dropouts. Second, recruitment was constrained by the declining number of post-COVID-19 OD cases following the epidemic's resolution in China after December 2022. Consequently, the study was terminated early. These factors limit the generalizability and statistical power of our findings. Therefore, the current results need to be confirmed in a sufficiently large, pre-calculated validation trial. Future research should recruit larger samples, employ extended follow-up periods, and explore the optimal timing and duration of acupuncture therapy for post-COVID OD.

Conclusion

This study provides preliminary evidence that acupuncture may be a beneficial, safe, and well-tolerated intervention for OD following COVID-19 infection. Early initiation of treatment appears to increase the likelihood of successful recovery. Given the encouraging findings

Table 5

Median scores and interquartile ranges observed within- and between-group differences for primary and secondary outcome measures

	Group A (n = 7)				Group B (n = 6)				Between-group
	n	Median	IQR	P value	n	Median	IQR	P value	P value
SOC									
Baseline	7	3.00	2.50–5.50	Ref.	6	3.50	3.00–4.75	Ref.	0.942
Cycle-1 treatment	7	7.00	7.00–7.00	0.006*	3	5.00	4.00–5.50	0.427	0.015*
2-Week washout	7	6.00	5.00–7.00	0.069	3	5.00	4.00–5.50	0.427	0.197
Cycle-2 treatment	7	7.00	7.00–7.50	0.015*	2	4.50	4.25–4.75	0.497	0.125
2-Week follow-up	6	7.00	6.25–7.75	0.036*	2	5.50	5.25–5.75	0.175	0.238
SRP									
Baseline	7	2.00	1.90–2.30	Ref.	6	2.70	2.25–3.15	Ref.	0.061
Cycle-1 treatment	7	3.20	3.10–3.60	0.003*	3	3.40	3.20–3.40	0.147	0.818
2-Week-washout	7	3.00	3.00–3.50	0.002*	3	3.20	3.10–3.30	0.089	0.906
Cycle-2 treatment	7	3.20	2.70–3.20	0.005*	2	3.20	3.10–3.30	0.238	0.550
2-Week follow-up	6	3.40	2.90–3.75	0.018*	2	3.40	3.30–3.50	0.088	1.000
ORQ									
Baseline	7	2.50	1.83–3.00	Ref.	6	2.84	2.42–3.25	Ref.	0.280
Cycle-1 treatment	7	4.00	3.75–4.25	0.002*	3	3.33	3.25–3.50	0.243	0.039*
2-Week-washout	7	4.17	3.92–4.25	0.002*	3	3.67	3.42–3.84	0.154	0.108
Cycle-2 treatment	7	4.00	3.75–4.08	0.002*	2	3.42	3.30–3.54	0.317	0.104
2-Week follow-up	6	4.08	4.00–4.66	0.006*	2	3.66	3.50–3.83	0.177	0.302
sQOD-NS									
Baseline	7	12.00	7.50–14.00	Ref.	6	8.50	6.25–15.25	Ref.	0.886
Cycle-1 treatment	7	15.00	11.00–15.00	0.270	3	11.00	10.00–12.00	0.606	0.296
2-Week-washout	7	15.00	13.00–18.00	0.139	3	11.00	9.50–13.50	0.607	0.358
Cycle-2 treatment	7	15.00	12.50–18.00	0.109	2	11.50	11.25–11.75	0.505	0.186
2-week follow-up	6	16.00	13.75–16.75	0.052*	2	12.00	9.50–14.50	0.736	0.611
UPSIT-TC†									
Baseline	7	23.00	18.00–26.00	Ref.	6	19.00	17.25–26.75	Ref.	0.829
Cycle-1 treatment	7	26.00	25.50–29.00	0.157	3	18.00	14.50–19.50	0.696	0.085
2-Week-follow-up	7	29.00	25.50–30.00	0.047	3	20.00	17.50–20.50	0.896	0.039*

IQR: Interquartile range; ORQ: Olfactory-related quality of life; SOC: Subjective olfactory capability; sQOD-NS: Short version of the Questionnaire of Olfactory Disorders-Negative Statements; SRP: Self-reported capability of perceiving specific odors; UPSIT-TC: Traditional Chinese version of the University of Pennsylvania smell identification test.

*$P < 0.05$.

†UPSIT-TC was checked only in cycle 1.

and minimal adverse effects, acupuncture warrants further investigation in larger, multicenter RCTs to confirm its therapeutic efficacy and establish standardized treatment protocols.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

Dongjue Wei, Choryin Leung, Yiping Wong, and Peipei Du drafted the manuscript. Shu Yang and Peipei Du analyzed the data. Alan Yatlun Wong, Ka Ming Yau, and Choryin Leung conducted the clinical research. Dongjue Wei and Yiping Wong performed the systematic reviews. Linda Zhong designed the study and revised the manuscript. Chifung Choy and Hungwai Cho monitored the clinical research and assessed patients. Bacon FL Ng and Rowena Wong provided valuable comments on the drafts and data analysis of the Phase II Pilot Randomized Control Study.

Table 6

Linear mixed effects of olfactory dysfunction-related outcome measures in groups A and B

	SOC	SRP	ORQ	sQOD-NS	UPSIT-TC
Group	–0.19 (0.92)	0.58 (0.27)	0.44 (0.29)	0.12 (2.52)	–1.81 (3.86)
TP1–TP2	2.47 (1.67)	1.71** (0.46)	2.54** (0.66)	4.03 (3.92)	9.36 (6.26)
TP1–TP3	4.76** (1.67)	1.81** (0.46)	2.61** (0.66)	6.79 (3.92)	11.65 (6.26)
TP1–TP4	4.21* (1.77)	1.33* (0.48)	2.46** (0.69)	7.68 (4.15)	-
TP1–TP5	3.02 (1.82)	1.31* (0.50)	2.58** (0.71)	6.80 (4.27)	-
Group × TP1–TP2	–0.47 (1.18)	–0.54 (0.32)	–1.02* (0.46)	–1.60 (2.79)	–5.22 (4.45)
Group × TP1–TP3	–1.61 (1.18)	–0.56 (0.32)	–0.94* (0.46)	–2.64 (2.79)	–5.36 (4.45)
Group × TP1–TP4	–1.35 (1.32)	–0.33 (0.36)	–0.96 (0.50)	–3.40 (3.10)	-
Group × TP1–TP5	–0.26 (1.33)	–0.22 (0.37)	–0.90 (0.51)	–2.71 (3.14)	-
Constant	4.05 (1.42)	1.50 (0.42)	2.01 (0.45)	10.60 (3.89)	22.95 (5.97)
Observations	50	50	50	50	33
Log likelihood	–85.48	–22.39	–32.60	–130.91	–103.53
Akaike Inf. Crit.	194.97	68.78	89.19	285.82	233.07
Bayesian Inf. Crit	217.91	91.72	112.14	308.77	235.04

ORQ: Olfactory-related quality of life; SOC: Subjective olfactory capability; SRP: Self-reported capability to perceive specific odors; TP: Time point; TP1: Baseline; TP2: Cycle-1 treatment; TP3: 2-week-washout; TP4: Cycle-2 treatment; TP5:2-week follow-up; SE: Standard error; sQOD-NS: Short version of the Questionnaire of Olfactory Disorders-Negative Statements; UPSIT-TC: Traditional Chinese version of the University of Pennsylvania smell identification test.

Values indicate the estimated effect (β) and corresponding SE.

UPSIT-TC was only checked in Cycle-1.

*$P < 0.05$; **$P < 0.01$.

Table 7

Robust linear mixed effects in olfactory dysfunction-related outcome measures in groups A and B

	SOC	SRP	ORQ	sQOD-NS	UPSIT-TC
Group	–0.32 (0.85)	0.58 (0.27)	0.44 (0.29)	0.12 (2.52)	–1.81 (3.86)
TP1–TP2	2.28 (1.56)	1.71** (0.46)	2.54** (0.66)	4.03 (3.92)	9.36 (6.26)
TP1–TP3	4.53** (1.56)	1.81** (0.46)	2.61** (0.66)	6.79 (3.92)	11.65 (6.26)
TP1–TP4	4.02* (1.65)	1.33* (0.48)	2.46** (0.69)	7.68 (4.15)	-
TP1–TP5	2.92 (1.70)	1.31* (0.50)	2.58** (0.71)	6.80 (4.27)	-
Group × TP1–TP2	–0.55 (1.10)	–0.54 (0.32)	–1.02* (0.46)	–1.60 (2.79)	–5.22 (4.45)
Group × TP1–TP3	–1.67 (1.10)	–0.56 (0.32)	–0.94* (0.46)	–2.64 (2.79)	–5.36 (4.45)
Group × TP1–TP4	–1.37 (1.22)	–0.33 (0.36)	–0.96 (0.50)	–3.40 (3.10)	-
Group × TP1–TP5	–0.33 (1.24)	–0.22 (0.37)	–0.90 (0.51)	–2.71 (3.14)	-
Constant	4.54 (1.31)	1.50 (0.42)	2.01 (0.45)	10.60 (3.89)	22.95 (5.97)
Observations	50	50	50	50	33

ORQ: olfactory-related quality of life; SOC: subjective olfactory capability; SE: Standard error; sQOD-NS: short version of the Questionnaire of Olfactory Disorders-Negative Statements; SRP: self-reported capability to perceive specific odors; TP: Time point; TP1: baseline; TP2: Cycle-1 treatment; TP3: 2-Week-washout; TP4: Cycle-2 treatment; TP5: 2-Week follow-up; UPSIT-TC: traditional Chinese version of the University of Pennsylvania smell identification test.

Values indicate the estimated effect (β) and corresponding SE.

UPSIT-TC was only checked in cycle 1.

*$P < 0.05$; **$P < 0.01$.

Ethical approval of studies and informed consent

The study was approved by the Hong Kong Baptist University Human Research Ethics (Clinical) Committee (Hong Kong, China) on the Use of Human Subjects for Teaching and Research (REC/20e21/0508) and the Hospital Authority Kowloon Central/Kowloon East Research Ethics Committee (KC/KE-21-0054/FR-3). Informed consent was obtained from all individual participants included in the study.

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None.

Data availability

All data generated or analyzed during this study are included in this published article.

Declaration of generative AI in scientific writing

The conceptual framework, study design, and original manuscript writing were conducted by the authors. Artificial intelligence was utilized solely to refine linguistic coherence and revise punctuation. The intellectual content, data interpretation, and clinical conclusions remain entirely original. All references in this publication were manually searched, cross-referenced, and inserted by the authors to ensure accuracy. Following the use of linguistic tools, the authors have reviewed and revised the content as needed and take full responsibility for the content of this publication.

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