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RESPONSE TO LETTER

Managing Sleep, Emotional Well-Being, and Quality of Life in Hemodialysis Patients via Acupressure [Response to Letter]

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Dear editor

We sincerely appreciate the insightful comments and constructive suggestions from Zhao et al[1] regarding our systematic review and meta-analysis on acupressure for hemodialysis (HD) patients.[2] Their perspectives on methodological optimization are of great value for improving the quality of evidence synthesis in this field and guiding subsequent clinical research and practice. We hereby respond to each of their concerns point by point with rigorous evidence and methodological explanations.

Response to the Limitation of Single Timepoint Selection in Meta-Synthesis

We recognize that selecting the most frequently reported follow-up timepoint for outcome analysis may mask the temporal and cumulative effects of acupressure. This is a methodological trade-off made under the premise of balancing study heterogeneity and statistical validity. First, the 27 included studies showed significant heterogeneity in follow-up durations (28 days, 30 days, 56 days, 90 days, etc.), and consistent timepoint selection is a standardized processing method recommended by the PRISMA 2020 guidelines for meta-analyses with high follow-up time heterogeneity, which can avoid the bias caused by mixing different timepoint data in a single analysis.[3]

Second, we have explicitly stated this limitation in the Strengths and Limitations section of our original study and pointed out that subsequent research should explore the time-effect relationship of acupressure through long-term follow-up and stratified analysis. Third, the dose-response meta-analysis and subgroup analysis by intervention duration suggested by Zhao et al[1] are indeed valuable research directions, but the current included studies lack unified reporting of acupressure dose (eg, pressure intensity, cumulative operation time) and long-term follow-up data (≥6 months), which makes it impossible to conduct valid dose-response and long-term effect analysis.[4] In the future, we will follow their suggestion to conduct further evidence synthesis when more high-quality studies with standardized timepoint and dose reporting are available.

Response to Low-Certainty Evidence Does Not Imply Limited Clinical Relevance

We appreciate Zhao et al's[1] careful verification of the weighted mean difference (WMD) and minimal important difference (MID) for social functioning outcomes. Our description of acupressure having "little impact" on social functioning is a comprehensive judgment that combines Grading of Recommendations, Assessment, Development and Evaluation (GRADE) evidence certainty and clinical effect reliability, rather than a negation of the observed effect size.

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First, although the WMD of social functioning (15.37, 95% CI 10.67–20.06) exceeded the MID of 10 points, the evidence certainty was rated as low according to the GRADE approach, which was mainly due to the small number of included studies (only 3 Randomized Controlled Trials (RCTs), 209 participants) and serious risk of bias (no allocation concealment, no blinding).[5] The GRADE system emphasizes that the clinical application of evidence should be based on both effect size and the certainty of the evidence. Low-certainty evidence means that the true effect may differ substantially from the observed effect, so it is inappropriate to directly conclude that acupressure has a definite clinical effect on social functioning.

Second, we did not deny the potential clinical relevance of the effect size; instead, we pointed out in the discussion that the positive trend of social functioning improvement needs to be verified by more high-quality RCTs with large samples and low risk of bias. Our original position is to remain cautious about the clinical conclusions drawn from low-certainty evidence, consistent with the GRADE evaluation principle that "evidence certainty determines the strength of recommendation".

Response to Inconsistencies in Control Selection and Study Inclusion

We clarify that the control selection and study inclusion in our research strictly followed the pre-specified eligibility criteria registered in PROSPERO (ID: CRD420251010657), and the perceived "inconsistencies" are due to insufficient detailed description in the original text. We respond to the three sub-questions as follows:

Ambiguity of the Medication Control Scope

The included studies with medication control all used sedative-hypnotic drugs related to the study outcomes (estazolam, zolpidem, etc.), which are the first-line drugs for treating HD patients' sleep disorders in clinical practice. We have listed the specific control drugs for each study in Table 1 of the original paper,[2] and the data extraction process strictly excluded studies with irrelevant control drugs (eg, antihypertensive drugs, hypoglycemic drugs).

Rationale for Excluding Sham/Acupressure or Routine Care Controls

Routine care was not excluded in our study. The waitlist (no-intervention) control mentioned in the original article[2] actually included routine clinical care for patients with HD. Our definition of the "waitlist control" in our study refers to the absence of additional pharmacological or targeted nursing interventions to improve study outcomes, such as insomnia and mood disorders. Routine care for HD patients is limited to fixed clinical dialysis procedures and basic vital sign monitoring and does not involve specialized care for insomnia, psychological problems, and other conditions in the study. Therefore, such routine care constitutes a basic medical measure received by both the experimental and control groups, and is not categorized as a "targeted intervention" as defined in this study.

Regarding the exclusion of sham-acupressure controls, we have elaborated on this issue in Section – Response to Blinding Feasibility in Acupressure Trials – as the design of sham-acupressure is closely linked to the feasibility of blinding in acupressure trials for HD patients.

Inclusion of the Study Comparing Auricular Acupressure + Acupoint Scraping with Acupoint Scraping Alone

Lin's study[6] was included because acupoint scraping was a standard routine intervention in both the experimental and control groups, and the only difference between the two groups was the addition of auricular acupressure in the experimental group. In essence, the study compared "auricular acupressure + basic scraping" with "basic scraping", which is consistent with our eligibility criteria of "acupressure as the experimental intervention".

Response to Blinding Feasibility in Acupressure Trials

We agree with Zhao et al[1] that blinding of participants and outcome assessors is theoretically feasible in acupressure trials, and their suggested methods (light touch on non-acupoints, recruiting acupressure-naïve participants, masked outcome assessors) are valuable methodological references for subsequent research.[7] However, our statement that

"blinding participants and operators is inherently challenging" is based on the actual research status of the included studies and the clinical characteristics of HD patients.

First, none of the 27 included RCTs used the above blinding methods, and all studies lacked blinding of participants and operators, a common methodological defect in acupressure trials in current clinical research of HD patients. Our description is a factual reflection of the existing evidence, not a denial of blinding's feasibility.

Second, HD patients have unique clinical characteristics: most of them have long-term dialysis history, accompanied by cognitive impairment, fatigue, and other complications, and the compliance of participating in complex blinding operations (eg, receiving non-acupoint light touch) is low. In addition, acupressure is a physical manipulation with an intuitive sensory component (eg, pressure sensation at acupoints), which makes it difficult to effectively blind participants in actual operation, even when non-acupoint stimulation is used.

Third, we explicitly proposed in the Implications section of the original text that subsequent acupressure trials should implement participant and outcome assessor blinding to reduce performance and detection bias, which is consistent with the suggestion of Zhao et al.[1]

Response to the Underexplored Moderator of Intervention Provider Variability

The reason for not conducting this analysis is insufficient statistical power due to extreme imbalance in sample sizes across provider types. The small sample size of self-administered acupressure studies makes subgroup analysis at high risk of type II error (false negative result), which cannot accurately reflect the true efficacy difference between the two delivery modes.

In addition, we have pointed out in the Discussion section of the original paper[2] that standardizing the implementation of acupressure interventions is a key direction for subsequent research, including unifying provider training and exploring self-administered acupressure protocols suitable for HD patients. We fully agree with Zhao et al[1] that future systematic reviews should incorporate provider type as a subgroup or meta-regression variable, and we will conduct this analysis when more self-administered acupressure studies with large samples are available in this field.

Response to the Conclusion and Suggestions for Methodological Optimization

We highly appreciate the comprehensive methodological suggestions put forward by Zhao et al,[1] which are highly consistent with the research directions we proposed in the Implications and Conclusion sections of the original paper. Our systematic review aims to provide the latest evidence on the clinical application of acupressure in HD patients, and we have fully acknowledged and elaborated on the methodological limitations of the existing evidence (eg, high risk of bias, small sample size, non-standardized intervention protocols) in the original paper. The suggestions of Zhao et al[1] (eg, temporal stratification analysis, rational interpretation of GRADE evidence, standardized control selection, implementation of blinding, and exploration of provider-type effect) further enrich and improve the methodological optimization plan for subsequent research in this field. We will take their valuable comments as an important reference, and in follow-up research, we will focus on the above methodological points to conduct more rigorous evidence synthesis and clinical trial design, thereby providing higher-quality evidence to support the integration of acupressure into HD clinical care.

Abbreviations

GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HD, Hemodialysis; MID, Minimal Important Difference; QoL, Quality of Life; RCT(s), Randomized Controlled Trial(s); WMD, Weighted Mean Difference.

Data Sharing Statement

The datasets generated and analyzed during the present communication are available from the corresponding author (Dr. Li-Wei Chou, chouliwe@gmail.com) on reasonable request.

Author Contributions

Yiting Wang: Conceptualization, Formal analysis, Writing – original draft; Li-Wei Chou: Conceptualization, Supervision, Writing – review & editing. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this communication.

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