ANNALS OF MEDICINE
2025, VOL. 57, NO. 1, 2566397
https://doi.org/10.1080/07853890.2025.2566397

PROTOCAL

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# Preoperative electroacupuncture for prevention of postoperative delirium in older adults undergoing total knee arthroplasty: protocol for a multicenter randomized controlled trial

Yifen Zhuo[a*], Jialin Yang[b*], Xuezhen Shi[c*], Huifen Lin[d], Xincheng Liao[e], Yusheng Yao[b] and Lei Chen[f]

[a]Department of Anesthesiology, Xiamen Haicang Hospital, Xiamen, China; [b]Department of Anesthesiology, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou, China; [c]Department of Anesthesiology, General Hospital of Taining County, Taining, China; [d]Department of Anesthesiology, Sanming First Hospital Affiliated to Fujian Medical University, Sanming, China; [e]Department of Anesthesiology, The Second Affiliated Hospital of Fujian University of Traditional Chinese Medicine, Fuzhou, China; [f]Department of Anesthesiology, People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, Fuzhou, China

**ABSTRACT**

**Introduction:** Postoperative delirium is a common and serious complication following total knee arthroplasty in older adults, leading to increased mortality, prolonged hospitalization, and cognitive decline. Although electroacupuncture has shown promise in improving cognitive function, its efficacy in preventing postoperative delirium following arthroplasty remains unknown. This study investigates whether preoperative electroacupuncture prevents postoperative delirium in older adults undergoing total knee arthroplasty.

**Methods and analysis:** This multicenter, randomized, double-blind, sham-controlled trial will enroll 1460 participants aged 65–90 years scheduled for elective total knee arthroplasty. Participants will be randomly assigned (1:1) to receive either active electroacupuncture (at GV24 and bilateral GB13 acupoints, 1 mA for 30 min before anesthesia induction; $n=730$) or sham electroacupuncture ($n=730$). The primary outcome is delirium incidence within 72 h after surgery, assessed using the Confusion Assessment Method. Secondary outcomes include delirium severity and subtypes, cognitive function, anxiety, depression, sleep quality, pain scores, cumulative morphine consumption, recovery quality, length of hospital stay, and adverse events.

**Ethics and dissemination:** The protocol was approved by the Institutional Review Board of Fujian Provincial Hospital (K2023-02-004/02). All participating centers obtained ethics committee approval before enrollment. Written informed consent will be obtained from all participants. Results will be published in peer-reviewed journals, regardless of the outcome.

**ARTICLE HISTORY**
Received 4 September 2024
Revised 11 September 2025
Accepted 12 September 2025

**KEYWORDS**
Electroacupuncture; postoperative delirium; total knee arthroplasty; older adults; randomized controlled trial; perioperative neurocognitive disorders

## Introduction

### *Background*

Total knee arthroplasty (TKA) remains the definitive treatment for end-stage knee osteoarthritis, with over 1.6 million procedures performed in the United States between 2012 and 2022 [1]. As the global population ages, the demand for TKA is projected to increase substantially, yet older patients face significant perioperative risks [2].

Postoperative delirium (POD) stands out as a particularly serious complication. This acute neuropsychiatric syndrome involves fluctuating attention and consciousness within seven days after surgery [3].

**CONTACT** Yusheng Yao fjslyys@fjmu.edu.cn Department of Anesthesiology, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, 134 Dongjie, Fuzhou 365001, China; Lei Chen chenlei@fjtcm.edu.cn Department of Anesthesiology, People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, 602 Bayiqi Road, Fuzhou 350004, China.
*These authors contributed equally to this work.

While delirium affects 15–25% of older patients after major elective surgery and exceeds 50% in high-risk procedures [4,5], arthroplasty patients show variable rates: 6–17% following hip replacement versus 8–24% following TKA, with incidence doubling in patients over 75 years [6]. POD carries significant implications: immediate risks include a 2-fold increased mortality and 3–5 day prolonged hospitalization, while long-term consequences include a 2.3-fold increased risk of cognitive decline [7].

Current prevention strategies face significant limitations. The American Society of Anesthesiologists' Perioperative Brain Health Initiative recommends non-pharmacological strategies as first-line delirium prevention [8]. Although multicomponent interventions effectively reduce delirium by 30–40%, their complexity and resource requirements limit practical implementation [9]. These barriers have prompted exploration of complementary approaches, particularly electroacupuncture, which combines traditional acupuncture with controlled electrical stimulation to reduce neuroinflammation and enhance cerebral perfusion [10].

Evidence for electroacupuncture in TKA-related delirium prevention remains limited. A recent meta-analysis examining electroacupuncture in arthroplasty found promising results but included only three studies with inconsistent delirium assessment methods [11]. A systematic review demonstrated that transcutaneous electrical acupoint stimulation reduced delirium in mixed surgical populations but lacked TKA-specific data [12]. Consequently, high-quality evidence for electroacupuncture's effectiveness in preventing delirium specifically in older TKA patients is still lacking.

### *Objective*

This study determines whether electroacupuncture, added to standard non-pharmacological care, reduces delirium incidence in older patients undergoing TKA. We hypothesize that electroacupuncture will provide additional benefit beyond current best practices for this vulnerable population.

## Patients and methods

### *Setting and design*

This multicenter, prospective, randomized, double-blinded, parallel-group, sham-controlled trial will be conducted at four hospitals in Fujian Province, China: Fujian Provincial Hospital (primary center), Sanming First Hospital, The Second Affiliated Hospital of Fujian University of Traditional Chinese Medicine, and People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine. The study is scheduled to run from September 2024 to August 2026 and adheres to the principles outlined in the Declaration of Helsinki. Table 1 presents the study timeline, and Figure 1 shows the Consolidated Standards of Reporting Trials (CONSORT) flow diagram. This protocol adheres to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines [13].

### *Participants*

We will enroll patients aged 65–90 years undergoing elective unilateral total knee arthroplasty under general anesthesia. Eligible participants must have American Society of Anesthesiologists (ASA) physical status class II or III, indicating mild to moderate systemic disease.

Exclusion criteria include: cognitive impairment (Mini-Mental State Examination [MMSE] score <24); implanted electrical devices; infection at acupuncture sites; severe bleeding disorders; communication barriers (inability to communicate in Mandarin or severe audiovisual impairments); alcohol or substance use disorder; current sedative, antidepressant, or glucocorticoid use; acupuncture exposure within six months; and any condition deemed unsafe by the research team.

Designated researchers will screen patients scheduled for total knee arthroplasty. Initial screening occurs one day before surgery (Friday for Monday surgeries) during preoperative evaluation and includes MMSE assessment to evaluate baseline cognitive function, with scores below 24 resulting in immediate exclusion. Following MMSE screening, the first Confusion Assessment Method (CAM) evaluation is conducted to detect any pre-existing delirium, with CAM-positive patients excluded immediately. Researchers

**Table 1.** Study timeline and assessment schedule.

| | Study period | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Enrollment | Randomization/ Allocation | | Post-allocation | | | | | | | | |
| | Day −1 | Day 0 | | | Day 1 | Day 2 | Day 3 | | 1 m | 3 m | 6 m | 12 m |
| Timepoint | Screening/ Consent | Morning (Baseline) | Intervention (30 min pre-anesthesia) | Intraoperative | Postoperative | | | Discharge | Follow-up | | | |
| Enrolment | | | | | | | | | | | | |
| MMSE | X | | | | | | | | | | | |
| Eligibility screening | X | | | | | | | | | | | |
| Informed consent | X | | | | | | | | | | | |
| Demographic data collection | X | | | | | | | | | | | |
| Interventions | | | | | | | | | | | | |
| Allocation | | | X | | | | | | | | | |
| Active electroacupuncture | | | X | | | | | | | | | |
| Sham electroacupuncture | | | X | | | | | | | | | |
| Blinding assessment (post-intervention) | | | X | | | | | | | | | |
| Assessments | | | | | | | | | | | | |
| CAM | X | X | | | 2X | 2X | 2X | | | | | |
| DRS-R-98 (If delirium present) | | | | | X | X | X | | | | | |
| RASS (If delirium present) | | | | | X | X | X | | | | | |
| AMTS | | X | | | | | | | X | X | X | X |
| HADS | | X | | | X | X | X | | | | | |
| RCSQ | | X | | | X | X | X | | | | | |
| NRS | | X | | | X | X | X | | | | | |
| Cumulative morphine consumption | | | | | | | X | | | | | |
| In-hospital antipsychotic /sedative use | | | | | | | | X | | | | |
| QoR-15 | | | | | X | X | X | X | | | | |
| LOS | | | | | | | | X | | | | |
| Adverse events monitoring | | | X | X | X | X | X | X | | | | |

Abbreviations: AMTS, Abbreviated Mental Test Score; CAM, Confusion Assessment Method; DRS-R-98, Delirium Rating Scale-Revised-98; HADS, Hospital Anxiety and Depression Scale; LOS, length of stay; MMSE, Mini-Mental State Examination; NRS, Numerical Rating Scale; QoR-15, 15-item Quality of Recovery questionnaire; RASS, Richmond Agitation-Sedation Scale; RCSQ, Richards-Campbell Sleep Questionnaire.
Notes: CAM assessment performed at both Day −1 screening and Day 0 morning to exclude pre-existing delirium; Formal enrollment and randomization occur after negative Day 0 morning CAM; 2X indicates twice-daily assessments (09:00–11:00 and 18:00–20:00) on postoperative days 1–3; DRS-R-98 and RASS administered only when CAM positive; NRS assessed at 1, 3, 6, 12, 24, 36, 48, 60, 72 h postoperatively; HADS and RCSQ assessed at Day 0 baseline then daily for 3 postoperative days; Cumulative morphine consumption calculated at 72 h; Adverse events monitored from intervention through discharge CAM assessment at Day −1 and Day 0 morning confirms absence of pre-existing delirium; positive.

will explain study objectives, methods, benefits, risks, and adverse event procedures to eligible patients who pass both MMSE and CAM screening. Written informed consent will be obtained from patients or legal representatives. On the surgery morning, eligibility is reconfirmed with a second CAM assessment. Only patients with negative CAM at both timepoints proceed to randomization, ensuring all enrolled participants meet criteria at intervention.

## *Randomisation and blinding*

Enrolled patients will undergo 1:1 randomization to active or sham electroacupuncture using block randomization (size 4) stratified by center. An independent statistician generates the allocation sequence using R version 4.0.5 ('blockrand' package). Allocations remain concealed in sequentially numbered, opaque envelopes until enrollment confirmation. Unblinded researchers prepare equipment according to the allocation.

Participants, surgeons, and outcome assessors remain blinded; acupuncturists cannot be blinded due to the intervention's nature. Identical-appearing devices ensure participant blinding. Sham electroacupuncture

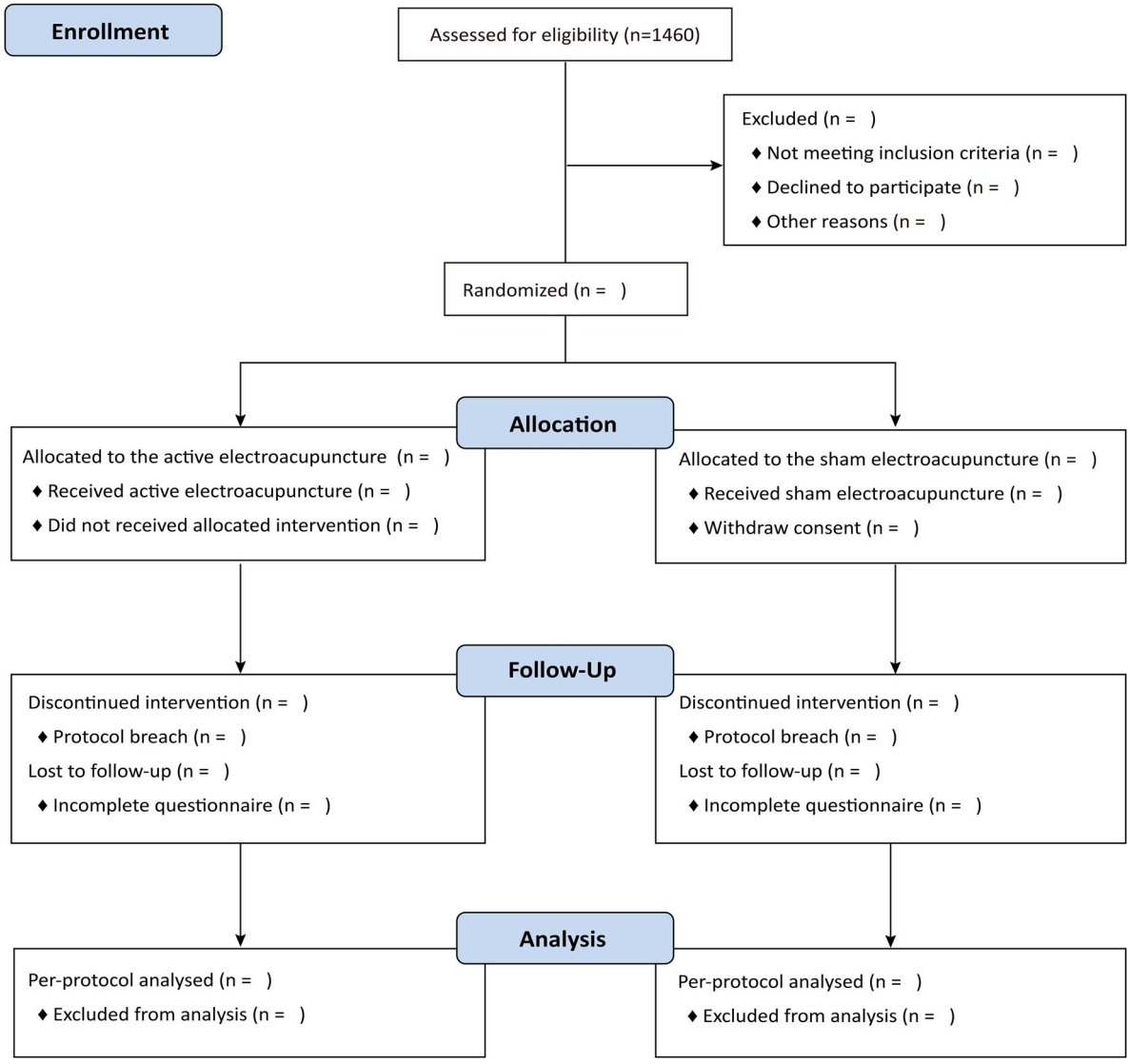


**Figure 1.** Consolidated Standards of reporting trials (CONSORT) flow diagram.

uses retractable placebo needles without electrical output, simulating insertion without penetration [14]. Blinding success is assessed by asking participants which treatment they believe they received.

### *Electroacupuncture administration*

We selected Shenting (GV24) and bilateral Benshen (GB13) acupoints, which are associated with cognitive function in Traditional Chinese Medicine and have been shown to reduce cognitive impairment in prior studies [15]. GV24 is located 0.5 cun (≈10 mm) above the anterior hairline midpoint, with GB13 positioned 3 cun (≈60 mm) lateral to GV24 (Figure 2), following WHO standardized locations [16]. Equipment included disposable acupuncture needles (0.30 mm × 75 mm), non-penetrating needles (0.30 mm × 25 mm) for sham treatment, and SDZ-V electroacupuncture devices (Hwato, China). All participants received 30-minute treatment sessions before anesthesia induction.

For active treatment, certified acupuncturists inserted needles 20–24 mm into the subgaleal layer at oblique angles, then manually manipulated them to elicit de qi (sensations of fullness, numbness, or soreness). Electrodes delivered alternating stimulation (2/15 Hz, 1 mA), producing mild skin movement without pain. Sham treatment targeted non-acupoints 20 mm above GV24 and 20 mm lateral to GB13, placing them in different dermatomes to prevent location-specific effects [17]. The sham protocol used non-penetrating needles without manipulation, de qi sensation, or electrical stimulation.

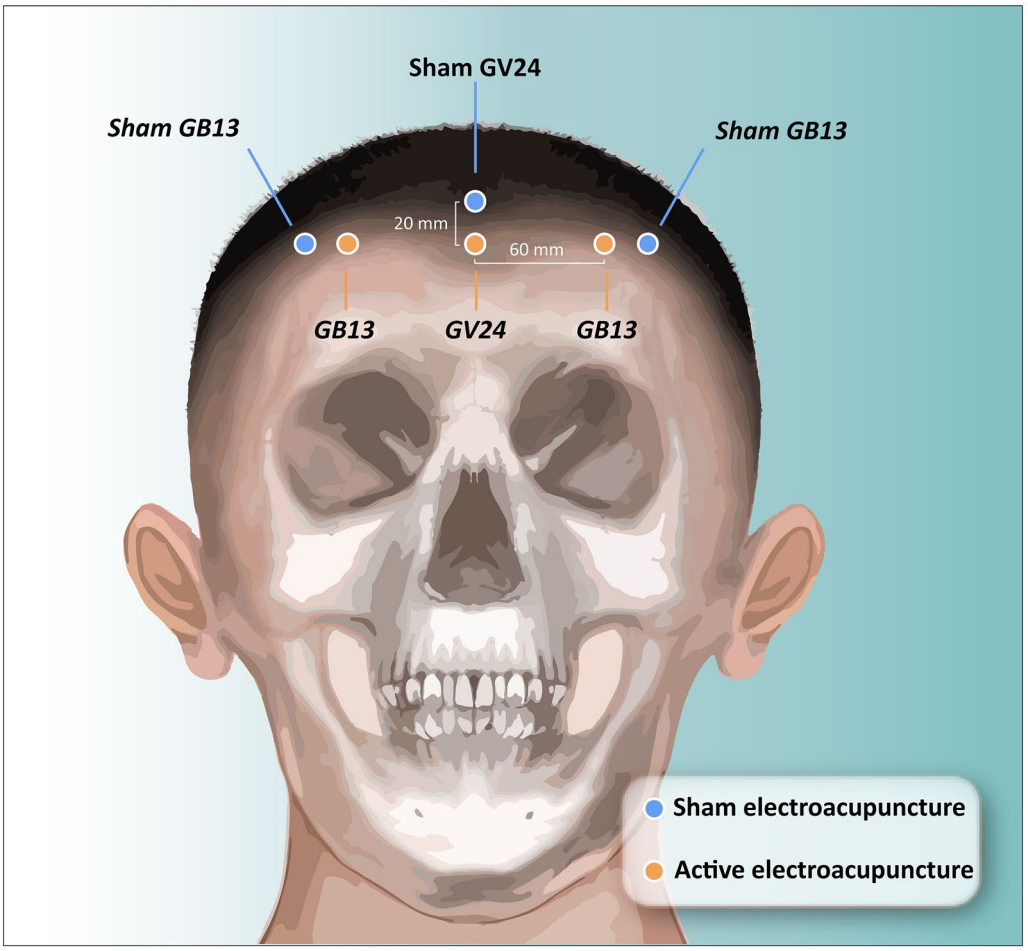


**Figure 2.** Location of acupoints for patients receiving active electroacupuncture and sham electroacupuncture.
Notes: Frontal view showing acupuncture point locations. Active electroacupuncture points (orange) at bilateral GB13 (Benshen) and GV24 (Shenting). Sham electroacupuncture points (blue) positioned 20 mm lateral to GV24 and 20 mm posterior to bilateral GB13. GB13 = Gallbladder 13; GV24 = Governing Vessel 24.

### *Standard anesthetic management*

All patients will receive standardized anesthetic care with continuous monitoring throughout surgery. The protocol includes: pre-oxygenation (100% oxygen, 3 min); induction with propofol 1.5–2.0 mg/kg, sufentanil 0.3 μg/kg, and rocuronium 0.6 mg/kg; laryngeal mask airway insertion; and maintenance with sevoflurane 1.5% and remifentanil 0.05–0.2 μg/kg/min. Hemodynamics will be maintained within 20% of baseline with a bispectral index between 40 and 60. Additional rocuronium 0.15 mg/kg maintains muscle relaxation as needed. At surgery completion, sugammadex reverses neuromuscular blockade before airway removal. Immediate postoperative analgesia includes wound infiltration (20 mL 0.5% ropivacaine), intravenous flurbiprofen axetil (50 mg initially, then every 6 h for 72 h), and patient-controlled morphine (2.0 mg bolus, 10-minute lockout) for pain exceeding 3/10.

### *Postoperative care*

After achieving recovery criteria (Aldrete score ≥9), patients will be transferred to orthopedic wards with 1:4 nurse ratios (during days) and 1:6 (at nights). Monitoring includes: 24-hour oximetry, vital signs every 4 h (for 48 h) then every 8 h, and daily wound checks. Analgesia continues for 72 h: scheduled flurbiprofen (50 mg every 6 h), patient-controlled morphine for breakthrough pain, ice therapy (20 min every 2 h while awake), and transition to oral celecoxib (200 mg twice daily) from day 3. Pain assessment occurs every 4 h.

Structured mobilization begins immediately: Day 0—bed exercises; Day 1—bedside sitting, passive motion (0–40°), assisted walking; Day 2—50-meter ambulation, active flexion to 60°; Day 3+ – independent walking, progressive flexion targeting 90°. Physical therapy occurs twice daily (30-minute sessions). Patients will be discharged when meeting criteria: independent 100-meter ambulation, 90° knee flexion, controlled pain (score <4), absence of complications, and confirmed home support.

### Delirium prevention protocol

Both groups will receive identical evidence-based prevention measures: orientation boards displaying date and care teams; physiotherapy-assisted mobilization from postoperative day one; family visitation (08:00–20:00) with reorientation participation; immediate access to sensory aids with functionality checks; clustered nighttime care with quiet protocols after 21:00; and optimized analgesia for pain scores >3. These evidence-based interventions represent current best practice, allowing assessment of electroacupuncture's additional benefit beyond standard care.

### Outcomes and assessments

The primary outcome is the incidence of POD within 72 h after surgery, assessed using the CAM, a diagnostic tool specifically designed to identify delirium [18]. This differs from the MMSE used during initial screening, which evaluates baseline cognitive function for eligibility determination rather than acute confusional states. Baseline CAM assessments occur at screening (day −1) and surgery morning (day 0) to detect any pre-existing delirium, not to assess general cognition. CAM-positive patients are excluded and referred for clinical care. The Day 0 morning CAM serves as the definitive baseline, confirming the absence of pre-existing delirium immediately before intervention. CAM diagnoses delirium when criteria 1 (acute onset/fluctuation) and 2 (inattention) are present, plus either criterion 3 (disorganized thinking) or 4 (altered consciousness). Postoperative assessments will occur 2 h post-surgery, then twice daily (09:00–11:00, 18:00–20:00) for three days. Blinded assessors will perform all evaluations. This schedule balances comprehensive detection with feasibility, capturing the period when 90% of POD cases manifest.

Secondary outcomes comprise delirium severity measured using the Delirium Rating Scale-Revised-98 (DRS-R-98) [19]; delirium subtypes classified by the Richmond Agitation-Sedation Scale (RASS) [20]; cognitive function assessed longitudinally using the Abbreviated Mental Test Score (AMTS) at baseline, 1, 3, 6, and 12 months, which provides a brief cognitive screening tool suitable for repeated assessments distinct from the initial MMSE screening [21]; anxiety and depression measured with the Hospital Anxiety and Depression Scale (HADS) assessed preoperatively and daily for 72 h [22]; pain intensity evaluated using the Numeric Rating Scale (NRS) at 1, 3, 6, 12, 24, 36, 48, 60, and 72 h post-surgery; cumulative morphine consumption over 72 h; antipsychotic and sedative medication use including drug type, dose, and duration; recovery quality measured by the Quality of Recovery-15 (QoR-15) questionnaire assessed at discharge and daily for 72 h [23]; and sleep quality evaluated using the Richards-Campbell Sleep Questionnaire (RCSQ) assessed preoperatively and daily for 72 h [24]. Adverse events will be coded using Medical Dictionary for Regulatory Activities (MedDRA) standards.

### Monitoring

The Institutional Review Board appoints monitors for quarterly verification, who recommend trial continuation or termination based on safety and adherence. Quality control ensures multicenter consistency. Personnel undergo standardized training with certification: CAM assessors achieve kappa >0.80 through video cases; acupuncturists demonstrate proficiency *via* practical examination. Monthly calibration meetings maintain assessment consistency. The electronic case report form (eCRF) system provides real-time monitoring with automated validations, triggering 48 h resolution queries. Quarterly visits include 20% source verification and protocol assessment; sites exceeding 5% error rates receive additional support. Discrepancies will be resolved within two weeks.

Safety monitoring employs dual surveillance: structured assessment for electroacupuncture events (ecchymosis, dizziness, hematoma, needle pain) and daily record review for all events. Adverse events

(AEs) will be coded (MedDRA), graded (CTCAE v5.0), and assessed for causality. Serious AEs will be reported within 24 h. The principal investigator will determine intervention-relatedness with independent monitoring. For participants with serious AEs, follow-up is modified to minimize burden while maintaining oversight. Assessments may be adapted (telephone replacing visits) or deferred, documented as missing data, not violations. All AEs will be followed to resolution.

One-year follow-up includes all participants. Lost participants will not be replaced. To minimize attrition, multiple contact methods will be used; reminder calls precede assessments. Participants may withdraw without justification; reasons will be documented when possible to assess bias.

### Sample size calculation

Sample size was calculated using PASS software version 15.0 (NCSS LLC, Kaysville, UT, USA). Based on 23.9% postoperative delirium incidence in older surgical patients [25], 660 participants per group provide 90% power to detect a 30% relative reduction (from 23.9% to 16.8%) with $\alpha = 0.05$ (two-sided). Accounting for 10% attrition, we will enroll 730 participants per group (1460 total). Recognizing that TKA-specific studies report lower incidence (14–16%) [6,26], our protocol includes adaptive sample size re-estimation at the planned interim analysis to maintain statistical power if the observed incidence falls below 20% [27].

### Data collection, management, and analysis

Trained assessors blinded to group allocation will collect all study data, including baseline characteristics, primary and secondary outcomes, and adverse events. Statistical analysis will follow intention-to-treat principles using SPSS version 26.0 (IBM SPSS Inc., Chicago, IL, USA). After normality assessment *via* Shapiro-Wilk tests and Q-Q plots, continuous variables will be reported as mean ± SD (normal) or median (IQR) (non-normal), with group comparisons using Student's t-test or Mann-Whitney U test accordingly. Categorical variables will be expressed as n (%) and compared using $\chi^2$ or Fisher's exact tests. POD incidence will be analyzed using Kaplan-Meier curves with log-rank testing, reporting relative risks and 95% confidence intervals. Statistical significance is set at $p < 0.05$ (two-tailed).

Secondary outcomes will be analyzed using generalized linear mixed models accounting for repeated measures and relevant covariates. Missing data will be handled through multiple imputation with sensitivity analyses evaluating robustness under different assumptions. Post-hoc subgroup analyses will explore effect modification across six predefined categories: age (65–74 vs. ≥75 years), baseline cognition (MMSE 24–26 vs. 27–30), comorbidity burden (Charlson Comorbidity Index ≤2 vs. >2), frailty status (Clinical Frailty Scale), surgery duration (<90 vs. ≥90 min), and preoperative anxiety (HADS-$A$ < 8 vs. ≥8). Treatment-by-subgroup interactions will be tested using regression models with interaction p-values <0.10 indicating potential differential effects. Forest plots will visualize subgroup-specific treatment effects.

An interim analysis at 50% enrollment will evaluate safety and efficacy using predetermined stopping boundaries for futility or harm. The Data Safety Monitoring Board will review results and recommend trial continuation, modification, or termination based on pre-specified criteria.

### Ethics and confidentiality

The Institutional Review Board of Fujian Provincial Hospital approved the study protocol (K2023-02-004/02). The trial is registered at ClinicalTrials.gov (NCT06564506). Written informed consent will be obtained from all participants before study initiation. Each participant will receive a unique identification code for data linkage and eCRF generation. Personal data will remain confidential, requiring explicit authorization from the principal investigator, Yusheng Yao (ORCID: 0000-0001-8488-8876), for disclosure. Study documents will be retained for 10 years post-completion.

### Patient and public involvement

No patient or public involvement occurred in the design or implementation of this study.

### Protocol amendments

Protocol modifications affecting study conduct will be reported to the Institutional Review Board of Fujian Provincial Hospital by the principal investigator, Yusheng Yao (ORCID: 0000-0001-8488-8876), who retains final decision-making authority for all amendments.

### Dissemination plan

Study results will be published in peer-reviewed journals regardless of outcome and presented at scientific conferences. Findings will be shared with participating institutions. The principal investigator, Yusheng Yao (ORCID: 0000-0001-8488-8876), oversees dissemination activities.

## Discussion

Postoperative delirium, the most common surgical complication in older people, manifests as an acute, fluctuating state of confusion, inattention, and altered consciousness within seven days post-surgery [28]. This heterogeneous syndrome confers increased mortality, prolonged hospitalization, and long-term cognitive deterioration [29]. Incidence in patients ≥65 years undergoing orthopedic procedures ranges from 12 to 51% [30].

Total knee arthroplasty provides an optimal model for delirium prevention research due to converging risk factors and rehabilitation demands. TKA uniquely combines multiple delirium precipitants: tourniquet-induced ischemia-reperfusion injury (up to 90 min), bone cement embolization with hemodynamic instability, and severe postoperative pain requiring high-dose opioids [31]. Unlike hip arthroplasty, TKA requires immediate intensive knee mobilization to prevent arthrofibrosis—precisely when delirium risk peaks. Delirium-related mobilization delays increase complications by 35% and extend hospitalization 3–5 days, directly compromising surgical outcomes [32]. This convergence of elevated delirium risk with mandatory early rehabilitation makes TKA ideal for testing preventive interventions with measurable functional impact.

Acupuncture-based interventions demonstrate established perioperative benefits, including pain reduction, nausea relief, and decreased opioid consumption [33,34]. Beyond these conventional applications, emerging evidence suggests specific efficacy in preventing postoperative delirium. Clinical studies indicate that acupuncture techniques represent safe and effective non-pharmacological strategies for delirium prevention [35]. These benefits are especially important for older adults, who face heightened delirium risk from age-related declines in cognitive reserve [36]. Proposed mechanisms include reduced neuroinflammation and neuronal injury, decreased blood-brain barrier permeability, and enhanced cerebral perfusion and metabolism [37]. Among available modalities, electroacupuncture emerges as particularly promising due to its standardizable parameters and consistent therapeutic delivery.

Critically, electroacupuncture is tested as an adjunctive intervention to standard non-pharmacological delirium prevention, not a replacement. Both groups receive identical prevention protocols comprising orientation strategies, early mobilization, family involvement, and sensory optimization [38]. This design isolates electroacupuncture's incremental benefit beyond current best practices, which reduce delirium from 20 to 14%—a 30% relative reduction—in orthopedic populations [39,40]. Unlike multicomponent interventions requiring sustained staffing over multiple days, electroacupuncture provides a pragmatic single-session treatment readily integrated into surgical workflows while targeting distinct neuroinflammatory pathways.

Sham acupoints were carefully selected and validated to maintain blinding integrity. Positioned 20 mm from true acupoints in different dermatomes, these locations minimize neurological overlap. Preliminary studies confirmed no measurable physiological responses, including absent brain activation patterns on functional imaging and no autonomic changes. The retractable needle design prevents skin penetration while maintaining visual similarity to active treatment, and absence of electrical stimulation eliminates the therapeutic component. This protocol provides methodologically rigorous control while preserving participant blinding and ethical standards.

Optimal electroacupuncture parameters—including acupoint selection, frequency, intensity, and timing—remain incompletely defined. In Traditional Chinese Medicine, the scalp points GV24 (Shenting) and

bilateral GB13 (Benshen) are linked to cognitive function [41]. This combination, termed 'Acupuncture at 3-points for intelligence', effectively treats cognitive impairment in neurodegenerative conditions including Alzheimer's disease [42]. Given these established cognitive benefits, we hypothesize that preoperative electroacupuncture at GV24 and bilateral GB13 will reduce postoperative delirium incidence in older people undergoing TKA.

We selected electroacupuncture parameters of alternating 2/15 Hz (dense-disperse waves) at 1 mA intensity, consistent with standard clinical practice for perioperative adjuvant treatments [43]. This wave pattern alternates between sparse and dense stimulation, potentially reducing tolerance while enhancing metabolism, blood circulation, and anti-inflammatory effects. Intensity was determined by observed skin trembling and participant comfort, as sensory and tolerance thresholds for scalp acupoints range from 0.2 to 2.5 mA [44]. Our selected intensity of 1 mA produces minimal skin trembling at the acupoint without eliciting pain, ensuring patient comfort and safety.

Timing of electroacupuncture administration is critical for this study. While electroacupuncture can be delivered preoperatively, intraoperatively, or both, we selected a preoperative approach. Participants receive electroacupuncture for 30 min, beginning 30 min before anesthesia induction. This timing was chosen for three reasons: first, it ensures patients receive the full therapeutic effect without anesthetic interference; second, it modulates the autonomic nervous system before surgical stress; and third, it enables treatment during the conscious state, which enhances both efficacy and safety [45]. This design allows clear assessment of electroacupuncture's independent effect on postoperative outcomes. While this timing aligns with established perioperative acupuncture protocols, optimal timing remains to be definitively established through further research.

This multicenter, randomized, double-blind, sham-controlled trial provides robust methodological rigor through standardized training with inter-rater reliability testing (kappa > 0.80), multimodal analgesia protocols, and comprehensive blinding procedures. Our sample size of 1460 participants, calculated based on 23.9% anticipated POD incidence, provides 90% power to detect clinically meaningful differences. The protocol incorporates adaptive sample size re-estimation at interim analysis to maintain statistical power if observed incidence falls below 20%, ensuring robust conclusions regardless of baseline event rates.

Several limitations merit consideration. First, blinding challenges exist despite identical-appearing devices. The de qi sensation unique to active electroacupuncture and potential recognition by patients with remote acupuncture experience (beyond our six-month exclusion window) may compromise masking. We address this through formal blinding verification and planned sensitivity analyses stratified by blinding success. Second, our strict eligibility criteria limit generalizability. Excluding patients on psychotropic medications eliminates approximately 30% of typical TKA candidates, while restricting enrollment to ASA II–III excludes those at highest delirium risk. Using general anesthesia rather than neuraxial techniques diverges from enhanced recovery protocols, and requirements for trained acupuncturists further restrict implementation feasibility. Third, temporal and mechanistic constraints affect interpretation. The 72-hour monitoring period, while capturing peak delirium incidence and aligning with major trials, may miss delayed cases. Twice-daily assessment may underestimate true incidence compared to continuous monitoring. Without biomarkers, we cannot elucidate whether benefits derive from reduced neuroinflammation, improved perfusion, or other mechanisms. Despite these constraints, this trial provides essential efficacy data. Competing risks from mortality and attrition will be addressed through intention-to-treat and sensitivity analyses, with pre-specified subgroup analyses exploring treatment effects across age, cognition, comorbidity, frailty, surgery duration, and anxiety phenotypes.

This study aims to investigate the effects of electroacupuncture on postoperative delirium in older adults undergoing TKA. Our findings will establish whether electroacupuncture warrants inclusion in multimodal delirium prevention protocols for older TKA patients.

## Acknowledgments

The authors acknowledge the contributions of all study participants and their families, as well as the healthcare professionals involved in this trial. We thank the investigators, anesthesiologists, and support staff at participating institutions for their dedication and expertise.

## Author contributions

CRediT: **Yifen Zhuo**: Conceptualization, Funding acquisition, Investigation, Methodology, Resources, Writing – original draft; **Jialin Yang**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Writing – original draft; **Xuezhen Shi**: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft; **Huifen Lin**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software; **Xincheng Liao**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization; **Yusheng Yao**: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing; **Lei Chen**: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – review & editing.

## Patient consent for publication

Not applicable.

## Trial registration

ClinicalTrials.gov; Identifier: NCT06564506.

## Administrative information

This manuscript is based on protocol version 4.0_2024.06.10. Trial sponsor: Yusheng Yao.

## Disclosure statement

The authors report no conflicts of interest in this work.

## Funding

This study is supported by the Science and Technology Program of Haicang District of Xiamen (350205Z20232004), Natural Science Foundation of Xiamen (3502Z202374068), Scientific Research Project from Fujian University of Traditional Chinese Medicine (XB2024002), Natural Science Foundation of Fujian Province (2025J01071), and Joint Funds for the Innovation of Science and Technology, Fujian Province (2023Y9275). The funders had no role in study design, data collection, analysis, or manuscript preparation.

## ORCID

Yifen Zhuo http://orcid.org/0009-0009-1312-5367
Jialin Yang http://orcid.org/0009-0004-7538-8684
Xuezhen Shi http://orcid.org/0009-0008-2444-2299
Huifen Lin http://orcid.org/0000-0003-1315-508X
Xincheng Liao http://orcid.org/0000-0001-5388-5971
Yusheng Yao http://orcid.org/0000-0001-8488-8876
Lei Chen http://orcid.org/0009-0003-5642-155X

## Data availability statement

Individual participant data, study protocol, statistical analysis plan, and clinical study report will be available upon reasonable request from the principal investigator (Yusheng Yao, ORCID: 0000-0001-8488-8876) after publication.

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