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Intraoperative electroencephalogram patterns as predictors of postoperative delirium: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - Risk of bias assessment.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202420001

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 February 2024 and was last updated on 01 February 2024.

INTRODUCTION

Review question / Objective The aim of this systematic review and meta-analysis is to synthesize existing evidence on the predictive value of intraoperative EEG for postoperative delirium (POD) in adults, examining the correlation between specific intraoperative EEG patterns and the subsequent development of postoperative delirium.
(i) population: adult patients following surgery.
(ii) intervention (exposure): presence of intraoperative EEG pattern associated with POD.
(iii) comparator: absence of intraoperative EEG pattern associated with POD.
(iv) outcomes: POD.
(v) study design: prospective and retrospective observational studies, post-hoc analyses of randomized controlled trials.

Rationale Postoperative delirium (POD) is a critical neuropsychiatric complication observed in patients following surgical procedures, characterized by acute disturbances in attention, cognition, and consciousness. It is linked to increased morbidity, extended hospital stays, and a heightened risk of long-term cognitive decline, presenting a pivotal challenge in perioperative care. The growing frequency of surgeries, particularly among the elderly, underscores the importance of understanding and mitigating risks of postoperative delirium. This issue is not only significant for patient well-being but also impacts healthcare systems globally, highlighting the urgent need for effective prediction and management strategies.
In this clinical study, the focus is on intraoperative electroencephalography (EEG) monitoring, a promising approach that differs from preoperative evaluations by providing real-time insights into

cerebral function during the surgical process. This dynamic monitoring could be crucial in identifying early neural markers of POD, potentially enabling interventions at a stage where they might be most effective.
Recent developments, including a meta-analysis, have raised doubts about the efficiency of Bispectral Index (BIS) monitoring in reducing the incidence of POD. This finding emphasizes the need to explore alternative monitoring approaches that may offer better predictive value for POD.
Furthermore, the paradigm of intraoperative EEG monitoring has evolved in response to contemporary guidelines aimed at managing postoperative delirium. These guidelines advocate a return to native EEG and density spectral array patterns during intraoperative monitoring as a proactive measure against POD. This shift is based on new evidence suggesting that these methods may provide more accurate and timely identification of early neural markers associated with POD development.
The aim of this systematic review and meta-analysis is to synthesize existing evidence on the predictive value of intraoperative EEG for POD in adults, examining the correlation between specific intraoperative EEG patterns and the subsequent development of postoperative delirium.

Condition being studied Postoperative delirium is a common complication in the older surgical population, with significant sequelae and associated burden on healthcare.

METHODS

Search strategy A systematic literature search of studies published between January 1, 2003, and October 23, 2023 was conducted in PubMed, Medline and Cochrane CENTRAL by three independent investigators. Both backward and forward snowballing methods were also used for an exhaustive search (Litmaps service). Language restrictions were not applied.

Participant or population Adult patients (without restrictions on age, sex, race, or ethnicity) following surgery.

Intervention Presence of intraoperative EEG pattern associated with postoperative delirium, e.g. presence of burst suppression.

Comparator Absence of intraoperative EEG pattern associated with postoperative delirium.

Study designs to be included We included prospective and retrospective observational studies, and also considered post-hoc analyses of randomized controlled trials.

Eligibility criteria We focused on prospective and retrospective observational studies that explored predictors of POD using intraoperative native EEG signal analysis in adult patients. Studies were excluded if they met one of the following criteria: 1) were review articles, case reports or letters to the editors; 2) followed EEG-guided anesthesia; 3) reported no outcome data; 4) utilized non-intraoperative EEG; 5) evaluated bispectral index (BIS).

Information sources PubMed, Medline, Cochrane CENTRAL and databases from Litmaps service (Crossref, Semantic Scholar, OpenAlex).

Main outcome(s) The meta-analysis specifically focused on the burst suppression pattern in EEG, examining its duration, ratio, and presence.

Additional outcome(s) We also analyzed EEG wave patterns (alpha, beta, delta, theta).

Quality assessment / Risk of bias analysis The internal validity and risk of bias of the included studies will be assessed by two independent investigators using the “Tool to assess risk of bias in cohort studies” contributed by the CLARITY Group at McMaster University.
Publication bias and small-study effects will be assessed using Egger's test and funnel plot analysis. The certainty of evidence will be assessed with the GRADE systematic approach.

Strategy of data synthesis Data extraction was performed by three independent authors. The data extracted included study design, sample size, first author, publication year, journal name, method of POD assessment, study setting, participant age and sex, American society of anesthesiologists (ASA) score, type of anesthesia used, duration of surgery and anesthesia, length of intensive care unit (ICU) and hospital stay, intraoperative EEG timing, and the types and characteristics of EEG patterns in both POD and non-POD groups.
We will convert the data to the mean ± standard deviation (SD) format if needed.
STATA 17.0 software (StataCorp LLC, Texas, US) will be used to calculate and visualize the results of the meta-analysis. Inter-study heterogeneity will be evaluated using the I-squared (I2) statistic and the Cochrane Q test. Standardized mean differences (SMD) with 95% confidence intervals (CIs) will be calculated for quantitative data. We will follow the Cochrane Handbook guidelines to interpret SMD using rules of thumb for effect size (0.70 = large

effect) [https://training.cochrane.org/handbook/archive/v6/chapter-15].
A fixed-effects inverse-variance model will be applied in cases of low statistical heterogeneity (I^2 0.05), while a random-effects model (restricted maximum likelihood [REML]) was used for $I^2 \geq 60\%$ and/or $p < 0.05$.
Statistical significance for hypothesis testing will be set at the 0.05 level. Diagnostic accuracy of burst suppression presence will be evaluated through pooled metrics: sensitivity, specificity, positive and negative likelihood ratios (PLR and NLR), along with the summary receiver-operating characteristic (SROC) area under the curve (AUC), employing the 'midas' module in STATA 17.0. We will also calculate a weighted average AUC based on the type of detected EEG wave (alpha, beta, delta, theta).

Subgroup analysis None.

Sensitivity analysis For a more convenient way of comparing effect sizes, direct mean difference (MD), odds ratio (OR) and risk ratio (RR) values will be additionally calculated and analyzed.

Language restriction No language limitations.

Country(ies) involved Russian Federation.

Keywords Electroencephalography; postoperative delirium; burst suppression; surgery.

Contributions of each author
Author 1 - Valery Likhvantsev - conceived and designed the analysis, revised the manuscript, wrote the paper.
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