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Intraoperative Frontal Electroencephalogram Alpha Power Is Associated with Postoperative Mortality and Other Adverse Outcomes

Rory Vu Mather, M.S., Ryan Nipp, M.D., M.P.H., Gustavo Balanza, M.D., Tom A. D. Stone, M.S., Rodrigo Gutierrez, M.D., Ph.D., Praachi Raje, M.D., Masaya Higuchi, M.D., M.P.H., Ran Liu, Ph.D., Laura A. Santa Cruz Mercado, M.D., Edward A. Bittner, M.D., Ph.D., Hiroko Kunitake, M.D., M.P.H., Patrick L. Purdon, Ph.D.

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ABSTRACT

Background: With estimated global postoperative mortality rates at 1% to 4% leading to approximately 3 million to 12 million deaths per year, an urgent need exists for reliable measures of perioperative risk. Existing approaches suffer from poor performance, place a high burden on clinicians to gather data, or do not incorporate intraoperative data. Previous work demonstrated that intraoperative anesthetics induce prefrontal electroencephalogram (EEG) oscillations in the alpha band (8 to 12 Hz) that correlate with postoperative cognitive outcomes.

Methods: The authors analyzed a retrospective cohort of 1,081 patients undergoing surgery with general anesthesia at Massachusetts General Hospital (Boston, Massachusetts) with intraoperative EEG recordings. The association between EEG alpha power and adverse outcomes was characterized using statistical models that were fitted on propensity weighted data. The primary outcome was postoperative mortality, measured from date of surgery to date of death or last follow-up. Secondary outcomes included mortality within prespecified time windows (30 days, 90 days, 180 days, and 1 yr), hospital and postanesthesia care unit lengths of stay, discharge to long-term care, and 30-day hospital readmission.

Results: Alpha power was associated with mortality risk (hazard ratio, 0.92; 95% CI, 0.85 to 0.99; $P = 0.039$). Within specified time windows, alpha power was associated with 30-day mortality (odds ratio, 0.81; 95% CI, 0.66 to 0.95; $P = 0.010$), 90-day mortality (odds ratio, 0.68; 95% CI, 0.55 to 0.79; $P < 0.001$), 180-day mortality (odds ratio, 0.75; 95% CI, 0.66 to 0.83; $P < 0.001$), and 1-yr mortality (odds ratio, 0.85; 95% CI, 0.79 to 0.91; $P < 0.001$). Additionally, alpha power was associated with discharge to long-term care (odds ratio, 0.91; 95% CI, 0.86 to 0.96; $P < 0.001$). We did not find significant associations among alpha power and 30-day readmission and hospital or postanesthesia care unit lengths of stay.

Conclusions: Intraoperative EEG alpha power is independently associated with postoperative mortality and adverse outcomes, suggesting it could represent a broad measure of postoperative physical resilience and provide clinicians with a low-burden, personalized measure of postoperative risk.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- There are a variety of postoperative mortality prediction models based on preoperative comorbidities and features of surgery, but the complexity of the required information puts a burden on their widespread usage
- It is known that cognition is related to patient resilience

What This Article Tells Us That Is New

- A low intraoperative electroencephalogram alpha power was an independent risk factor for increased postoperative mortality
- Anesthetic-induced alpha electroencephalogram power can be seen as a broad measure of postoperative resilience

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Rory Vu Mather, M.S.: Harvard/MIT MD-PhD Program, Boston, Massachusetts; Harvard-MIT Program in Health Sciences and Technology, Cambridge, Massachusetts; Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts; Department of Anesthesia, Perioperative and Pain Medicine, Stanford University School of Medicine, Palo Alto, California.

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Global access to life-saving surgical procedures has dramatically increased in recent years. There were an estimated 234 million surgeries performed in 2004 worldwide, which increased to greater than 310 million in 2012.[1] Global estimates of early postoperative mortality rates are 1% to 4%, leading to approximately 3 million to 12 million deaths per year, a number around half that of cardiovascular disease and similar to death due to cancer.[1–4] High-risk patients who are older, have coexisting medical diseases, or undergo major surgery have even worse outcomes, accounting for 84% of postoperative deaths.[5] Accurately identifying patients at risk for complications or death after surgery in order to prioritize limited resources remains a challenge. Thus, there is an urgent need for perioperative risk stratification tools to optimize surgical care and postoperative outcomes.

Various physician groups, including the American Heart Association (Dallas, Texas), European Society of Cardiology (Sophia Antipolis, France), and European Society of Anesthesiology and Intensive Care (Brussels, Belgium), recommend using preoperative prediction models to estimate postoperative mortality risk.[6–9] Examples they recommend include the American Society of Anesthesiologists (ASA; Schaumburg, Illinois) Physical Status, Physiologic and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM), and American College of Surgeons (Chicago, Illinois) National Surgical Quality Improvement Program (ACS-NSQIP). While these models have been validated for clinical use, they have yet to achieve mainstream use due to suboptimal performance and/or the high burden placed on physicians to gather the information necessary to use the algorithm.[10] It is now widely recognized that cognition plays an important role in physical resilience, but the aforementioned models do not incorporate robust measures of cognition.[11] In addition, these tools also do not take into account intraoperative data. Multiple studies have found that the inclusion of intraoperative data in risk prediction algorithms leads to better performance than preoperative data alone, but obtaining these data during surgery can be a barrier.[12–14] An opportunity therefore exists to improve postoperative outcome prediction by incorporating information related to cognition and from the intraoperative period.

Intraoperative electroencephalogram (EEG) recordings hold potential as a low-burden, novel, and scalable measure of postoperative risk. EEG has become a standard component of anesthetic monitoring at many medical institutions, and past studies have shown EEG abnormalities related to hypoxia, sepsis, and mortality.[15–19] Previous work demonstrated that the anesthetics propofol and sevoflurane inhibit thalamocortical circuits, inducing prefrontal cortical oscillations in the alpha band of EEG frequencies (8 to 12 Hz) that are correlated with postoperative delirium and cognitive decline.[20–23] These studies highlight the ability of EEG biomarkers to provide a real-time measure of patient health and risk for adverse outcomes after surgery.

In this study, we sought to determine whether intraoperative frontal EEG alpha power is independently associated with postoperative outcomes. We used data from a large, retrospective cohort of surgical patients with intraoperative EEG recordings to evaluate associations of alpha power with postoperative mortality and other adverse outcomes. By understanding these associations of intraoperative EEG recordings with important postoperative clinical outcomes, findings from this work will help to inform future efforts to develop and test proactive strategies for enhancing perioperative care delivery and outcomes.

Materials and Methods

Design, Data Source, and Study Population

The study design and a waiver of informed consent were approved by the Massachusetts General Hospital (Boston, Massachusetts) institutional review board (#2021P000892 and #2019P002417). Informed consent was waived because we only analyzed retrospective clinical data collected as part of standard of care for the institution, and analyses of these data posed minimal risk. We established an *a priori* statistical analysis plan that defined all variables, exposures, and outcomes, and outlined analysis procedures (see statistical analysis plan, https://links.lww.com/ALN/D766).

We included a retrospective cohort of patients who underwent a surgical procedure requiring general anesthesia at Massachusetts General Hospital between April 2016 and December 2019 with an intraoperative EEG

Ryan Nipp, M.D., M.P.H.: Section of Hematology/Oncology, Department of Internal Medicine, University of Oklahoma, Health Sciences Center, Stephenson Cancer Center, Oklahoma City, Oklahoma.

Gustavo Balanza, M.D.: Department of Anesthesia, Perioperative and Pain Medicine, Stanford University School of Medicine, Palo Alto, California.

Tom A. D. Stone, M.S.: Department of Anesthesia, Perioperative and Pain Medicine, Stanford University School of Medicine, Palo Alto, California; Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts.

Rodrigo Gutierrez, M.D., Ph.D.: Department of Anesthesia, Perioperative and Pain Medicine, Stanford University School of Medicine, Palo Alto, California; Department of Anesthesia and Perioperative Medicine, University of Chile, Santiago, Chile.

Praachi Raje, M.D.: Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts.

Masaya Higuchi, M.D., M.P.H.: Department of Medicine, Division of Palliative Care and Geriatric Medicine, Massachusetts General Hospital, Boston, Massachusetts; Department of Neurosurgery, Graduate School of Medicine, Tohoku University, Sendai, Japan.

Ran Liu, Ph.D.: Department of Anesthesia, Perioperative and Pain Medicine, Stanford University School of Medicine, Palo Alto, California.

Laura A. Santa Cruz Mercado, M.D.: Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Hospital, Boston, Massachusetts.

Edward A. Bittner, M.D., Ph.D.: Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts.

Hiroko Kunitake, M.D., M.P.H.: Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts.

Patrick L. Purdon, Ph.D.: Department of Anesthesia, Perioperative and Pain Medicine, Stanford University School of Medicine, Palo Alto, California.

(fig. 1). We extracted patient data from the electronic health record and conducted a complete case analysis. Race and ethnicity were included as patient baseline variables; their associations with our alpha power variable were controlled for through propensity score reweighting. They were also collected to present the demographics characteristics of our study cohort. Cases were excluded if they did not have a complete EEG recording or electronic health record data for analysis, and if their EEG did not have artifact-free regions for window selection necessary for spectral analysis. To identify any potential selection bias in our study population, we compared the set of demographics, baseline comorbidities, past surgical history, and characteristics of surgery between subjects excluded and included in our study (eMethods in Supplemental Digital Content, https://links.lww.com/ALN/D767).

Exposure

Our exposure variable was intraoperative frontal EEG alpha power, defined as the spectral power within the alpha band of frequencies (8 to 12 Hz) measured in decibels. Frontal EEG recordings were collected using the SedLine Brain Function Monitor (Masimo Corporation, USA). The SedLine SEDTrace (Masimo Corporation) electrode array records from electrodes located at Fp1, Fp2, F7, and F8, with a ground electrode at Fpz and reference electrode around 1 cm above Fpz.

Spectral Analysis Methods and EEG Analysis Window Selection

We used multitaper spectral estimation methods implemented in the MNE-Python toolbox to compute the EEG power spectra and spectrogram for each patient.[24] EEG data were lowpass filtered at 40 Hz. We estimated the spectra and spectrograms using the following parameters: detrended windows of length 4 s with no overlap and spectral resolution of 1 Hz, thus time half-bandwidth product of 2 and 3 tapers. Power in the alpha band was computed by integration of the multitaper spectrum between 8 and 12 Hz, averaging across each 4-s window and channel, and then converting to the decibel scale.

For each patient, we visually selected the first 2-min time window greater than 10 min past induction that did not contain any artifacts or burst suppression and had stable EEG dynamics on the spectrogram (*i.e.*, no transitions with emergence or burst suppression). Burst suppression is a state of profound brain inactivation that can be induced by high anesthetic doses, which has a characteristic "flickering" between high-power broad-spectrum peaks and isoelectricity in the EEG spectrogram.[25] The investigator conducting the visual EEG assessment was blinded to all outcomes while performing window selection.

Outcomes

Our primary outcome was postoperative mortality, extracted from the patient's electronic health record or the

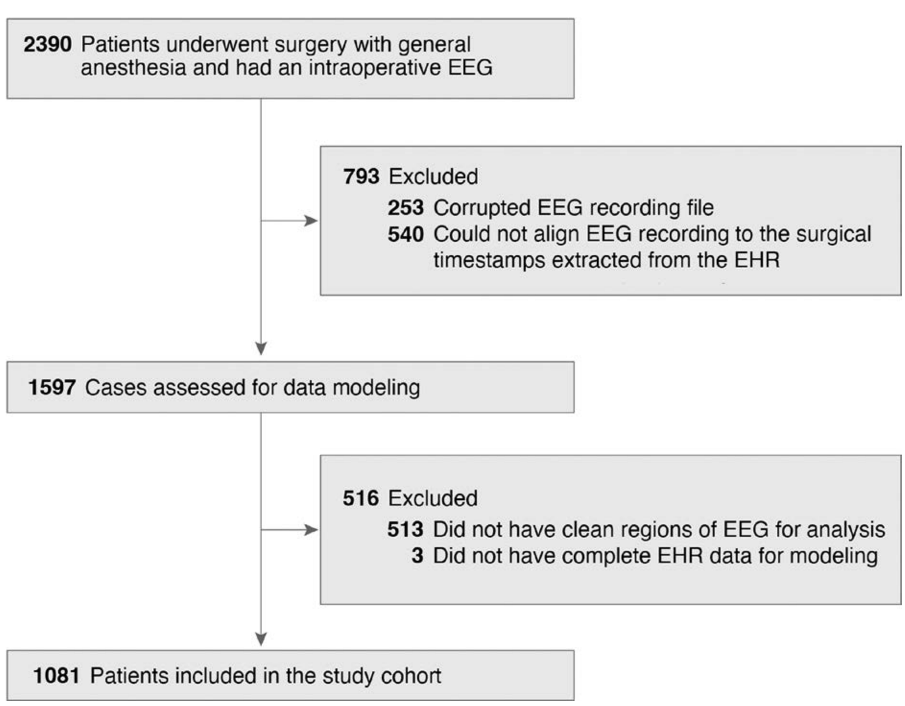

Fig. 1. Flow diagram of our study population. EEG, electroencephalogram; EHR, electronic health record.

State of Massachusetts death registry, and measured from the date of surgery to date of death or last follow-up, up until the data collection date: November 21, 2022. Secondary outcomes included mortality within prespecified time windows (*i.e.*, 30 days, 90 days, 180 days, and 1 yr), hospital and postanesthesia care unit (PACU) lengths of stay, discharge to long-term care, and 30-day hospital readmission (eMethods in Supplemental Digital Content, https://links.lww.com/ALN/D767).

Statistical Analysis

To account for potential preoperative confounders that could affect intraoperative EEG alpha power, the data set was weighted using a multivariable propensity score that incorporated prespecified confounding variables (table 1). These variables included patient demographics, preoperative baseline comorbidities, medical treatment history, history of surgical complications, and neurologic diagnoses known to correlate with anesthetic-induced EEG alpha power (*i.e.*, dementia, delirium, and Alzheimer disease; eMethods in Supplemental Digital Content, https://links.lww.com/ALN/D767). We calculated propensity scores using a generalized boosted model and the "mlrMBO" package in R (Version 4.3.3, accessed February 2, 2024) to perform Bayesian optimization for hyperparameter selection, modeling our intraoperative EEG alpha power exposure dependent on the set of prespecified confounding variables.[26,27] We reweighted the data using this score to control for the effects of these confounding variables on the exposure.[28] Correlations between the propensity score variables and the alpha power exposure before and after reweighting are presented in table 1. Variables that were not well-balanced after weighting (defined as absolute weighted correlation with alpha power above 0.1) were included in the regression model as covariates to account for residual confounding.

We also included additional adjustment variables as covariates to each model to account for potential confounds occurring intraoperatively (table 1). These included characteristics of surgery, intraoperative vital sign measures, blood loss, and anesthetic dosing measured as average end-tidal concentration for inhalatory agents and cumulative infused dose for propofol. We conducted a sensitivity analysis to determine the impact of these covariates on primary and secondary outcomes (eFigure 2 in Supplemental Digital Content, https://links.lww.com/ALN/D767).

We performed multivariable regression analysis to determine whether intraoperative frontal EEG alpha power was associated with adverse postoperative clinical outcomes. Cox proportional hazards regression was used to model time-to-event outcomes (postoperative mortality, PACU length of stay, and hospital length of stay). Logistic regression was used to model binary outcomes (mortality within 30 days, 90 days, 180 days, and 1 yr after surgery, discharge to long-term care, and 30-day hospital readmission). A Bonferroni correction was applied to the analysis of our secondary outcomes to account for multiple comparisons. Given the low prevalence of our outcomes, the odds ratios from our models approximated risk ratios, and we interpreted them as such.[29] All analyses were conducted in R (version 4.2.1).

Results

The study cohort included 1,081 individuals (table 1). Our cohort had a mean ± SD age of 56.3 ± 16.53 yr, and 56.4% (n = 609) were female. General surgery (n = 222; 20.5%), orthopedic (n = 155; 14.3%), and urology (n = 145; 13.4%) were the most common types of surgery, together accounting for 48.2% of all procedures. Propofol was the most common anesthetic administered (n = 1,069; 98.9%) with a median (interquartile range) cumulative dose of 200.00 mg (150.00 to 260.00 mg; fig. 2). Sevoflurane was the second most common anesthetic (n = 779; 72.1%) with a median (interquartile range) of 1.00% (0.00 to 1.39%) for the average end-tidal concentration. Our analysis to identify possible sources of selection bias in those excluded from our study cohort found no meaningful differences in demographics, baseline comorbidities, past surgical history, or features of surgery.

The median (interquartile range) of frontal EEG alpha power was 8.04 dB (4.52 to 11.26 dB). The time from the start of surgery to window selection for EEG alpha power calculation had a median (interquartile range) of 23 min (14 to 43 min). Across the postoperative time windows selected, alpha power was markedly lower in the cohort that died (fig. 3). The cohort overall had a 1,480-day median length of postoperative survival through follow-up, with 99 deaths (9.16%) during the follow-up period. For secondary outcomes, there was a 1.67% 30-day mortality rate, 2.40% 90-day mortality rate, 3.05% 180-day mortality rate, 4.07% 1-yr mortality rate, 7.59% 30-day rate of readmission, 7.40% rate of discharge to long-term care, 2.08-h median PACU length of stay, and 1.24-day median inpatient length of stay.

For our primary outcome, frontal EEG alpha power was associated with mortality with a hazard ratio of 0.92 (95% CI, 0.85 to 0.99; $P = 0.039$) per decibel of alpha power (fig. 4). For our secondary outcomes modeling mortality within specified time windows, alpha power was associated with 30-day mortality, with an odds ratio of 0.81 (95% CI, 0.66 to 0.95; $P = 0.010$), 90-day mortality, with an odds ratio of 0.68 (95% CI, 0.55 to 0.79; $P < 0.001$), 180-day mortality, with an odds ratio of 0.75 (95% CI, 0.66 to 0.83; $P < 0.001$), and 1-yr mortality, with an odds ratio of 0.85 (95% CI, 0.79 to 0.91; $P < 0.001$). Alpha power was associated with discharge to a long-term care facility with an odds ratio of 0.91 (95% CI, 0.86 to 0.96; $P < 0.001$). We did not find a significant association between alpha power and 30-day readmission, hospital length of stay, or PACU length of stay. Our sensitivity analysis found that removing the intraoperative adjustment covariates did not meaningfully change the magnitude or direction of our modeled

Table 1. Baseline Statistics and Clinical Characteristics with Propensity-Weighted Correlations of the Study Population

Statistic	No. (%)	Correlation with Alpha Power (Unweighted/Weighted)
Demographics		
Total No. of patients	1,081	
Age, yr, mean ± SD	56.33 (16.53)	0.527/0.187
Female	609 (56.4%)	0.205/0.182
Race		
White	849 (78.6%)	
Asian	48 (4.4%)	0.056/0.024
Black	47 (4.4%)	0.013/0.033
Hispanic	71 (6.6%)	0.125/0.117
Other	66 (6.1%)	0.026/0.053
Baseline variables		
Body mass index, mean ± SD	28.05 (6.77)	0.038/0.056
Elixhauser Comorbidity Index, mean ± SD	1.18 (1.49)	0.016/0.031
Diagnosis of dementia, delirium, or Alzheimer's disease	49 (4.5%)	0.142/0.079
Anemia diagnosis	359 (33.2%)	0.224/0.062
History of anticoagulant use	539 (49.9%)	0.082/0.085
History of preoperative cancer treatment	222 (20.6%)	0.127/0.060
Cancer diagnosis	611 (56.6%)	0.069/0.096
Cancer metastasis diagnosis	31 (2.9%)	0.090/0.033
History of surgical complication	37 (3.4%)	0.001/0.052
Exposure		
Alpha power, dB, median (interquartile range)	8.04 (4.52–11.26)	
Surgical baseline variables		
Surgery service		
General surgery	222 (20.5%)	
Plastic surgery	89 (8.2%)	
Surgical oncology	113 (10.5%)	
Gynecology	102 (9.4%)	
Urology	146 (13.5%)	
Thoracic surgery	87 (8.0%)	
Orthopedic surgery	155 (14.3%)	
Other	167 (15.4%)	
Inpatient	785 (72.7%)	
Elective surgery	283 (26.2%)	
Vasopressors administered intraoperatively	936 (86.7%)	
Laparoscopic surgery	274 (24.5%)	
Conversion from laparoscopic to open surgery	2 (0.2%)	
Dalton Procedural Severity Score		
Mortality, median (interquartile range)	40.59 (24.64–53.60)	
Morbidity, median (interquartile range)	73.23 (0.00–81.41)	
Surgical duration, h, median (interquartile range)	3.02 (2.03–4.50)	
Blood loss, l, median (interquartile range)	0.01 (0.00–0.14)	
Hypotensive duration, min, median (interquartile range)	2.00 (0.00–11.00)	
Tachycardic duration, min, median (interquartile range)	0.00 (0.00–5.00)	
Bradycardic duration, min, median (interquartile range)	12.00 (0.00–58.00)	
Anesthesia		
Nitrous oxide	652 (60.3%)	
Desflurane	5 (0.5%)	
Isoflurane	117 (10.8%)	
Sevoflurane	779 (72.1%)	
Propofol	1,069 (98.9%)	
Outcomes		
Postoperative survival through follow-up, d, median (interquartile range)	1,480 (1,405.00–1,621.00)	
30-d mortality	18 (1.7%)	
90-d mortality	26 (2.4%)	
180-d mortality	33 (3.1%)	
1-yr mortality	44 (4.1%)	
30-d readmission	82 (7.5%)	
Discharge to long-term care	80 (7.4%)	
PACU length of stay, h, median (interquartile range)	2.08 (1.44–2.93)	
Hospital length of stay, d, median (interquartile range)	1.24 (0.25–3.92)	

PACU, postanesthesia care unit.

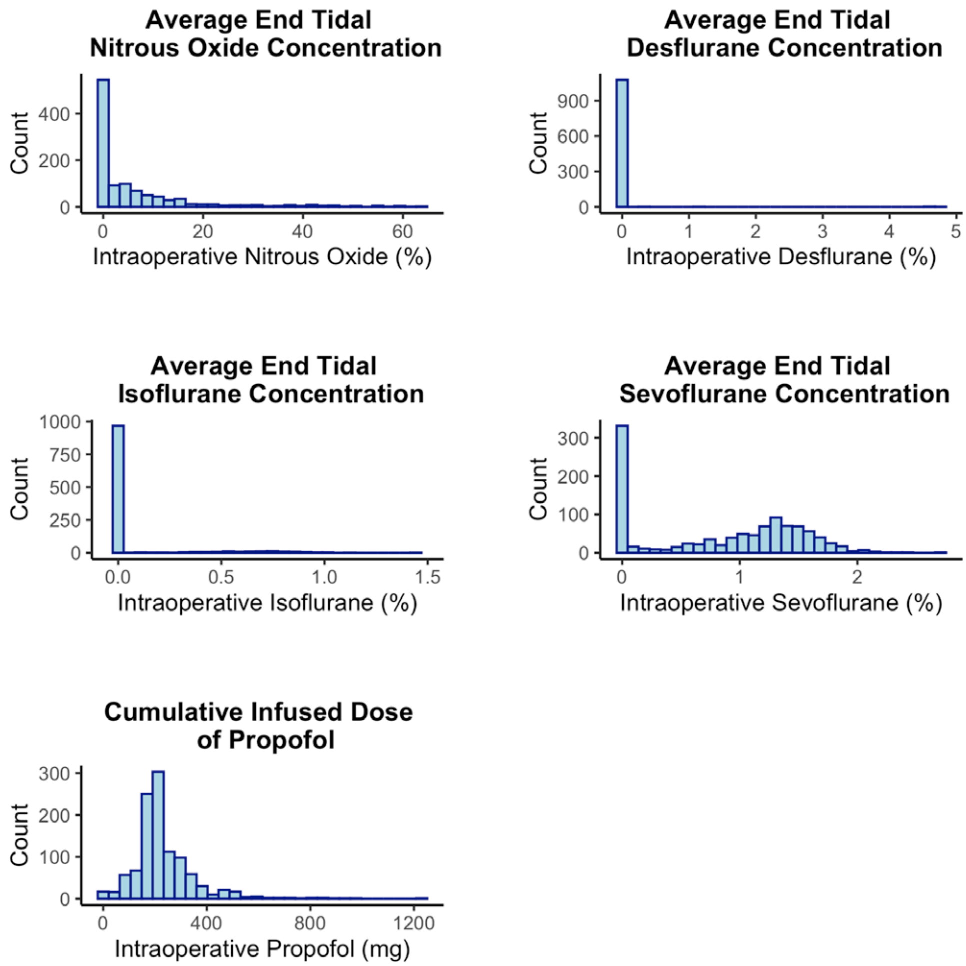

Fig. 2. Distributions of intraoperative anesthetic dosing across our sample population.

effects, and therefore these variables were kept in the model to increase modeling precision (eFigure 2 in Supplemental Digital Content, https://links.lww.com/ALN/D767).

Discussion

In this study, we observed that intraoperative frontal EEG alpha power is associated with adverse postoperative clinical outcomes. Specifically, our data suggest that 1 dB lower alpha power is correlated with a 18.7% increased risk of death at 30 days, 15.2% increased risk of death at 1 yr, and 8.8% increased risk of discharge to long-term care. Alpha power in our population had a 95th percentile of –2.43 to 17.81 dB, and thus these associations represent substantial differences in patient outcomes that could readily be measured in surgical patients.

Previous work has shown that a "triple low" state consisting of low mean arterial pressure, low minimum alveolar concentration fraction of gas anesthetics, and low EEG Bispectral Index correlates with mortality.[30] However, low EEG Bispectral Index only correlated with mortality when paired with other physiologic markers.[30,31] In our study, we found that a single metric extracted only from the intraoperative EEG is independently associated with mortality and other adverse postoperative outcomes, allowing it to be used alongside most anesthetic regimens. We also see that the association between intraoperative EEG alpha power and mortality varies with increasing time after surgery, likely reflecting confounding causes of patient death after surgery not due to their surgical procedure.

We hypothesize that anesthetic-induced EEG alpha power could represent a broad measure of postoperative physical resilience, with potential underlying mechanisms explained by the relationship between EEG alpha power and brain aging. Physical resilience is an emerging concept within geriatric medicine that defines the maintenance or recovery of function after biomedical or pathologic challenges and health stressors.[32] Cognition is thought to be a major determinant of physical resilience, and could serve as an intervenable target for enhancing resilience.[11] Decreased

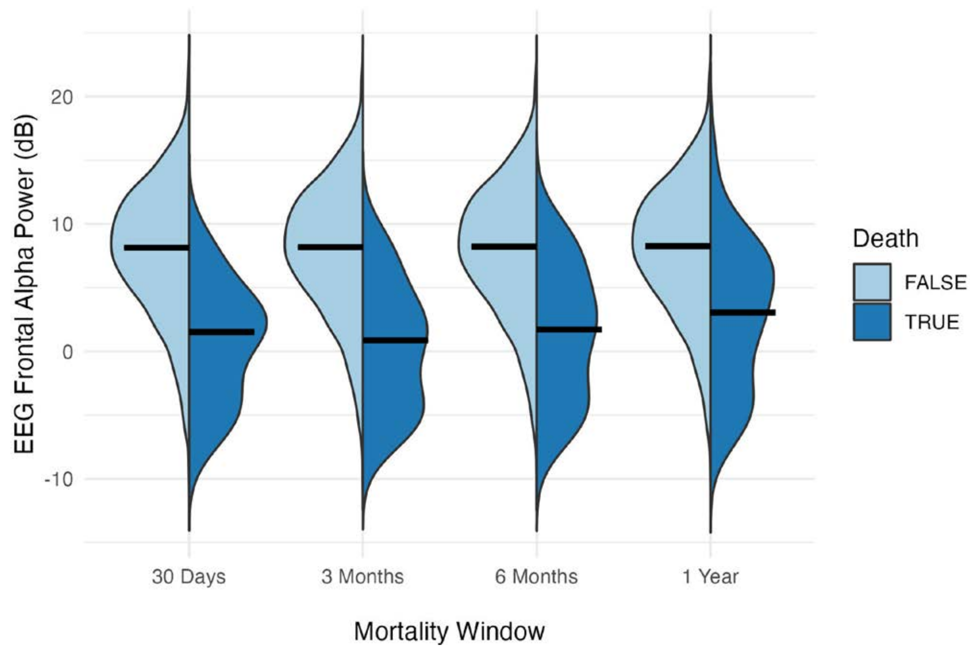

Fig. 3. Violin plots of alpha power split by mortality across specified time windows. Each *violin plot* represents the distribution of alpha power for those who died and survived at 30 days, 3 months, 6 months, and 1 yr after surgery. The *black lines* represent the median of the distribution. EEG, electroencephalogram.

intraoperative EEG alpha power is associated with lower preoperative cognitive function and higher risk of postoperative delirium and cognitive decline.[21–23,33] Past studies have demonstrated that intraoperative EEG alpha power decreases with age, which is likely caused by age-dependent cortical thinning and changes in brain metabolism.[34,35] Together, these results suggest that low anesthetic-induced EEG alpha power could reflect the cognitive component of physical resilience, linking this biomarker with the risk of postoperative complications such as mortality. Given the brain's central role in regulating the human body especially in periods of trauma and stress during and after surgery, it is not surprising that intraoperative EEG alpha power, a direct measure of brain activity shown to relate to cognitive and brain health, could provide additional insight into the physical resilience of a patient after surgery.[36]

To determine whether this hypothesis is reflected in our study cohort, clinical staff on our research team performed a manual chart review of all patients who died within 1 yr after surgery. There were 44 patients within this group, with an older average age compared to the full study cohort (64.97 yr *vs*. 56.33 yr) and lower proportion of female patients (40.9% *vs*. 56.4%). In this cohort of patients that died within 1 yr after surgery, there was a higher proportion of patients diagnosed with cancer as compared to the full study cohort (63.6% *vs*. 56.6%) as well as those who had a history of dementia, delirium, or Alzheimer disease (15.9% *vs*. 4.5%). Median alpha power was markedly lower in the subjects that died (interquartile range) of 3.04 dB (–2.55 to 6.53 dB) as compared to the full study cohort of 8.25 dB (4.80 to 11.37 dB). These patients died on average 96.5 days after their surgery: 25 patients (56.8%) died due to complications from malignancy or associated cancer treatment, 13 patients (29.6%) died due to postsurgical cardiorespiratory failure or sepsis, and 6 patients (13.6%) died while on hospice care for an ongoing chronic disease. This analysis highlights that for these patients who died within a year after surgery, their markedly lower intraoperative alpha power potentially signaled a decreased physical resilience to surgical trauma, complications from surgery, or ongoing chronic disease. While this analysis cannot provide definitive explanations for why this association exists, intraoperative EEG alpha power can still play a role in identifying patients at the highest risk for postoperative mortality and adverse outcomes.

As access to surgical care continues to expand globally, alongside an increasing number of patients with postoperative complications, clinicians and healthcare systems need tools to guide the allocation of limited resources such as ICU beds and blood transfusions.[37] In order for such a predictive tool to be implemented effectively into current medical workflow, it needs to be easy to use by clinicians, personalize predictions to each unique patient, and provide these predictions in real time using only preoperative and/or intraoperative data. There have been a number of

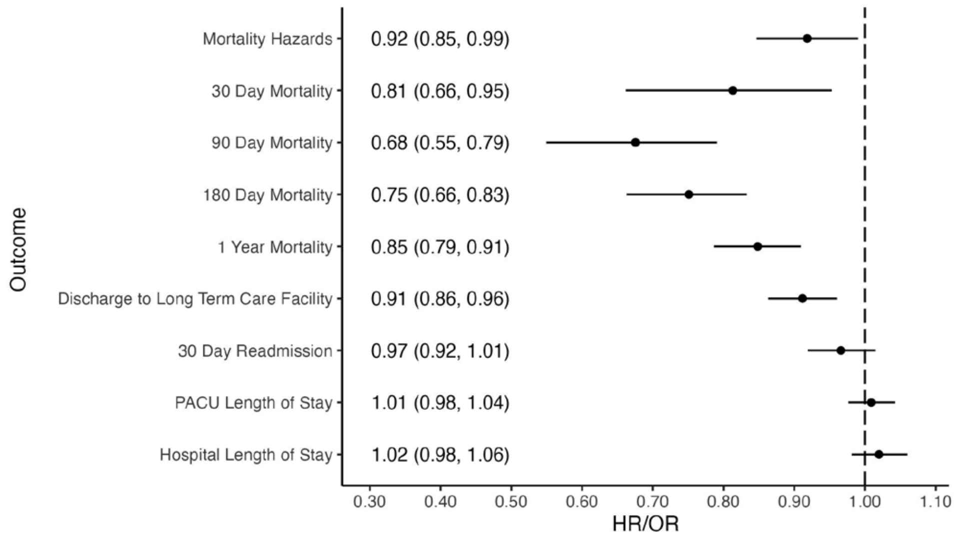

Fig. 4. Model estimates for primary and secondary outcomes. This *forest plot* presents the model estimates with CIs for each outcome with electroencephalogram frontal alpha power as the exposure. Hazard ratios (HR) were estimated for time-to-event outcomes (mortality hazards, postanesthesia care unit [PACU] length of stay, and hospital length of stay) and odds ratios (OR) estimated for binary outcomes (mortality within 30 days, 90 days, 180 days, and 1 yr after surgery, discharge to long-term care (LTC), and 30-day hospital readmission). Odds ratios were calculated by exponentiating model coefficients. We computed the HR by exponentiating the coefficients of the Cox proportional hazards models, which are ratios of event occurrence to population baseline rates. Greater hazard rates predict shorter event occurrence times. Secondary outcome CIs were adjusted using the Bonferroni correction for multiple comparisons.

preoperative risk prediction tools that have been able to achieve some of these features. However, these tools have several limitations, including wide variability among users (ASA Physical Status), inclusion of variables not always available for each patient preoperatively or intraoperatively (POSSUM and ACS-NSQIP), or complex models that require extensive manual chart review to obtain the necessary data to produce individual predictions (ACS-NSQIP).[38–40]

While these preoperative risk prediction tools incorporate data related to physiologic derangement, severity of comorbidities, or invasiveness of surgery, they do not incorporate robust measures of cognitive or brain health. We believe that measuring intraoperative EEG alpha power could supplement preoperative risk predictions and provide clinicians with an additional low-burden, scalable, and personalized method for postoperative risk prediction. Intraoperative alpha power is easy to measure using adhesive disposable EEG electrodes, making implementation into current perioperative workflow potentially easy with little additional burden on healthcare providers and enabling rapid assessment and efficient coordination of follow-up care. More broadly, our results suggest that preoperative information about a patient's cognitive ability could augment existing postoperative risk prediction approaches.

Follow-up care tailored to high-risk patients could take different forms, depending on the particular characteristics of the patient and their surgery. Some patients with low intraoperative EEG alpha power could be flagged for increased postoperative monitoring or evaluated by geriatrics, which has been shown to increase the functional recovery for elderly patients.[41] EEG alpha power could inform clinicians on resource allocation decisions such as transfers to the ICU after surgery. In other scenarios, case management and social work teams could be consulted early in the postoperative period to potentially begin coordination of postdischarge care planning and prioritize patients with the highest predicted risk. Collectively, all of these examples underscore the potential for how risk assessment incorporating intraoperative data could inform systems-level efficiencies in resource allocation to optimize outcomes for the highest-risk surgical patients.

This study did not find an association between intraoperative EEG alpha power and PACU or hospital length of stay. However, we do not believe that this result is inconsistent with our mortality outcomes given that patients who die early may have shorter hospitalizations than comparable patients who recover normally after surgery. Sessler *et al.*, in their study describing the "triple low" state, found that low EEG Bispectral Index was only associated with hospital length of stay when combined with other physiologic markers, and even then, they describe that the magnitude of change was not clinically significant.[30] In total, our findings alongside previous work could suggest that while EEG recordings can provide insight into a patient's postoperative resilience, there are many other factors that influence when a patient is discharged postoperatively.

Further work will be needed to understand the mechanism for how intraoperative EEG alpha power is associated with postoperative mortality and outcomes. Elucidating this pathway could provide methods for clinicians to optimize brain resilience and postoperative care to subsequently improve postoperative outcomes for patients.

Limitations

Limitations of our study include the observational design and potential for residual confounding. Because not all EEG recordings analyzed as part of this study were collected with the intention of performing spectral analysis, many subjects were excluded due to inadequate data quality necessary for alpha power calculation. Our analysis to identify potential sources of selection bias in those excluded from our study found no meaningful differences in patient demographics, baseline comorbidities, past surgical history, or features of surgery (eMethods in Supplemental Digital Content, https://links.lww.com/ALN/D767). Therefore, we suspect that the source of this EEG noise is due to specific features of the EEG monitors used at our institution. In future work, the optimal electrode impedance across all EEG channels could be readily verified before the start of surgery to help mitigate this problem.

Our observational study design also prevents us from making inferences on interventions that could potentially influence intraoperative EEG alpha power and influence postoperative outcomes for patients. Our study population is derived from a single medical center, and thus our findings could reflect patterns of practice limiting the generalizability of our results. This study population also potentially lacks racial and socioeconomic diversity, limiting its generalizability to a broader patient population. Due to study design and sample size limitations, we could not comprehensively account for all potential confounding variables. E-values were used to assess unmeasured confounding (eTable 10 in Supplemental Digital Content, https://links.lww.com/ALN/D767). Our sensitivity analysis suggested that removing the set of adjustment variables to account for sources of intraoperative confounding marginally influenced the magnitude of modeled effects but did not change their direction or interpretation (eFigure 2 in Supplemental Digital Content, https://links.lww.com/ALN/D767).

Conclusions

In this study, we found that intraoperative frontal EEG alpha power is independently associated with mortality and adverse postoperative outcomes for patients undergoing surgery with general anesthesia. EEG monitoring is increasingly incorporated into routine anesthesia monitoring, and therefore intraoperative alpha power could provide clinicians with a low-burden, scalable, real-time personalized measure of each patient's postoperative risk. More broadly, our results suggest that information about a patient's cognitive function could enhance existing approaches for postoperative risk assessment.

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Competing Interests

Dr. Purdon is a cofounder of PASCALL Systems, Inc. (Boston, Massachusetts), a start-up company developing closed-loop physiologic control systems for anesthesiology. The other authors declare no competing interests.

Correspondence

Address correspondence to Dr. Purdon: Department of Anesthesia, Perioperative and Pain Medicine, Stanford University, 3145 Porter Dr. E130, Palo Alto, California 94304. ppurdon@stanford.edu

Supplemental Digital Content

Supplementary Digital Content, https://links.lww.com/ALN/D767

Statistical Analysis Plan, https://links.lww.com/ALN/D766

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