EEG Changes Correlated with Ischemia Across the Sexes in Carotid Endarterectomy

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I. Introduction

In surgical procedures that are at high risk for intraoperative cerebral ischemia, such as carotid endarterectomy (CEA), continuous intraoperative monitoring (IONM) with electroencephalography (EEG) is routinely performed [1, 2]. In IONM, a neurophysiologist visually monitors the EEG and alerts the surgical team when the risk of ischemia is present. During CEA, the risk of ischemia is high in the period immediately after the clamping of the carotid artery. Typical changes reflective of cerebral ischemia that are visually observed on the EEG include an ipsilateral decrease in amplitude of faster frequencies or ipsilateral increase in activity of slower frequencies. Human visual monitoring of the EEG can be tedious and error-prone, and quantitative EEG (QEEG) parameters can enhance visual EEG review. However, it is not known if sex affects QEEG parameters. Thus, in this study, we focus on evaluating the difference in QEEG parameters between females and males, correcting for age and side of surgery.

II. Methods

A database of 1,512 patients who underwent CEA monitored with intraoperative EEG was used for QEEG analysis. EEG was recorded using electrodes placed on the scalp according to the International 10–20 system, and eight channels were recorded: F3-P3, P3-O1, F3-T3, T3-O1, F4-P4, P4-O2, F4-T4, and T4-O2. The EEG recordings were reviewed by a physician trained in IONM, who annotated the time periods in each recording that were indicative of ischemia. For each patient, we extracted a 10-minute recording post-clamp; this recording was partitioned into 20-second intervals, and QEEG parameters were computed from Fourier-transformed power spectra of delta, theta, alpha, beta, and gamma frequency bands [3]. We computed ten QEEG parameters that included normalized alpha, beta, theta, delta power values averaged over four ipsilateral channels, alpha power to delta power ratio (ADR), beta power to delta power ratio (BDR), alpha-plus-beta power to delta-plus-theta power ratio (ABDTR), spectral edge frequency 90% (SEF90) and amplitude-integrated EEG (aEEG). QEEG parameters were calculated from each 20-second post-clamp interval and normalized using a baseline 120-second EEG recorded before carotid clamping. We calculated the maximal trough and peak values for the QEEG parameters compared to the baseline and restricted our analyses to the ipsilateral channels.

We partitioned the database by sex (630 female and 882 male patients). We used the nonparametric Mann-Whitney U test to identify ipsilateral QEEG parameters that were statistically significantly different between the ischemic-change and no-ischemic-change intervals as determined by the physician-assessed time periods of ischemic EEG change. In addition, we performed multivariate logistic regression to predict the odds of ischemic-change for sex, correcting for age and side of surgery.

III. Results

Table 1 shows that for females and males, QEEG trough z-scores were statistically significantly decreased from the pre-clamp baseline for all parameters (ipsilateral 4-channel averaged alpha, beta, theta, delta power values, ADR, BDR, ABDTR, SEF90, and aEEG) in the ischemic-change group. In contrast, QEEG peak z-

Table 1. Comparison of z-scores of ipsilateral QEEG parameters in the ischemic-change versus no-ischemic-change groups for females and males

QEEG Parameter	Females			Males		
	Ischemic-Change Group (n=47)	No-Ischemic-Change Group (n=583)	P-value	Ischemic-Change Group (n=35)	No-Ischemic-Change Group (n=847)	P-value
Delta						
Trough, median	-1.36	-0.97	**<0.001**	-1.86	-1.01	**<0.001**
Peak, median	+0.97	+1.27	0.449	+1.14	+1.48	0.199
Theta						
Trough, median	-1.48	-0.47	**<0.001**	-1.62	-0.46	**<0.001**
Peak, median	+0.47	+1.01	**0.033**	+0.70	+1.04	**0.002**
Alpha						
Trough, median	-2.03	-0.75	**<0.001**	-2.37	-0.78	**<0.001**
Peak, median	+0.35	+0.71	**0.004**	+0.16	+0.80	**<0.001**
Beta						
Trough, median	-1.71	-0.70	**<0.001**	-1.77	-0.70	**<0.001**
Peak, median	+0.54	+0.78	0.059	+0.30	+1.03	**<0.001**
Gamma						
Trough, median	-1.28	-0.61	**<0.001**	-1.12	-0.62	**<0.001**
Peak, median	+1.57	+1.39	0.447	+1.02	+1.88	**0.008**
ADR						
Trough, median	-1.65	-0.98	**<0.001**	-2.22	-1.03	**<0.001**
Peak, median	+0.65	+0.84	0.062	+0.63	+0.92	0.093
BDR						
Trough, median	-1.33	-0.85	**<0.001**	-1.90	-0.95	**0.001**
Peak, median	+0.64	+0.84	0.074	+0.80	+0.95	0.114
ABDTR						
Trough, median	-1.45	-0.91	**<0.001**	-1.59	-1.05	**<0.001**
Peak, median	+0.54	+0.73	**0.048**	+0.44	+0.76	0.191
SEF90						
Trough, median	-1.44	-0.85	**0.011**	-1.52	-0.96	**0.046**
Peak, median	+0.92	+0.99	0.199	+0.92	+1.01	0.248
aEEG						
Trough, median	-1.23	-0.57	**<0.001**	-1.37	-0.54	**<0.001**
Peak, median	+0.75	+0.97	0.178	+0.71	+1.26	0.052

scores were significantly increased from the pre-clamp baseline for fewer parameters; for females, three peak z-scores, and for males, four peak z-scores were significantly increased from the pre-clamp baseline, though the significant parameters were different between the sexes. A decreased trough value is a key indicator of intraoperative cerebral ischemia that neurophysiologists visually monitor during surgery. The results support this observation as all troughs showed a statistically significant difference from baseline for both male and female groups, while each specific QEEG parameter significance difference, the magnitude of the difference, and z-score for each sex allow for comparisons of QEEG values between males and females.

Table 2 provides the results of logistic regression analyses. The background characteristics included in the three models are sex (882 males and 630 females), age (range from 41-96 years old, split into intervals of 10), and side of surgery (746 with left-sided CEA and 766 patients with right-sided CEA), with the outcome variable of ischemic event (82 with event and 1,430 without event). The age distribution was 1% between 40-50 years old, 11% between 50-60 years old, 34% between 60-70 years old, 37% between 70-80 years old, 16% between 80-90 years old, and 1% between 90-100 years old. Multivariate logistic regression shows that the odds of an ischemic-change for a female is 1.98 times the odds of such a change for a male

Table 2. Coefficients of logistic regression for sex, age and side of surgery. Models 1 – 3 are univariate and model 4 is multivariate

	Model 1	**Model 2**	**Model 3**	**Model 4**
Sex	1.95* [1.24-3.06] p-value = 0.004			1.98* [1.26-3.11] p-value = 0.003
Age		1.03* [1.01-1.06] p-value = 0.012		1.03* [1.01-1.06] p-value = 0.010
Side of surgery			1.14 [0.73-1.77] p-value = 0.577	1.17 [0.75-1.84] p-value = 0.483

*$p < 0.05$. 95% confidence intervals included in brackets.

($p<0.05$), and the odds of an ischemic-change increases by 1.03 times for each 1-year increase in age ($p<0.05$). The odds of an ischemic-change for the right-sided CEA is 1.17 times the odds of such a change for left-side CEA; however, this change is not statistically significant at the 0.05 level.

Our results confirm prior studies that a decrease in QEEG parameters is more commonly seen after carotid clamping when compared with an increase [1, 4]. Further, this pattern of change in QEEG parameters is similar in both sexes. Our results also indicate that females have a higher risk of EEG ischemic change during CEA than males, and increasing age increases the risk of EEG ischemic change.

IV. Future Work

In future work, we plan to explore the causes of our finding that women are at higher risk of ischemia during CEA. The patient's overall health and comorbidities may partially explain the differences we saw between males and females, so more of these characteristics will be included in future studies. Another possibility is that women undergo CEA at an older age than men and thus have a higher risk due to increased age. Additionally, potential confounders such as contralateral carotid occlusion, hemispheric versus retinal transient ischemic attack as qualifying events, and ulcerated plaque should be investigated in future work. Some of the limitations of our work include a single physician reviewer who assessed the EEGs for ischemia and the patients in our database underwent CEA in a single health system.

Acknowledgments

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Introduction

Background

- Perioperative stroke is the 3rd leading cause of death.
- Intraoperative neurophysiological monitoring (IONM) is used to monitor for cerebral ischemia.
- Early detection is important for intervention (i.e., mechanical clot removal) to preserve brain tissue.

Figure 1. Example of IONM.

Objective

- Evaluate differences in quantitative EEG (QEEG) parameters between the sexes, correcting for age and side of surgery.

Data Processing

1. **Source**: EEG data for patients collected using 8 channels (4 channels on each side of head).
2. **Preprocessing**: Fast Fourier Transform performed on the raw EEG to obtain power spectrum, which is then transformed by 10 x log_10(power).
3. **Baseline**: region with least variance selected before clamp.
4. **Features**: averages per minute after clamp for each EEG band.

Methods

- 1,512 patients who underwent carotid endarterectomy (CEA) monitored with intraoperative EEG was used for 10 QEEG analysis.
- Data split by sex: 630 female and 882 male patients.
- Analysis: nonparametric Mann Whitney U test & multivariate logistic regression

1) nonparametric Mann Whitney U test to identify ipsilateral QEEG parameters that were statistically significantly different between the ischemic-change and no-ischemic-change intervals as determined by physician assessment

2) multivariate logistic regression to predict the odds of ischemic-change for sex, correcting for age and side of surgery

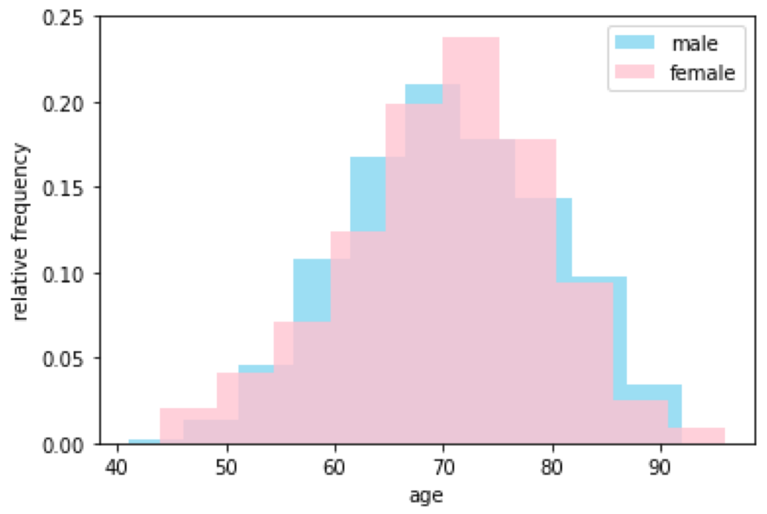

Figure 2. Relative frequency vs. age for patients in the dataset, split by sex.

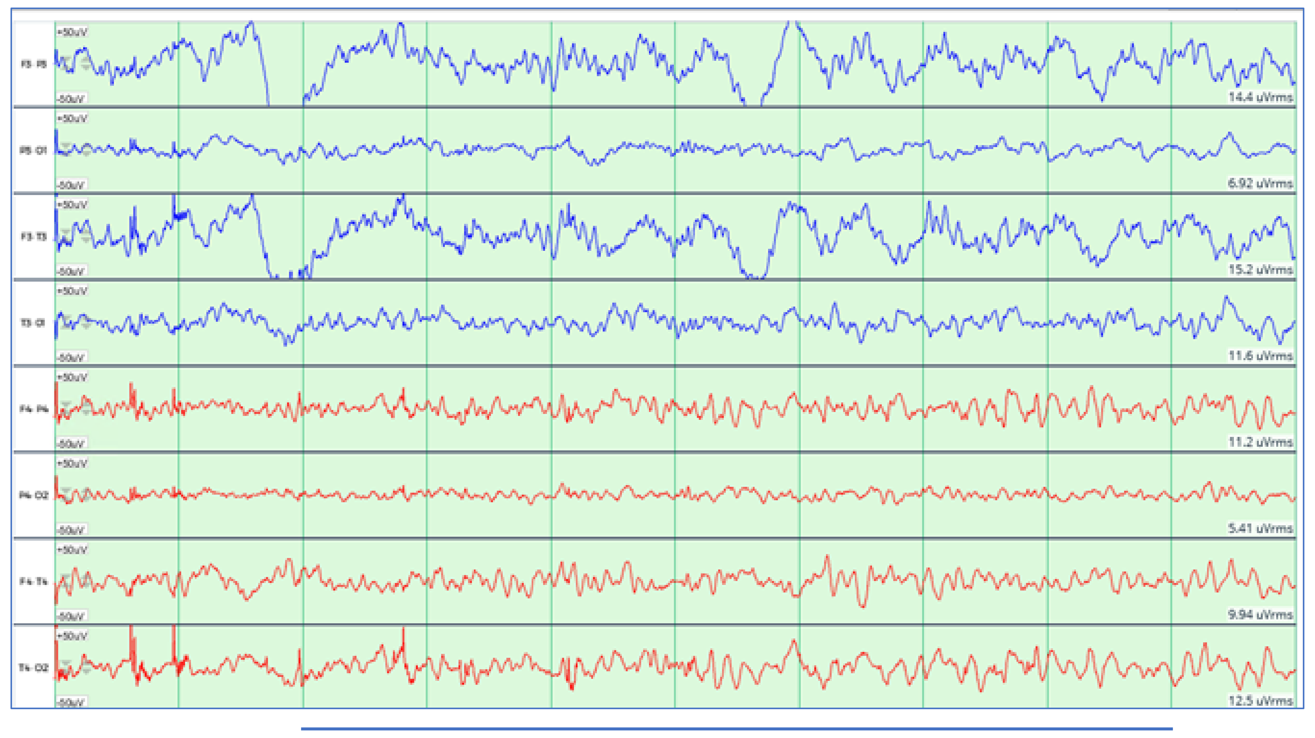

Figure 3. 8-channel EEG data collected during IONM monitoring. The blue line at the bottom indicates an ischemic event as assessed by a monitoring physician.

Results

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Conclusions

- Results confirm prior studies that a decrease in QEEG parameters is more commonly seen in CEA.
- Increased age increases the risk of EEG ischemic change during CEA.
- *Females have a higher risk of EEG ischemic change during CEA compared to males.*