Electroencephalography for detection of vasospasm and delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: a retrospective analysis and systematic review

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OBJECTIVE Good functional outcomes after aneurysmal subarachnoid hemorrhage (aSAH) are often dependent on early detection and treatment of cerebral vasospasm (CVS) and delayed cerebral ischemia (DCI). There is growing evidence that continuous monitoring with cranial electroencephalography (cEEG) can predict CVS and DCI. Therefore, the authors sought to assess the value of continuous cEEG monitoring for the detection of CVS and DCI in aSAH.

METHODS The cerebrovascular database of a quaternary center was reviewed for patients with aSAH and cEEG monitoring between January 1, 2017, and July 31, 2019. Demographic data, cardiovascular risk factors, Glasgow Coma Scale score at admission, aneurysm characteristics, and outcomes were abstracted from the medical record. Patient data were retrospectively analyzed for DCI and angiographically assessed CVS. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and odds ratio for cEEG, transcranial Doppler ultrasonography (TCDS), CTA, and DSA in detecting DCI and angiographic CVS were calculated. A systematic literature review was conducted in accordance with PRISMA guidelines querying the PubMed, Cochrane Controlled Trials Register, Web of Science, and Embase databases.

RESULTS A total of 77 patients (mean age 60 years [SD 15 years]; female sex, $n = 54$) were included in the study. Continuous cEEG monitoring detected DCI and angiographically assessed CVS with specificities of 82.9% (95% CI 66.4%–93.4%) and 94.4% (95% CI 72.7%–99.9%), respectively. The sensitivities were 11.1% (95% CI 3.1%–26.1%) for DCI ($n = 71$) and 18.8% (95% CI 7.2%–36.4%) for angiographically assessed CVS ($n = 50$). Furthermore, TCDS detected angiographically determined CVS with a sensitivity of 87.5% (95% CI 71.0%–96.5%) and specificity of 25.0% (95% CI 7.3%–52.4%). In patients with DCI, TCDS detected vasospasm with a sensitivity of 85.7% (95% CI 69.7%–95.2%) and a specificity of 18.8% (95% CI 7.2%–36.4%). DSA detected vasospasm with a sensitivity of 73.9% (95% CI 51.6%–89.8%) and a specificity of 47.8% (95% CI 26.8%–69.4%).

CONCLUSIONS The study results suggest that continuous cEEG monitoring is highly specific in detecting DCI as well as angiographically assessed CVS. More prospective studies with predetermined thresholds and endpoints are needed to assess the predictive role of cEEG in aSAH.

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KEYWORDS aneurysm; EEG; electroencephalography; delayed cerebral ischemia; SAH; subarachnoid hemorrhage; vasospasm

ANEURYSMAL subarachnoid hemorrhage (aSAH) causes significant morbidity and mortality.^{1,2} This debilitating condition affects as many as 10 individuals per 100,000 population per year.³ More than 10% of individuals who experience aSAH die before reach-

ing the hospital, and an additional one-third of patients die within 24 hours of onset or remain in a poor clinical condition.³ Furthermore, approximately 50% of survivors remain cognitively disabled and unable to return to work.² Cerebral vasospasm (CVS) and delayed cerebral is-

ABBREVIATIONS aSAH = aneurysmal subarachnoid hemorrhage; cEEG = cranial electroencephalography; CVS = cerebral vasospasm; DCI = delayed cerebral ischemia; GCS = Glasgow Coma Scale; NPV = negative predictive value; PPV = positive predictive value; TCDS = transcranial Doppler ultrasonography.

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chemia (DCI) are significant factors associated with poor functional outcomes in aSAH.⁴ CVS typically occurs between postbleed days 3 and 21, with a peak between days 6 and 8.⁵ Although CVS is known to be the main driving force in the pathogenesis of DCI, the current understanding of DCI is that it is an evolving multifactorial process comprising cerebral edema, blood-brain barrier disruption, sympathetic nervous system activation, autoregulatory failure, microthrombosis, spreading depolarizations, and inflammation starting as early as 24 hours postbleed and lasting as long as 3 weeks.⁶ Although the diagnosis of DCI relies on serial neurological examinations in adjunct to CT or MRI, the diagnosis of CVS can be established using transcranial Doppler ultrasonography (TCDS), CTA, or DSA.⁷

The early recognition and management of CVS and DCI are critical to prevent the debilitating sequelae of aSAH.⁸ However, the detection of these considerable pathological states remains challenging because of the restricted neurological examination possible in patients with poor-grade aSAH.⁹ Recently, there has been growing evidence that continuous monitoring with cranial electroencephalography (cEEG) may predict CVS and DCI.⁹ In this study, we assess the value of continuous cEEG monitoring for the detection of CVS and DCI in aSAH.

Methods

Retrospective Analysis

The Post-Barrow Ruptured Aneurysm Trial database was reviewed for patients with aSAH and cEEG from January 1, 2017, to July 31, 2019. Demographic data, cerebrovascular risk factors, Glasgow Coma Scale (GCS) score at admission, aneurysm characteristics, and outcomes were abstracted from the medical record and retrospectively analyzed. The cerebrovascular risk profile comprises hypertension, diabetes, smoking status, and cardiovascular disease.

The diagnostic modalities used to detect CVS were TCDS, CTA, DSA, clinical deterioration (defined as a new focal neurological deficit or a decrease in the level of consciousness), and continuous cEEG monitoring. The diagnosis of DCI was established in concordance with the universally valid definition, as either 1) a new focal neurological deficit, a decrease in the level of consciousness, and/or a decrease in the GCS score of at least 2 points for more than 1 hour in the absence of a relatable ischemic event; or 2) an infarct area emerging on CT, MRI, or confirmed on autopsy, after exclusion of procedure-related infarctions.¹⁰ The clinical assessment of DCI was limited for a subset of patients in poor cognitive condition. The cEEG findings were considered positive if the final report of the attending epileptologist indicated vasospasm that occurred on the same day or within 24 hours after DCI diagnosis or angiographic indication of CVS.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and odds ratio (OR) were calculated for each diagnostic modality in patients with DCI and patients with angiographically assessed CVS. The study was approved by the IRB at St. Joseph's Hospital and Medical Center (Phoenix, Arizona).

The need for written consent was waived because of the low risk to study subjects.

Data analysis was performed using R version 4.0.1 (The R Foundation). Data are represented as mean, standard deviation, and 25th and 75th percentile, when appropriate. Sensitivity, specificity, PPV, NPV, and OR are reported as percentages with 95% confidence intervals. The level of statistical significance was set at $p < 0.05$. Data were graphed with Prism version 9.0.2 (GraphPad Software).

Systematic Literature Review

In addition to analyzing our institutional experience, we conducted a systematic literature review in accordance with PRISMA guidelines.¹¹ The PubMed, Cochrane Controlled Trials Register, Web of Science, and Embase databases were queried on September 31, 2021, using the terms “vasospasm, intracranial” or “delayed cerebral ischemia,” in combination with “electroencephalography,” “diagnosis,” and “detection,” either as Medical Subject Headings or as any other variation. No time period restrictions were applied. The resulting articles were screened by title and abstract and collected in an EndNote (Clarivate) library by a single reviewer. Data points that captured the prognostic and diagnostic values of cEEG, including sensitivity, specificity, PPV, and NPV measurements, were extracted. Clinical studies that allowed for data extraction related to the use of cEEG for the diagnosis and/or prognosis of vasospasm were included. We excluded all non-English-language articles and those not conducted on human subjects.

Results

Patient and Aneurysm Characteristics

A total of 77 patients met inclusion criteria during the study period. Following aSAH, 50 patients (65%) were assessed for vasospasm angiographically and 71 patients (92%) were assessed for DCI. The mean patient age was 60 years (SD 15 years), and 54 patients (70%) were women. Hypertension, diabetes, and cardiovascular disease were present in 51 (66%), 14 (18%), and 25 (32%) patients, respectively. Thirty-three patients (43%) were active smokers. The mean GCS score at admission was 9.8 (SD 4.1). Aneurysms were diagnosed predominantly in the anterior circulation ($n = 50$, 65%) and had a mean diameter of 6.1 mm (SD 3.8 mm). At follow-up, 57 patients (74%) had a modified Rankin Scale score greater than 2 (Table 1).^{7,12}

Assessment of DCI

In patients with DCI ($n = 71$), cEEG detected vasospasm with a sensitivity of 11.1% (95% CI 3.1%–26.1%) and specificity of 82.9% (95% CI 66.4%–93.4%). TCDS, CTA, and DSA detected vasospasm with much greater sensitivities of 85.7% (95% CI 69.7%–95.2%), 70.6% (95% CI 52.5%–84.9%), and 73.9% (95% CI 51.6%–89.8%), respectively. Compared with cEEG, TCDS, CTA, and DSA were significantly less specific, at 18.8% (95% CI 7.2%–36.4%), 40.0% (95% CI 21.1%–61.3%), and 47.8% (95% CI 26.8%–69.4%), respectively (Table 2 and Fig. 1).

In this cohort of patients with DCI, cEEG had a PPV of 40% (95% CI 17.1%–68.4%) and an NPV of 47.5% (95% CI 42.8%–52.3%). TCDS, DSA, and CTA had greater

TABLE 1. Demographic and clinical characteristics of patients with aSAH and cEEG monitoring between January 1, 2017, and July 31, 2019

Characteristic	Value (n = 77)
Mean age, yrs (SD)	60 (15)
Female sex, n (%)	54 (70)
Vascular risk profile, n (%)	
Hypertension	51 (66)
Diabetes	14 (18)
Cardiovascular disease	25 (32)
Smoking	33 (43)
GCS score at admission, n (%)	
3–6	18 (23)
7–11	28 (36)
12–15	31 (40)
Mean GCS score at admission (SD)	9.8 (4.1)
GCS score at admission, IQR	7, 12
Mean aneurysm size, mm (SD)	6.1 (3.8)
Anterior circulation location, n (%)	50 (65)
mRS score >2 at follow-up, n (%)	57 (74)

mRS = modified Rankin Scale.

PPVs of 53.6% (95% CI 48.2%–58.9%), 58.6% (95% CI 47.2%–69.2%), and 61.5% (95% CI 52.1%–70.2%), respectively. In comparison with cEEG, TCDS and CTA both had similar NPVs of 54.6% (95% CI 28.8%–78.0%) and 50.0% (95% CI 33.0%–67.0%), respectively. DSA had the greatest NPV at 64.7% (95% CI 44.9%–80.5%) (Table 2).

In clinically assessed patients with DCI, the OR was highest with DSA, with an OR of 2.6 (95% CI 0.77–9.44), and lowest in cEEG, with an OR of 0.6 (95% CI 0.14–2.33). CTA was associated with a higher OR of 1.6 (95% CI 0.54–4.82) compared with TCDS (OR 1.38, 95% CI 0.37–5.31) (Table 2 and Fig. 2). These findings were not statistically significant.

Assessment of Vasospasm

In patients with angiographic findings that indicated vasospasm, cEEG had a sensitivity of 18.8% (95% CI 7.2%–36.4%) and a specificity of 94.4% (95% CI 72.7%–99.9%). Comparatively, TCDS and CTA had 4.5-fold greater sensitivities of 87.5% (95% CI 71.0%–69.5%) and 85.7% (95% CI 67.3%–96.0%), respectively, followed by clinical examination, with a 3-fold greater sensitivity of 58.6%

(95% CI 38.9%–76.5%). Compared with cEEG, CTA and clinical examination had lower specificities of 57.1% (95% CI 28.9%–82.3%) and 64.7% (95% CI 38.3%–85.8%), respectively. TCDS had the lowest specificity of 25.0% (95% CI 7.3%–52.4%) (Table 3 and Fig. 1).

In this cohort with angiographic findings positive for vasospasm, cEEG had the greatest PPV of 85.7% (95% CI 43.9%–97.9%), followed by CTA with 80.0% (95% CI 68.2%–88.2%), clinical examination with 73.9% (95% CI 58.2%–85.3%), and TCDS with 70.0% (95% CI 63.1%–76.1%). Additionally, cEEG had the lowest NPV of 39.5% (95% CI 34.9%–44.4%), followed by clinical examination at 47.8% (95% CI 34.4%–61.6%), TCDS at 50.0% (95% CI 22.3%–77.7%), and CTA at 66.7% (95% CI 42.0%–84.7%) (Table 3).

In angiographically assessed CVS, CTA had the highest reported OR of 8.0 (95% CI 1.9–39.7), which was found to be statistically significant ($p = 0.006$). The OR for cEEG monitoring was next highest with an OR of 3.92 (95% CI 0.6–77.6), followed by clinical assessment with an OR of 2.6 (95% CI 0.77–9.44) and TCDS with an OR of 2.33 (95% CI 0.48–11.4) (Table 3 and Fig. 2). These findings were not statistically significant.

Results of the Systematic Literature Review

The database search generated 720 articles. After excluding duplicates, articles not on human subjects, and non-English-language articles, as well as commentaries, editorials, and letters to the editor, the systematic literature review yielded a total of 53 articles. The full-text screening for appropriateness and availability for data extraction yielded 12 articles (Fig. 3). The articles were abstracted for key findings and conclusions to compare the findings of our institutional review with findings reported in the literature (Table 4).^{8,9,12–21}

Discussion

Aneurysmal SAH is a devastating disease with a high morbidity and a 30-day mortality of 30% to 40%, which is largely attributable to the occurrence of CVS and DCI.² Although the current standard of care for recognition of neuronal damage depends on serial neurological examinations and vascular imaging studies, such as TCDS and CTA, recent studies have indicated that continuous cEEG monitoring may assist in the detection of CVS and DCI.^{8,9,12–15,18,20} We conducted a retrospective analysis of the utility of continuous cEEG monitoring in a cohort of patients with poor-grade aSAH.

Continuous cEEG monitoring was highly specific for

TABLE 2. Detection of vasospasm in 71 patients with DCI

Diagnostic Method	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Youden Index	PPV, % (95% CI)	NPV, % (95% CI)	OR (95% CI)	p Value
cEEG	11.1 (3.1–26.1)	82.9 (66.4–93.4)	0.53	40.0 (17.1–68.4)	47.5 (42.8–52.3)	0.60 (0.14–2.33)	0.5
TCDS	85.7 (69.7–95.2)	18.8 (7.2–36.4)	0.52	53.6 (48.2–58.9)	54.6 (28.8–78.0)	1.38 (0.37–5.31)	0.6
CTA	70.6 (52.5–84.9)	40.0 (21.1–61.3)	0.55	61.5 (52.1–70.2)	50.0 (33.0–67.0)	1.60 (0.54–4.82)	0.4
DSA	73.9 (51.6–89.8)	47.8 (26.8–69.4)	0.61	58.6 (47.2–69.2)	64.7 (44.9–80.5)	2.60 (0.77–9.44)	0.13

FIG. 1. Sensitivity and specificity of diagnostic methods in patients with clinically assessed DCI and angiographically assessed CVS. **A:** Forest plot showing the sensitivities of DSA, CTA, TCDS, and cEEG in clinically assessed DCI. **B:** Forest plot showing the specificities of DSA, CTA, TCDS, and cEEG in clinically assessed DCI. **C:** Forest plot showing the sensitivities of clinical assessment, CTA, TCDS, and cEEG in angiographically assessed vasospasm. **D:** Forest plot showing the specificities of clinical assessment, CTA, TCDS, and cEEG in angiographically assessed vasospasm.

FIG. 2. OR of diagnostic methods in patients with clinically assessed DCI and angiographically assessed CVS. **A:** Forest plot showing the OR and 95% CI of DSA, CTA, TCDS, and cEEG in clinically assessed DCI. **B:** Forest plot showing the OR and 95% CI of clinical assessment, CTA, TCDS, and cEEG in angiographically assessed vasospasm.

TABLE 3. Detection of vasospasm in 50 patients with angiographically assessed CVS

Diagnostic Method	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Youden Index	PPV, % (95% CI)	NPV, % (95% CI)	OR (95% CI)	p Value
cEEG	18.8 (7.2–36.4)	94.4 (72.7–99.9)	0.57	85.7 (43.9–97.9)	39.5 (34.9–44.4)	3.92 (0.60–77.6)	0.2
TCDS	87.5 (71.0–96.5)	25.0 (7.3–52.4)	0.56	70.0 (63.1–76.1)	50.0 (22.3–77.7)	2.33 (0.48–11.4)	0.3
CTA	85.7 (67.3–96.0)	57.1 (28.9–82.3)	0.71	80.0 (68.2–88.2)	66.7 (42.0–84.7)	8.00 (1.90–39.7)	0.006
Clinical	58.6 (38.9–76.5)	64.7 (38.3–85.8)	0.62	73.9 (58.2–85.3)	47.8 (34.4–61.6)	2.60 (0.77–9.44)	0.13

angiographically assessed CVS and DCI, with specificities ranging from 80% to 95%. However, we also found cEEG monitoring to be associated with sensitivities as low as 11% for DCI and 19% for angiographically assessed CVS. In 2004, Claassen et al. reported a similar specificity of 84% among patients, with a single cEEG recording showing greater than 50% decrease in the alpha-delta ratio from baseline.¹⁵ However, the sensitivities that they reported for DCI detection were significantly higher than our findings, at 89% to 100%.¹⁵ Likewise, in 2016, Rots et al. observed a high specificity of 83.3% in a cohort of 8 patients with

confirmed DCI.¹² They also found cEEG monitoring to be 100% sensitive for detection of DCI, using a greater than 38% decrease in either the alpha-delta ratio or the alpha variability as the threshold.¹² In 2018, a study by Balança et al. verified the use of continuous cEEG monitoring as a feasible predictor to detect DCI, based on 100% sensitivity and 88.9% specificity observed with a regional 30% alpha-theta/delta ratio decrease lasting more than 3.7 hours.⁸ In a prospective study, Rosenthal et al. concluded that continuous cEEG monitoring accurately predicted DCI.²⁰ Their claims were substantiated by a 91% sensitivity and an 83%

FIG. 3. PRISMA flowchart outlining the systematic literature review.

TABLE 4. Systematic literature review on the utility of EEG to detect vasospasm and DCI in aSAH

Authors & Year	Title	No. of Pts	Key Findings & Conclusions
Rivierez et al., 1991 ¹³	"Value of electroencephalogram in prediction and diagnosis of vasospasm after intracranial aneurysm rupture"	151	Early prognostic value of EEG on 1st postbleed day: among 46 pts w/ normal EEG findings, 33 (72%) did not present w/ further electrical ischemic features or delayed angiographic vasospasm; among 78 pts w/ aberrant EEG findings, 76 (97%) exhibited EEG signs of ischemia & angiographic vasospasm several days later. Late diagnostic value of EEG on postbleed day 5: among 107 pts w/ aberrant EEG findings, 103 (96%) were assessed for vasospasm angiographically.
Vespa et al., 1997 ¹⁴	"Early detection of vasospasm after acute subarachnoid hemorrhage using continuous EEG ICU monitoring"	32	In 19/19 pts w/ angiographically assessed vasospasm, the relative alpha activity was low but improved w/ resolution of vasospasm. In 10/19 pts, the EEG abnormalities preceded the diagnosis of vasospasm by a mean of 2.9 days (SD 1.73 days). PPV, 76%; NPV, 100%. 12/19 pts exhibited clinical signs of vasospasm at the time of EEG alterations. Decreased relative alpha variability provides early detection of vasospasm in pts before clear clinical symptoms & signs occur.
Claassen et al., 2004 ¹⁵	"Quantitative continuous EEG for detecting delayed cerebral ischemia in patients with poor-grade subarachnoid hemorrhage"	34	EEG had a 100% sensitivity & 76% specificity when 6 consecutive recordings had a >10% decrease in alpha-delta ratio from baseline. EEG had a 89% sensitivity & 84% specificity when any single measurement had a >50% decrease in alpha-delta ratio from baseline.
Stuart et al., 2010 ¹⁶	"Intracortical EEG for the detection of vasospasm in patients with poor-grade subarachnoid hemorrhage"	5	Intracortical EEG showed a decrease in alpha-delta ratio from baseline (>25% for ≥4 hrs) in all 3 pts w/ angiographically confirmed vasospasm & not in the 2 pts w/o vasospasm. Early predictive value of intracortical EEG: the decline occurred 1–3 days before angiographic confirmation. Intracortical continuous EEG may be superior to scalp EEG in detecting vasospasm.
Rathakrishnan et al., 2011 ¹⁷	"Using continuous electroencephalography in the management of delayed cerebral ischemia following subarachnoid hemorrhage"	13	Sensitivity of predicting clinical deterioration w/ EEG improved from 40% to 67% & of predicting clinical improvement w/ EEG improved from 8% to 50%. Predictive value of EEG in clinical deterioration: 67% sensitivity & 73% specificity. In 3/12 pts, EEG was predictive >24 hrs before clinical change. Tracking the daily mean alpha power accurately identified DCI recurrence & poor responders to first-line therapy at preclinical stages. EEG is a useful noninvasive tool to supplement routine clinical parameters in the prediction of DCI. It can dynamically monitor the response to treatment & might aid preclinical management decisions.
Gollwitzer et al., 2015 ⁹	"Early prediction of delayed cerebral ischemia in subarachnoid hemorrhage based on quantitative EEG: a prospective study in adults"	12	EEG had 89% sensitivity & 77% specificity w/ decrease of >40% in power persisting >5 hrs in the alpha band & >6 hrs in the theta band. EEG changes preceded detection of vasospasm & DCI in standard procedures by 2.3 days. Focal reduction in alpha power may represent a valid, observer-independent, noninvasive, & continuous marker for vasospasm & DCI in pts w/ SAH.
Rots et al., 2016 ¹²	"Continuous EEG monitoring for early detection of delayed cerebral ischemia in subarachnoid hemorrhage: a pilot study"	20	Early detection of DCI: all 8 pts w/ DCI showed a decrease of >38% of either alpha-delta ratio or alpha variability (100% sensitivity, 83.3% specificity). In 5/8 pts, the DCI-compatible EEG changes were found before clinical DCI diagnosis. Continuous EEG detected DCI 7 hrs earlier than clinical deterioration & 44 hrs earlier than CT.
Kim et al., 2017 ¹⁸	"Epileptiform abnormalities predict delayed cerebral ischemia in subarachnoid hemorrhage"	124	Presence of IICAs was associated w/ higher risk of DCI, especially if they emerged late in the acute period after SAH. Quantification of IICA features may assist in the development of an algorithm to predict DCI risk.
Wickering et al., 2016 ¹⁹	"Automation of classical QEEG trending methods for early detection of delayed cerebral ischemia: more work to do"	85	The highest sensitivity & specificity of alpha-delta ratio decrease detected by the automated EEG-based early DCI-detection system were 95% & 34%, respectively. The mean time btwn the 1st change in EEG activity & the clinical DCI was 3.9 days. Improved methods to detect decreases in alpha-delta ratio & relative alpha variability are needed before an automated EEG-based early DCI-detection system is ready for clinical use.

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TABLE 4. Systematic literature review on the utility of EEG to detect vasospasm and DCI in aSAH

Authors & Year	Title	No. of Pts	Key Findings & Conclusions
Balança et al., 2018 ⁸	"Diagnostic accuracy of quantitative EEG to detect delayed cerebral ischemia after subarachnoid hemorrhage: a preliminary study"	15	A regional 30% alpha-theta/delta ratio decrease outlasting 3.7 hrs reached 100% sensitivity & 88.9% specificity to detect DCI. A regional 50% alpha-theta/delta ratio decrease outlasting 3.7 hrs reached 89.9% sensitivity & 83.3% specificity to detect DCI. Prolonged alpha-theta/delta ratio decrease starting in 1 territory seems to be a good biomarker of DCI.
Rosenthal et al., 2018 ²⁰	"Continuous electroencephalography predicts delayed cerebral ischemia after subarachnoid hemorrhage: a prospective study of diagnostic accuracy"	103	EEG alarms occurred in 96.2% of pts w/ & 19.6% of pts w/o subsequent DCI (1.9-day median latency). Predictive value of EEG in DCI: sensitivity, 96.2%; specificity, 80.4%; PPV, 83.3%; & NPV, 95.4%. Among alarm subtypes, late-onset epileptiform abnormalities had the highest predictive value. Prespecified EEG findings predicted DCI among pts w/ low (91% sensitivity, 83% specificity) & high (95% sensitivity, 77% specificity) baseline risk. Continuous EEG accurately predicts DCI after SAH.
Spalletti et al., 2019 ²¹	"Amplitude instability of somatosensory evoked potentials as an indicator of delayed cerebral ischemia in a case of subarachnoid hemorrhage"	1	A 55-yr-old man w/ aSAH was monitored w/ continuous EEG-SSEPs. A prolonged phase of SSEP amplitude instability correlated w/ a phase of ischemic penumbra, as demonstrated by CT perfusion. EEG monitoring remained relatively uninformative due to neurosedation. Continuous EEG-SSEP monitoring could be included in the multimodal assessment of vasospasm from TCDS & DSA.

IICA = ictal-interictal continuum abnormality; pts = patients; SSEP = somatosensory evoked potential.

specificity in patients with a low baseline risk of DCI, as well as a 95% sensitivity and a 77% specificity in patients with an elevated baseline risk of DCI.²⁰

All the above studies suggest a high diagnostic accuracy of cEEG monitoring in detecting CVS and DCI. Although our findings affirm the high specificity of cEEG reported in the literature, we found much lower sensitivity than other studies. The lower sensitivity of cEEG monitoring in DCI may be attributable to institutional differences or biases among observers. For instance, although the clinical aspect of the standard DCI definition is provided by a new focal neurological deficit, a decrease in the level of consciousness, and/or a decrease in the GCS score of at least 2 points for more than 1 hour in the absence of a relatable ischemic event, institutions may have altered these guidelines in favor of better patient care and better outcomes.^{10,18,19,22} This change may be associated with a high rate of false-positive DCI diagnoses among patients with poor clinical condition.

Although other studies have assessed the diagnostic capacity of cEEG monitoring for detection of CVS,^{13,14} cEEG actually measures aberrant neuronal activity, which translates into the assessment of DCI. In contrast, DSA, TCDS, and CTA evaluate vasospasm on the basis of changes in vessel diameter and cerebral flow velocities. The paradigm stating that DCI results solely from vasospasm has long been abandoned, and recent studies have provided reason to believe that the pathogenesis of DCI is an evolving multifactorial process, implicating the role of microvasculature, coagulation and fibrinolysis, cortical spreading depressions, and the immune system.^{4,6} Therefore, although continuous cEEG monitoring does not directly measure CVS, it indirectly measures the processes that induce and maintain brain injury in DCI.

DSA is considered the diagnostic gold standard for the early recognition and treatment of CVS.^{23–25} Although DSA is associated with some risk because it is an invasive procedure, recent advances have made these procedures safer.^{26,27} Furthermore, DSA offers major advantages that include its accuracy and the ability to immediately administer vasodilatory agents intraarterially.^{23–25} Arias et al. assessed a sensitivity of 80% and a specificity of 71% for DSA in detecting CVS among patients who were transiently symptomatic or had poor neurological examination findings.²⁵ We found DSA to be less sensitive (73.9%) and less specific (47.7%) in patients with clinical deterioration. The decreased sensitivity and specificity of DSA in these patients may be attributed to the subset of patients in our cohort with significantly poor neurological examination findings, which can make the clinical interpretation of CVS challenging.

We also evaluated the capacity of TCDS to detect angiographically assessed CVS. TCDS detected angiographically determined CVS with an 87.5% sensitivity, 25.0% specificity, PPV of 70%, and NPV of 50%. These sensitivity findings are in accordance with previously reported values of 84% to 85%.^{24,28–31} In a prospective study by Mascia et al., TCDS was found to be 100% sensitive and 75% specific for angiographic CVS, with a PPV of 72% and NPV of 100%.³¹ Likewise, Sloan et al. found TCDS to be 100% sensitive for angiographic CVS; however, the authors reported a lower specificity of 58.6%.³⁰ The lower specificities of TCDS in angiographic CVS may be explained by the limitations associated with TCDS, which include interobserver variability and restricted access to the entire cerebral vasculature, resulting in diagnostic variation.²⁴ Nonetheless, the advantages of TCDS include that it is noninvasive, broadly available, low cost, and asso-

ciated with a low risk to patients, as well as having higher sensitivity and specificity than DSA.^{24,29}

Limitations

Potential limitations of our study include its retrospective nature and the small study population. In addition, the randomization of the study population was lost because continuous cEEG monitoring is reserved for patients with high-grade SAH who have particularly poor neurological examination findings. Subsequently, the large proportion of patients with poor clinical performance may have affected the observer's clinical assessment of DCI. In general, DCI is a challenging condition to diagnose, especially retrospectively. Despite the attempt to standardize the diagnosis of DCI with the help of uniform definitions, it remains a subjective diagnosis with potentially high interobserver variability. Furthermore, the guidelines for diagnosing vasospasm and DCI with use of different diagnostic modalities may vary among institutions, possibly creating a bias when the findings of individual studies are compared. This limitation becomes evident when comparing the studies identified by our literature review, as each has reported different thresholds and endpoints (Table 4). Finally, although cEEG findings were considered positive only when occurring on the same day or within 24 hours after DCI diagnosis or changes on DSA, this study has limited value in assessing the early predictive value of cEEG monitoring for CVS or DCI screening.

Conclusions

Altogether, continuous cEEG monitoring offers non-invasive, continuous real-time measurements of neuronal activity, which can be correlated with the development of DCI.⁸ Because one-fifth of patients with DCI remain asymptomatic, cEEG may be considered a feasible adjunct to the current standard of care techniques, such as TCDS and DSA.²² We found that continuous cEEG monitoring was highly specific for CVS and DCI for patients with aSAH. However, cEEG was found to have a low sensitivity, and it requires adjunct modalities for screening. Further prospective studies with predetermined thresholds and endpoints are needed to assess the role of continuous cEEG monitoring in detecting CVS and DCI after aSAH.

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Disclosures

Dr. Jha: consultant for Biogen. Dr. Ducruet: consultant for Penumbra, Cerenovus, Medtronic, Stryker, Koswire, and Oculus.

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Supplemental Information

Videos

Video Abstract. <https://vimeo.com/675878437>.

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