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Using cerebral regional oxygen saturation and amplitude-integrated electroencephalography in neonates on extracorporeal membrane oxygenation: preliminary experience from a single center

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Abstract

Objective This study aims to evaluate the application value in neurological outcome of cerebral regional oxygen saturation ($CrSO_2$) and amplitude-integrated electroencephalography (aEEG) monitoring during neonatal extracorporeal membrane oxygenation (ECMO) courses.

Methods We retrospectively analyzed 18 neonates receiving veno-arterial ECMO (V-A ECMO) support at our hospital from July 2021 to December 2022. Continuous monitoring of $CrSO_2$ and brain electrical activity was conducted using near-infrared spectroscopy (NIRS) and aEEG throughout the ECMO treatment. We collected and analyzed related clinical data.

Results Among the 11 survivors, 5 were categorized as the normal group (N group) and 6 as the abnormal group (AN group) based on post-ECMO brain MRI outcomes. The N group exhibited shorter time percentage of significant $CrSO_2$ reduction (> 25% from baseline or absolute value < 40%), better fractional tissue oxygen extraction (FTOE) rates, and more stable mean percentage changes in $CrSO_2$ compared to the AN group. Neonates in the N group predominantly showed mildly abnormal aEEG readings, with one patient displaying disrupted sleep-wake cycles. This particular patient also had more significant $CrSO_2$ reduction and poorer FTOE compared to others in the N group. Additionally, the Test of Infant Motor Performance (TIMP) scores indicated hypoevolutism in this patient before discharge, while others in the N group had normal TIMP scores. In the AN group, 4 exhibited moderate and 2 severe aEEG abnormalities; 5 had hypoevolutism TIMP scores, and 1 with moderate aEEG abnormalities maintained a normal TIMP score, exhibiting lesser $CrSO_2$ reduction and improved FTOE.

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Conclusion $CrSO_2$ and aEEG monitoring show potential as routine assessments for neurological outcomes during neonatal ECMO. In our cohort, a tendency was observed where neonates with greater reductions in $CrSO_2$ and more severe aEEG abnormalities experienced poorer neurological outcomes.

Keywords Neonates, ECMO, Cerebral regional oxygen saturation, Early results

Introduction

Extracorporeal membrane oxygenation (ECMO) is the ultimate treatment modality for neonates facing severe, reversible respiratory or circulatory failure. The ECMO procedure in neonates entails the ligation and cannulation of right cervical vessels, blood interfacing with artificial membranes, and anticoagulation therapy, all of which can lead to significant cerebral hemodynamic alterations. These procedural elements, combined with the potential for bleeding and embolization, increase the risk of severe brain injury and adverse neurodevelopmental outcomes [1]. Additionally, the inherent fragility and developmental immaturity of neonatal vascular networks, along with the possible impairment of cerebral autoregulation during ECMO, place these patients at an increased risk for brain injury [2]. Impaired cerebral autoregulation is associated with poor neurodevelopmental outcomes [3]. Cerebral hemorrhage, the most frequent neurological complication, is linked with the highest mortality. Other serious neurological complications, including ischemic stroke, hypoxic-ischemic encephalopathy, and epileptic seizures, can also lead to death [4]. Despite improvements in ECMO management techniques reducing deaths from neurological complications, the incidence of near-term and long-term adverse neurological outcomes remains high, particularly in neonates [4–6]. In neonates who survive ECMO support, neurological complications such as periventricular leukomalacia, cerebral palsy, sensorineural hearing loss, and intellectual impairment are common. Consequently, monitoring brain function during the ECMO period is crucial to identify and mitigate these risks effectively. This vigilant approach is essential for improving neurological outcomes and overall quality of life for these vulnerable patients.

Cerebral regional oxygen saturation ($CrSO_2$) monitoring, utilizing near-infrared spectroscopy (NIRS), is instrumental in detecting levels of cerebral oxyhemoglobin (HbO_2) and deoxygenated hemoglobin (HbR), thereby measuring regional blood oxygen saturation [7]. This technique has become a vital tool for monitoring neonatal tissue hypoxia and cerebral injuries [8]. Studies have shown that lower $CrSO_2$ measurements correlate with poorer neurological outcomes and increased perioperative mortality. Real-time monitoring of $CrSO_2$ offers early detection of hypoxia, often before it is evident through routine invasive hemodynamic monitoring, enabling prompt intervention to mitigate organ damage [9]. Due to its non-invasive nature, continuous bedside capability, absence of ionizing radiation, and compatibility with other monitoring equipment, $CrSO_2$ monitoring is increasingly recommended as a standard procedure during ECMO support [10]. Alongside $CrSO_2$, the amplitude-integrated electroencephalogram (aEEG) — a simplified, filtered, and compressed EEG trend — is gaining prominence in neonatal intensive care units (NICU) for assessing neurodevelopmental outcomes [11]. This dual monitoring strategy enhances the ability to predict and manage potential neurological issues in vulnerable neonatal populations.

The utility and empirical support for using $CrSO_2$ and aEEG to assess cerebral hypoxia and neurological outcomes in neonates during ECMO are not fully established. This study was designed to explore the application value and effectiveness of $CrSO_2$ and aEEG monitoring in evaluating neurological outcomes during neonatal ECMO treatment periods.

Materials and methods

We obtained written informed consent from the parents of the patients involved. This retrospective observational study collected data through our medical record system, focusing on 18 neonates who received venoarterial ECMO (V-A ECMO) support from July 2021 to December 2022. We excluded seven neonates due to death or pre-existing central nervous system conditions, including cerebral hemorrhage, cerebral infarction, and epilepsy, prior to ECMO support. Ultimately, 11 neonates were included in the study, all of whom were intubated nasally and managed with controlled ventilation settings before ECMO initiation. Our protocol adhered to the ELSO Neonatal Respiratory Support Guidelines [12]. ECMO assistance was considered when a patient's respiratory or hemodynamic status was unstable and met one of the following criteria: (1) reversible cardiopulmonary failure; (2) oxygenation index > 40 for over 4 h; (3) oxygenation index > 20 after 24 h of conventional treatment; (4) severe progressive respiratory failure or associated with circulatory failure, or prolonged use of high-dose cardiovascular drugs.

Following the removal of ECMO, brain magnetic resonance imaging (MRI) was conducted to detect any radiographic central nervous system abnormalities. Using the MAGNETOM Prisma 3.0T scanner, the MRIs were categorized, and a unified team of imaging doctors interpreted the results. The abnormal findings included reduced white matter around the posterior horn of the

bilateral lateral ventricles, widened subarachnoid space at the left infratemporal pole, slightly deeper bilateral frontotemporal sulci, right frontal softening focus with deeper sulci, enlarged ventricles, and deeper frontotemporal sulci on both sides. Based on the imaging results, 5 cases were classified as belonging to the N group (normal group) and 6 to the AN group (abnormal group), indicating variations in the severity and presence of neurological impairments.

Throughout the ECMO course, Near-Infrared Spectroscopy (NIRS) was employed to continuously monitor $CrSO_2$ using the INVOS™5100 C (Kehui Medical Equipment International Trading Co., LTD). Data from the device was exported via USB flash drive. The INVOS Monitoring Analytics TOOL software was used to analyze desaturation events and establish $CrSO_2$ baselines. A NIRS neonatal sensor was positioned at the median forehead of each patient, with a baseline reading recorded after a 5-minute stabilization period pre-ECMO. (Fig. 1) Desaturation was defined as a reduction in $CrSO_2$ greater than 25% from baseline or an absolute value of $CrSO_2$ less than 40% during ECMO, following criteria established in previous adult ECMO studies [13]. To minimize confounders, data from cannulation and de-cannulation phases were excluded from the analysis. Our approach was proactive, aiming to maintain $CrSO_2$ at normal baselines. Upon detecting desaturation, our first response was to check the sensor's position, patient's head, and the arterial and venous cannulas. If hypotension was suspected, cardiac output was optimized, and vasopressors were administered to maintain a mean perfusion pressure of 40–45 mmHg in normothermia. When mean arterial pressure (MAP) was normal, abnormal systemic oxygenation was corrected, a better acid-base balance and partial pressure of carbon dioxide ($PaCO_2$) levels were obtained by adjusting the ventilation or modifying the oxygenator. Red blood cell transfusions were considered to maintain hemoglobin levels above 100 g/L. If these steps didn't improve $CrSO_2$, deeper anaesthesia and analgesia, temperature adjustments, and anticonvulsants were considered to decrease cerebral oxygen consumption. (14–15) These events and interventions were all recorded in the INVOS monitor. Our management of pH and arterial gases during ECMO aimed for specific ranges: PH:7.35–7.45, SvO_2:65–80%, SPO_2>90%, PaO_2: 60–80 mmHg, $PaCO_2$: 40–45 mmHg, HCO_3-: 22–27 mmol/L, BE: ±3 mmol/L, and Lac: < 1.6mmol/L. Scalp electrodes and multichannel aEEG were implemented for continuous EEG activity monitoring throughout the ECMO treatment.

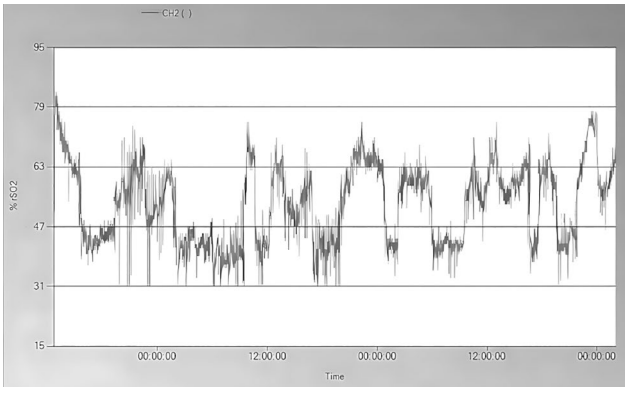

Fig. 1 $CrSO_2$ graphical value of one neonate during the study

Our study conducted a detailed statistical analysis, encompassing various aspects of the neonatal patients and their ECMO treatment. Data were gathered and analyzed, including: (1) general patient information like age, body weight, gender, primary disease, and clinical symptoms; (2) average heart rate (HR), peripheral blood oxygen saturation (SpO_2), MAP, and ECMO support duration; (3) time percentage of $CrSO_2$ reduction greater than 25% or absolute value less than 40% during ECMO (to calculate the time percentage of $CrSO_2$ reductions during ECMO, we divided the cumulative time that $CrSO_2$ was lower than the established cutoffs (greater than 25% reduction from baseline or an absolute value less than 40%) by the total duration of the ECMO course. This method provided us with a proportion, expressed as a percentage, indicating the extent of time the patient spent under these critical $CrSO_2$ thresholds while receiving ECMO support.); [16] (4) the mean percentage change in $CrSO_2$ (We recorded the $CrSO_2$ value of each hour during the ECMO support process, calculated the value of $CrSO_2$ less than or greater than the baseline at each time point, the positive value was above the baseline, the negative value was below the baseline, and then the sum of each time point was divided by the total monitoring time.); (5) fractional tissular oxygen extraction (FTOE) during ECMO; (6) aEEG monitoring results; and (7) post-ECMO brain MRI findings and Test of Infant Motor Performance (TIMP) scores before discharge. This comprehensive dataset aimed to provide a robust foundation for evaluating the efficacy of ECMO support and its impacts on neonatal patients, with a particular focus on neurological outcomes.

Neonatal EEG activity is classified according to amplitude and continuity using the aEEG with a widely accepted five-classification method proposed by Hellström-Westas et al. [17] The classifications are: (1) Continuous Normal Voltage, characterized by lower boundary amplitude fluctuations between 5 and 10 μV and upper boundary fluctuations between 10 and 25 μV, not exceeding 50 μV; (2) Discontinuous Normal Voltage, where background activity is discontinuous, lower boundary amplitude does not exceed 5 μV, and the upper boundary is greater than 10 μV; (3) Burst Suppression,

featuring discontinuous background activity, lower boundary amplitude between 0 and 2 μV, burst amplitude exceeding 25 μV, with burst density classified as BS+if≥100 bursts/h and BS- if<100 bursts/h; (4) Continuous Low Voltage, with continuous background activity and significantly reduced amplitude, upper boundary less than 10 μV and lower boundary less than 5 μV; (5) Inactive and Flat Trace, indicating very low voltage close to electrical silence with amplitude less than 5 μV. In this system, classification (1) is deemed normal, (2) mildly abnormal, (3) moderately abnormal, and (4) and (5) severely abnormal. This categorization aids in the detailed assessment of neonatal brain activity and potential neurological conditions.

The TIMP is a scale designed to assess motor and postural control in infants, specifically tailored for those aged from 34 gestational weeks to 4 months of corrected gestational age. It evaluates the infant's motor control and postural coordination, as well as their motor abilities in relation to functional activities, serving as a predictor for future motor development. The TIMP encompasses 42 items, with the first 13 being observational and the remaining 29 eliciting specific motor responses. Upon completion of the assessment, a total score is compiled, with scores above a certain cutoff considered "normal" and those below the threshold regarded as indicative of "hypoevolutism". Professional and trained rehabilitation doctors typically conduct the TIMP scoring to ensure accuracy and reliability in determining infants' motor developmental status [18].

Statistical analysis

All data were analyzed using IBM SPSS statistical software, version 20.0. Counts and percentages were used to describe the categorical data. The continuous variables were expressed as median and inter-quartile range (IQR).

Results

Patient characteristics and vital signs

This study included 11 surviving neonates who received V-A ECMO support, with primary indications including persistent pulmonary hypertension of the neonate (PPHN), acute respiratory distress syndrome (ARDS), meconium aspiration syndrome (MAS), postoperative congenital diaphragmatic hernia (CDH), pertussis with pulmonary artery hypertension (PAH), and PPHN with fetal edema. The clinical characteristics shared among these cases were progressively worsening respiratory and circulatory failure. When comparing the normal group (N) and abnormal group (AN) based on the MRI findings, the median age was 2.0 (1.5, 3.0) days for group N and 5.2 (1.0, 7.5) days for group AN, and the median weight was 3.7 (3.2, 3.8) kg for group N versus 3.4 (3.0, 3.8) kg for group AN. The median values for MAP, SpO_2, and HR during ECMO treatment were 47.0 (45.5, 48) mmHg vs. 46.5 (42.8, 49.3) mmHg, 95.0 (94.5, 96.0)% vs. 95.0 (93.8, 96.0)%, and 143.0 (142.5, 145.5) beats/min vs. 145.5 (141.8, 147.3) beats/min in groups N and AN respectively. Additionally, the median duration of ECMO support was 86.0 (78.0, 94.5) hours for group N and 84.3 (78.5, 92.5) hours for group AN. These findings and comparisons are further detailed in Tables 1 and 2 of the study.

CrSO2 changes during ECMO course

In our study, the median baseline $CrSO_2$ prior to ECMO initiation was 52.2 (52.0, 55.5) for the normal group (N) and 50.7 (51.0, 53.8) for the abnormal group (AN) as detailed in Table 2. The group N showed a smaller percentage of time with $CrSO_2$ reduction greater than 25% from baseline or absolute $CrSO_2$ less than 40%, indicating better oxygenation status than group AN. Furthermore, FTOE and the mean percentage change in $CrSO_2$ were more favorable in group N compared to group AN, suggesting more stable and effective oxygenation.

Table 1 Patient's characteristics

	Age (days)	Gender	Weight (kg)	Primary disease	Clinical symptoms
1	3	Male	3.9	PPHN, ARDS	Respiratory, circulatory failure
2	3	Male	3.8	PPHN, ARDS	Respiratory, circulatory failure
3	2	Female	3.7	MAS, PPHN	Respiratory, circulatory failure
4	2	Female	2.99	CDH, PPHN	Respiratory, circulatory failure
5	1	Female	3.5	MAS, PPHN	Respiratory, circulatory failure
6	2	Male	3.15	PPHN, ARDS	Respiratory, circulatory failure
7	1	Female	3	PPHN, ARDS	Respiratory, circulatory failure
8	1	Male	2.8	PPHN, ARDS	Respiratory, circulatory failure
9	24	Male	4.2	Pertussis, PAH	Respiratory, circulatory failure
10	1	Male	3.65	PPHN, fetal edema	Respiratory, circulatory failure
11	2	Male	3.6	CDH, PPHN,	Respiratory, circulatory failure

PPHN, persistent pulmonary hypertension of the new-born; ARDS, acute respiratory distress syndrome; MAS, meconium aspiration syndrome; CDH, congenital diaphragmatic hernia; PAH, pulmonary artery hypertension

Table 2 MAP, SpO_2, HR, and $CrSO_2$, FTOE during ECMO course

	Group *N* (*n* = 5)	Group AN (*n* = 6)
The mean value of MAP (mmHg)	47.0 (45.5, 48)	46.5 (42.8, 49.3)
The mean value of SpO_2 (%)	95.0 (94.5, 96.0)	95.0 (93.8, 96.0)
The mean value of HR (beats/min)	143.0 (142.5, 145.5)	145.5 (141.8, 147.3)
Duration of ECMO support (h)	86.0 (78.0, 94.5)	84.0 (78.5, 92.5)
$CrSO_2$ baseline prior to ECMO	52.0 (49.0, 55.5)	51.0 (47.3, 53.8)
Time percentage of $CrSO_2$ decline > 25% from baseline (%)	24.6 (17.9, 27.1)	43.3 (40.3, 46.9)
Time percentage of $CrScO_2$ < 40% (%)	18.8 (8.4, 22.6)	34.8 (22.2, 46.4)
The mean percentage change in $CrSO_2$ (%)	9.0 (7.5, 10.0)	1.0 (0.8, 4.0)
FTOE	0.36 (0.35, 0.38)	0.43 (0.42, 0.56)

The continuous variables were expressed as median and inter-quartile range (IQR). MAP, mean arterial pressure; SpO_2, peripheral blood oxygen saturation; HR, heart rate; FTOE: fractional tissular oxygen extraction; $CrSO_2$, cerebral regional oxygen saturation

Notably, within group N, one patient was identified with a TIMP score indicative of hypoevolutism; this patient experienced more significant $CrSO_2$ reduction and worse FTOE compared to others in the same group. Conversely, in group AN, one patient had a normal TIMP score and demonstrated lesser $CrSO_2$ reduction and better FTOE relative to peers in that group. The brain MRI of this particular patient revealed slightly deeper sulci but no other significant changes in brain parenchyma.

aEEG during ECMO course

In the study, neonates in group N with normal brain MRI results exhibited mildly abnormal aEEG results. Within this group, one patient lacked a sleep-wake cycle and was identified with a TIMP score indicative of hypoevolutism prior to discharge. Conversely, the neonates categorized in group AN due to abnormal brain MRI results displayed more significant aEEG abnormalities: four had moderate abnormalities and two severe. The brain MRI of those with moderate aEEG abnormalities typically showed reduced white matter around the bilateral lateral ventricles' posterior horns, widened subarachnoid space of the left infratemporal pole, and deeper frontotemporal sulci, right frontal softening focus, with one patient showing a normal TIMP score but slightly deeper sulci without other parenchymal changes. This patient also had less $CrSO_2$ reduction and better FTOE compared to others in AN. The patients with severe aEEG abnormalities and electrical silence had MRI results indicating enlarged ventricles and deeper frontotemporal sulci. These two patients experienced greater $CrSO_2$ reduction and worse FTOE compared to their peers in the same group and were all scored as hypoevolutism on the TIMP. (Table 3)

These findings illustrate a correlation between the severity of EEG abnormalities, structural brain changes, and functional outcomes, underscoring the importance of integrated neuro-monitoring in assessing and understanding the complex impacts of ECMO on neonatal neurological health.

Discussion

We performed a descriptive analysis and found the tendency that the neonates with lower $CrSO_2$ and worse aEEG during ECMO might have the worse TIMP score and abnormal MRI results. In this study, group N demonstrated a lower percentage of time with significant $CrSO_2$ reduction and exhibited better FTOE and mean percentage change in $CrSO_2$ compared to group AN. These observations align with those reported by Wong et al.,

Table 3 aEEG during ECMO course and TIMP score, brain MRI results after ECMO support

	aEEG during ECMO	The TIMP score before discharge	brain MRI results
1	Mild abnormality (no sleep and wake cycle)	Hypoevolutism	Normal
2	Mild abnormality	Nnormal	Normal
3	Mild abnormality	Nnormal	Normal
4	Mild abnormality	Nnormal	Normal
5	Mild abnormality	Nnormal	Normal
6	Moderate abnormality	Hypoevolutism	The white matter around the posterior horn of bilateral lateral ventricles was less.
7	Moderate abnormality	Hypoevolutism	The subarachnoid space of the left infratemporal pole was widened, and the frontotemporal sulcus on both sides was slightly deeper.
8	Severe abnormality, electrical silence	Hypoevolutism	The ventricles on both sides were larger and the frontotemporal sulcus on both sides was deeper.
9	Severe abnormality, electrical silence,	Hypoevolutism	The ventricles of both sides were larger and the frontotemporal sulcus of both sides was deepened.
10	Moderate abnormality	Hypoevolutism	Right frontal softening focus
11	Moderate abnormality	Nnormal	The sulcus was slightly deeper.

MRI, magnetic resonance imaging; aEEG, amplitude-integrated electroencephalography; TIMP, Test of Motor Infant Performance

who utilized NIRS for monitoring during ECMO support [13]. Their study identified brain desaturation in all 20 patients undergoing ECMO. Following interventions to correct potential mechanical issues and enhance oxygen and blood delivery (like adjusting head position, ECMO cannulae and sensor placement, increasing ECMO flow and oxygen supply, and ensuring adequate arterial pressure and hemoglobin levels), 16 patients showed recovery. However, two patients continued to exhibit bilateral persistent low $CrSO_2$, subsequently diagnosed with diffuse ischemic brain injury. The remaining two patients had unilateral persistent low $CrSO_2$, which was later confirmed as unilateral cerebral infarction through imaging. These findings highlight the criticality of continuous monitoring and timely intervention in managing cerebral oxygenation and mitigating potential adverse neurological outcomes during ECMO support.

In the realm of ECMO-supported patient care, prospective studies have linked acute brain injury to the frequency, duration, and intensity of desaturation episodes as detected by $CrSO_2$ monitoring [19]. A notable increase in acute brain injury rates has been observed correlating with decreased $CrSO_2$ levels. Another study confirmed the utility of $CrSO_2$ monitoring during ECMO in early detection of potential brain damage [20]. In recent years, $CrSO_2$ monitoring has become a prevalent method for assessing brain function during ECMO, particularly due to its ability to provide continuous, non-invasive insights into cerebral oxygenation trends. However, while it's widely used, the evidence and advantages of $CrSO_2$ in evaluating the extent of cerebral hypoxia and predicting neurological outcomes in neonates are not as robust. Given that cerebral perfusion and oxygenation disorders significantly contribute to neonatal brain injury and increase the risk of adverse neurodevelopmental outcomes, understanding and monitoring these parameters are crucial [21]. In our study, we defined desaturation based on a set reduction in $CrSO_2$ (>25% from baseline or an absolute value<40%) during ECMO, aligning with established criteria [13]. Additionally, we incorporated FTOE as an indicator of the balance between oxygen delivery and consumption, combining it with measurements like SpO_2, HR, MAP, and $CrSO_2$ to analyze cerebral metabolic demand [22]. Our findings revealed that patients with lesser $CrSO_2$ reduction and better mean percentage change in $CrSO_2$ typically had improved FTOE, mirroring the beneficial application of $CrSO_2$ in other neonatal care areas [9]. In our patient cohort, one individual in group N was noted to have hypoevolutism according to the TIMP score before discharge, with this patient also showing greater $CrSO_2$ reduction and worse FTOE compared to others in the group. Conversely, in group AN, one patient had a normal TIMP score before discharge, coupled with lesser $CrSO_2$ reduction and better FTOE, demonstrating the variable impacts and potential benefits of meticulous $CrSO_2$ and FTOE monitoring. These nuanced differences underscore the variability of outcomes and indicators within each group, emphasizing the importance of individualized monitoring and assessment in ECMO treatment.

Polito et al. reported that approximately 20% of neonates receiving ECMO support experienced neurological sequelae [23], a finding echoed by Madderom et al. [24] Additionally, of those children who suffered brain injury post-ECMO, 36–38% survived until 20 days post-discharge, with 9–26% exhibiting mild motor or cognitive impairments at longitudinal follow-up [25, 26]. These statistics underline the significant risk of neurological damage and neurodevelopmental delays among neonates and children recovering from critical illnesses treated with ECMO. Such individuals are also more susceptible to worsening of pre-existing medical conditions and development of new medical comorbidities [27]. These factors make the continuous monitoring of brain function an essential component of neonatal ECMO care, aiming to promptly identify and mitigate potential neurological complications.

NIRS, while effective in reaching the grey matter of the brain, has limitations in penetrating deeper into the brain parenchyma [8]. This limitation restricts NIRS's ability to monitor the entire brain parenchyma comprehensively. Additionally, NIRS has a lower spatial resolution compared to MRI and a lower temporal resolution than aEEG [7]. Therefore, utilizing various examination modalities is critical to objectively evaluate neonatal brain function, encompassing aspects of brain structure, electrophysiology, and oxygenation metabolism to identify potential brain injuries [8]. In our study, we employed a dual approach by combining aEEG and $CrSO_2$ monitoring to provide a comprehensive evaluation of brain function in neonates undergoing ECMO support. Additionally, post-ECMO support, MRI findings combined with TIMP scores were utilized as outcome indicators to assess the extent of any brain injury and the developmental prospects of the neonates.

Electroencephalography serves as a fundamental clinical neurophysiology tool, widely recognized for its effectiveness in diagnosing, monitoring, and prognosticating a variety of brain disorders in critically ill patients [28]. aEEG is particularly noted for its sensitivity in early outcome prediction, especially in term asphyxiated infants [29]. In our study, we observed a correlation where the severity of a patient's aEEG abnormalities was directly associated with more profound $CrSO_2$ reduction, deteriorated FTOE, poorer TIMP scores, and more adverse findings in brain MRI results. This pattern emphasizes the interconnectedness of these variables and highlights the utility of comprehensive monitoring for a holistic

understanding of the neonate's neurological status during ECMO support.

MRI is highly favored for neuroimaging in children, especially after ECMO support, due to its high sensitivity, specificity, and lack of radiation exposure [27]. In our center, all neonates receiving ECMO support underwent brain MRI before discharge. For the purposes of this retrospective study, patients were categorized based on their post-ECMO support brain MRI results. The abnormal brain MRI findings in 6 neonates from the AN (abnormal) group post-ECMO indicated various central nervous system abnormalities, including reduced white matter, deeper bilateral frontotemporal sulci, enlarged ventricles, and right frontal softening focus among others. These patients also exhibited more significant $CrSO_2$ reduction, worse mean percentage change in $CrSO_2$, and poorer FTOE, along with moderate to severe abnormalities in aEEG. The findings of our study align with those of Wintermark P et al., reinforcing the correlation between $CrSO_2$, aEEG, and MRI in assessing brain injury in neonates both during and post-ECMO support [30].

The TIMP scores were conducted on neonates post-tracheal intubation removal, serving as a prevalent method for assessing motor functions in neonates and preterm infants [31]. In our study, one neonate in group N displayed mildly abnormal aEEG patterns along with an absent sleep-wake cycle; this individual's TIMP score was recorded as hypoevolutism before discharge, while the remaining four in the group were scored as normal. Conversely, in group AN, one patient with moderate abnormal aEEG had a normal TIMP score, whereas the other five were classified as hypoevolutism. The variability in TIMP scores suggests a degree of subjectivity in the assessment. Despite this, within our limited sample size, a correlation still emerged: greater reductions in $CrSO_2$ and more pronounced abnormalities in aEEG were generally associated with poorer TIMP scores and more adverse brain MRI findings.

Limitation

This study, while insightful, has several limitations to consider. Firstly, as a single-center retrospective study with a small sample size, it lacks the robustness needed for comprehensive statistical comparative analysis and definitive conclusions. Therefore, the results might not have statistical significance. Secondly, our study only included neonates receiving V-A ECMO support, limiting the generalizability of our findings to all ECMO-supported children. Thirdly, the $CrSO_2$ monitoring employed in this study has its own limitations. It primarily reflects the oxygenation status of the brain tissue in the forehead area, potentially overlooking variations in other parts of the brain. Despite these limitations, our study observed a trend where greater reductions in $CrSO_2$ and more pronounced abnormalities in aEEG correlated with worse neurological outcomes. Although these findings provide some directional insight for clinical practice, they underscore the necessity for future, larger-scale, multicenter studies to validate and expand upon these preliminary conclusions.

Conclusion

$CrSO_2$ and aEEG monitoring show potential as routine assessments during neonatal ECMO to predict neurological outcomes. In our cohort, a tendency was observed where neonates with greater reductions in $CrSO_2$ and more severe aEEG abnormalities experienced poorer neurological outcomes.

Abbreviations

$CrSO_2$	Cerebral regional Oxygen Saturation
aEEG	Amplitude-Integrated Electroencephalography
ECMO	Neonatal Extracorporeal Membrane Oxygenation
NIRS	Near-Infrared Spectroscopy
NICU	Neonatal Intensive Care Units
FTOE	Fractional Tissue Oxygen Extraction
TIMP	Test of Infant Motor Performance
HbO_2	Oxyhemoglobin
HbR	Deoxygenated Hemoglobin
MRI	Brain Magnetic Resonance Imaging
MAP	Mean Arterial Pressure
$PaCO_2$	Partial Pressure of Carbon Dioxide
FTOE	Fractional Tissular Oxygen Extraction
PPHN	Persistent Pulmonary Hypertension of the Neonate
ARDS	Acute Respiratory Distress Syndrome
MAS	Meconium Aspiration Syndrome
CDH	Congenital Diaphragmatic Hernia
PAH	Pulmonary Artery Hypertension

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Author contributions

Ling-Shan Yu and Qiang Chen designed the study, performed the statistical analysis, participated in the operation, and drafted the manuscript. Xiu-Hua Chen and Si-Jia Zhou collected the clinical data. Yi-Rong Zheng and Zeng-Chun Wang supervised the study. All authors read and approved the final manuscript.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author at the reasonable request.

Declarations

Ethics approval and consent to participate

The ethics committee of Fujian Children's Hospital granted approval for this study (2022ETKLR12052). We obtained written informed consent from the parents of the patients involved.

Consent for publication

Not applicable.

Competing interests
The authors declare no competing interests.

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