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Electrical Impedance Tomography in Pediatric Acute Respiratory Distress Syndrome: Dynamic Ventilation Monitoring and Clinical Correlation Analysis from Intubation to Extubation

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Abstract

Objective: This study aims to investigate the dynamic evolution patterns of regional ventilation parameters monitored by bedside electrical impedance tomography (EIT) in pediatric patients with acute respiratory distress syndrome (ARDS) from endotracheal intubation to planned extubation, to analyze their correlation with traditional disease severity classification, and to evaluate their predictive value for extubation outcomes.

Methods: This study employed a retrospective single-center cohort design. Pediatric ARDS patients who received invasive mechanical ventilation and underwent EIT monitoring in our hospital's PICU from January 2023 to September 2025 were included. Baseline patient data, ARDS etiology (pneumonia-associated or non-pneumonia-associated), and disease severity (based on the oxygenation index) were collected. EIT parameters, including the center of ventilation, global inhomogeneity index, and regional ventilation delay index and ratio, were recorded during the stable post-intubation period (T1) and prior to planned extubation (T2). The primary outcome was reintubation within 72 hours after extubation. Paired sample tests were used to compare differences in parameters between T1 and T2. Spearman correlation analysis was employed to assess the correlation between T1 parameters and disease severity, and independent sample tests along with receiver operating characteristic curve analysis were used to evaluate the predictive efficacy of T2 parameters for extubation failure.

Results: A total of 42 pediatric patients were included, with a median age of 4.6 years. Pneumonia-associated ARDS accounted for 85.7% (36/42) of cases, and extubation failure occurred in 4 patients (9.5%). Compared to T1, both the global inhomogeneity index (GI) and regional ventilation delay parameters showed significant improvement at T2 (all $P < 0.01$), while the center of ventilation and regional distribution proportions exhibited no significant change. No significant correlation was found between EIT parameters at intubation and traditional ARDS severity grading (all $P > 0.05$). Although no statistically significant differences in pre-extubation EIT parameters were observed between the successful and failed extubation groups (all $P > 0.05$), strong internal consistency was noted among the EIT parameters. For example, a significant positive correlation was identified between the GI and the regional ventilation delay ratio ($rs = 0.609$, $P < 0.001$).

Conclusion: During the treatment of pediatric ARDS, EIT can non-invasively and dynamically monitor significant improvements in the homogeneity and synchrony of pulmonary ventilation, providing objective bedside physiological evidence for the recovery of lung function. However, this study found that pre-extubation regional ventilation parameters failed to independently predict extubation outcomes and showed no significant correlation with severity grading based on the traditional oxygenation index. This suggests that in the clinical management of pediatric ARDS, the core value of EIT may lie more in its real-time visual guidance for optimizing lung-protective ventilation strategies, rather than serving as a standalone tool for severity classification or weaning prediction. Future studies with larger sample sizes are needed to investigate the potential role of EIT in integrated physiological monitoring and personalized therapeutic decision support.

Background

Acute respiratory distress syndrome (ARDS) is a leading cause of acute respiratory failure and mortality in pediatric intensive care units (PICUs)[1] . Its pathological core lies in severe ventilation/perfusion mismatch resulting from diffuse alveolar damage[2]. Currently, the primary clinical framework for assessing the severity of

pediatric ARDS and guiding respiratory support—the 2015 “Berlin Definition for pediatric ARDS” [3]—relies heavily on the oxygenation index (PaO_2/FiO_2) [4] and chest imaging[5]. However, this classic paradigm has inherent limitations. The oxygenation index is a “final common pathway” indicator of overall gas exchange, insensitive to regional and heterogeneous pathological changes within the lungs. Bedside chest radiographs offer limited resolution, and while chest computed tomography (CT) is the “gold standard,” it cannot be used for dynamic monitoring due to radiation risks and logistical challenges of patient transport[6]. This assessment paradigm, which “sees the forest but not the trees,” makes it difficult for clinicians to accurately identify key pathologies—such as gravitational-dependent lung collapse and regional overdistention that lead to ventilator-induced lung injury (VILI)—during the implementation of lung-protective ventilation strategies. It also hinders the individualized assessment of lung recruitment potential and the optimal timing for weaning.

The emergence of electrical impedance tomography (EIT) technology offers a revolutionary bedside tool to address these challenges. EIT non-invasively and radiation-free monitors real-time changes in thoracic impedance via surface electrodes, enabling visualization and quantification of cross-sectional pulmonary ventilation distribution [7, 8]. In adult ARDS research [9], EIT has been validated for titrating optimal positive end-expiratory pressure (PEEP) [10], assessing lung recruitment [11], monitoring pulmonary ventilation heterogeneity [9], and has shown preliminary potential for predicting weaning outcomes[12]. However, extrapolating conclusions from adult studies to the pediatric population presents significant challenges. Children have distinct chest wall structure, respiratory system compliance, and ARDS etiological profiles (e.g., a higher proportion of pneumonia-associated cases) compared to adults; consequently, the patterns and evolution of their ventilatory mechanics may have unique characteristics[13, 14]. Presently, evidence for the application of EIT in pediatric ARDS remains scarce [15]. Existing studies are predominantly small-sample, cross-sectional descriptions. There is a lack of research involving paired dynamic monitoring at two decisive clinical timepoints—initial intubation (the phase of peak disease severity) and planned extubation (the point of functional recovery assessment)—and systematically investigating the association between EIT parameters and disease severity, particularly their link with the crucial clinical outcome of extubation.

Therefore, to address this gap, this study aims to answer three sequential scientific questions: First, what are the dynamic evolution patterns of regional ventilation distribution (characterized by parameters such as CoV%, GI, and RVD) in pediatric ARDS patients during treatment from intubation to extubation? Second, is ventilation heterogeneity at intubation correlated with traditional ARDS severity classification? Finally, and most directly relevant clinically, can pre-extubation EIT assessment provide incremental information beyond traditional metrics to help predict extubation success or failure?

Through this retrospective cohort study, we aim to provide critical physiological evidence and clinical insights to support the application of EIT in the precise management and safe weaning decision-making for pediatric ARDS.

Materials and Methods

1. Study Design and Population

This study was a single-center, retrospective, observational cohort study. The study protocol was approved by the Ethics Review Committee of the Capital Institute of Pediatrics, Capital Medical University (approval number:

SHERLLM2025058), and the requirement for informed consent was waived.

Inclusion criteria: Pediatric patients admitted to the Pediatric Intensive Care Unit (PICU) of our hospital between January 1, 2023, and September 31, 2025, aged ≥28 days and ≤18 years, who underwent Electrical Impedance Tomography (EIT) monitoring for acute respiratory failure.

Grouping criteria: The worst arterial blood gas and ventilator parameters within 24 hours of admission were used. Disease severity was classified according to the 2015 Pediatric Acute Lung Injury Consensus Conference (PALICC) criteria [16]. For this study, the Oxygenation Index (OI) was prioritized as the primary criterion for severity grading. For patients not receiving invasive mechanical ventilation and for whom Mean Airway Pressure (MAP) was unavailable, the Oxygenation Saturation Index (OSI) or the PaO_2/FiO_2 ratio was used. All classification cut-off values strictly adhered to the PALICC criteria.

Non-ARDS control group (n=45): Patients with respiratory failure who did not meet the PALICC diagnostic criteria for ARDS, i.e., OI < 4 or PaO_2/FiO_2 > 300.

Mild ARDS group (n=41): Patients meeting ARDS diagnostic criteria, with 4 ≤ OI < 8 or 200 ≤ PaO_2/FiO_2 < 300.

Moderate-to-severe ARDS group (n=17): Patients meeting ARDS diagnostic criteria, with OI ≥ 8 or PaO_2/FiO_2 < 200. To enhance statistical power, the moderate and severe ARDS categories defined by the PALICC criteria were combined into a single moderate-to-severe group[17].

Monitoring time points:

Intubation group (T1): Within 1-2 hours after endotracheal intubation, following stabilization of initial ventilator settings.

Pre-extubation group (T2): Within 1 hour before planned extubation, following a successful Spontaneous Breathing Trial (SBT) and immediately prior to the extubation procedure.

Exclusion criteria: (1) Poor-quality EIT signal precluding analysis; (2) Contraindications to EIT application (e.g., extensive chest dressings, implanted cardioverter-defibrillator); (3) Severely incomplete clinical medical records.

2. Data Collection

The following data were uniformly collected through the hospital's electronic medical record system:

Baseline Data: Sex, age (months), height (cm), weight (kg).

Clinical Characteristics: Primary diagnosis (categorized as "previously healthy" or "with underlying chronic conditions"), direct cause of ARDS (pneumonia-associated/non-pneumonia-associated), and primary pathogen.

Arterial Blood Gas Data: The arterial blood gas results closest in time to the baseline EIT measurement were collected. The fraction of inspired oxygen (FiO_2) and, for mechanically ventilated children, the mean airway pressure (MAP) at the time of blood gas sampling were also recorded to calculate the Oxygenation Index (OI = [FiO_2 × MAP × 100] / PaO_2).

3. Electrical Impedance Tomography (EIT) Measurement and Parameter Analysis

EIT Device and Data Acquisition: Monitoring was performed using the [PulmoVista 500] EIT device. With the patient in the supine position and ventilator settings stable, a 16-electrode belt was positioned around the thorax at the level of the 4th-6th intercostal spaces. Measurements were recorded for at least 2 minutes with a sampling frequency of 20 Hz.

EIT Parameter Analysis: Raw data were analyzed offline using the device's dedicated software, [SDMI EIT Evaluation Tool V2.0]. To avoid motion artifacts, data from at least one minute of stable, consecutive respiratory cycles were selected for calculation. The analyzed parameters included:

Center of Ventilation (CoV, %): Reflects the vertical distribution of ventilation along the ventral-dorsal axis. A higher value indicates ventilation is more concentrated in non-dependent lung regions [18, 19].

Global Inhomogeneity Index (GI): Quantifies the spatial heterogeneity of overall lung ventilation. The value ranges from 0 to 1, with a higher value representing a more inhomogeneous ventilation distribution [18, 20].

Regional Ventilation Delay (RVD) [21]**:**

RVD SD (ms): The average of the standard deviations of regional time-to-peak for tidal impedance variation.

RVD Ratio (%): The percentage of the total lung area exhibiting delayed ventilation.

Ventilation ROI Layer Distribution (%): Layer division is based on the ventilation gradient along the ventral-dorsal (gravity-dependent) axis, categorized into ROI1 (ventral-lateral), ROI2 (ventral-medial), ROI3 (dorsal-medial), and ROI4 (dorsal-lateral).

Dependent Region Ventilation Proportion = ROI3% + ROI4%

Non-dependent Region Ventilation Proportion = ROI1% + ROI2%

Ventilation ROI Quadrant Distribution (%): Quadrant division is based on the ventral-dorsal axis: ROI1 (right anterior), ROI2 (left anterior), ROI3 (right posterior), ROI4 (left posterior). For supine patients, the dependent region is defined as both lower lung quadrants.

Dependent Region Ventilation Proportion is calculated as the sum of the ventilation percentages in the right lower quadrant (ROI3) and the left lower quadrant (ROI4).

Definition of Baseline EIT: This study primarily analyzed the arterial blood gas data obtained closest in time to the first EIT measurement. The EIT parameter values from this measurement session were defined as the "Baseline EIT parameters" for subsequent analyses across the severity spectrum and for outcome prediction studies.

4. Statistical Analysis

Statistical analysis was performed using SPSS 26.0 software. A P value of < 0.05 was considered statistically significant. For the description and comparison of baseline characteristics, continuous variables conforming to a normal distribution are presented as mean ± standard deviation (Mean ± SD). Data with a non-normal

distribution are presented as median (interquartile range) [M (Q1, Q3)]. Categorical data are presented as number (percentage).

Results

3.1 Study Population and Baseline Characteristics

During the study period, 42 pediatric patients were ultimately included after applying the inclusion and exclusion criteria. The baseline characteristics of the children are presented in Table 1. Among them, 24 were male (57.1%), with a mean age of 4.6 ± 4.2 years. Based on etiological classification, pneumonia-associated ARDS accounted for 36 cases (85.7%), comprising 7 bacterial, 5 viral, and 24 mixed infection cases. Non-pneumonia-associated ARDS accounted for 6 cases (14.3%). There were 16, 15, and 11 cases in the control, mild ARDS, and moderate-to-severe ARDS groups, respectively.

Table 1: Baseline Characteristics of the Patients

Characteristic	Value / n (%)
Demographic Data	
Male，n (%)	24 (57.1%)
Age (years), M (IQR)	4.6± 4.2
Weight (kg), mean ± SD	20.4± 15.0
Initial ARDS Severity, n (%)	
Control (Non-ARDS)	16 (38.1%)
Mild	15 (35.7%)
Moderate-Severe	11 (26.2%)
ARDS Etiology, n (%)	
Pneumonia-Associated	36 (85.7%)
- Viral	5 (11.9%)
- Bacterial	7 (16.7%)
- Mixed Infection	24 (57.1%)
Non-Pneumonia-Associated	6 (14.3%)

3.2 Comparison of EIT Parameters at Intubation and Pre-Extubation

Compared to the intubation period (T1), the children's EIT parameters at pre-extubation (T2) showed a significant trend of improvement, indicating recovery of ventilation function (Table 2). No statistically significant difference was observed in the center of ventilation (CoV%) ($P > 0.05$). The overall ventilation distribution tended toward greater homogeneity, manifested as a significant decrease in the global inhomogeneity index (GI) ($P < 0.01$). Improvement in the indicators reflecting ventilation asynchrony was particularly notable, with

both the regional ventilation delay standard deviation (RVD SD) and the regional ventilation delay ratio (RVD%) showing significant reductions (P < 0.001). Analysis of ventilation distribution by layers and quadrants along the ventral-dorsal axis revealed no statistically significant differences between the pre-extubation and intubation periods (P > 0.05).

Table 2: Comparison of EIT Parameters at Intubation (T1) and Pre-Extubation (T2) (n = 42)

EIT Parameter	Intubation (T1)	Pre-Extubation (T2)	Statistic	P-value
Overall Ventilation Parameters				
Center of Ventilation (CoV, %), mean ± SD	44.6 ± 4.89	44.9 ± 4.61	F=0.068	0.795
Global Inhomogeneity Index (GI), mean ± SD	0.51 ± 0.11	0.46 ± 0.06	F=6.855	0.011
Regional Ventilation Delay				
RVD SD, mean ± SD	12.77 ± 0.78	6.43 ± 3.71	F=22.539	<0.001
RVD ratio (%), mean ± SD	21.34 ± 16.39	8.90 ± 7.93	F=17.934	<0.001
Ventilation ROI Layer Distribution (%)				
ROI 1	17.95 ± 6.78	17.62 ± 5.64	F=0.473	0.494
ROI 2	41.02 ± 7.03	41.45 ± 7.07	F=0.258	0.613
ROI 3	33.67 ± 9.16	32.23 ± 7.70	F=0.470	0.495
ROI 4	7.36 ± 3.34	8.69 ± 4.67	F=2.598	0.111
Dependent Region Ventilation (ROI3+4) (%), mean ± SD	41.02 ± 10.90	40.93 ± 9.37	F=0.098	0.755
Ventilation ROI Quadrant Distribution (%)				
ROI 1	29.12 ± 12.36	28.93 ± 11.03	F=0.297	0.587
ROI 2	29.60 ± 12.50	29.93 ± 11.80	F=0.001	0.975
ROI 3	20.88 ± 9.96	21.45 ± 9.51	F=0.149	0.701
ROI 4	20.43 ± 8.49	19.69 ± 8.12	F=0.089	0.767
Dependent Region Ventilation (ROI3+4) (%), mean ± SD	41.31 ± 10.67	41.14 ± 9.33	F=0.017	0.896

3.3 Correlation between EIT Parameters at Intubation and ARDS Severity

Spearman correlation analysis showed no significant correlation between ARDS severity grading at intubation and any of the EIT parameters (including GI, CoV%, RVD SD, RVD%, etc.) (all P > 0.05). However, significant correlations were found among the EIT parameters themselves, as expected. For example, the center of ventilation (CoV%) exhibited strong correlations with the proportion of ventilation in the dependent region (for

both layer and quadrant distributions) (r_s = 0.896, P < 0.001; r_s = 0.903, P < 0.001). The global inhomogeneity index (GI) showed strong positive correlations with both the regional ventilation delay standard deviation (RVD SD) and the proportion of delayed ventilation area (RVD ratio) (r_s = 0.746, P < 0.001; r_s = 0.609, P < 0.001). The regional ventilation delay standard deviation (RVD SD) showed a strong positive correlation with the proportion of delayed ventilation area (RVD ratio) (r_s = 0.799, P < 0.001). A strong correlation was also observed between the proportion of ventilation in the dependent region calculated from layers and that calculated from quadrants (r_s = 0.993, P < 0.001). These findings indicate that these parameters possess consistent internal relationships when assessing ventilatory mechanical dysfunction.

Table 3: Correlation Analysis between ARDS Severity Grading and EIT Parameters at Pre-Extubation (T2) (r, P)

	ARDS Severity	**CoV%**	GI	RVD SD	RVD ratio	**Layer ROI3+ROI4**	**Quadrant ROI3+ROI4**
ARDS Severity	**-**	**-0.080, 0.0614**	**0.160, 0.312**	**0.172, 0.277**	**0.240, 0.125**	**-0.081,0.610**	**-0.091, 0.566**
CoV%		**-**	**0.057, 0.722**	**0.241， 0.124**	**0.057， 0.721**	0.896， 0.000	0.903， 0.000
GI			**-**	0.746, 0.000	0.609， 0.000	**-0.023， 0.884**	**-0.018， 0.910**
RVD SD				-	0.799, 0.000	**0.202， 0.200**	**0.213， 0.176**
RVD ratio					**-**	**0.081,0.610**	**0.099， 0.531**
Layer ROI3+ROI4						**-**	0.993,0.000
Quadrant ROI3+ROI4							**-**

4. Predictive Value of Pre-Extubation EIT Parameters for Extubation Failure

Of the 42 patients included in this study, 38 had successful extubation and 4 experienced extubation failure. Univariate analysis showed that the differences in pre-extubation (T2) EIT parameters (such as GI, RVD%, and CoV) between the successful extubation group and the failure group were not statistically significant (all $P >$ 0.05).

	Extubation Success (n=38)	Extubation Failure (n=4)	P-value
ARDS Severity	0.87 ± 0.81	1.00 ± 0.82	0.419
CoV%	44.95 ± 4.72	44.18 ± 3.88	0.697
GI	0.46 ± 0.06	0.43 ± 0.06	0.640
RVD SD	6.36 ± 3.78	7.08 ± 3.31	0.641
RVD ratio	9.00 ± 7.96	8.00 ± 8.77	0.607
Layer ROI3+ROI4	41.13 ± 9.54	39.00 ± 8.45	0.616
Quadrant ROI3+ROI4	42.34 ± 9.52	39.25 ± 8.26	0.532

Discussion

This study is the first to systematically delineate the evolution of regional ventilation distribution parameters in pediatric acute respiratory distress syndrome (ARDS) from endotracheal intubation to planned extubation through dynamic electrical impedance tomography (EIT) monitoring. The main findings are as follows: First, lung ventilation homogeneity and synchrony in children were significantly improved at pre-extubation compared to the intubation period. Second, although the EIT parameters at intubation demonstrated good internal consistency, they showed no significant correlation with the traditional ARDS severity classification based on the oxygenation index. Most importantly, neither single-point EIT parameters at pre-extubation nor their changes relative to the intubation values effectively predicted extubation outcomes. These results collectively highlight a central issue: in the clinical management of pediatric ARDS, the recovery of regional ventilatory mechanics is an important manifestation of improved lung function. However, in the complex decision-making process determining extubation success, its significance may be superseded by other factors.

1.Dynamic Improvement in Regional Ventilatory Function: Direct Confirmation by EIT Monitoring

Our data demonstrate that from T1 to T2, both the GI index, reflecting overall ventilation inhomogeneity, and the RVD parameters, reflecting ventilation asynchrony, showed significant improvement. This provides visualized, objective physiological evidence for the gradual recovery of lung function supported by lung-protective ventilation strategies. However, CoV% and the proportional distribution of ventilation across the ventral-dorsal and left-right quadrants did not change significantly. This may suggest that during the recovery phase of pediatric ARDS, improvement in ventilatory function initially manifests as homogenization and enhanced synchrony of whole-lung ventilation. In contrast, the regional ventilation distribution patterns, influenced by factors such as gravity, local consolidation, or atelectasis, may have already established a relatively stable configuration in the short term and are not prone to fundamental restructuring prior to extubation[22]. This finding deepens our understanding of the sequence of lung function recovery in pediatric ARDS.

2.The “Dissociation” Between Traditional Severity Classification and EIT Assessment: Complementary Dimensions of Evaluation.

This study found no significant correlation between EIT parameters at intubation and the Berlin definition severity classification of ARDS (based on PaO_2/FiO_2). This "dissociation" phenomenon carries important clinical

implications. PaO_2/FiO_2 is a composite indicator reflecting the overall efficiency of gas exchange, whereas EIT reveals the spatial distribution and temporal synchrony of ventilation within the lungs. The two methods assess lung injury from distinct dimensions: "gas exchange" and "ventilatory mechanics." Our results indicate that a child with near-normal oxygenation indices may still exhibit significant ventilation inhomogeneity (high GI) and delay (high RVD) within the lungs, and vice versa. This strongly supports the use of EIT as an important complementary tool to the existing assessment framework. It can identify high-risk children who appear "normal" by traditional scoring but have underlying ventilatory dysfunction, and it may aid in defining novel, physiology-based ARDS subtypes.

3.Lack of Predictive Value of EIT Parameters for Extubation Failure: Rethinking Complex Clinical Decisions

The central and challenging finding of this study is that pre-extubation EIT parameters failed to demonstrate predictive value for extubation failure. Considering the objective context of a relatively low number of extubation failure cases in the sample (4/42, 9.5%), we posit that multiple plausible explanations underlie this result. First, from a physiological perspective, extubation success is an outcome dependent on the collective "readiness" of multiple systems. It relies not solely on regional lung ventilatory function (assessed by EIT) but is also critically constrained by numerous other factors, including upper airway patency, respiratory drive, diaphragmatic contractile function, airway clearance capacity, control of the primary disease, and metabolic status. In children who experience extubation failure, the cause may primarily originate in these domains not assessable by EIT, while their regional ventilation may have recovered sufficiently, rendering their EIT parameters indistinguishable from those of the success group. Second, from a clinical practice standpoint, the treating physician's decision to extubate is itself a comprehensive judgment based on multi-source information, including physical examination, blood gas analysis, imaging, and ventilator waveforms. The weaning screening and spontaneous breathing trial criteria employed in current clinical practice may already be sufficiently sensitive in identifying cases with severe ventilatory mechanical abnormalities, thereby "filtering out" these high-risk children. Consequently, for patients who ultimately proceed to the extubation assessment stage, the incremental predictive information provided by EIT may become limited.

4. Limitations of the Study

This study has several limitations. First, as a single-center retrospective study, the sample size is small. The particularly low number of extubation failure events (n=4) results in insufficient statistical power and a high risk of Type II error, meaning that actual differences might have been missed. Second, EIT monitoring provides a single cross-sectional view, which may not fully represent the ventilation status of the entire lung. Finally, clinical treatment decisions (such as PEEP settings and recruitment maneuvers) were not standardized, which could have influenced both the EIT parameters and the final outcomes.

5. Conclusions and Future Perspectives

In summary, this study confirms that EIT can effectively and non-invasively monitor the dynamic improvement of regional ventilatory function during the treatment of pediatric ARDS. The "ventilatory mechanics" dimension of information it provides serves as a crucial complement to the traditional "gas exchange" assessment. Although, within this cohort, pre-extubation EIT parameters did not independently predict extubation outcomes, this precisely reflects the complexity of clinical weaning decision-making. This "negative" finding carries a

positive implication: it suggests that future research should not simply position EIT as an isolated predictive tool but should explore its integration into a broader physiological monitoring network.

Future research directions should include: 1) conducting large-scale, prospective, multi-center studies to validate and extend the findings of this research; 2) developing multimodal prediction models that integrate EIT parameters, assessments of diaphragmatic function, respiratory drive monitoring, and clinical indicators; 3) more importantly, shifting the research focus from "prediction" to "guidance." This involves prospectively evaluating whether individualized lung recruitment and PEEP titration strategies based on EIT can improve clinical hard endpoints, such as "extubation success rate," thereby truly realizing the core value of EIT in bedside precision respiratory therapy.

Declarations

Ethics approval and consent to participate

Ethical approval for this study was granted by the Research Ethics Committee of the Capital Center for Children's Health, Capital Medical University (Approval No.: SHERLLM2025058). All methods were performed in strict accordance with relevant guidelines and regulations. Written informed consent was obtained from all participants.

Consent for publication

Not applicable

Availability of Data and Materials

The datasets generated and/or analysed during the current study are not publicly available due ethical concerns but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Chuanzhi Li collected and analyzed the data and wrote the main manuscript text. **Shuang Liu** participated in experimental design. All authors reviewed and approved the final manuscript.

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