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Original Article

Factors influencing prognostic outcomes in children on noninvasive continuous positive airway pressure ventilation: A retrospective study

Peiqing Huo[1], Minglei Liang[2], Yuhui Cui[3], Jianhua Liu[4], Lili Ji[5]

ABSTRACT

Objective: To investigate factors influencing prognostic outcomes in children receiving non-invasive continuous positive airway pressure (nCPAP) ventilation.

Methodology: Clinical data of 158 children who received nasal nCPAP at Hebei Children's Hospital from February 2023 to May 2024 were retrospectively analyzed. During 72 hours of treatment, the patients were divided into a favorable-prognosis group (112 cases) and a poor-prognosis group (46 cases). Logistic regression was used to identify risk factors for poor prognosis. Receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive value of the identified factors.

Results: Of the 158 children, 112 (70.9%) had a favorable prognosis and 46 (29.1%) had a poor prognosis. Significant between-group differences were observed in age and underlying diseases ($P < 0.05$). A decreased P/F ratio, elevated PCT, higher initial CPAP pressure, higher initial FiO_2, and vasoactive drug administration were independently associated with poor prognosis ($P < 0.05$). The respective AUCs of these factors were 0.944, 0.820, 0.850, 0.868, and 0.594.

Conclusion: A decreased P/F ratio, elevated PCT, higher initial CPAP pressure, higher initial FiO_2, and vasoactive drug administration were independently associated with poor prognosis in children receiving nCPAP.

KEYWORDS: Non-invasive continuous positive airway pressure ventilation; Prognostic outcome; Influencing factor.

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INTRODUCTION

Non-invasive continuous positive airway pressure (nCPAP) is a first-line respiratory support technique for children with respiratory insufficiency, offering the advantages of being minimally invasive, easy to perform, and effective in improving oxygenation and pulmonary ventilation.[1] It is widely used in the clinical management of respiratory distress syndrome, bronchitis, and severe pneumonia in infants and young children.[2,3] However, there is significant heterogeneity in the prognostic outcomes of pediatric patients after receiving nCPAP.[4–6] While some children receiving nCPAP can be quickly weaned from ventilation support and recover and discharge smoothly, a small number of children experience treatment failure, requiring conversion to invasive mechanical ventilation, and even progressing to respiratory failure and multiple organ dysfunction syndrome.[7,8]

Currently, most studies on pediatric nCPAP treatment focus on selecting indications, optimizing ventilation parameters, and evaluating short-term efficacy. Although studies have shown that initiation of FiO_2 (commonly used to assess the severity of lung function) >30% and radiographic severe respiratory distress syndrome are predictors of CPAP failure, systematic research on the regularity of prognostic outcomes and influencing factors

in children remains scarce, and a unified risk assessment system has yet to be developed.[9-11] Therefore, identifying factors that influence prognosis and developing a scientifically reliable prognostic model can not only assist clinicians in the early identification of high-risk children and the formulation of individualized intervention strategies, but also provide a crucial basis for optimizing the allocation of medical resources and reducing the incidence of adverse outcomes.

This study retrospectively analyzed clinical data from children treated with nCPAP to describe prognostic outcomes and identify key factors associated with poor prognosis. The findings may support early clinical assessment and targeted treatment planning.

METHODOLOGY

The clinical data of 158 children who received nCPAP at the Hebei Children's Hospital from February 2023 to May 2024 were retrospectively reviewed.

Ethical Approval: The ethics committee of our hospital approved this retrospective study with the number 148, Date: January 29th 2021. All treatments and respiratory-support adjustments were determined by the attending physicians as part of routine clinical practice and were not influenced by the present retrospective study.

***Inclusion criteria*:**

- Age ≤ 15 years.
- nCPAP treatment initiated for respiratory insufficiency with a treatment duration of ≥ 2 hour.
- Complete clinical data.
- Continuous monitoring records with accessible changes in vital signs and oxygenation indicators every 24 hour during nCPAP treatment.

***Exclusion criteria*:**

- Patients who had received invasive mechanical ventilation (endotracheal intubation/tracheotomy) or other advanced respiratory support technologies before nCPAP treatment.
- Patients complicated with congenital airway malformation, complex congenital heart disease, or genetic metabolic diseases.
- Patients who were transferred to another hospital, discharged against medical advice, or lost to follow-up during treatment with unclear final prognosis.
- Patients for whom nCPAP treatment was only used for short-term postoperative respiratory support with non-respiratory primary diseases.

Treatment Methods: All pediatric patients received nasal nCPAP ventilation support with a dedicated nCPAP device. Appropriately sized and matched nasal prongs were selected based on the children's age and nasal cavity size.

Ventilation parameter settings: The initial CPAP pressure was set at 2–8 cmH_2O, with an initial FiO_2 of 0.3–0.6. The parameters were subsequently adjusted according to the patient's oxygenation status, respiratory effort, arterial blood gas results, and clinical response.

Principle of parameter adjustment: The treatment target was to maintain percutaneous oxygen saturation (SpO_2) at 92%~97%, partial pressure of arterial oxygen (PaO_2) at 50~80 mmHg, and partial pressure of arterial carbon dioxide ($PaCO_2$) at 35~50 mmHg. Vital signs and SpO_2 were monitored every 1~2 hours, and arterial blood gas analysis was rechecked every 4~6 hours. Parameters were adjusted gradually based on the results, with priority given to reducing FiO_2, followed by adjusting pressure levels.

Adjuvant therapy: Targeted treatment was administered according to the underlying disease, including pulmonary surfactant (PS) replacement therapy, anti-infective therapy, fluid management, nutritional support, and maintenance of internal environment stability. Vasoactive drugs (e.g., dopamine, dobutamine) were administered when necessary to maintain circulatory stability.

Criteria for Evaluating Prognostic Outcomes: For the purposes of this retrospective analysis, clinical status at 72 hours after initiation of nCPAP was extracted from the medical records and used to classify the patients' prognostic outcomes. Based on the data collected at that time point, combined with subsequent treatment and outcomes, patients were stratified into a favorable prognosis group and a poor prognosis group, with the evaluation criteria as follows:

Favorable prognosis:

- Within 72 hours of nCPAP treatment, respiratory distress symptoms (suprasternal/intercostal/subcostal retractions, grunting, tachypnea) were completely relieved or significantly improved, and the respiratory rate returned to the normal range for the corresponding age;
- The PaO_2/FiO_2 ratio was ≥ 300 mmHg, and SpO_2 was stably maintained within the target range; The patient was successful weaned from nCPAP, converted to nasal cannula oxygen inhalation ($FiO_2 \leq 0.3$) or complete oxygen withdrawal, without the need for further respiratory support, and no subsequent disease recurrence, with a smooth recovery and discharge.

Poor prognosis:

- Within 72 hours of nCPAP treatment, respiratory distress symptoms showed no improvement or progressive deterioration, the P/F ratio was <200 mmHg, and effective oxygenation could not be maintained despite optimization of the CPAP pressure and FiO_2.
- Requirement for conversion to invasive mechanical ventilation (endotracheal intubation + ventilator-assisted ventilation).
- Development of severe complications during treatment, including respiratory failure, septic shock, and multiple organ dysfunction syndrome (MODS).
- Death during treatment.

Data Collection: Relevant clinical data were retrospectively extracted from the hospital's electronic medical records and monitoring records using a standardized data-extraction procedure.

Baseline characteristics: gender, age (days/months/years), body weight, type of underlying disease (respiratory distress syndrome, severe pneumonia, bronchitis, acute laryngotracheobronchitis, etc.), and presence or absence of pulmonary hypertension.

Clinical indicators on admission: respiratory rate, arterial blood pH, PaO_2/FiO_2 ratio (P/F ratio). The P/F ratio was calculated as arterial partial pressure of oxygen (PaO_2, mmHg) divided by the fraction of inspired oxygen (FiO_2).

Laboratory test indicators: white blood cell count (WBC), C-reactive protein (CRP), procalcitonin (PCT). WBC counts were determined using a fully automated hematology analyzer (Shenzhen Mindray Biomedical Electronics Co., Ltd (BC-7500INRICS)). PCT levels were determined using a fully automated chemiluminescence immunoassay analyzer (Xingtong Medical Technology Co., Ltd CHBET-JYK-SHA08))

Table-I: Univariate Analysis of Prognosis in Children with nCPAP.

Baseline Characteristics	*Favorable Prognosis (n=112)*	*Poor Prognosis (n=46)*	χ^2/t	*P*
Gender[n(%)]				
Male	62(55.36)	27(58.70)	0.148	0.701
Female	50(44.64)	19(41.30)		
Age[n(%)]				
Infant (<1 year)	45(40.18)	31(67.39)	10.240	0.006
Preschool child (1–6 years)	48(42.86)	9(19.57)		
School-age child (>6 years)	19(16.96)	6(13.04)		
Body Weight (±s, kg)	9.81±3.09	10.03±2.82	0.417	0.678
Underlying Disease[n(%)]				
Respiratory distress syndrome	22(19.64)	20(43.48)	25.207	<0.001
Severe pneumonia	53(47.32)	15(32.61)		
Bronchitis	10(8.93)	11(23.91)		
Other	27(24.11)	0(0.00)		
Pulmonary Hypertension[n(%)]				
Yes	8(7.14)	15(32.61)	17.002	<0.001
No	104(92.86)	31(67.39)		
Respiratory Rate ($\bar{x}\pm s$, breaths/min)	53.41±5.32	54.68±6.79	1.254	0.212
Arterial Blood pH ($\bar{x}\pm s$)	7.33±0.12	7.29±0.10	1.993	0.048
P/F ratio($\bar{x}\pm s$, mmHg)	352.13±45.71	246.34±30.38	14.429	<0.001
WBC($\bar{x}\pm s$, ×109/L)	16.89±4.11	17.61±5.24	0.921	0.359
CRP($\bar{x}\pm s$, mg/L)	26.25±8.91	30.52±10.24	2.618	0.010
PCT($\bar{x}\pm s$, ng/mL)	2.39±1.07	4.62±2.13	8.739	<0.001
Initial CPAP pressure($\bar{x}\pm s$, cmH2O)	5.09±1.04	6.92±1.37	9.127	<0.001
Initial FiO_2($\bar{x}\pm s$)	0.37±0.08	0.53±0.12	9.791	<0.001
Pulmonary Surfactant (PS) Administration[n(%)]				
Yes	30(26.79)	20(43.48)	4.200	0.040
No	82(73.21)	26(56.52)		
Vasoactive Drug Administration[n(%)]				
Yes	35(31.25)	23(50.00)	4.934	0.026
No	77(68.75)	23(50.00)		

with electrochemiluminescence as the detection method. CRP levels were determined using a protein analyzer (Shenzhen Mindray Biomedical Electronics Co., Ltd CBC-7500INRICS)).

Ventilation-related indicators: initial CPAP pressure and FiO_2 of nCPAP. FiO_2 was determined by the oxygen delivery device (Fisher & Paykel MR850).

Clinical intervention indicators: administration of pulmonary surfactant (PS) and administration of vasoactive drugs.

Study Outcomes:

- Prognostic outcomes of children with nCPAP in this group were statistically analyzed.
- Univariate analysis of poor prognosis was conducted by taking prognostic outcome as the dependent variable, and all collected variables including general demographic characteristics, underlying diseases, clinical indicators on admission, laboratory test results, ventilation-related parameters and clinical interventions as independent variables to identify potential influencing factors associated with poor prognosis.
- Multivariate analysis of poor prognosis was conducted to incorporate the statistically significant potential influencing factors screened by univariate analysis into a multivariate logistic regression model, and analyze and identify the independent risk factors for poor prognosis in children after nCPAP treatment.
- The receiver operating characteristic (ROC) curve was generated, and the area under the curve (AUC) was calculated. The predictive value of each factor for poor prognosis in children with nCPAP was evaluated.

Statistical Analysis: Data was analyzed using SPSS 26.0. Quantitative variables were expressed as mean ± standard deviation (SD), and differences between the two groups were compared using independent-sample t-test. Categorical variables were expressed as frequency and constituent ratio (%), and differences between the two groups were compared using χ^2 test. Variables associated with poor prognosis were screened by univariate analysis and then included in multivariate logistic regression analysis to identify independent risk factors for prognostic outcomes in children on nCPAP ventilation Variables with P<0.2 on univariate analysis were entered into the multivariate model. Because one disease category contained zero poor-prognosis events, Firth's penalized-likelihood (bias-reduced) logistic regression was used, and the model was reduced to a final set of independent predictors by backward elimination. The predictive value of prognostic factors was assessed using the ROC curve. A P value < 0.05 was considered statistically significant.

RESULTS

Among the 158 children with nCPAP in this group, 112 had a favorable prognosis, accounting for 70.9%; 46 cases had poor prognosis, accounting for 29.1%. Among the children with poor prognosis, 40 cases were converted to invasive mechanical ventilation due to continuous deterioration of oxygenation function, 6 cases had secondary hospital acquired infections (pneumonia/ sepsis), and 3 cases died during treatment. These adverse outcomes were not necessarily mutually exclusive. There were no significant differences in gender, weight, respiratory rate, and WBC count among children with different prognoses of nCPAP (P>0.05), while significant between-group differences were observed in age, underlying disease, pulmonary hypertension, arterial blood pH, P/F ratio, CRP, PCT, initial CPAP pressure, initial FiO_2, pulmonary surfactant administration, and vasoactive drug administration (P<0.05; Table-I).

With poor prognosis as the dependent variable, variables with P<0.2 on univariate analysis were entered into a multivariate logistic regression model. Because one disease category contained zero poor-prognosis events, Firth's penalized-likelihood method was used, and the model was reduced by backward elimination. The analysis identified a decreased P/F ratio, elevated PCT, higher initial CPAP pressure, higher initial FiO_2, and vasoactive drug administration as factors independently associated with poor prognosis in children receiving nCPAP (P<0.05. Table-II and ; Table-III.

ROC analysis showed that the AUCs of P/F ratio, PCT, initial CPAP pressure, initial FiO_2, and vasoactive drug administration for discriminating poor prognosis after nCPAP treatment were 0.944, 0.820, 0.850, 0.868, and 0.594, respectively (Table-IV and Fig.1). ROC analysis showed good discriminatory performance for the P/F ratio, PCT, initial CPAP pressure, and initial FiO_2. In contrast, vasoactive drug administration alone showed limited discriminatory ability, with an AUC of 0.594.

Table-II: Variable Coding Table.

Variable	*Coding*
P/F ratio	Continuous variable; OR reported per 10-mmHg increase
PCT	Continuous variable; OR reported per 1-ng/mL increase
Initial CPAP pressure	Continuous variable; OR reported per 1-cmH_2O increase
Initial FiO_2	Continuous variable; OR reported per 1-unit increase
Vasoactive drug administration	Yes = 1; No = 0

DISCUSSION

The study identified decreased P/F ratio, elevated PCT, higher initial CPAP pressure, higher initial FiO_2, and use of vasoactive drugs as independent risk factors affecting prognosis after nCPAP treatment in children. This study identified multiple objective indicators associated with poor prognosis after nCPAP treatment that can be rapidly evaluated at the bedside, providing additional real-world clinical evidence for early risk assessment.

The incidence of poor prognosis (29.1%) in this study was consistent with the 25%-30% reported in similar studies, yet it is significantly higher than the 18.9% -22.4% reported in multicenter study by the foreign Neonatal Respiratory Distress Syndrome Collaborative Group.[12,13] We may speculate that the core mechanism of this regional difference is not the difference in ventilation technology itself, but the variability in intervention timing, comprehensive treatment strategies, and the underlying diseases. NCPAP is typically initiated early in infants with respiratory distress syndrome and is combined with PS (in over 80% of cases), strict fluid management, infection control, and circulatory support.[14] A possible reason is that a large proportion of children in our study were referred from primary centers and hence, initiation of nCPAP was delayed by some hours after disease onset. The PS utilization rate was also low and some children received standardized treatment only after developing severe hypoxemia. The important clinical value of the above results lies in suggesting that early initiation of nCPAP, standardized use of pulmonary surfactant, and strengthened comprehensive support management are key pathways to reduce poor prognosis, and have important guiding significance for primary hospitals and referral systems.

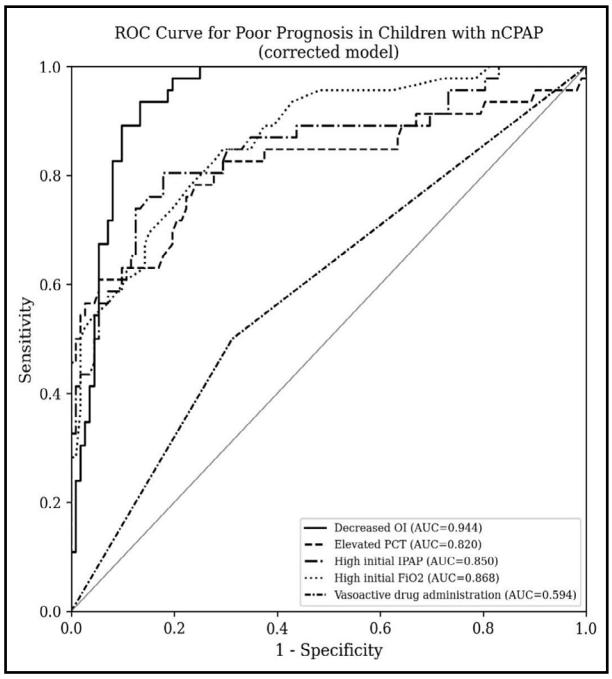

Fig.1: ROC Curve for Poor Prognosis in Children with nCPAP.

This study identified a higher initial CPAP pressure as a risk factor independently associated with poor

Table-III: Multivariate Analysis of Poor Prognosis in Children Receiving nCPAP.

Variable	*βvalue*	*S.E value*	*Waldχ^2 value*	*P value*	*OR value*	*95% CI*
P/F ratio (per 10-mmHg increase)	-0.933	0.322	8.402	0.004	0.393	0.209–0.739
PCT (per 1-ng/mL increase)	1.349	0.600	5.057	0.025	3.855	1.189–12.494
Initial CPAP pressure (per 1 cmH_2O increase)	2.741	1.075	6.508	0.011	15.507	1.887–127.407
Initial FiO_2 (per 1-unit increase)	2.525	0.846	8.914	0.003	12.489	2.381–65.514
Vasoactive drug administration	4.824	1.970	5.995	0.014	124.457	2.618–5916.584

Table-IV: ROC Analysis of Poor Prognosis in Children with nCPAP.

Variable	*AUC*	*S.E. Value*	*P value*	*95% CI*
Decreased P/F ratio	0.944	0.017	<0.001	0.907–0.975
Elevated PCT	0.820	0.045	<0.001	0.728–0.900
High initial CPAP pressure	0.850	0.037	<0.001	0.770–0.917
High initial FiO_2	0.868	0.030	<0.001	0.803–0.923
Vasoactive drug administration	0.594	0.043	0.028	0.508–0.678

prognosis (OR=15.507 per 1-cmH_2O increase). Because initial CPAP pressure is titrated upward when spontaneous respiratory effort and oxygenation remain inadequate at lower pressures, a higher starting pressure requirement is a bedside marker of greater baseline severity of respiratory compromise. Children who require higher initial pressures at nCPAP initiation may represent a subgroup with more advanced pulmonary pathophysiology, translating into a higher likelihood of nCPAP failure. Age < 12 months was significant on univariate analysis but was not retained as an independent predictor once P/F ratio, PCT, initial CPAP pressure, FiO_2, and vasoactive drug use were accounted for in the multivariate model.[15] From a pathophysiological perspective, the respiratory system of infants is extremely immature, with insufficient pulmonary surfactant production, poor lung compliance, and weak respiratory muscle strength.[16,17] Therefore, they often respond less to nCPAP support and are prone to persistent deterioration of oxygenation function due to increased airway resistance and insufficient gas exchange efficiency.[18,19] In addition, infants' hypothalamic-pituitary-adrenal axis function is not yet fully developed, and their stress response to hypoxia and inflammation is weak, which further increases the risk of disease progression.[20]

The study also demonstrated the clinical significance of elevated PCT levels on admission. As previously shown, for every 1 ng/mL increase in PCT, the risk of poor prognosis increases by 3.855-fold, consistent with the corrected Table-III estimate.[21] The essence of this difference lies in the variation of infection types and intervention timing.[22] In this study, some of the children had hospital-acquired infections, with distinct initiation mechanisms and progression rates of the inflammatory response. Moreover, antibiotic administration was delayed in some children due to limitations in their primary medical conditions, leading to differences in the predictive value of PCT for prognosis.

This study demonstrated the potential early warning value of a decreased P/F ratio combined with elevated initial FiO_2. The P/F ratio is a clinically accessible indicator of pulmonary gas exchange, and a lower value indicates more severe hypoxemia.[23] Previous research has shown that for every 10 mmHg decrease in P/F ratio, the risk of poor prognosis increases by 1.294-fold.[24] In the present cohort, each 10-mmHg decrease in the P/F ratio was associated with a 2.545-fold increase in the odds of poor prognosis. Previous studies have identified a higher initial FiO_2 requirement as a predictor of CPAP failure.[9,10,25] CPAP failure entails a more than 20-fold increased risk of death and pneumothorax, as well as a 2- to 5-fold increased risk of typical complications in prematurity.[25] Similarly, the present study found that the incidence of poor prognosis increased significantly with increasing initial nCPAP FiO_2. From a pathophysiological perspective, an abnormal P/F ratio indicates severe impairment of pulmonary gas exchange, while an elevated initial FiO_2 suggests severe hypoxic stress.[26] Therefore, a decreased P/F ratio combined with an elevated initial FiO_2 may indicate more severe respiratory compromise and the need for closer monitoring and timely escalation of respiratory support.

This study showed that the risk of poor prognosis was increased in children receiving vasoactive drugs, which is consistent with the conclusions of previous research.[27] This effect may be due to the combined involvement of the respiratory and circulatory systems, which form a vicious circle. Although the administration of vasoactive drugs can temporarily maintain blood pressure, the exacerbation of pulmonary congestion and edema further impairs pulmonary oxygenation, ultimately leading to a significantly increased failure rate of nCPAP.[28] This suggests that early identification of tissue hypoperfusion and timely initiation of circulatory support are the keys to improving the prognosis of children with combined respiratory and circulatory involvement. In the corrected multivariate model, the 95% CI around the vasoactive-drug association was wide (2.618–5916.584), reflecting the limited number of poor-prognosis events relative to the number of predictors screened; this estimate should be interpreted cautiously and would benefit from confirmation in a larger cohort.

In addition, ROC curve analysis further demonstrated the value of decreased P/F ratio, elevated PCT, high initial CPAP pressure, high initial FiO_2, and vasoactive drug administration in evaluating the prognosis of children receiving nCPAP. The findings of this study enrich the clinical research content in the field of pediatric non-invasive respiratory support, providing new evidence for early clinical warning, stratified management, and precise intervention, and have important theoretical significance and clinical application value.

Strengths and Limitations: This study evaluated objective and quantifiable risk factors covering multiple dimensions, including age, inflammation, oxygenation, ventilation, and circulation. These indicators can be rapidly assessed at the bedside and may assist with early clinical warning. The study also has some limitations. It was a single-center retrospective study with a relatively small sample size, and all included children were from our hospital's pediatric intensive care unit (PICU), which may introduce selection bias. The multivariate model retained 5 predictors against 46 poor-prognosis events (approximately 9 events per variable), and one disease category required Firth's bias-reduction method to manage a zero-event cell. Several 95% CIs, particularly for initial CPAP pressure and vasoactive drug administration, remained wide, and the model was not internally validated, so the point estimates should be interpreted with appropriate caution. Additionally, the correlation between dynamic adjustments of nCPAP parameters during treatment and children's prognosis was not analyzed, nor were the differential expression characteristics of influencing factors among subgroups with different underlying diseases explored. Future multicenter prospective cohort studies are needed to

expand the sample size and source, further validate the conclusions of the present study, and perform subgroup analyses stratified by gestational age and infection type to clarify differences in prognostic factors across distinct populations.

CONCLUSION

Children receiving nCPAP are at a certain risk of poor prognosis. Decreased P/F ratio, elevated PCT, high initial CPAP pressure, high initial FiO_2, and administration of vasoactive drugs are independent risk factors for poor prognosis. Close monitoring of these factors can facilitate the early identification of high-risk groups and the development of timely, targeted interventions, thereby improving their prognosis.

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PH and ML: Literature search, study design and manuscript writing.
YC, JL and LJ: Data collection, data analysis and interpretation. Critical review.
PH and ML: Manuscript revision and validation and are responsible for the integrity of the study.
All authors have read and approved the final manuscript.