

ORIGINAL RESEARCH



Incidence and risk factors of pediatric post-bronchoscopy fever in west China: a retrospective study

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Abstract

Post-bronchoscopy fever (PBF) is a common complication in pediatrics without clear causative reasons. It can affect the rehabilitation of children, increase hospitalization costs, and lead to stress and anxiety in parents. Yet, there are no direct strategies to prevent its occurrence, and data on Chinese patients are limited. This study evaluated the incidence and risk factors associated with PBF in children from West China. The data of children who underwent bronchoscopy from January 2019 to December 2019 in West China Second University Hospital were retrieved. Their demographic characteristics, bronchoscopic results, temperature change after bronchoscopy, and associated indicators were assessed. Differences were compared using the paired *t*-test, chi-squared test, or Fisher's exact test, as appropriate. Risk factors associated with PBF were calculated using multivariate logistic regression analyses. In total, the data of 867 patients were retrieved for final analysis. Of them, 88 patients had PBF, with an incidence rate of 10.15%. General anesthesia (odds ratio (OR) = 1.855, 95% confidence interval (CI): 1.482, 2.321) and length of procedure (OR = 1.02, 95% CI: 1.00, 1.03) were identified as risk factors for PBF in pediatrics. This study found that the type of anesthesia and length of procedure were risk factors for PBE in children from West China.

Keywords

Pediatric; Fever; Bronchoscopy; Risk factors

1. Introduction

Flexible bronchoscopy is commonly used in clinical practice. Despite being invasive, it is well-tolerated and safe for diagnosing pediatric respiratory diseases [1]. However, flexible bronchoscopy may also lead to complications, such as airway trauma and laryngeal spasm [2], which often prolong hospital stays and increase family burdens [3]. According to a small cohort size study, post-bronchoscopy fever (PBF) has been reported to be a common complication of flexible bronchoscopy, affecting almost 5–10% of adults and 2–33% of children [3, 4], but the underlying pathogenesis of PBF remains unclear [5].

Based on previous studies and clinical practices, we found that despite the high incidence of PBF in pediatrics and its association with increased stress and anxieties in parents, there are no standard guidelines or strategies to prevent its occurrence [6–9]. PBF is assumed to occur due to inflammatory factors released from transient bacteremia after bronchoscopy and bronchoalveolar lavage (BAL) [7–9]. However, the use of the prophylactic anti-inflammatory drug ibuprofen has not been effective in reducing the incidence of PBF [10]. In this study, we retrospectively assessed the data of children who underwent bronchoscopy in West China to investigate the

incidence of PBF and identify associated risk factors.

2. Materials and Methods

In this retrospective study, the records of children who underwent flexible bronchoscopy between January 2019 to November 2019 at the West China Hospital of Sichuan University (Sichuan, China) were retrieved and analyzed.

2.1 Study population

2.1.1 Inclusion criteria

The criteria for patient selection were: (1) patients with indications for bronchoscopy, such as laryngeal stridor, recurrent wheezing, chronic cough, recurrent respiratory tract infections, hemoptysis, abnormal chest imaging, suspected foreign body aspiration; (2) were aged from 0 to 18 years old; (3) had a normal immune function, and; (4) had no fever before the bronchoscopic intervention.

2.1.2 Exclusion criteria

Cases were excluded if: (1) 24 h before the bronchoscopic intervention, their ear temperature was >37.5 °C; (2) were given preoperative intravenous glucocorticoids or immuno-

suppressants; (3) had chronic or malignant diseases such as impaired immune function, diabetes, malignant hepatopathy, autoinflammatory disease, hyperthyroidism, and malignant tumor, and; (4) data needed for study assessment could not be retrieved.

2.2 Definition of study terminology

2.2.1 Bronchoscopy

Bronchoscopy is a widely performed intervention for diagnosis and treatment in clinical practice. It can be divided into flexible, rigid, or combined bronchoscopy [11, 12]. In pediatrics, flexible bronchoscopy is most commonly used [13]. The bronchoscopic procedures of this study were carried out according to the Chinese flexible bronchoscopy management clinical practice [14]. All patients included in this study underwent fiberoptic bronchoscopy.

2.2.2 Pre-bronchoscopy fever

Pre-bronchoscopy fever was defined as an ear temperature >37.5 °C within 24 h before the bronchoscopic intervention.

2.2.3 Post-bronchoscopy fever (PBF)

PBF was defined as an ear temperature >37.5 °C within 24 h after bronchoscopy. The temperature was taken immediately after returning to the ward after surgery and monitored every 6 h until the temperature normalized. In case of fever, the temperature was monitored every hour. The highest temperature was recorded every 4 h and was continuously monitored for 3 days after the temperature normalized.

2.3 Bronchoscopy procedures

2.3.1 Preparation before intervention

All patients underwent preoperative examinations such as chest computed tomography (CT), electrocardiogram and laboratory examination before the procedure. The patients and their caregivers were informed of the risks, complications and cost of bronchoscopy, and provided signed informed consent. Further, the participating anesthesiologist enquired for a history of anaphylaxis to anesthesia drugs and also signed the consent form for general anesthesia. For uniform management, the nurse in charge informed the guardian that the child would start fasting from 3:00 AM on the day of bronchoscopy. At the time of bronchoscopy, the patients were given local anesthesia with 1% lidocaine nebulization (0.2 mL/kg), which was repeated if necessary. Patients who underwent general anesthesia were given intravenous atropine (0.1–0.3 mg/kg) before the bronchoscopy procedure. The initial decision on the type of anesthesia was at the discretion of the attending physician. Usually, general anesthesia is opted for children with confirmed or suspected foreign body aspiration, and local anesthesia for the other remaining conditions. After evaluation by the respiratory therapist and anesthesiologist, the final type of anesthesia was confirmed.

2.3.2 Anesthesia

Upon arrival in the operating room, vital signs were continuously monitored, and adequate support was used to prevent the

child from falling out of the operating bed. Almost all children underwent the bronchoscopy procedure through the nasal route to prevent damage to the device. Transoral insertion was preferred in special cases such as neonates and those with narrow nostrils. Midazolam (0.1–0.3 mg/kg) was used for intravenous sedation with local anesthesia [14]. Children underwent general anesthesia with laryngeal mask ventilation, and mask bars were cut to facilitate the bronchoscope insertion. The mask model was selected according to the child's weight. Usually, a size of 1.0 was chosen for children less than 5 kg, a size of 1.5 for those between 5–10 kg, and a size of 2.0 for those between 10–20 kg. For general anesthesia, propofol and fentanyl were used. Scoline was used if muscle relaxation was needed [15].

2.3.3 Post-examination monitoring

After bronchoscopy, a proper handover was performed upon returning to the ward. The nurses communicated promptly with the parents, and the children were given oxygen inhalation at 0.5–1 L/min through the nasal passage. The patients' vital signs were monitored until they could start to eat. Nebulized inhalation of glucocorticoids to reduce bronchial mucosal edema was given when necessary. The guardians were advised to make their child fast for 3 h after local anesthesia and 6 h after general anesthesia, and were also given intravenous rehydration when necessary.

2.4 Selection of study indicators

Based on literature search and available information, epidemiological characteristics, preoperative laboratory tests, types of anesthesia, preoperative infusion of fibrinogen and antibiotics, duration of surgery, BAL, and surgical biopsy data were retrieved to assess their influence on PBF.

2.5 Statistical analysis

Continuous variables were presented as mean with standard deviation or violin plot, non-normally distributed measurement data were represented by median (quartile), and discrete variables were shown as absolute number and percentage. The Microsoft Excel (version 2019, Microsoft, Redmond, WA, USA) and SPSS (version 26.0, IBM, Chicago, IL, USA) software were used for statistical analysis. Differences were compared using the paired *t*-test, chi-squared test, or Fisher's exact test, as appropriate. Differences were considered statistically significant for *p* values < 0.05 . The risk factors of PBF were further evaluated using multivariate logistic regression analyses.

3. Results

3.1 Study Population

The data of 867 patients who underwent flexible bronchoscopy were included in the final analysis. Of them, 288 patients were excluded because they had preoperative glucocorticoids ($n = 91$), immunodeficient conditions ($n = 5$), or fever within 24 h before bronchoscopy ($n = 192$). We observed that 88 patients had PBF, with an incidence rate of 10.15%. The age of the patients ranged from 2 days to 15 years old. In all,

there were 498 (57.57%) males and 369 (42.56%) females. In the fever group, the top three main diagnoses were foreign body aspiration (FBA) (25%), severe pneumonia (14.77%) and pneumonia (12.5%). Similar to the fever group, the top three main diagnoses in the non-fever group were also FBA (22.59%), severe pneumonia (19.13%) and pneumonia (15.40%). The patients' clinical characteristics and preoperative examination indicators are presented in Table 1.

3.2 Temperature change within 24 h post-bronchoscopy

The descriptions of temperature change within 24 h post-bronchoscopy of the fever group are shown in Table 2 and the corresponding violin plot in Fig. 1. In the fever group, the temperature was measured every hour after the onset of fever until the body temperature was normal, and the highest point of temperature was recorded every 4 h within the first 24 h of fever. Our results showed that the mean temperature of the fever group was 36.78 °C to 38.06 °C, the median temperature was 36.5 °C to 38.20 °C, and the maximum temperature was 41.0 °C at the third time point.

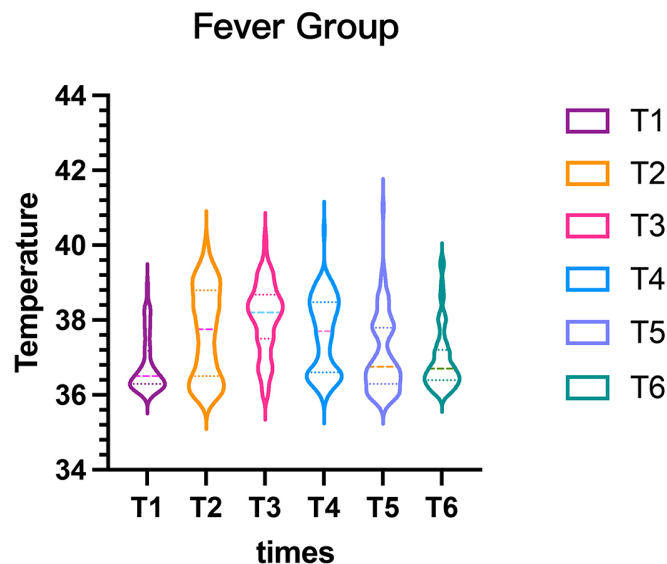


FIGURE 1. Violin plot of temperature descriptive of fever group.

Descriptions of temperature change within 24 h post-bronchoscopy of the non-fever group are shown in Table 3, and the corresponding violin plot in Fig. 2. The patients' temperature was measured 4 times within the first 24 h post-bronchoscopy. Their median temperature was 36.4 °C to 36.50 °C, and their maximum temperature was 37.4 °C.

3.3 Antipyretics use

In total, 45 (51.15%) patients received a total of 54 doses of antipyretic drugs within 24 h post-bronchoscopy. The antipyretics used were ibuprofen (66.67%), acetaminophen (25.93%), naproxen (5.55%), and glucocorticoid (1.85%). Antipyretics were prescribed as oral medications for 38 cases, enemas were performed 12 times, tube feedings were given 3 times, and intravenous infusion was administered in 1 case.

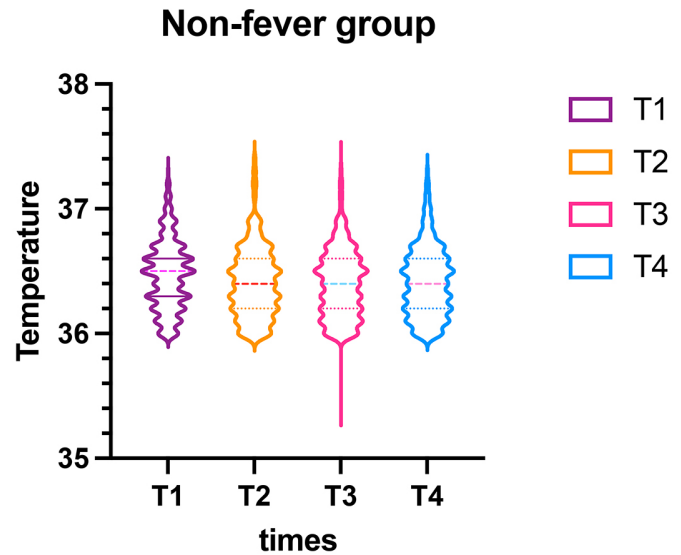


FIGURE 2. Violin plot of temperature descriptive of the non-fever group.

3.4 Risk factors of PBF

3.4.1 Integral analysis

Risk factors of PBF were identified using binary logistic regression. The type of anesthesia used (OR = 0.353, 95% CI: 0.226, 0.551) and length of procedure (OR = 1.02, 95% CI: 1.00, 1.03) were identified as significant factors associated with PBF, while no difference in other indicators such as gender, weight, laboratory examination and BAL was observed (Table 4). Our results showed that a longer duration of bronchoscopy was associated with a higher incidence of PBF. In regard to the mode of anesthesia and occurrence of PBF, a positive association between general anesthesia and risk of PBF (OR = 1.855, 95% CI: 1.482, 2.321) was observed, compared to local anesthesia (OR = 0.654, 95% CI: 0.521, 0.822).

3.4.2 Age-based subgroup analysis

The patients were divided into 3 subgroups according to their age: less than 1 year old, 1–3 years old, and more than 3 years old, and binary logistic regression for PBF risk factors was performed (Table 5). The results showed that the main influencing factor for the less than 1 year old group was the length of the procedure (OR = 1.042, 95% CI: 1.002, 1.084). For the 1–3 years old group, the main influencing factor was general anesthesia (OR = 1.625, 95% CI: 1.311, 2.014), while for the more than 3 years old group, the influencing factors were length of procedure (OR = 1.027, 95% CI: 1.004, 1.050) and general anesthesia (OR = 2.593, 95% CI: 1.467, 4.582).

4. Discussion

In this study cohort (n = 88), the incidence of PBF was 10.15%. Heat peaks above 38.5 °C were observed in 27 (30.68%) patients. The most significant factors associated with PBF occurrence were the type of anesthesia and the length of the procedure. Regarding treatment safety, no bronchoscopy-related adverse events or deaths occurred.

TABLE 1. Clinical characteristics of patients after bronchoscopy.

Indicators	Fever (n = 88)	Non-fever (n = 779)	df	t/x ²	p
Age (years)			2	1.94	0.37
<1	23	184			
1–3	44	353			
>3	21	242			
Gender			1	0.34	0.57
Male	48	450			
Female	40	329			
Weight (mean ± s)	13.56 ± 7.90	14.94 ± 9.71	863	–1.28	0.2
Complication			1	0.02	0.51
Yes	7	59			
No	81	720			
Anesthesia			2	21.58	< 0.001*
Local	41	554			
General	47	224			
WBC (× 10 ⁹ /L)	10.58 ± 5.03	9.53 ± 5.06	863	1.84	0.07
GRA (mean ± s)	4.76 ± 3.38	4.17 ± 3.10	863	1.67	0.10
Lymphocytes (%)	44.25 ± 19.14	45.58 ± 17.86	862	–0.65	0.51
Neutrophil (%)	43.74 ± 19.85	42.70 ± 18.27	863	0.50	0.62
Platelet (× 10 ⁹ /L)	404.41 ± 150.14	388.57 ± 142.41	863	0.98	0.33
Hemoglobin (g/L)	118.44 ± 15.17	122.60 ± 43.47	863	–0.89	0.37
C-reactive protein (mg/L)			1	1.54	0.22
Normal	68	642			
Abnormal	20	135			
Lactic dehydrogenase (U/L)	381.70 ± 315.52	373.21 ± 242.19	862	0.30	0.76
Fibrous protein (g/L)	297.87 ± 105.31	287.71 ± 112.02	862	0.81	0.42
Preoperative infusion of fibrinogen			1	0.17	0.44
Yes	6	63			
No	82	716			
Preoperative use of antibiotics			1	0.04	0.48
Yes	77	687			
No	11	92			
Length of procedure (min)	23.90 ± 20.62	17.26 ± 12.24	863	4.43	< 0.001*
Bronchoalveolar lavage			1	1.23	0.19
Yes	84	718			
No	4	61			
Intraoperative biopsy			1	1.15	0.22
Yes	4	20			
No	84	779			

WBC: white blood cell; GRA: absolute value of neutrophil count. *Indicates that the difference is statistically significant.

TABLE 2. Temperature descriptive of fever group after bronchoscopy (°C).

Variables	T1	T2	T3	T4	T5	T6
Minimum	36.00	36.00	36.00	36.00	36.00	36.00
25% Percentile	36.30	36.50	37.50	36.60	36.30	36.40
Median	36.50	37.75	38.20	37.70	36.75	36.70
75% Percentile	37.18	38.80	38.68	38.48	37.80	37.20
Maximum	39.00	40.00	40.20	40.40	41.00	39.60
Mean	36.78	37.66	38.06	37.61	37.09	36.94
SD	0.74	1.20	0.95	1.01	1.02	0.84
SE	0.08	0.13	0.10	0.11	0.11	0.09

T1–T6: Timing 1–Timing 6; SD: Standard Deviation; SE: Standard Error.

TABLE 3. Temperature descriptive of the non-fever group after bronchoscopy (°C).

Variables	T1	T2	T3	T4
Minimum	36.00	36.00	35.40	36.00
25% Percentile	36.30	36.20	36.20	36.20
Median	36.50	36.40	36.40	36.40
75% Percentile	36.60	36.60	36.60	36.60
Maximum	37.30	37.40	37.40	37.30
Mean	36.47	36.41	36.40	36.42
SD	0.28	0.28	0.28	0.28
SE	0.01	0.01	0.01	0.01

T1–T4: Timing 1–Timing 4; SD: Standard Deviation; SE: Standard Error.

TABLE 4. Risk factors of post-bronchoscopy fever.

Factors	B	S.E.	Wals	Sig.	OR	95% CI
Gender	−0.28	0.24	1.37	0.24	0.76	0.47, 1.21
Weight	−0.01	0.02	1.10	0.29	0.98	0.95, 1.01
Anesthesia			12.21	0.00		
Local	19.69	40194.5	0.00	1.00	0.65	0.52, 0.82
General	20.63	40194.5	0.00	1.00	1.85	1.48, 2.32
WBC count	0.02	0.03	0.46	0.50	1.02	0.96, 1.09
GRA	0.00	0.07	0.00	0.95	1.01	0.88, 1.15
Lymphocytes	−0.02	0.02	1.44	0.23	0.98	0.95, 1.01
Neutrophil	−0.02	0.02	0.78	0.38	0.99	0.95, 1.02
Platelet	0.00	0.00	0.36	0.55	1.00	0.99, 1.00
Hemoglobin	−0.01	0.01	2.01	0.16	0.99	0.97, 1.00
CRP	0.19	0.38	0.27	0.60	1.22	0.58, 2.54
Lactic dehydrogenase	0.00	0.00	0.43	0.51	1.00	0.99, 1.00
Fibrous protein	0.00	0.00	0.10	0.75	1.00	0.99, 1.00
Preoperative infusion of fibrinogen	0.04	0.49	0.01	0.93	1.04	0.40, 2.73
Preoperative use of antibiotics	−0.04	0.37	0.01	0.90	0.96	0.47, 1.97
Operating time	0.02	0.01	5.53	0.02	1.02	1.00, 1.03
Bronchoalveolar lavage	0.79	0.64	1.58	0.21	2.22	0.64, 7.72
Intraoperative biopsy	0.58	0.63	0.84	0.36	1.78	0.52, 6.15
Constant	−20.34	40194.5	0.00	1.00	0.00	

B: Unstandardized Coefficients; S.E.: Std. Error; Wals: Wald; Sig.: significance; OR: Odds Ratio; CI: confidence interval; WBC: white blood cell; GRA: absolute value of neutrophil count; CRP: C-reactive protein.

TABLE 5. Risk factors of post-bronchoscopy fever based on age-subgroup.

Subgroup	Factors	B	S.E.	Wals	Sig.	OR	95% CI
<1 year	Length of procedure	0.041	0.02	4.19	0.041	1.042	1.002, 1.084
	Constant	-2.784	0.43	42.21	0.000	0.062	
	Anesthesia			10.59	0.005	0.304	0.152, 0.609
1-3 years	Local	18.42	40191.14	0.00	1.000	0.494	0.302, 0.807
	General	19.581	40191.14	0.00	1.000	1.625	1.311, 2.014
	Constant	-21.203	40191.14	0.00	1.000	0.000	
>3 years	Length of procedure	0.026	0.01	5.14	0.023	1.027	1.004, 1.050
	Anesthesia	-1.051	0.50	4.36	0.037	0.350	0.130, 0.937
	Local					0.685	0.471, 0.996
	General					2.593	1.467, 4.582
	Constant	-2.268	0.53	18.26	0.000	0.104	

B: Unstandardized Coefficients; S.E.: Std. Error; Wals: Wald; Sig.: significance; OR: Odds Ratio; CI: confidence interval.

The incidence of PBF in this study was within the range of that reported in previous studies [16, 17] but was much lower than that reported in a study by Picard E *et al.* [16] (48%). The reasons for the different incidence rates are not only related to the study population and sample size, but also to inconsistencies in existing diagnostic criteria for fever. Some guidelines and studies have defined fever as a rise in body temperature to over 38 °C [16–21], while in this present study, fever was defined as a body temperature above 37.5 °C, which was based on Chinese guidelines [22, 23].

Despite the advantages of bronchoscopy, this procedure may also be a route for bacterial infection. Bacteremia and sepsis after bronchoscopy have been reported in both immunocompromised and immunocompetent patients, with a frequency range of 0.7–6.5% and 3.5% in adults, respectively [5]. With developments in medical technology, improvements in the sterilization of bronchoscopic equipment and operating room environments have reduced the risks of infections. An interesting observation in this study was that inflammatory biomarkers were not routinely examined in children with PBF. Thus, we could not determine whether the postoperative fever was non-specific or caused by infection, and determining the type and cause of fever will be our focus in the future.

This study also found that the type of anesthesia and length of bronchoscopy were significant risk factors associated with PBF in children. Further assessments showed that the influence of these factors was different in different age groups. Although the underlying pathogenesis and mechanism of PBF remain unclear, it is assumed that PBF is caused by the release of BAL-induced cytokines from alveolar cells [6]. However, in this present study, our findings showed that BAL, age less than 2 years and preoperative use of antibiotics were not related to PBF, which was different from other studies [3, 6, 24–27]. Other causes for cytokine release could also be lidocaine installation or physical irritations such as suctioning through the bronchoscope, but it was reported that the corresponding temperature peak would be under 38.5 °C [28]. Comparatively, in this study, we found that almost 30.68% of patients had at least one temperature above 38.5 °C within 24h after

bronchoscopy. Elevated fever peaks should not rule out other infections.

For fever management, ensuring patient comfort is an important aspect of treatment that divides the use of drugs. In this study, 51.15% of patients received Nonsteroidal Anti-inflammatory Drugs (NSAIDs), at least one time, within 24h after bronchoscopy, and oral administration was the main treatment route. In 15 patients, enema was performed, and the enteral route was preferred in 2 patients. Findings from a randomized controlled study showed that ibuprofen was not efficient in preventing PBF in children, especially in those undergoing BAL [6]. In regard to the prophylactic administration of antipyretics, our results showed that the preoperative use of antibiotics was not associated with a reduction in PBF ($p = 0.48$), which was concordant with that of previous studies [29, 30].

Despite the interesting findings observed in this study, there were some limitations worth mentioning. First, the retrospective and single-center design of this study could have led to some unavoidable bias in patient selection. Second, the type of infections associated with PBF could not be determined because postoperative blood tests were not routinely performed. Lastly, the study results could have also been impacted by the fact that almost all patients underwent BAL and the institution’s protocol, which led to prolonged fasting and drinking in children who underwent bronchoscopy. Thus, avoiding these limitations would be a focus of our future research.

5. Conclusion

In this study, the observed incidence of PBF was 10.15%. General anesthesia and the length of bronchoscopy were the most significant risk factors associated with PBF, and these should be carefully planned before bronchoscopy.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

YZ—designed the research study, collected the data. QW—contributed to analysis and manuscript preparation data curation, original draft writing. LL and LC—performed the research, distributed staff resources. All authors contributed to editorial changes in the manuscript, read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the institution review board of West China Hospital of Sichuan University (Medical Research 2021, Ethical Approval No. 213). Informed consent was obtained from all subjects involved in the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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