Journal of Acute Disease

Original Article

jadweb.org

doi: 10.4103/jad.jad_64_25

Clinical value of early bronchoalveolar lavage for severe pneumonia in older adult patients

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ABSTRACT

Objective: To evaluate the effects of early bronchoalveolar lavage (BAL) on inflammatory response, oxidative stress, and clinical outcomes in older adult patients with severe pneumonia using generalized estimating equations (GEE).

Methods: Eighty-three older adult patients (⩾60 years) hospitalized with severe pneumonia between August 2024 and December 2024 were enrolled and assigned to either a control group (n=47), which received standard therapy (including antimicrobials, expectorants, and mechanical ventilation), or an intervention group (n=36), which received additional BAL at 12 and 48 hours post-admission. Clinical efficacy and time to symptom improvement were compared between groups. Serum concentrations of inflammatory markers—interleukin (IL)-6, procalcitonin, and C-reactive protein (CRP)—and oxidative stress markers—superoxide dismutase and malondialdehyde (MDA)—were measured at baseline (T0) and at 24 (T1), 72 (T2), and 144 hours (T3) following admission. Intergroup differences were analyzed using GEE.

Results: Compared with the control group, the intervention group demonstrated significantly lower Clinical Pulmonary Infection Score, Acute Physiology and Chronic Health Evaluation Ⅱ score, Murray Lung Injury Score, duration of lung inflammation, and length of hospital stay (all P<0.05). GEE analyses indicated that the intervention group exhibited significantly reduced levels of IL-6, procalcitonin, CRP, and MDA (all P<0.05), and significantly increased superoxide dismutase levels (P<0.05).

Conclusions: Early administration of BAL significantly mitigates systemic inflammation and oxidative stress, while improving clinical outcomes in older adult patients with severe pneumonia. These findings support further investigation of broader clinical application of early BAL in this population.

KEYWORDS: Alveolar lavage; Generalized estimating equations; Inflammatory markers; Oxidative stress; Severe pneumonia

Summary

Question: What are the effects of early implementation of bronchoalveolar lavage (BAL) on clinical outcomes, inflammation, and oxidative stress factors in older adult patients with severe pneumonia?

Findings: This study found that older adult patients with severe pneumonia who received early BAL experienced faster improvement in lung inflammation, shorter hospital stays, and a quicker reduction in inflammatory markers such as interleukin-6, procalcitonin, and C-reactive protein compared to the control group. Additionally, there was an earlier increase in antioxidant factors, such as superoxide dismutase levels, and a significant decrease in the pro-oxidant factor malondialdehyde levels.

Meaning: The research on early intervention using BAL in older adult patients with severe pneumonia is currently insufficient. This study provides valuable clinical data on BAL-based early intervention for this patient group.

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How to cite this article: Li GX, Gu W, Guo W. Clinical value of early bronchoalveolar lavage for severe pneumonia in older adult patients. J Acute Dis 2025; 14; 14.

Article history: Received 15 May 2025; Revision 29 May 2025; Accepted 9 July 2025; Available online 24 July 2025

1. Introduction

Pneumonia remains a leading cause of morbidity and mortality worldwide, particularly among vulnerable populations such as infants, young children, and the older adult patients. In older adults (⩾60 years), the condition frequently progresses to life-threatening complications, including multi-organ dysfunction and septic shock. With the continued demographic shift toward an aging population in China, the incidence of severe pneumonia in the older adult patients has dramatically risen. In the absence of timely and effective intervention, mortality rates in this population may exceed 40%, largely attributable to age-related immunosenescence and compromised host defenses[1,2]. Despite the routine use of antibiotics, expectorants, and respiratory support[3], the clinical outcomes of older adult patients with severe pneumonia remain suboptimal.

Bronchoalveolar lavage (BAL), commonly performed in conjunction with flexible bronchoscopy, is a frequently employed therapeutic approach that involves the repeated instillation and aspiration of saline and pharmacologic agents into the alveolar space. This technique facilitates the removal of inflammatory mediators and airway secretions, thereby enhancing the pulmonary microenvironment, improving ventilation-perfusion matching, and supporting lung function recovery[4]. However, limited evidence is available regarding the longitudinal effects of early BAL as an adjuvant therapy in older adult patients with severe pneumonia. In this study, we conducted a longitudinal analysis of inflammatory and oxidative stress biomarkers, collected at multiple time points from older adult patients diagnosed with severe pneumonia. To assess the therapeutic efficacy of BAL, we employed a generalized estimating equation (GEE) model. The findings aimed to provide empirical support for the clinical integration of early BAL in the management of severe pneumonia in this high-risk population.

2. Patients and methods

2.1. Study setting

This is a short-term exploratory intervention study. Between August 2024 and December 2024, older adult patients with severe pneumonia requiring invasive mechanical ventilation were enrolled from three institutions: 82nd Group Army Hospital of the People's Liberation Army Ground Force, the First Central Hospital of Baoding City, and Chuiyangliu Hospital affiliated to Tsinghua University. This study was approved by the Ethics Committee of 82nd Group Army Hospital of the People's Liberation Army Ground Force (2025007) as well as the Ethics Committee of Baoding

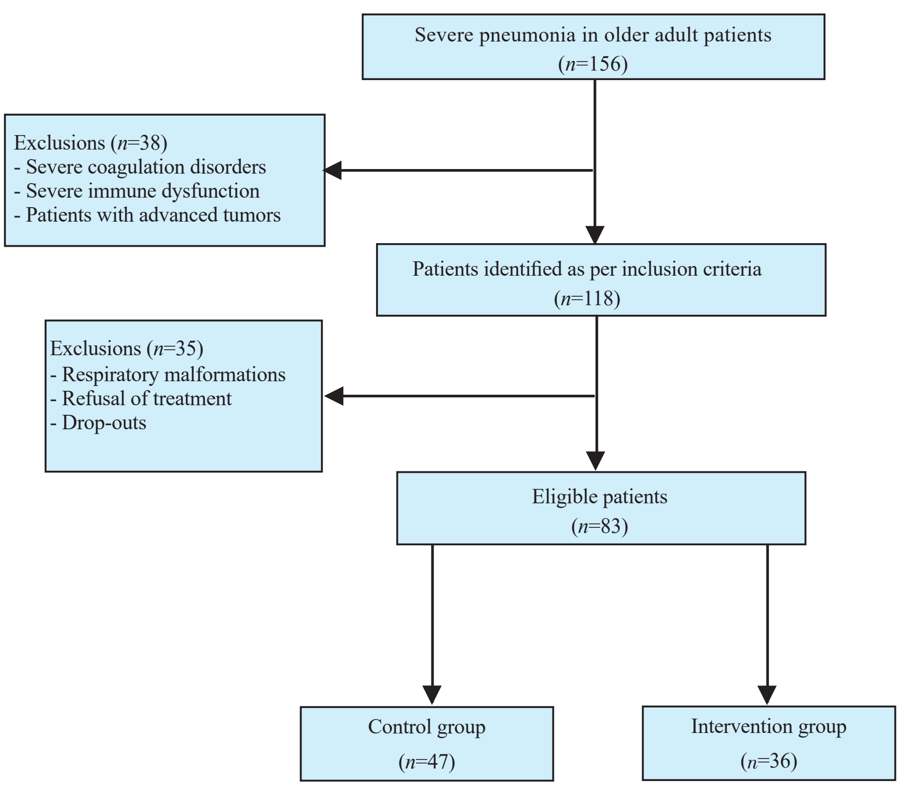

Figure 1. The study flowchart.

First Central Hospital ([2024]-31). The inclusion criteria were: (1) fulfillment of the Infectious Disease Society of America/American Thoracic Society (IDSA/ATS) 2007 criteria for severe pneumonia[5], confirmed by definitive imaging findings; (2) adult patients (60-80 years); and (3) availability of complete medical records with informed consent obtained. Exclusion criteria included: (1) presence of severe coagulopathy and/or immune dysfunction; (2) structural anomalies of the respiratory tract; (3) confirmed contraindications to bronchial lavage; (4) advanced malignancies with cachexia ; (5) explicit refusal of the proposed treatment. According to the random number table, they were divided into intervention group and control group, 55 cases were in each group. Since the presence of patients who dropped out and the presence of missing values in the indicators, 36 cases in the intervention group and 47 cases in the control group were included in the analysis.

2.2. Measurements

The control group received standard care, including analgesia, sedation, mechanical ventilation, antimicrobial therapy, chest physiotherapy, and nutritional support. The intervention group received the same standard care in addition to BAL. Following a fasting period of 6 hours, a bronchofiberscope was carefully advanced through the artificial airway. Subsequently, 10 mL of 37℃ sterile normal saline was slowly instilled and withdrawn *via* negative pressure. This lavage cycle was repeated 6 to 8 times until the aspirated fluid appeared clear. Throughout the procedure, patients' vital signs were continuously and closely monitored.

2.2.1. Arterial blood gas

Arterial blood gas (ABG) parameters—including oxygen saturation (SO_2), partial pressure of oxygen (PO_2), and the PaO_2/FiO_2 ratio—were analyzed by the clinical laboratory.

2.2.2. Inflammatory and oxidative stress markers

This study set four time points for test, with specific information as follows: T0 represents admission, with the aim of obtaining baseline data for two groups of patients. Due to the first implementation of BAL within 16 hours of patient admission, we set a T1 time point (24 hours after admission) to evaluate the patient's inflammation and oxidative stress indicators. The second BAL was performed 48 hours after the patient's admission, and we conducted testing at T2 time (72 hours after admission) to analyze the differences in inflammation and oxidative stress indicators between the two groups of patients. A comprehensive evaluation of the patient is required one week after admission (168 hours), and we took the median value (120 hours) between 72 hours and 168 hours of admission as the T3 time point. The detection of these indicators, C-reactive protein (CRP), procalcitonin (PCT), and interleukin-6 (IL-6), was carried out by the laboratory department.

Similarly, venous blood samples (5 mL) were obtained at each of the four designated time points. Following centrifugation at 4℃, supernatants were separated and stored at −80℃ pending analysis. Quantification of oxidative stress markers was performed using a superoxide dismutase (SOD) assay kit (NBT method; catalog no. YT311-TLQ; BALB, Beijing, China) and a malondialdehyde (MDA) colorimetric assay kit (TBA method; catalog no. SNM208-FZM; BALB, Beijing, China).

2.2.3. Pneumonia–related scoring systems

To assess disease severity and pulmonary involvement, the Acute Physiology and Chronic Health Evaluation Ⅱ (APACHE-Ⅱ)[6], Clinical Pulmonary Infection Score (CPIS; maximum score=12)[7], and Murray Lung Injury Score (MLIS)[8] were recorded at admission and on day 7 post-admission. Changes in these scores between the two time points were compared between the study groups.

2.2.4. Clinical efficacy

Clinical outcomes were evaluated by comparing the two groups with respect to the following parameters: time to radiographic improvement on lung CT, time to maximum defervescence, and overall length of hospital stay.

2.3. Statistical analysis

Due to the correlation within the repeated measurements data, we were unable to calculate the sample size using traditional software such as G Power and PASS. This study had to refer to the sample sizes of published relevant studies. A study of the effect of antiplatelet therapy on patients with sepsis was performed by generalized estimating equations analysis. There were at least 30 cases in the control group and 31 cases in the intervention group[5]. In this study, 36 cases in the intervention group and 47 cases in the control group were included, meeting the above conditions. Numerical variables with normal distribution are expressed as mean±standard deviation (mean±SD), and intergroup comparisons were performed using the independent samples *t*-test. Non-normally distributed variables are reported as median with interquartile range [Median (P25, P75)] and compared using the Mann-Whitney *U* test. Categorical variables are presented as counts and percentages [*n* (%)] and analyzed using the *chi*-square test. All statistical analyses were conducted using GraphPad Prism version 8.0. GEE models were implemented with the "geepack" and "emmeans" packages in R software (version 4.2.1)[9,10]. A two-tailed $P<0.05$ was considered statistically significant.

Table 1. Demographic and baseline characteristics.

Variable	Control group (n=47)	Intervention group (n=36)
Age, years	69.83±5.83	69.06±5.76
BMI, kg/m^2	25.45±3.14	26.04±3.95
Sex		
Male	25 (53.2%)	20 (55.6%)
Female	22 (46.8%)	16 (44.4%)
COPD		
Yes	13 (27.7%)	12 (33.3%)
No	24 (72.3%)	24 (66.7%)
Smoking history		
Yes	17 (36.2%)	11 (30.6%)
No	30 (63.8%)	25 (69.4%)
SO_2, %	72.02±3.60	72.76±3.13
PO_2, mmHg	56.72±5.24	54.97±7.59
PaO_2/FiO_2 ratio	220.80±14.78	218.40±13.96
APACHE-Ⅱ	20.89±2.87	19.61±3.35
CPIS	9 (8, 11)	9 (9, 10)
MLIS	12 (10, 13)	11 (12, 10)

BMI: body mass index; COPD: chronic obstructive pulmonary disease; SO_2: oxygen saturation; PO_2: partial pressure of oxygen; APACHE-Ⅱ: Acute Physiology and Chronic Health Evaluation Ⅱ; CPIS: Clinical Pulmonary Infection Score. MLIS: Murray Lung Injury Score.

3. Results

3.1. Patient characteristics

The intervention and control groups were matched with respect to demographic characteristics, ABG parameters, and pneumonia-related severity scores at the time of admission (all P>0.05; Table 1).

3.2. Changes in ABG parameters and pneumonia-related scores

After 7 days of treatment, the intervention group exhibited significant improvements in SO_2, PO_2, and PaO_2/FiO_2 ratio (all P<0.05). In addition, the intervention group demonstrated significantly greater reductions in APACHE-Ⅱ, CPIS, and MLIS scores compared with the control group (all P<0.05) (Table 2).

3.3. Clinical outcomes

Compared with the control group, the intervention group demonstrated significantly shorter time to radiographic improvement on lung CT (10.42±1.61 *vs* 11.62±2.02, t-Statistic =2.75, P=0.007), time to maximum defervescence [3 (2.25, 3) *vs* 3 (3, 4) days, U-Statistic=620.00, P=0.02] and overall length of hospital stay [15 (13, 15.75) *vs* 16 (16, 18) days, U-Statistic=285.50, P<0.001].

3.4. Longitudinal effects of intervention on inflammatory and oxidative stress markers

GEE models revealed significant time × group interactions for IL-6 (Wald χ^2=10, P=0.02), CRP (Wald χ^2=97, P<0.001), and PCT (Wald χ^2= 17, P<0.001), indicating differential temporal changes in these inflammatory markers between groups, potentially attributable to the specific effects of the intervention. There were no significant differences in IL-6 and CRP levels between the groups at baseline (T0). However, PCT levels were significantly higher in the intervention group at T0 (P=0.04). At T1 (24 hours post-admission), the intervention group exhibited significantly lower IL-6 levels relative to the control group following the initial lavage (P=0.03) (Tables 3 & 4). Subsequent measurements at T2 (72 hours) and T3 (144 hours) showed significantly lower IL-6 and CRP levels in the intervention group. Although PCT levels remained higher in the intervention group at T1 and T2, they were significantly lower at T3 (P=0.02), suggesting that alveolar lavage may have contributed to attenuating the systemic inflammatory response in patients with severe pneumonia.

GEE analysis identified a significant time×group interaction for SOD levels (Wald χ^2=29, P<0.001). SOD levels did not differ significantly between groups at T0 (P=0.19), T1 (P=0.62), or T2 (P=0.17), but were significantly elevated in the intervention group at T3 (P<0.001). No significant time×group interaction was observed for MDA (Wald χ^2=6, P=0.1); therefore, only main effects were examined. Analysis of the pooled population revealed significant main effects of both time (Wald χ^2=654, P<0.001) and group (Wald χ^2=5, P=0.02). MDA levels significantly declined from T0

Table 2. Comparisons of arterial blood gas (ABG) parameters and pneumonia-related scores between groups after 7 days of treatment.

Item	Control group (n=47)	Intervention group (n=36)	Statistics	P
ABG				
SO_2, %	90.87±2.92	92.50±2.44	2.70^a	0.008
PaO_2, mmHg	81.96±5.21	84.83±6.38	2.26^a	0.03
PaO_2/FiO_2 ratio	341.90±14.52	349.30±10.55	2.56^a	0.01
Pneumonia-related scores				
APACHE-Ⅱ	10.36±3.01	8.58±2.27	2.96^a	0.004
CPIS	4 (3, 5)	3 (4, 2)	535.50^b	0.003
MLIS	7 (6, 8)	4 (3, 5)	82.00^b	P<0.001

^{a}t test, ^{b}Mann-Whitney U test.

to T1 in both groups (mean difference: 0.81; P=0.02), with similar trends observed at T2 and T3. These findings indicate a general reduction in oxidative stress over time in both groups, with a more pronounced decline in the intervention group (Tables 3 & 4).

4. Discussion

Severe pneumonia is a prevalent and life-threatening condition frequently encountered in the emergency department and is often associated with serious complications, including sepsis[11]. Older adult patients, who commonly present with underlying chronic diseases, poor nutritional status, and immunosenescence, are particularly vulnerable, exhibiting significantly higher case-fatality rates compared with younger individuals[12]. Current therapeutic strategies for severe pneumonia in older adults primarily include antimicrobial agents, corticosteroids, expectorants, bronchodilators, agents targeting microcirculatory stabilization, and various forms of respiratory support. Although these interventions provide symptomatic relief and modest improvements in prognosis, their overall efficacy in this population remains limited[13]. Bronchoalveolar lavage, a widely accessible procedure, has emerged as a promising adjunctive treatment for severe pneumonia. By facilitating the removal of alveolar secretions and inflammatory mediators, BAL can attenuate pulmonary inflammation, enhance alveolar ventilation, and improve systemic oxygenation[14]. The present study investigated the therapeutic impact of BAL in older adult patients with severe pneumonia, with a particular focus on dynamic changes in inflammatory and oxidative stress markers, aiming to provide robust clinical evidence to support its use in improving patient outcomes.

Our findings indicate that early intervention with BAL in this patient population led to marked improvements in clinical symptoms, pneumonia severity scores, oxygenation parameters, biomarkers of inflammation and oxidative stress, compared with conventional therapy alone. ABG analysis, a critical tool

Table 3. Changes of levels in inflammatory and oxidative stress markers at different time points.

Time point	Grouping	Inflammatory markers			Oxidative stress markers	
		IL-6, pg/mL	CRP, mg/L	PCT, ng/L	SOD, U/mL	MDA, mmol/L
T0	Intervention group	99.30±6.37	86.80±10.27	10.87±2.19	4.11±1.07	10.39±2.45
	Control group	97.28±12.68	85.89±8.02	9.85±2.32	4.41±0.99	11.09±2.85
T1	Intervention group	88.95±8.04	67.25±6.18	9.08±1.09	4.60±1.06	9.96±1.32
	Control group	94.70±15.86	68.99±6.63	8.45±1.88	4.49±1.07	9.74±1.56
T2	Intervention group	80.89±10.61	54.75±5.25	5.63±1.23	5.53±1.13	7.19±1.42
	Control group	87.43±14.58	60.10±6.67	4.99±1.06	5.18±1.21	7.36±2.16
T3	Intervention group	35.53±5.20	35.53±5.20	3.58±0.94	7.78±1.18	5.04±1.34
	Control group	54.11±6.77	54.10±6.77	4.00±0.71	6.25±1.40	5.82±1.26

T0: baseline, T1: 24 hours, T2: 72 hours, T3: 144 hours. CRP: C-reactive protein; PCT: procalcitonin; SOD: superoxide dismutase; MDA: malondialdehyde.

Table 4. Comparisons of the individual effects of different interventions on inflammatory markers within the same time intervals using the generalized estimating equation.

Parameter	Time point	Estimates	SE	*T*	*P*
IL-6	T0	2.02	2.11	0.96	0.34
	T1	5.75	2.64	–2.18	0.03
	T2	–6.54	2.73	–2.39	0.002
	T3	–4.88	1.46	–3.34	0.001
CRP	T0	0.92	2.05	0.45	0.65
	T1	–1.74	1.39	–1.24	0.21
	T2	–5.35	1.29	–4.14	<0.001
	T3	–18.58	1.30	–14.32	<0.001
PCT	T0	1.03	0.49	2.09	0.04
	T1	0.63	0.32	1.93	0.05
	T2	0.64	0.25	2.53	0.01
	T3	–0.42	0.19	–2.26	0.02
SOD	T0	–0.30	0.23	–1.33	0.19
	T1	0.12	0.23	0.50	0.62
	T2	0.35	0.26	1.38	0.17
	T3	1.53	0.28	5.48	<0.001
MDA	T0 (Reference)	/	/	/	/
	T1	–0.81	0.36	/	0.02
	T2	–3.40	0.41	/	*P*<0.001
	T3	–5.21	0.33	/	*P*<0.001

for evaluating pneumonia severity, demonstrated significantly higher PO_2, SO_2, and PaO_2/FiO_2 ratios in the intervention group on day 7 post-admission, suggesting that BAL facilitates recovery from hypoxemia and respiratory failure. Inflammatory markers, particularly IL-6, are closely associated with pneumonia prognosis. As a key pro-inflammatory cytokine, IL-6 activates the immune response during pathogen invasion, promoting immune cell differentiation and further cytokine release. Elevated IL-6 levels have been correlated with poor clinical outcomes in older adult patients and may reflect incomplete clearance of pathogenic toxins[15]. In this study, IL-6 levels were significantly reduced in the intervention group following the first lavage session. Moreover, the rate of IL-6 decline over time was more pronounced in this group, suggesting that BAL contributed to the effective removal of pro-inflammatory mediators, mitigated pulmonary injury, and promoted tissue repair. Under normal physiological conditions, CRP and PCT levels are low but increase significantly in response to severe infection and systemic inflammation. PCT, in particular, is a stable biomarker that correlates with pneumonia severity and is less affected by confounding variables such as corticosteroid use or immunodeficiency[16,17]. In our study, the intervention group exhibited significantly lower CRP levels after the second BAL. Despite initially higher baseline PCT levels, the intervention group demonstrated significantly lower PCT levels at 120 hours post-admission (T3), further supporting the role of BAL in attenuating both systemic and pulmonary inflammation.

Oxidative stress, defined as an imbalance between pro-oxidant and antioxidant mechanisms within the human body, induces the infiltration of inflammatory cells and promotes the excessive production of reactive oxygen species, ultimately leading to tissue injury. This pathological process plays a pivotal role in the onset and progression of pneumonia. During the course of pneumonia, the oxygenation capacity of the alveoli is compromised, resulting in the generation of a large quantity of free radicals. These radicals can disrupt the structural integrity of lung cell membranes, thereby worsening clinical outcomes[18,19]. SOD and MDA are well-established biomarkers of oxidative stress. SOD mitigates oxidative damage by neutralizing oxygen free radicals and maintaining redox homeostasis; notably, decreased SOD activity is strongly associated with poor prognosis in pneumonia[20]. In our present study, SOD levels significantly increased in the intervention group at T3. Additionally, the relatively slower decline in SOD compared with inflammatory markers may reflect the systemic, multi-organ involvement characteristic of severe pneumonia in older adult patients. While BAL predominantly resolves local pulmonary inflammation, leading to a reduction in inflammatory mediators, systemic inflammatory resolution may require a longer duration. Notably, BAL appears to facilitate this process. MDA, a terminal byproduct of lipid peroxidation, interferes with cellular metabolism and has been closely associated with pneumonia-induced myocardial injury and adverse outcomes[21,22].

This study suggested that early intervention with BAL in older adult patients with severe pneumonia can improve symptoms and reduce inflammatory factors. Nevertheless, the study still has some weaknesses. First, the sample size estimates used in randomized controlled trials were not applicable due to the presence of internal sample correlation in repeated measures data. As an alternative, we had to refer to the sample size in similar studies. Although the data were originated from the three hospitals, some patients dropped out during treatment or missing data, which was another important reason for the low sample size. Second, some efficacy has been achieved after early BAL intervention. It is an invasive procedure, which is prone to tracheal mucosal injury. Hence, it is need to be carefully evaluated for older adult with severe pneumonia. Thirdly, older adult people often suffered from chronic diseases such as high blood pressure and diabetes, which tend to aggravate pneumonia. Unfortunately, these variables were not included in this model, which may lead to bias in some of the results. In future trial designs, we should increase the number of data sources and expand the sample size. More covariates should be included when analyzing the data to reduce bias.

In summary, early application of BAL may attenuate systemic inflammation, reduce pulmonary oxidative stress, promote restoration of lung function, and consequently ameliorate clinical symptoms in older adult patients with severe pneumonia.

Conflict of interest statement

The authors report no conflict of interest.

Funding

This work was supported by the Beijing Clinical Key Specialty Project (2023).

Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Authors' contributions

Study concept and design: LGX, Gu W and Guo W; Data colletction and nalysis: LGX and Gu W; Drafting of the manuscript:

LGX; Critical revision of the manuscript for important intellectual content: LGX, Gu W and Guo W; Statistical analysis: LGX.

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Edited by Liu JJ

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