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European Journal of Medical Research (2025) 30:208
https://doi.org/10.1186/s40001-025-02451-4

European Journal of Medical Research

RESEARCH Open Access

Reducing stroke-associated pneumonia through pulmonary rehabilitation in moderate-to-severe acute ischemic stroke

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Abstract

Objectives This study investigated the effect of a comprehensive pulmonary rehabilitation (CPR) program on stroke-associated pneumonia (SAP) in patients with moderate-to-severe acute ischemic stroke (AIS) after thrombolysis.

Methods This study was a prospective randomized controlled intervention study. Eighty patients with moderate-to-severe AIS were divided into the conventional rehabilitation (CR) and CPR groups. Demographic and general clinical data were collected. Patients were evaluated by the Fatigue Severity Scale (FSS), Fugl–Meyer Assessment (FMA), and Fugl–Meyer balance (FMB). The incidence of pneumonia in the acute phase and the treatment efficacy were compared.

Results FSS scores at T1 and T2 (2 weeks and 4 weeks after treatment), FMA scores, and FMB scores were higher than those at T0 (first day of admission). FSS scores in the CPR group were lower, while FMA and FMB scores were higher than those in the CR group at T1 and T2. The incidence of pneumonia was 10.00% in the CPR group and 25.00% in the CR group. The rehabilitation effective rate was 92.50% in the CPR group and 80.00% in the CR group, but the proportion of rehabilitation effect in the CPR group was higher than that in the CR group.

Conclusions CPR program improves fatigue and motor function and reduces the occurrence of SAP in AIS patients.

Keywords Comprehensive pulmonary rehabilitation, Acute ischemic stroke, Fatigue, Motor function, Stroke-associated pneumonia

Introduction

Stroke is a clinical syndrome in which there is a sudden loss of brain function, either focal or global, that lasts for more than 24 h or results in death [1]. Stroke is now the second leading cause of death, characterized by high morbidity, mortality, and disability [2]. The incidence of acute cerebral infarction (ACI) is about 60–70% of all stroke patients [3]. Intravenous thrombolysis has become a common treatment for ACI [4–6]. After intravenous thrombolysis, rehabilitation aids patients in slowly recovering the functions of the affected limbs, such as muscle strength, coordination, and balance. Moreover, systematic rehabilitation can reduce the incidence of disability after stroke [7]. Pulmonary rehabilitation has been increasingly recognized and applied by healthcare professionals, since it was introduced in 1994. In 2016, the American Stroke Association recommended early intervention for post-stroke patients through pulmonary rehabilitation exercises, such as vibration expectoration, active exercises, and respiratory muscle training [8]. However, there are few studies that apply comprehensive

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pulmonary rehabilitation to patients with moderate-to-severe acute ischemic stroke (AIS).

Post-stroke fatigue (PSF) is the subjective feeling of extreme fatigue due to lack of mental and/or physical energy, which appears suddenly after a stroke event [9]. PSF is a common and long-lasting sequela of stroke, which affects the patient's recovery and increases disability and mortality rates [10–12]. Fatigue not only manifests itself in physical weakness, but also in mental lethargy, making it difficult for patients to adhere to the necessary rehabilitation treatments, which in turn hinders the process of neurological recovery [13]. Physical activity after stroke improves physical fitness and stimulates cortical excitability, which may help reduce fatigue [13]. Meanwhile, motor dysfunction is also a key problem for patients with moderate-to-severe AIS. Due to the damage of motor neurons caused by cerebral ischemia, patients often suffer from paralysis of limbs, loss of muscle strength, and poor motor coordination. This not only restricts the patient's ability to move independently, making it impossible for the patient to perform basic life actions, but also may lead to a series of complications, such as muscle atrophy, joint contracture, etc., which will further aggravate disability of the patient. In addition, stroke-associated pneumonia (SAP) is a common cause of death in clinical practice, and the incidence of SAP ranges from 3.0 to 56.6% [14]. Patients with moderate-to-severe AIS are highly susceptible to aspiration due to swallowing dysfunction, weakened cough reflex, and impaired consciousness, which can lead to lung infection [15]. Once SAP occurs, the patient's hospitalization time is prolonged, medical costs increase, and the prognosis becomes significantly worse [16]. The focus on preventing and controlling SAP in stroke treatment has increased, with research and guidelines worldwide showing that pulmonary rehabilitation can improve pulmonary function and daily activities in patients with stroke [17].

In recent years, comprehensive pulmonary rehabilitation (CPR) programs have gradually gained attention and been applied in clinical practice. Pulmonary rehabilitation aims to improve respiratory function, exercise capacity, and overall health through a series of planned and targeted interventions, including respiratory training, physical therapy, exercise training, nutritional support, and psychological counseling [18]. For patients with moderate-to-severe AIS, the implementation of a CPR program after thrombolysis is potentially important. On the one hand, respiratory training and physical therapy can improve patients' respiratory function, enhance the ability to cough up sputum, and reduce the risk of aspiration, thereby reducing the incidence of SAP [19]. On the other hand, systematic exercise training can promote the recovery of patients' motor function, improve muscle strength and motor coordination, reduce fatigue symptoms, and enhance patients' daily self-care ability and quality of life [20].

Although some studies have explored the application of pulmonary rehabilitation in stroke patients, there are still relatively few studies on the effects of CPR program on fatigue, motor function, and the incidence of SAP after thrombolysis in patients with moderate-to-severe AIS. It is of great theoretical and practical significance to conduct such studies to clarify the role and value of CPR programs in the treatment of patients with moderate-to-severe AIS to optimize the clinical treatment strategy and improve the rehabilitation effect and quality of life of patients. The aim of this study was to investigate the effects of a post-thrombolysis CPR program on fatigue, motor function, and the incidence of SAP in patients with moderate-to-severe AIS through rigorous clinical observation and data analysis, and to provide a reference for the implementation of integrated pulmonary rehabilitation in clinical practice.

Materials and methods

Study population

This prospective study recruited 80 patients with moderate-to-severe AIS who received intravenous thrombolysis from January 2020 to June 2024 at Zibo Central Hospital.

Inclusion criteria: (1) patients who underwent head computed tomography or magnetic resonance imaging at admission were diagnosed with ischemic stroke and received rt-PA intravenous thrombolysis; (2) patients who were at least 18 years, had their first stroke with onset time < 4.5 h, and had persistent signs and symptoms of neurological deficit; (3) patients had a pre-thrombolysis National Institutes of Health Stroke Scale (NIHSS) score of 5–24; (4) patients were treated throughout their stay in our hospital, and no patients were transferred to another hospital; and (5) during the COVID-19 outbreak, patients were admitted to our hospital with nucleic acid negative results.

Exclusion criteria: (1) patients with contraindications to thrombolysis; (2) patients with severe hepatic and renal insufficiency; (3) patients with COVID-19 infection; (4) patients with previous pneumonia, active infection before hospitalization, or previous antibiotic treatment; (5) patients with incomplete clinical data; (6) patients with ischemic stroke in the posterior circulation; (7) pregnant patients; and (8) patients with surgical treatments, such as arterial thrombolysis, stenting, or bone flap decompression.

Post-thrombolytic rehabilitation

The patients were numbered according to the order of consultation. The Rand function in Excel software was used to generate the corresponding random numbers for each patient. The 80 random numbers generated were sorted according to the size, and after sorting, the first 40 cases were divided into the conventional rehabilitation group (CR group), and the last 40 cases were divided into the CPR group. The study involved a single-blind method for patients and data analyzers. Patients in both groups were treated with anticoagulation and antiplatelet aggregation medications (dual antiplatelet drugs and low molecular heparin calcium).

CR group: Stroke patients were provided with comprehensive management and systematic rehabilitation, such as limb function training, language training, activity training, cognitive training, psychological rehabilitation, and health education [21]. CPR group: CPR was performed based on the above conventional training. Pulmonary rehabilitation includes abdominal breathing training, costal breathing, breath control, respiratory muscle endurance training, airway clearance techniques, and upper and lower extremity training [22].

Data collection

Demographic and clinical characteristics of the enrolled patients were collected, including age, gender, BMI, smoking history, drinking history, comorbidities, NIHSS score, time of disease onset, time from admission to administration of thrombolysis, hospitalization stay, and Trial of Org 10,172 in acute stroke treatment (TOAST) classification.

Fatigue severity evaluation

The fatigue severity scale (FSS) was used to assess PSF at baseline T0 (day 1 of admission, before rehabilitation), T1 (2 weeks of rehabilitation), and T2 (4 weeks of rehabilitation), respectively [23]. The total score greater than or equal to 36 points was defined as PSF, and the severity of fatigue was proportional to the total score.

Motor function evaluation

Motor function: The motor function (including upper and lower limb motor function) was evaluated at the same timepoints mentioned above using the Fugl–Meyer assessment (FMA) scale. Out of 100 points, a higher score indicates better motor function [24].

Balance function: The Fugl–Meyer balance (FMB) scale consists of 3 sitting and 4 standing positions, with each item scored at 3 levels: 0, 1, and 2 points. 0 indicates failure to replicate the posture, 1 indicates replication of the posture, and 2 indicates complete replication of the posture. The higher the score, the better the recovery of balance function [25].

Incidence of pneumonia and severity of pneumonia

During the acute phase (14 days), both groups were evaluated for pneumonia development through sputum culture and chest radiography. The Pneumonia Severity Index (PSI) is a well-validated pneumonia scoring system used to assess the severity of pneumonia in patients with SAP. For patients with SAP, severe SAP was defined as PSI IV and V (PSI score > 90), whereas non-severe SAP was defined as PSI I–III (PSI score ≤ 90) [26, 27].

Rehabilitation efficacy

Rehabilitation efficacy was assessed according to the efficacy criteria established by the National Conference of Neurology of Chinese Medical Association. Clinical efficacy was categorized into three levels: significantly effective, effective, and ineffective. Symptom disappearance, improvement in physical activity, activities of daily living, limb movement and quality of life, and a reduction in NIHSS score > 45% were considered to be significantly effective; Improvement in symptoms, activities of daily living, limb motor function and quality of life, and an 18–45% reduction in NIHSS score were considered effective; No improvement in symptoms and limb movement, etc., with significant sensory, mobility, and motor deficits, and a reduction of < 18% in NIHSS score was considered ineffective. The total effective rate = (significantly effective + effective)/number of observed patients. All patients were evaluated by the same experienced rehabilitation physician after 4 weeks of rehabilitation treatment.

Statistical analysis

The obtained data were statistically analyzed using SPSS 24.0 software and visualized by Graph Pad Prism 8.0. Measurements that conformed to normal distribution were expressed as mean ± standard deviation, with independent samples t test used for between-group comparisons and paired samples t test for pairwise comparisons. Measurements that were not normally distributed were expressed as M (P_{25},P_{75}), with two-independent samples rank-sum (Mann–Whitney U) test used for between-group comparisons, and Wilcoxon test for pairwise comparisons. Count data were expressed as frequency or rate (%) using the χ^2 test for comparisons, with $P < 0.05$ indicating statistical significance.

Table 1 Demographic and clinical characteristics of the patients

Data	CPR group ($n=40$)	CR group ($n=40$)	*P* value
Age	60.69 ± 11.41	61.35 ± 12.05	0.802
Gender			0.622
Male	27 (67.50%)	30 (75.00%)	
Female	13 (32.50%)	10 (25.00%)	
BMI (kg/m^2)	24.4 ± 1.64	23.87 ± 1.83	0.177
Smoking history	26 (65.00%)	21 (52.50%)	0.364
Drinking history	9 (22.50%)	13 (32.50%)	0.453
Hypertension	29 (72.50%)	26 (65.00%)	0.63
Diabetes	7 (17.50%)	9 (22.50%)	0.781
Hyperlipidemia	10 (25.00%)	12 (30.00%)	0.803
Coronary heart disease	24 (60.00%)	26 (65.00%)	0.818
Atrial fibrillation	7 (20.00%)	9 (22.50%)	0.781
NIHSS score at admission	9 (6–13)	10 (7–14)	0.143
Onset time min	142 (120–170)	144 (116–172)	0.555
Time from admission to administration of intravenous thrombolysismin	35.95 ± 6.20	34.13 ± 7.05	0.304
TOAST typing			0.968
Large artery atherosclerosis	14 (35.50%)	13 (32.50%)	
Cardiogenic embolism	7 (174.50%)	6 (15.00%)	
Small artery atherosclerosis	15 (37.50%)	16 (40.00%)	
Other etiology	4 (10.00%)	5 (12.5%)	

Table 2 Comparison of FSS scores between the two groups of patients M (P_{25}, P_{75})

Groups	T0	T1	T2	*P* value (T0 vs. T1)	*P* value (T1 vs. T2)
CPR group ($n=40$)	45 (35–52)	38 (30–45)	30 (22–40)	< 0.0001	< 0.0001
CR group ($n=40$)	43 (36–56)	39.5 (30–46)	33 (24–43)	< 0.0001	< 0.0001
P value	0.309	0.048	0.0003	/	/

Results

Baseline characterization

The differences were not statistically significant when comparing the general information of the two groups ($P>0.05$) (Table 1).

PSF in patients with moderate-to-severe ASI

At baseline, there was no statistically significant difference between the FSS scores of the patients in the CPR group and those in the CR group ($P>0.05$). At T1, the FSS scores in the CPR group were lower than those in the CR group ($P<0.05$). After rehabilitation in the CPR group, the FSS scores were significantly lower compared with those before the rehabilitation period ($P<0.05$), and PSF was improved; patients in the CR group had lower FSS scores than at baseline after 2 weeks of rehabilitation, and the difference was statistically significant ($P<0.05$). At T2, the FSS scores decreased again. The difference between the CPR group and the CR group was

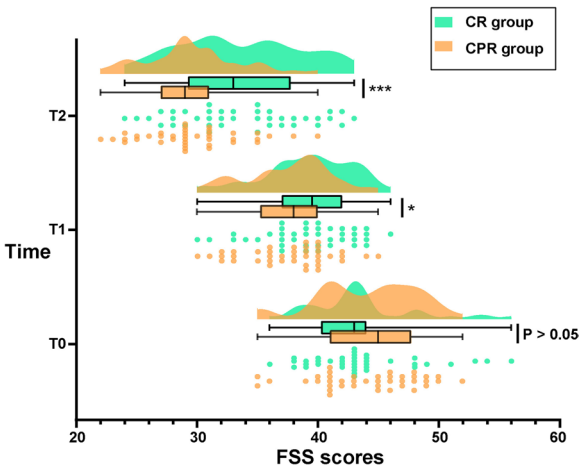

Fig. 1 Comparison of FSS scores between the two groups of patients

statistically significant. The difference in the FSS scores at T1 and T2 was statistically significant ($P<0.05$), as shown in Table 2 and Fig. 1.

Motor function in patients with moderate-to-severe ASI

Motor function between the two groups before rehabilitation showed no statistically significant difference ($P>0.05$). At T1, the FMA scores in both groups were improved compared with those at T0, and motor function was improved ($P<0.05$). The FMA scores in both groups further improved at T2, and the difference between the two groups was statistically significant ($P<0.05$). Compared with T0, the FMB scores of patients in both groups at T1 improved, and the FMB scores in both groups at T2 improved compared with those at T1, and the differences between the groups were statistically significant (T0 vs. T1 and T1 vs. T2, $P<0.05$) (Tables 3 and 4, Fig. 2).

Incidence of pneumonia and the severity of pneumonia after rehabilitation

Ten patients in the CR group developed pneumonia during the acute stage, with an incidence rate of 25.00%; four patients in the CPR group developed pneumonia, with an incidence rate of 10.00%. The difference in the incidence of SAP between the two groups was not statistically significant ($P>0.05$). The severity of patients who developed pneumonia in both groups after rehabilitation was further analyzed by PSI score. Among the patients who developed SAP in the CR

Table 3 Comparison of FMA motor function scores between the two groups of patients M (P_{25}, P_{75})

Groups	T0	T1	T2	*P* value (T0 vs. T1)	*P* value (T1 vs. T2)
CPR group ($n=40$)	23 (14–38)	28 (17–43)	36.5 (26–49)	<0.001	<0.001
CR group ($n=40$)	22 (12–34)	25.5 (13–36)	30 (20–43)	0.0099	0.0004
P value	0.475	0.0131	<0.001	/	/

Table 4 Comparison of FMB balance function scores between the two groups of patients M (P_{25}, P_{75})

Groups	T0	T1	T2	*P* value (T0 vs. T1)	*P* value (T1 vs. T2)
CPR group ($n=40$)	3 (1–7)	4.5 (2–7)	6 (2–10)	0.0002	0.0008
CR group ($n=40$)	3 (1–6)	4 (1–7)	5 (2–9)	0.0093	0.015
P value	0.853	0.196	0.022	/	/

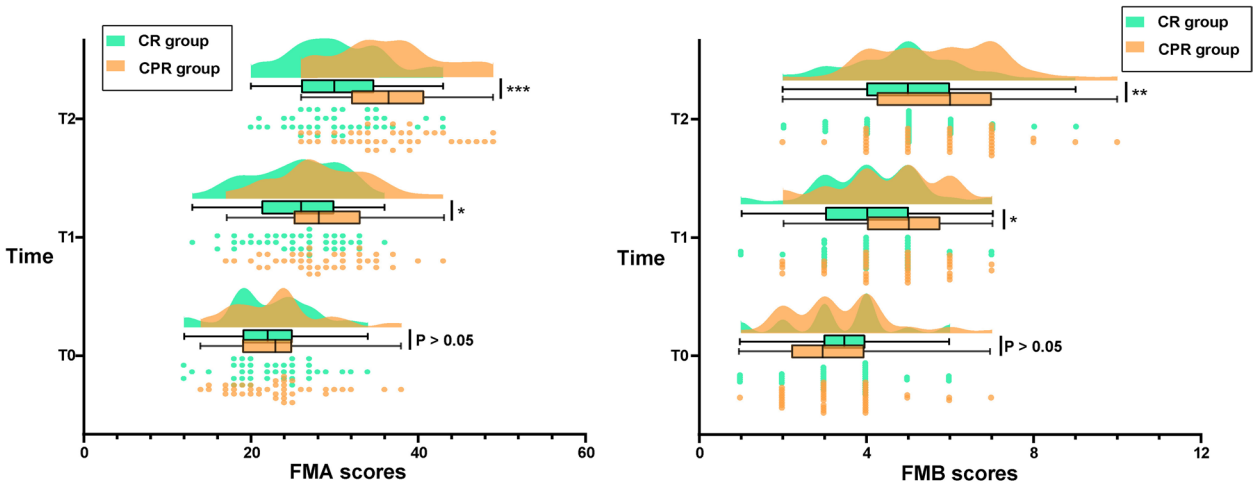

Fig. 2 Comparison of FMA and FMB scores between the two groups of patients

Table 5 Incidence of pneumonia after rehabilitation in both groups of patients

Groups	CPR group ($n=40$)	CR group ($n=40$)	*t* value	*P* value
Incidence of pneumonia *n* (%)	4 (10.00%)	10 (25.00%)	1.765	0.0775

group, two patients had PSI scores greater than 90, presenting moderate-risk pneumonia, and were admitted to the ward for treatment. Among the 4 patients with pneumonia occurring in the CPR group, all patients had PSI scores less than 90, presenting low-risk pneumonia and were treated in the general ward (Table 5).

Clinical efficacy of the two rehabilitation methods

The efficacy of the two rehabilitation programs is shown in Table 6. The total effective rate between the two programs did not show statistical significance ($P>0.05$), but the CPR group had a higher number of significantly effective cases than the CR group ($P<0.05$). This indicates that while both programs were equally effective in terms of overall efficiency, CPR program outperformed CR program in prompting a significant recovery.

Discussion

Acute cerebrovascular disease has become a global public health problem, with AIS being the most prevalent and common, accounting for approximately 60–80% of all strokes [28]. Despite advances in medical technology, more than 70% of patients are still left with varying degrees of limb dysfunction, and their quality of life is severely compromised [29]. Stroke can lead to significant respiratory dysfunction [30]. In the past, post-stroke rehabilitation focused on the restoration of limb function and sensation, and often neglected the rehabilitation of trunk and respiratory muscles. In 2013, the American Thoracic Society and the European Respiratory Society proposed that pulmonary rehabilitation is a comprehensive intervention following individualized treatment, based on a comprehensive assessment of the patient, which includes but is not limited to exercise training, health education, and behavioral interventions aimed at improving the physiological and psychological status of patients with chronic respiratory diseases, as well as increasing long-term adherence to health-favoring behaviors [17]. In the 2016 guidelines for adult stroke rehabilitation published by the American Heart Association and the American Stroke Association, it is clearly proposed that pulmonary rehabilitation, including expectoration rehabilitation, be implemented early in patients with combined pneumonia after stroke [8]. In recent years, with the development of rehabilitation medicine, pulmonary rehabilitation has received increasing attention from researchers.

PSF is one of the most common post-stroke complications, in which the patient presents with fatigue along with depression, which is a persistent and pathologic [31, 32]. PSF is a predictor of long-term mortality in post-stroke patients, making early intervention for PSF particularly important [33]. This study showed that both CPR program and CR program were able to improve PSF and reduce FSS scores. Fatigue relief was better in the CPR group than in the CR group. Some post-stroke patients have compromised respiratory pathways, reduced central respiratory drive, and significant decreases in maximal inspiratory and maximal expiratory pressures [34]. Pulmonary rehabilitation is a central part of the treatment of patients with chronic respiratory diseases [35]. It has been indicated that pulmonary rehabilitation alleviates dyspnea and fatigue due to chronic obstructive pulmonary disease and improves exercise tolerance and quality of life [36]. Likewise, CPR might aid in reducing PSF and allow AIS patients to engage more actively in other rehabilitation activities by enhancing oxygen use and respiratory efficiency.

Improved lung function may help improve overall exercise capacity in stroke patients [37]. Strengthening muscles involved in respiration, such as the diaphragm and intercostal muscles, may allow patients to breathe more efficiently and improve their exercise training performance [38]. In addition, effective respiratory control helps to optimize blood circulation, which may further facilitate the recovery of muscle function. Similar

Table 6 Evaluation of the efficacy of the two rehabilitation methods

Groups	Significantly effective (cases)	Effective (cases)	Ineffective (cases)	Total effective rate (%)
CPR group ($n=40$)	25	12	3	92.50%
CR group ($n=40$)	15	16	9	80.00%
t value	2.236	0.938	1.87	1.87
P value	0.0253	0.348	0.06	0.06

to these findings, CPR improved patients' respiratory muscle endurance and respiratory control through abdominal breathing training, promotes recovery of diaphragm function, respiratory muscles, improves trunk stabilization and body control, and improves motor function. In addition, the FMA and FMB scores in the CPR group and the CR group improved over time, and CPR had a better improvement effect.

AIS patients have a higher risk of developing SAP due to dysphagia, motor limitation, and impaired consciousness [39, 40]. For stroke patients, early intervention is the process of taking steps to prevent complications, including pneumonia, for patients as early as possible when they are found to have a stroke. Early intervention for stroke patients significantly reduces the incidence of pneumonia in stroke patients [19]. Similar to this study, this study showed that patients in the CPR group had a lower incidence of SAP than the CR group. This may be related to the fact that pulmonary rehabilitation can help to improve the patients' cough reflex and sputum clearance and reduce the accumulation of respiratory secretions, thus reducing the incidence of pneumonia [22]. In the evaluation of the efficacy of the two programs, although the difference in the effective rate of the two programs was not statistically significant, our results showed that CPR program had a higher effective rate. It is important to note that pulmonary rehabilitation programs should be individualized and designed according to the patient's specific condition.

In summary, our results found that CPR program after thrombolysis relieves fatigue, improves dyskinesia, and enhances motor function in patients with moderate-to-severe AIS. Even though SAP incidence was lower in the CPR group, the difference from the CP group was not statistically significant, which might be attributed to the small sample size. This study focused solely on FSS, FMA, and FMB scores. Future research will integrate various assessment methods. From the perspective of clinical practice, this study provides a new path for stroke rehabilitation. CPR program integrates multiple interventions to comprehensively meet the physical, psychological, and quality-of-life rehabilitation needs of patients, which has obvious advantages over traditional single rehabilitation methods. At the same time, the program is easy to operate, feasible, and easy to promote at all levels of medical institutions. This will not only help to improve the rehabilitation effect of stroke patients, reduce the burden on families and society, but also promote the overall improvement of stroke rehabilitation treatment.

Acknowledgements
Not applicable.

Author contributions
QingSha Zhang designed the research study. QingSha Zhang performed the research. Jie Sun provided help and advice. HongKun Liu and HongGe Shi analyzed the data. QingSha Zhang wrote the manuscript. HongGe Shi reviewed and edited the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Funding
Not applicable.

Availability of data and materials
The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The present study was approved by the Ethics Committee of Zibo Central Hospital (No. 2019ZBCH033) and written informed consent was provided by all patients prior to the study start. All procedures were performed in accordance with the ethical standards of the Institutional Review Board and The Declaration of Helsinki, and its later amendments or comparable ethical standards. Clinical Trial Number: ChiCTR21000439223.

Competing interests
The authors declare no competing interests.

Received: 9 October 2024 Accepted: 10 March 2025
Published online: 26 March 2025

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