

Clinical Neuroscience Research

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Clinical Neuroscience Research

Focus and Scope

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The journal provides a platform for studies that explores the diagnosis, nature, causes, treatment, and public health aspects of neurological illnesses.

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Safety Study of Monosialotetrahexosylganglioside Sodium in the Treatment of Stroke

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Abstract: *Objective:* To retrospectively analyze the safety and efficacy of monosialotetrahexosylganglioside sodium (GM1) in the treatment of stroke, and to provide a reference for clinical rational drug use. *Methods:* This study was a multicenter, single-arm, retrospective, observational study, which recruited stroke patients who were treated with GM1 from January 1, 2020, to December 31, 2023, as the research subjects, analyzed their adverse events and grades, and performed chi-square test and t-test on NIHSS scores and Barthel before and after intervention. Compare the scores before and after. *Results:* A total of 4405 patients were enrolled, and the NIHSS score of the patients decreased and the Barthel score increased after GM1 intervention, and there was a significant statistical difference before and after intervention ($P < 0.05$). A total of 1635 patients had adverse events, and 99.4% were mild, and severe was not seen. *Conclusion:* In this study, GM1 has high safety and significant efficacy in the treatment of stroke, and results suggest potential for clinical application, subject to further validation.

Keywords: Stroke; Tetrahexose ganglioside monosialic acid; Safety; Efficacy; Adverse events

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1. Introduction

Stroke refers to acute cerebrovascular disease caused by rupture or blockage of cerebral blood vessels, which ranks first among the causes of disability and death in China, with a rapid course and high fatality rate, and a serious poor prognosis is often seen in significant decline in language, motor and cognitive functions. In order to improve the quality of life of patients, therapeutic intervention is necessary for trunk muscle strength, balance and control of stroke patients. However, the current rehabilitation treatment process is mostly several years or even more than ten years, which is a heavy financial and mental burden for patients and their families. Based on the above, the research and development of some drugs to assist in the rehabilitation process has been put on

the agenda in the industry. Monosialotetrahexosylganglioside (GM1) is one of the cell membrane components of mammals, which is mainly extracted from pig brain and has the potential to promote the repair of central nervous system injury. GM1 is the highest content in the central nervous tissue, which can effectively slow down the process of neurodegeneration, so that the damaged central nervous system can be repaired, and has an important regulatory role in the generation and regeneration of neurons.

In recent years, with the widespread application of the drug, adverse events have occurred frequently, but the treatment measures have been rarely reported, especially when the patient has dyspnea, anaphylactic shock and symptoms other than the adverse events indicated in the drug instructions, how to quickly and standardize the rescue treatment is particularly important, which can directly affect the health and life safety of the patient.

Therefore, this study solicited a retrospective and descriptive survey of stroke patients who used GM1 from January 1, 2020, to December 31, 2023, to provide a reference for the rational use of GM1 in the clinical treatment of stroke.

2. Data and methods

2.1. General information

This study is a multicenter, single-arm, retrospective, descriptive study. A total of 4405 stroke patients who received GM1 intervention in different hospitals from January 1, 2020, to December 31, 2023, were recruited and their clinical data were retrospectively analyzed. Inclusion criteria: (1) Language function deterioration, some facial and limb sensory dysfunction, symptoms for more than 24 hours, and CT and other imaging clinical examination results are stroke; (2) Previous use of GM1. Exclusion Criteria: (1) Patients who are allergic to GM1; (2) The body is currently accompanied by serious diseases of important organs such as heart, liver, and lungs; (3) Patients who are currently accompanied by mental illness and whose degree of mental abnormality cannot be graded^[1,2].

2.2. Information collection

The main data information collected is as follows:

- (1) Basic information: gender, age, height, weight, BMI;
- (2) Disease diagnosis and past history information: including various clinical diagnosis medical records and reports, drug use and allergy history;
- (3) Medication information: GM1 start time, administration method, intake medium, intake dose, infusion rate, combination medication, intake end time, etc.;
- (4) Adverse events: specific time of occurrence and disappearance, affected organs and specific symptoms, degree of grading, what kind of intervention measures, etc.;
- (5) Efficacy evaluation information: NIHSS and Barthel Index before and after treatment.

2.3. Statistical analysis

All statistical analyses were performed using R4.3.2, and the median, interquartiles, minimum, maximum, mean and standard deviation were used for the quantitative variables, and the number and proportion of patients were used for the qualitative variables. The evaluation of intervention effect describes the frequency and composition ratio of the indicators. The NIHSS score before and after the intervention was compared using the paired t-test

method, and the Barthel Index before and after the intervention was compared using the McNemar test, and the statistical criterion was $p < 0.05$ ^[3].

3. Results

3.1. Demographic characteristics of patients

In this study, a total of 4411 stroke patients who were treated with GM1 between January 1, 2020, and December 31, 2023, were collected, and a total of 6 patients were found to be excluded because their data did not meet the requirements, and finally, 4405 patients were included for analysis ^[4]. Among them, there were 2,701 male patients and 1,704 female patients, with an average age of 59.1 years, an average height of 168.0cm, a weight of 67.2kg, and a BMI of 23.7. The results are shown in **Table 1**.

Table 1. Demographic characteristics of patients

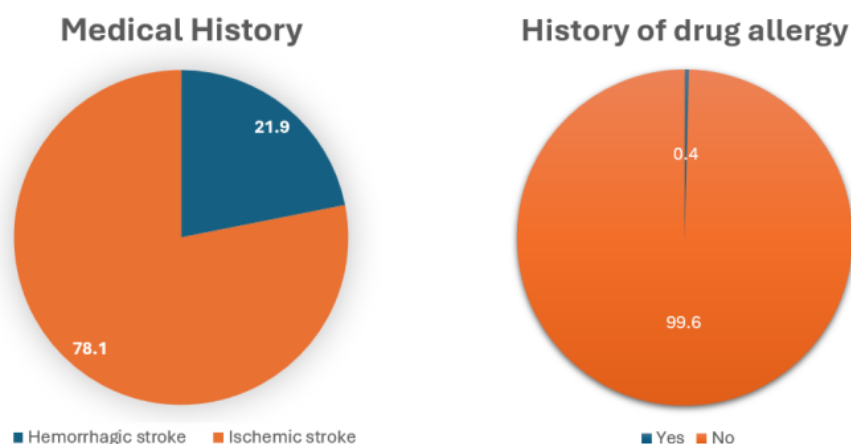
Number of patients included	N = 4405
Age	
The mean \pm standard deviation	59.1 \pm 11.9
Range	16.8–97.4
Median (Q1–Q3)	59.6 (52.0–66.9)
Gender	
Man	2701 (61.3)
Woman	1704 (38.7)
Height (cm)	
The mean \pm standard deviation	168.0 \pm 7.6
Min-Max	142.0–191.0
Median (Q1–Q3)	169.0 (162.0–174.0)
Weight (kg)	
The mean \pm standard deviation	67.2 \pm 11.4
Min-Max	40.0–168.0
Median (Q1–Q3)	68.0 (60.0–75.0)
BMI	
The mean \pm standard deviation	23.7 \pm 3.2
Min-Max	14.5–55.4
Median (Q1–Q3)	23.6 (21.8–25.6)

3.2. Patient's disease diagnosis and anamnesis information

Among the 4405 patients, 3440 patients were diagnosed with ischemic stroke, accounting for 78.1%, and 965 patients were diagnosed with hemorrhagic stroke, accounting for 21.9%. Sixteen of all patients, accounting for 0.4%, had a history of drug allergy. The results are shown in **Table 2** and **Figure 1**.

Table 2. Diagnostic information and drug allergy history [*n*(%)]

Anamnes/allergy history	Number of people (percentage)
Past history	
Hemorrhagic stroke	965 (21.9)
Ischemic stroke	3440 (78.1)
History of drug allergy, <i>n</i> (%)	
Be	16 (0.4)
Not	4389 (99.6)

**Figure 1.** Diagnostic information and drug allergy history.

3.3. Patient medication information

The average number of days GM1 was 11.8 days in the included studies. A total of 4241 cases (96.3%) were mainly intravenous infusion, and 164 cases (3.7%) were intramuscular injection. Among the patients with intravenous infusion, 4041 patients received GM1 solvent, were 0.9% sodium chloride injection, accounting for 95.3%. There were 200 patients with 5% glucose injection as the solvent, accounting for 4.7%. Among the patients with intravenous infusion, there were 337 patients with a GM1 infusion time of 0–40 minutes, 2581 patients with 40–60 minutes, 1095 patients with 60–90 minutes, and 228 patients with more than 90 minutes. Among all patients, there were 130 patients with GM1 doses of 0–20 mg/day, 1748 patients with 20–80 mg/day, and 2527 patients with more than 80 mg/day. Among all patients, 3886 patients were treated alone, accounting for 88.2%; 519 cases were combined with drugs, accounting for 11.8%. The results are shown in **Table 3** and **Figure 2**.

Table 3. Patient medication information table

Medication information		
Days of GM1 medication (days)		
The mean \pm standard deviation		11.8 \pm 8.3
Min–Max		1.0–90.0
Median (Q1–Q3)		8.0 (7.0–14.0)
GM1 dosage mode		
Intravenous drip		4241 (96.3)
intramuscular injection		164 (3.7)
GM1 drug solvent		
0.9% sodium chloride injection		4041 (95.3)
5% glucose injection		200 (4.7)
GM1 instillation time		
0–40 minutes		337 (7.9)
40–60 minutes		2581 (60.9)
60–90 minutes		1095 (25.8)
More than 90 minutes		228 (5.4)
GM1 dosage (mg/day)		
0–20		130 (3.0)
20–80		1748 (39.6)
> 80		2527 (57.4)
Combination medication		
Medication alone		3886 (88.2)
Combination medication		519 (11.8)

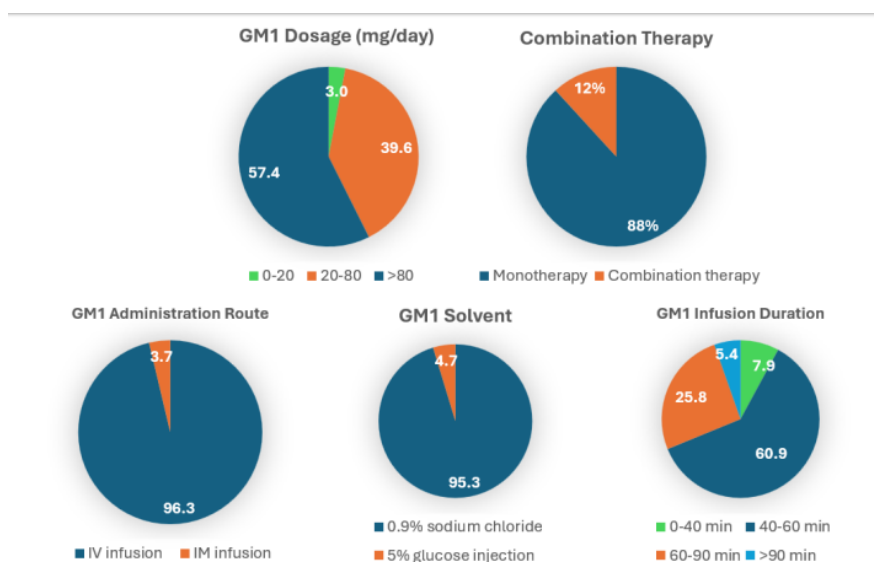


Figure 2. Patient medication information.

3.4. Information on adverse events of patients

Of the total 4405 participants, 1635 had adverse events, with an incidence rate of 37.1%. Digestive symptoms (such as bloating, abdominal pain, diarrhea, vomiting, decreased appetite, etc.) occurred in up to 70.9% of all adverse events. The vast majority (99.4%) of adverse events were mild, and no serious adverse events occurred. Of these, 244 patients (14.9%) had management measures for adverse events^[5–7]. The results are shown in **Table 4** and **Figure 3**.

Table 4. Information table of adverse events of patients

Name	
Total adverse events	
Yes	1635 (37.1)
Not	2777 (62.9)
Adverse reactions affect the system and symptoms	
Digestive system (such as bloating, abdominal pain, diarrhea, vomiting, decreased appetite, etc.).	1160 (70.9)
Neurological system (e.g., transient speech disorders, confusion, lethargy, rare seizures, tinnitus, deafness, dizziness, etc.).	310 (19.0)
respiratory system (respiratory distress, respiratory paralysis, shortness of breath, etc.).	33 (2.0)
Systemic symptoms (profuse sweating, chills and tremors in the limbs, sore limbs, bruising of the lips and limbs, etc.).	44 (2.7)
Eye diseases (such as blurred vision, pain in both eyes, swelling of the upper eyelids, conjunctival congestion, tearing, etc.).	22 (1.3)
other	66 (4.0)
Adverse event severity	
Mild	1625 (99.4)
Moderate	10 (0.6)
Severe	0 (0.0)
Whether to take treatment measures	
Be	244 (14.9)
Not	1391 (85.1)

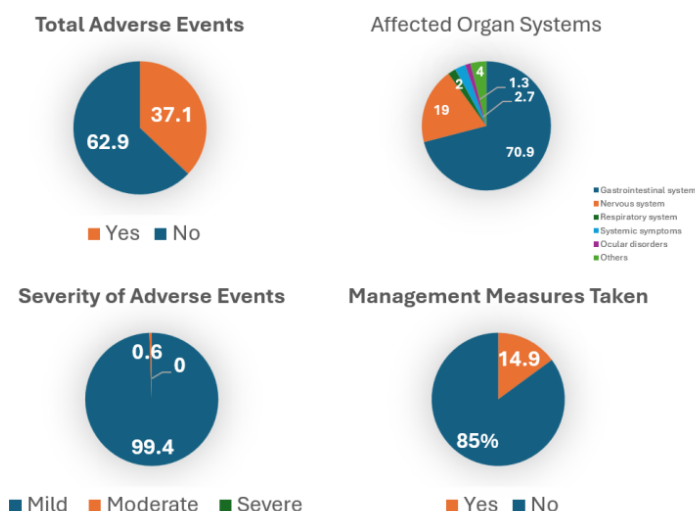


Figure 3. Infographic of patient adverse events.

3.5. Efficacy evaluation information

Before GM1 treatment, the mean NIHSS score of all patients was 14.0 points, and the mean NIHSS score after treatment was 10.1, with an average decrease of 3.9 points. Before GM1 treatment, there were 742 patients with Barthel scores below 20 points, 1575 cases with 20–40 points, 1667 cases with 40–60 points, and 421 cases with 60 points or more. A total of 741 cases had Barthel scores below 20 points, 935 cases with 20–40 points, 1056 cases with 40–60 points, and 1673 cases with more than 60 points after medication. The Wilcoxon test results showed statistical significance. The results are shown in **Table 5**.

Table 5. Patient efficacy evaluation table

	Before medication	After medication	Statistics	P-value
NIHSS score (mean \pm SD)	14.0 \pm 8.0	10.1 \pm 8.6	37.974	< 0.001
Barthel Index			1122162	< 0.001
20 points or less	742 (16.8)	741 (16.8)		
20–40	1575 (35.8)	935 (21.2)		
40–60	1667 (37.8)	1056 (24.0)		
60 or more	421 (9.6)	1673 (38.0)		

4. Discussion

Stroke is a sudden cerebrovascular disease, and its urgency and severity have always been a major medical and health problem at home and abroad. With the change of modern lifestyle, the incidence of stroke is gradually getting younger, which has triggered scholars in the industry to rethink the treatment of this disease^[8,9]. At present, the management of the disease is gradually changing from traditional treatment methods to individualized and personalized treatment, not only considering the patient's clinical symptoms, but also taking into account the patient's physique, economic situation and personal needs. Under the trend of individualized treatment, the application of GM1 has shown significant therapeutic effects and high safety.

Of the total 4405 patients in this study, only 1635 cases experienced adverse events, with an incidence rate of 37.1%. Among them, digestive system symptoms were the main ones, accounting for 70.9%; 19.0% of neurological symptoms and 2.7% of systemic symptoms, such as profuse sweating, chills, and trembling limbs, sore limbs, etc.; There are also a few respiratory symptoms, eye diseases, and other symptoms that occur. It is worth noting that 99.4% of the adverse events were only mild, and no patients had severe adverse events, which can be considered to be safe for GM1 in the treatment of stroke.

In terms of treatment effectiveness, the average NIHSS score of all patients before treatment with GM1 was 14.0 points, and the average NIHSS score after treatment was 10.1, with an average decrease of 3.9 points. The Barthel Index after treatment was statistically significant by Wilcoxon's test, and it can be considered that GM1 effectively improved the recovery of stroke patients and improved their daily living ability of stroke patients.

5. Conclusion

To sum up, GM1, as a highly safe brain-protective drug, can treat stroke well, and it has a significant effect

in promoting neurological function recovery and improving quality of life. In the face of the trend of younger stroke, individualized and personalized treatment strategies are particularly important. Future research should focus on how to optimize the treatment regimen of GM1 to improve its safety and therapeutic efficacy to better meet the treatment needs of different patients. At the same time, strengthening the study of GM1 mechanisms may provide a theoretical basis and technical support for the development of new therapeutic drugs.

Disclosure statement

The authors declare no conflict of interest.

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Efficacy and Safety of Monosialotetrahexosylganglioside Sodium in the Treatment of Acute Ischemic Stroke: A Real-World Study

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Abstract: *Objective:* The purpose of this study was to evaluate the efficacy and safety of monosialotetrahexosylganglioside (GM1) in patients with acute ischemic stroke (AIS) based on real-world data. *Methods:* From March 2022 to January 2023, patients with AIS treated with GM1 were included in this study. Functional outcomes were assessed using the modified Rankin Scale (mRS) and the NIH Stroke Scale (NIHSS) at baseline and at 2, 6, and 10 weeks after treatment initiation. Safety was evaluated through adverse event (AE) monitoring. *Results:* A total of 1772 patients with AIS were collected for analysis after the exclusion of the exclusion criteria. GM1 treatment significantly improved functional outcomes. The mRS score decreased from a baseline of 1.32 to 0.97 at the third follow-up (mean reduction: 0.35 points, $P < 0.05$). The NIHSS score decreased from 5.14 to 2.32 (mean reduction: 2.82 points, $P < 0.05$). A total of 128 AEs were reported in 98 patients (5.5%). The majority of AEs were mild to moderate (124 events, 7.0%), with only 4 severe AEs (Grade 3, 0.2%) observed. No life-threatening or fatal AEs occurred. *Conclusion:* GM1 treatment significantly improves the mRS score and NIHSS score of AIS patients, and the safety is high. AIS patients showed obvious advantages in neurological function recovery after GM1 treatment, and these results provide a clinical basis for GM1 in the real diagnosis and treatment environment of AIS patients.

Keywords: Acute ischemic stroke; GM1; mRS score; NIHSS score

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1. Introduction

Acute ischemic stroke (AIS) has a high incidence and recurrence rate, and is one of the leading causes of death and disability worldwide. At present, some progress has been made in the treatment of AIS in the acute stage, such as the popularization and application of intravenous drug thrombolysis and mechanical thrombectomy, but the long-term efficacy is still limited by many factors, such as treatment time window, access to medical resources, and

patient differences. Therefore, exploring new treatments to improve the long-term prognosis of AIS remains one of the important topics in the field of neuroscience. As a ganglioside, monosialotetrahexosylganglioside (GM1) has multiple effects, such as neuroprotection, improving nerve repair, and delaying apoptosis, and is widely used in the clinical treatment of neurological diseases. Previous studies have confirmed that GM1 can protect ischemic brain injury by resisting inflammatory responses, reducing oxidative stress, maintaining cell membrane morphology, and promoting energy metabolism. However, large-scale, multi-center, high-quality evidence on the clinical efficacy of GM1 in the treatment of AIS is still lacking, especially with limited data on real-world application effects. This study evaluates the efficacy and safety of GM1 in patients with AIS based on real-world research data, filling in the gaps of previous studies. We hope that through this study, we will provide stronger evidence-based data for clinical practice, thereby promoting the standardized application of GM1 in AIS and providing more treatment options to improve the prognosis of AIS patients.

2. Data and methods

2.1. General information

This multicenter, prospective, observational, real-world enrolled AIS patients who used GM1 from March 2022 to January 2023 were included in this study. Inclusion criteria: (1) Age ≥ 18 years old; (2) The diagnostic criteria meet the diagnostic criteria for acute ischemic stroke in the 2018 Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke, and are confirmed by head CT or MRI; (3) Patients who received standardized acute treatment, including thrombolysis, mechanical thrombectomy, etc., and were treated with GM1^[1–3]. Exclusion criteria: (1) Allergy to GM1 and its components or drug contraindications; (2) History of other serious diseases of the central nervous system (such as severe brain trauma, skull tumor, cerebral hemorrhage, etc.); (3) Previously combined with heart, liver, renal insufficiency or other systemic major diseases, with an expected survival time of < 3 months; (4) Pregnant and lactating women; (5) Patients who have received other drug treatments or interventions that may affect the study outcomes before admission; (6) Patients who are in critical condition at the time of admission and are not expected to benefit in the short term (such as malignant large-scale cerebral infarction, etc.)^[4,5]. The GM1 treatment regimen was administered in accordance with the instructions. For the acute phase of ischemic stroke, the recommended dosage was 100 mg once daily, administered via intravenous infusion. The duration of the acute phase high-dose treatment was 2 to 3 weeks, followed by a maintenance phase of 20–40 mg once daily via intramuscular injection or intravenous infusion for a subsequent 3 to 4 weeks. The total treatment course was approximately 6 weeks. Follow-ups were conducted at 2, 6, and 10 weeks after treatment. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of Wuhan University People's Hospital as well as the ethical committees of all participating sites. Written informed consent was obtained from all participants or their legally authorized representatives prior to any study-specific procedures.

2.2. Research indicators

- (1) The basic condition and disease status of the patient;
- (2) Evaluation of long-term functional prognosis of patients: the primary efficacy endpoint was the proportion of patients achieving an excellent functional outcome (modified Rankin Scale [mRS] score of 0 to 1) and a favorable functional outcome (mRS score 0 to 2) over time. The mRS score was also presented as an ordinal measure for descriptive purposes^[6].
- (3) Evaluation of the degree of neurological deficit in patients: The secondary functional outcome was the

NIHSS score, which is a quantitative tool for assessing the degree of neurological deficit in patients with acute stroke, and is used to quickly judge the severity of stroke and changes in the condition^[7];

(4) Adverse event (AE) evaluation: The CRF scale was used to collect related AEs before and after treatment.

2.3. Statistical methods

SPSS 26.0 software was used for statistical analysis. The continuity index is represented by “mean ± standard deviation (SD).” The categorical indexes were expressed as “*n*,%”, and the differences between groups were compared by the χ^2 test. Changes in NIHSS over time was analyzed by repeated-measures analysis of variance (ANOVA). The difference was statistically significant by two-sided $P < 0.05$.

3. Results

3.1. Patient demographic data

A total of 1772 patients with AIS were included in this study, including 1069 males (60.3%) and 703 females (39.7%), as shown in **Table 1**.

Table 1. Demographic data of patients [*n*,(%)]

Variable	Patients with AIS (<i>n</i> = 1772)
Gender	
Male	1069 (60.3)
Female	703 (39.7)
Age	
18–45 years old	57 (3.2)
46–60 years old	818 (46.2)
61–79 years	750 (42.3)
> 80 years old	147 (8.3)
Hypertension	
Yes	1321 (74.5)
Not	451 (25.5)
Diabetes	
Yes	646 (36.5)
Not	1126 (63.5)
Dyslipidemia	
Yes	607 (34.4)
Not	1165 (65.6)
Heart disease	
Yes	378 (21.3)
Not	1394 (78.7)
Vasculitis	
Yes	142 (8.0)
Not	1630 (92.0)

3.2. Clinical symptoms of stroke and previous treatment methods

The clinical manifestations of the enrolled patients with confirmed acute ischemic stroke were as follows: 44.2%

presented with a progressive stroke, 31.7% with a complete stroke, 20.7% with reversible ischemic neurological deficits, and 3.4% with other clinical manifestations (**Table 2**).

Table 2. Clinical symptoms and previous treatment methods of stroke [*n*,(%)]

Variable	Statistics
Clinical manifestations	
Progression stroke	783(44.2)
Complete stroke	562(31.7)
Reversible ischemic neurological deficits	367(20.7)
Other clinical manifestations	640(3.4)
Stroke duration	
< 1 year	1432(80.8)
1–2 years	177(10.0)
> 2 years	163(9.2)
Prior medication	
Yes	1536(86.7)
Not	236(13.3)
Rehabilitation training	
Yes	511(28.8)
Not	1261(71.2)
surgery	
Yes	306(17.3)
Not	1466(82.7)

3.3. Changes in mRS score before and after treatment

Compared with the baseline assessment, the distribution of patients across modified Rankin Scale (mRS) categories showed significant improvement after GM1 treatment. The proportion of patients with a favorable outcome (mRS score 0–1) significantly increased from 25.0% at baseline to 34.0%, 40.0%, and 43.0% at the first, second, and third follow-ups, respectively (P for trend < 0.001) (**Table 3**).

Table 3. Changes in mRS score before and after treatment

Patient	n	mRS score	mRS 0–1, <i>n</i> (%)	mRS 0–2, <i>n</i> (%)
Baseline	1772	1.32 ± 0.78	443 (25.0%)	1418 (80.0%)
The first follow-up visit	894	1.07 ± 0.62	304 (34.0%)	847 (94.7%)
Second follow-up visit	795	1.01 ± 0.58	318 (40.0%)	763 (96.0%)
Third follow-up visit	654	0.97 ± 0.54	281 (43.0%)	637 (97.4%)
P	< 0.001			

Note: Data are presented as mean ± standard deviation for descriptive purposes. The statistical significance of the ordered change in mRS distributions over time was analyzed using the χ^2 test.

3.4. Changes in NIHSS score before and after treatment

Compared with the first treatment, the NIHSS score of AIS patients was significantly reduced after GM1 treatment ($P < 0.001$). Post hoc analyses confirmed that scores at all follow-up time points were significantly reduced compared to baseline (all $P < 0.05$) (**Table 4**).

Table 4. Changes in NIHSS score before and after treatment

Patient	n	NIHSS score
First diagnosis	1772	6.82 ± 6.50
The first follow-up visit	894	4.21 ± 5.20
Second follow-up visit	795	3.15 ± 4.60
Third follow-up visit	654	2.32 ± 4.11
F	185.7	
P	< 0.001	

Note: Data presented as mean ± standard deviation. The *P*-value represents the result of the omnibus test for the main effect of time using repeated-measures ANOVA. Post hoc pairwise comparisons with baseline were performed using Bonferroni-adjusted tests.

3.5. Safety evaluation

The safety profile of GM1 was evaluated in all 1772 treated patients. A total of 128 adverse events (AEs) were reported in 98 patients (5.5%). The vast majority of AEs were mild to moderate in severity (Grade 1-2), accounting for 124 events (7.0%). Only 4 severe AEs (Grade 3, 0.2%) were observed, which included 2 cases of severe vomiting and 2 cases of severe headache; all resolved with appropriate medical intervention and without sequelae. No Grade 4-5 AEs were reported. The most common AEs were gastrointestinal disorders, affecting 45 patients (2.5%) with 62 events (3.5%), primarily nausea (1.7%) and vomiting (1.2%) (**Table 5**).

Table 5. Summary of adverse events by severity (Safety population, *N* = 1772)

Preferred term (System organ class)	Patients, <i>n</i> (%)	Events, <i>n</i> (%)	Grade 1–2, <i>n</i> (%)	Grade ≥ 3, <i>n</i> (%)
Any Adverse Event	98 (5.5)	128 (7.2)	124 (7.0)	4 (0.2)
Gastrointestinal disorders	45 (0.5)	62 (3.5)	60 (3.4)	2 (0.1)
Nausea	25 (1.4)	30 (1.7)	30 (1.7)	0 (0.0)
Vomiting	15 (0.8)	22 (1.2)	20 (1.1)	2 (0.1)
Diarrhea	5 (0.3)	10 (0.6)	10 (0.6)	0 (0.0)
Nervous system disorders	27 (1.5)	35 (2.0)	33 (1.9)	2 (0.1)
Dizziness	15 (0.8)	18 (1.0)	18 (1.0)	0 (0.0)
Headache	10 (0.6)	15 (0.8)	13 (0.7)	2 (0.1)
Somnolence	2 (0.1)	2 (0.1)	2 (0.1)	0 (0.0)
Skin and subcutaneous tissue disorders	12 (0.7)	15 (0.8)	15 (0.8)	0 (0.0)
Rash	8 (0.5)	10 (0.6)	10 (0.6)	0 (0.0)
Pruritus	4 (0.2)	5 (0.3)	5 (0.3)	0 (0.0)
General disorders and administration site conditions	8 (0.5)	10 (0.6)	10 (0.6)	0 (0.0)
Injection site reaction	5 (0.3)	7 (0.4)	7 (0.4)	0 (0.0)
Fatigue	3 (0.2)	3 (0.2)	3 (0.2)	0 (0.0)
Others	6 (0.3)	6 (0.3)	6 (0.3)	0 (0.0)
Insomnia	3 (0.2)	3 (0.2)	3 (0.2)	0 (0.0)
Palpitations	2 (0.1)	2 (0.1)	2 (0.1)	0 (0.0)
Increased ALT	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)

Note: Adverse events were graded according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. No Grade 4 (life-threatening) or Grade 5 (fatal) adverse events were observed. ALT: Alanine Aminotransferase.

4. Discussion

The results of this study showed that GM1 treatment significantly improved the mRS score and NIHSS score of AIS patients, and the treated patients showed more obvious advantages in functional prognosis and neurological function recovery. These results show that the application of GM1 in AIS patients can effectively reduce disability rates and improve quality of life, further proving its clinical value in the field of neuroprotection.

This study also inevitably has the following limitations. First, based on data analysis from real-world studies, this study can reflect the application effect of GM1 in actual clinical diagnosis and treatment settings, but compared with clinical trials with strict quality control and full-process implementation management, there may be inherent systemic bias due to the type of study. Second, the follow-up time of this study is relatively short, and it is impossible to comprehensively evaluate the impact of GM1 on the long-term prognosis of AIS. Finally, due to the limited sample size, this study cannot extensively explore the differences in response to GM1 treatment in different subgroups (such as different ages, stroke severity, comorbidities, etc.), and we will explore the impact of different clinical factors on long-term prognosis in future studies.

AIS is one of the leading causes of disability and mortality worldwide, with a high burden of disease. A large number of AIS patients are accompanied by limited daily physiological functions and impaired quality of life, which has a long-term heavy impact on families and society. The pathophysiological process of AIS mainly involves ischemia-induced nerve cell damage, inflammatory response, oxidative stress, and disruption of the blood-brain barrier. GM1 stimulates multiple pathways to play protective neuronal functions at the same time: first, GM1 can maintain the stability of nerve cell membranes, delay the circulation of calcium ions, and reduce ischemic injury^[8,9].

At the same time, GM1 hinders the release of a large number of inflammatory factors, keeping the inflammatory response in the internal environment at a low level. In addition, GM1 reduces free radical damage to nerve cells by reducing oxidative effects^[10]. In addition, GM1 can promote nerve repair and regeneration, helping to improve patients' nerve function and daily life ability^[11,12]. Under the combined effect of these multiple mechanisms, GM1 can significantly improve the outcomes of adverse clinical events in patients with AIS. In addition, no adverse reactions were found in all patients during multiple follow-up visits after treatment, indicating a high safety profile with GM1 treatment^[13,15].

5. Conclusion

In summary, this study verified the efficacy and safety of GM1 in the treatment of acute ischemic stroke using real-world data, and the results showed that GM1 significantly improved functional outcome and neurological recovery, and reduced the burden of disease in patients. This study provides a strong evidence-based basis for the clinical application of GM1 in AIS, and lays a foundation for further exploration of the mechanism of action of GM1 and the optimization of treatment options in the future.

Disclosure statement

The authors declare no conflict of interest.

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Real-world Study of Citicoline on the Neurological Prognosis of Acute and Convalescent Patients with Ischemic Stroke

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Abstract: *Objective:* To evaluate the effect and safety of citicoline on the improvement of neurological function in patients with ischemic stroke. *Methods:* The Mini-Mental State Examination (MMSE) score and National Institutes of Health Stroke Scale (NIHSS) score were analyzed in 8780 patients with ischemic stroke who received citicoline therapy from January 2023 to April 2024 at 1 month, 2 months, and 3 months after treatment. *Results:* With the prolongation of treatment, the MMSE and NIHSS scores of the patients improved significantly, and the total clinical effectiveness rate at three months was 43.08%. The incidence of adverse reactions was 0.14%, mainly mild gastrointestinal reactions and central nervous system reactions. *Conclusion:* Citicoline has a significant effect on improving neurological function in patients with ischemic stroke, and its safety is high.

Keywords: Ischemic stroke; Citicoline; Neurological function; Safety; MMSE; NIHSS

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1. Introduction

Ischemic stroke refers to acute cerebrovascular disease caused by occlusion or stenosis of the cerebral blood supply artery, which in turn causes related signs and symptoms. The pathogenesis of stroke is complex, and vascular risk factors (such as cerebral embolism, hypertension) and lifestyle factors (age, smoking, poor diet) may lead to the onset of the disease. If effective treatment measures are not taken in time to improve cerebral blood circulation, it can lead to excessive damage to neuromotor conduction pathways and neurons, about 50% of survivors have obvious disabilities, and 10% need long-term hospitalization. Stroke has caused a great mental and economic burden on patients and their families. Citicoline is a natural endogenous compound that is a precursor to the synthesis of phosphatidylcholine (one of the components of cell membranes) and is commonly used in clinical

settings for brain protection. At present, the neuroprotective effect of stroke clinical patients in different treatment periods (e.g., acute, subacute, and convalescent) has not been clearly reported. Therefore, this study collected real-world data to evaluate the effect of citicoline on the neurological function prognosis of patients with acute and convalescent ischemic stroke.

2. Data and methods

2.1. General information

This study analyzed patients with ischemic stroke who were treated with citicoline as assessed by the investigator between January 2023 and April 2024^[1]. Inclusion criteria: (1) Age > 18 years old; (2) Meet the diagnostic criteria related to stroke in the “Key Points for the Diagnosis of Various Cerebrovascular Diseases”; (3) The Barthel index is 21–99 points; (4) Accompanied by symptoms of neurological deficits caused by stroke, such as movement disorders, cognitive disorders, and speech and swallowing disorders. Exclusion criteria: (1) Concomitant use of other neuroprotective drugs, such as butylphthaloin, edaravone, etc.; (2) Non-stroke diseases that cause cognitive impairment, such as intracranial mass lesions, brain trauma, etc.; (3) Patients with a NIHSS score of > 25 points and unable to cooperate with cognitive and related functional assessments; (4) Those with allergies; Those who are allergic to the test drug or its related medicinal flavors or ingredients; (5) Patients with severe liver impairment (ALT or AST levels are more than 15 times higher than normal); (6) Patients with severe renal impairment (serum creatinine is more than 1.5 times higher than normal); (7) Patients with severe cardiac insufficiency (echocardiography showing cardiac insufficiency or cardiac function rating of grade III or above).

2.2. Research methods

This study was a single-arm trial in which all included patients were treated with citicoline at 200 mg × 3 doses per day for one month per treatment cycle. Among them, 8,780 people were included at baseline and evaluated by MMSE and NIHSS. After one month of treatment, 5,588 people were evaluated for retention, after a total of two months of treatment, 3,990 people were evaluated for neurological function, and after a total of three months of treatment, 2,862 people were evaluated^[2,3].

2.3. Observation indicators

2.3.1. Main observation indicators

- (1) Observe the neurological deficits at 1 month, 2 months, and 3 months after medication (changes in National Institutes of Health Stroke Scale (NIHSS) score and Mini-Intelligent State Examination (MMSE) score;
- (2) Total clinical effective rate. The grading criteria are: the NIHSS score decreases by more than 90%, the patient's ability to live after treatment is restored, the clinical symptoms basically disappear, and there is no focal neurological dysfunction: improvement: the NIHSS score decreases between 60% and 89%, the patient's ability to live is significantly restored after treatment, the clinical symptoms improve, and the focal neurological function is mild; Effective: NIHSS score was reduced by 30%-59%, and the patient's living ability and clinical symptoms improved after treatment. Ineffective: The above criteria are not met, that is, there are no obvious benign changes in the patient's clinical symptoms and NIHSS score after treatment. Total effective rate = apparent efficiency + improvement rate + effective rate^[4].

2.3.2. Secondary observation indicators

- (1) Observe the incidence of adverse drug reactions/adverse events during medication;
- (2) Abnormal safety examination with clinical assessment.

2.4. Statistical analysis

Statistical analysis was performed using Stata SE/14.0 software. The number of cases, mean, and standard deviation are evaluated based on whether the measurement data conforms to or approximates the normal distribution. Categorical data evaluates its frequency and composition ratio. Analysis of variance was used for comparison between baseline groups of continuous data. Chi-square test or rank-sum test was used for comparison of categorical data between groups, and repeated-measures analysis of variance (ANOVA) was used to compare the continuous data (MMSE and NIHSS scores) across different time points (baseline, 1 month, 2 months, 3 months). Differences were considered statistically significant at $P < 0.05$.

3. Results

3.1. Demographic characteristics and source distribution of patients

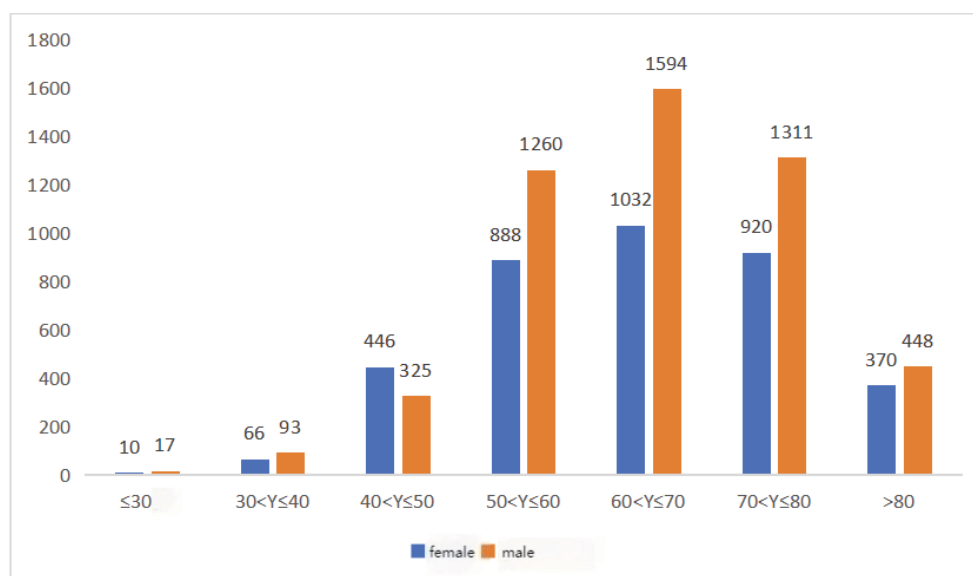
A total of 8780 cases were included at baseline and followed up three times, that is, NIHSS score, MMSE score, and total effective rate data were collected at 1 month, 2 months, and 3 months after medication. At baseline, there were 5169 male patients (58.8%) and 3611 female patients (41.1%), with an average age of 65.06 ± 11.83 years and a normal age distribution. The specific results are shown in Table 1. The patients came from 21 provinces, and the distribution is shown in Table 2, and the age distribution by gender is shown in Figure 1.

Table 1. Demographic characteristics of patients

	Baseline (<i>N</i> = 8780, %)	One month (<i>N</i> = 5588, %)	Two months (<i>N</i> = 3990, %)	Three months (<i>N</i> = 2862, %)
Gender				
Male	5169 (58.87)	3334 (59.66)	2371 (59.42)	1695 (59.22)
Female	3611 (41.13)	2254 (40.34)	1619 (40.58)	1167 (40.78)
Age (years, mean \pm SD)				
	65.06 \pm 11.83	64.97 \pm 11.76	65.05 \pm 11.79	65.12 \pm 11.94
Education				
No formal education	1540 (17.54)	949 (16.98)	686 (17.19)	502 (17.54)
Primary school education	3368 (38.36)	2150 (38.48)	1522 (38.15)	1134 (39.62)
Junior high school education	2181 (24.84)	1398 (25.02)	995 (24.94)	681 (23.79)
Senior high school education	1032 (11.75)	670 (11.99)	469 (11.75)	324 (11.32)
Associate degree	479 (5.46)	300 (5.37)	225 (5.64)	159 (5.56)
Bachelor's degree	169 (1.92)	111 (1.99)	85 (2.13)	55 (1.92)
Graduate student	11 (0.13)	10 (0.18)	8 (0.2)	7 (0.24)

Table 2. Geographical distribution of patients

Province	Number	Proportion
Anhui	486	5.5%
Beijing	41	0.5%
Guangdong	913	10.4%
Guangxi	105	1.2%
Guizhou	15	0.2%
Hebei	90	1.0%
Henan	729	8.3%
Hubei	60	0.7%
Hunan	515	5.9%
Jiangsu	866	9.9%
Jiangxi	1413	16.1%
Liaoning	79	0.9%
Ningxia	8	<0.1%
Shandong	2235	25.5%
Shanxi	34	0.4%
Shaanxi	181	2.1%
Sichuan	90	1.0%
Tianjin	142	1.6%
Yunnan	8	<0.1%
Zhejiang	750	8.5%
Chongqing	20	0.2%

**Figure 1.** Age distribution of patients of different genders.

3.2. Patient's disease diagnosis and anamnesis information

As shown in **Table 3**, among the 8780 patients included at baseline, 4082 patients had a Toast classification of stroke, accounting for 46.49%, 3263 patients had arteriole occlusion, accounting for 37.16%, 507 patients had cardioembolism, 895 patients had other clear causes, accounting for 10.19%, and 33 patients had other causes, accounting for 0.38%. The number and proportion of stroke treatment stages were as follows: 5186 (59.07) in the recovery period, 1656 (18.86) in the acute stage, and 1938 (22.07) in the subacute stage. The number and proportion of symptoms of neurological impairment in stroke were as follows: sensory and motor dysfunction 3657 (41.65), communication dysfunction 1079 (12.29), cognitive dysfunction 3548 (40.41), psychological dysfunction 216 (2.46), and other dysfunction 280 (3.19).

Table 3. Patient disease diagnosis and anamnesis information

	Baseline (N = 8780, %)	One month (N = 5588, %)	Two months (N = 3990, %)	Three months (N = 2862, %)
Toast typing of stroke				
Large-artery atherosclerosis	4082 (46.49)	299 (5.35)	2743 (49.09)	1509 (52.73)
Small-vessel occlusion	3263 (37.16)	2264 (40.52)	2074 (37.12)	1022 (35.71)
Cardioembolism	507 (5.77)	711 (12.73)	304 (5.44)	119 (4.16)
Other determined etiology	895 (10.19)	576 (10.31)	450 (8.05)	204 (7.13)
Undetermined etiology	33 (0.38)	28 (0.50)	17 (0.3)	8 (0.28)
Stroke treatment staging				
convalescence	5186 (59.07)	3382 (60.52)	2474 (62.01)	1812 (63.31)
Acute phase	1656 (18.86)	1089 (19.49)	805 (20.18)	626 (21.87)
Subacute phase	1938 (22.07)	1117 (19.99)	711 (17.82)	424 (14.81)
Symptoms of stroke neurological injury				
Sensory and motor dysfunction	3657 (41.65)	2358 (42.2)	1673 (41.93)	1175 (41.06)
Communication dysfunction	1079 (12.29)	693 (12.4)	475 (11.9)	351 (12.26)
Cognitive dysfunction	3548 (40.41)	2260 (40.44)	1633 (40.93)	1170 (40.88)
Psychological disorders	216 (2.46)	102 (1.83)	68 (1.7)	47 (1.64)
Other functional impairments	280 (3.19)	175 (3.13)	141 (3.53)	119 (4.16)

3.3. Evaluation of citicoline efficacy

The results showed that there were significant differences between at least two groups ($P < 0.05$) between different treatment periods, indicating that there were statistical differences in the changes in MMSE levels of ischemic stroke patients treated with citicoline during the treatment cycle. Further between-group comparisons of MMSE and NIHSS measured at different time periods found statistically significant changes in MMSE and NIHSS after citicoline therapy, indicating an improvement in neurological function with citicoline therapy (**Table 4** and **Table 5**).

Table 4. Evaluation of the effect of citicoline treatment in patients with ischemic stroke

	Baseline (N = 8780, %)	One month (N = 5588, %)	Two months (N = 3990, %)	Three months (N = 2862, %)	Statistics	P-value
MMSE (Mean ± SD)	15.71 ± 6.60	16.85 ± 6.43	18.33 ± 6.24	19.41 ± 6.50	F = 1865.65	P < 0.05
NIHSS (Mean ± SD)	10.19 ± 6.27	9.75 ± 6.18	8.79 ± 6.32	8.15 ± 6.61	F = 2654.62	P < 0.05

Table 5. Efficacy of different treatment cycles

Treatment cycle	Markedly effective	Improved	Effective	Ineffective	Total Effective Rate (%)
One month	19 (0.34%)	85 (1.52%)	1032 (18.44%)	4462 (79.71%)	20.29 %
Two months	46 (1.15%)	387 (9.63%)	989 (24.62%)	2595 (64.60%)	35.40 %
Three months	13 (0.45%)	646 (22.57%)	574 (20.06%)	1629 (56.92%)	43.08 %

3.4. Adverse reactions

A total of 30 adverse reactions occurred, with an average duration of 1.63 days, a minimum duration of 0 days, a maximum duration of 5 days, and a total of 8 occurrences, an average duration of gastrointestinal reactions of 3.74 days, a minimum duration of 0 days, and a maximum duration of 34 days, a total of 19 occurrences, and an average duration of anaphylaxis of 3.33 days, a minimum duration of 2 days, and a maximum duration of 6 days, with a total of 3 occurrences. Adverse reactions accounted for 0.14% of total events. 63.3% of them are gastrointestinal reactions, such as taste, loss of appetite, diarrhea, abdominal pain, nausea, etc.; 10% are allergic reactions, such as rash, itching, etc.; 26.7% were central nervous system reactions, such as limb numbness, tremor, insomnia, etc. The above adverse reactions are mild, and the subsequent symptom relief disappears, and no serious consequences will affect the subsequent treatment of the patient. Only one was recorded to be discharged due to adverse reactions, which were further determined by physicians to be unrelated to citicoline (**Table 6**).

Table 6. Adverse reactions

Type	Number of occurrences	Average number of days lasting	Frequency of serious adverse events (%)	Extent
Gastrointestinal reactions (e.g. abnormal taste, loss of appetite, diarrhea, abdominal pain, nausea, etc.)	19	3.74	63.3	Mild
Central nervous system reactions (e.g., limb numbness, tremors, insomnia)	8	1.63	26.7	Mild
Allergic reactions (such as rash, itching, etc.)	3	3.33	10	Mild

4. Discussion

This study evaluated the effect of citicoline on improving neurological function in patients with ischemic stroke and its safety. The results showed that citicoline had a significant clinical effect on improving the neurological function of patients with ischemic stroke, and the MMSE and NIHSS scores of the patients were significantly improved after treatment. The incidence of adverse reactions was low, and the safety was high. This result is consistent with previous experimental studies and further supports the important role of citicoline in stroke treatment.

As a natural endogenous compound, citicoline can restore the structure and function of nerve cell membranes and promote the recovery of neuronal function by participating in the biosynthesis of phosphatidylcholine. This mechanism helps improve the neurological function of stroke patients. In addition, citicoline can further support nerve repair by increasing cerebral blood flow and promoting brain metabolism. In addition, previous data suggest that citicoline has a neuroprotective effect on cerebral ischemia models, promoting vascular and nerve regeneration and enhancing neuronal plasticity by increasing the number of peripheral endothelial progenitor cells^[5,6]. These pharmacological mechanisms provide a biological basis for explaining the clinically observed improvement in neurological function symptoms.

The results of this study also showed that patients had a low incidence of adverse reactions after taking citicoline, mainly mild gastrointestinal reactions and central nervous system reactions. This suggests that oral citicoline treatment is not only effective but also has a high safety profile. In particular, most of the symptoms of adverse reactions disappear on their own during the treatment process and do not adversely affect subsequent treatment, which provides a strong safety guarantee for the use of citicoline in the treatment of ischemic stroke in clinical practice^[7].

However, there are some limitations to this study. First, this study is a single-arm trial and lacks a control group, so it is not possible to fully evaluate the relative efficacy of citicoline. Future studies should consider adding a control group with a randomized controlled trial design to more precisely assess the efficacy of citicoline. Secondly, the follow-up period of this study is short, limited to three months, and the long-term effects have not been fully evaluated. Therefore, long-term follow-up studies are recommended in the future to observe the continued efficacy and safety of citicoline.

5. Conclusion

In summary, citicoline has significant clinical effects in improving neurological function in patients with ischemic stroke, and its safety is high. Future studies should further verify its efficacy and explore the best treatment options to provide a more scientific basis for clinical treatment.

Disclosure statement

The authors declare no conflict of interest.

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Study on the Mechanism of H19/miR-93-5p/STAT3 in Regulating the Expression of Inflammatory Factors and Oxidative Stress in Microglia

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Abstract: *Objective:* To investigate the regulatory mechanism of the H19/miR-93-5p/STAT3 pathway on the expression of inflammatory factors and oxidative stress in microglia, providing potential therapeutic targets for neuroinflammatory-related diseases. *Methods:* Twenty patients with chronic subdural hematoma admitted to our hospital from August 2023 to December 2024 were selected as the study subjects. BV2 microglia were extracted from their local inflammatory hyperplastic tissues for experimental analysis. The cells were randomly divided into an LPS-induced group and a normal cell control group, with 10 cases each. The LPS-induced group was further subdivided into an H19 knockdown group ($n = 3$) constructed by transfecting with an H19 knockdown vector; an miR-93-5p overexpression group ($n = 4$) formed by transfecting with an miR-93-5p mimic; and further subdivided into an H19 knockdown group ($n = 3$) and an miR-93-5p overexpression group ($n = 4$) by transfecting with an miR-93-5p mimic/inhibitor and an H19 knockdown vector. The mRNA levels of H19, miR-93-5p, and inflammatory factors (IL-1 β , IL-6, TNF- α) were detected by RT-qPCR. The expression of STAT3 phosphorylation (p-STAT3), the Nrf2/HO-1 axis, and oxidative stress markers (MDA, GSH) were analyzed by Western blot. The binding relationship between STAT3 and the miR-93-5p promoter was verified by dual-luciferase assay. *Results:* After LPS induction, H19 expression was upregulated, miR-93-5p expression was decreased, and the levels of p-STAT3, inflammatory factors, and MDA were significantly increased ($P < 0.01$), while the GSH level was decreased ($P < 0.05$). Knockdown of H19 or overexpression of miR-93-5p could reverse these changes, inhibit p-STAT3, and activate the Nrf2/HO-1 axis, while reducing inflammatory factors and MDA ($P < 0.01$) and increasing GSH ($P < 0.05$). Dual-luciferase assay confirmed that STAT3 directly binds to the miR-93-5p promoter. *Conclusion:* The H19/miR-93-5p/STAT3 pathway affects the release of inflammatory factors and oxidative stress in microglia by regulating STAT3 phosphorylation and the Nrf2/HO-1 axis, providing a new strategy for the treatment of neuroinflammatory diseases.

Keywords: H19; miR-93-5p; STAT3; Microglia; Inflammatory factor expression; Oxidative stress mechanism

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1. Introduction

Chronic subdural hematoma (CSDH) is a common neurosurgical condition characterized by pathological features such as chronic intracranial hemorrhage, hematoma formation, and a series of symptoms including increased intracranial pressure and neurological dysfunction^[1]. Activated microglia release a large number of inflammatory factors, triggering neuroinflammatory responses, while elevated levels of oxidative stress lead to neuronal damage. Long non-coding RNA H19, microRNA miR-93-5p, and Signal Transducer and Activator of Transcription 3 (STAT3) play significant roles in cellular physiological and pathological processes^[2]. This study aims to delve into the regulatory mechanisms of the H19/miR-93-5p/STAT3 pathway on inflammatory factor expression and oxidative stress in microglia, providing a new perspective for the study of the pathogenesis of chronic subdural hematoma and exploring potential therapeutic targets. The findings are reported as follows.

2. Subjects and methods

2.1. Subjects

Twenty patients with chronic subdural hematoma admitted to our hospital from August 2023 to December 2024 were selected as the sample source. BV2 microglia were extracted from their local inflammatory hyperplastic tissues for experimental purposes. The basic grouping included an LPS-induced group and a normal cell control group. The LPS-induced group was further subdivided into an H19 knockdown group ($n = 3$) constructed by transfecting with an H19 knockdown vector, and an miR-93-5p overexpression group ($n = 4$) formed by transfecting with an miR-93-5p mimic.

Inclusion criteria: (1) Meeting the clinical diagnostic criteria for chronic subdural hematoma; (2) Complete clinical data and an admission duration of ≥ 3 days; (3) Absence of other severe neurological diseases; (4) No use of immunosuppressants in the past 3 months; (5) Signed informed consent from the patient or their family.

Exclusion criteria: (1) Presence of severe cardiac, hepatic, or renal dysfunction; (2) Coexistence of other types of dementia or psychiatric disorders; (3) Recent history of major surgery or severe infection; (4) Allergy to reagents used in the experiment.

2.2. Research methods

An LPS-induced group was established in the study, where BV2 microglial cells were cultured in a medium containing 100 ng/mL LPS for 24 hours to simulate a neuroinflammatory environment. Meanwhile, normal cells were set up as the control group, and cell transfection procedures were carried out. In LPS-induced BV2 microglial cells, the H19 knockdown vector and miR-93-5p mimic were transfected, respectively. The transfection process strictly adhered to the instructions of the transfection reagent to ensure transfection efficiency and accuracy. After transfection, the cells were further cultured for a certain period to allow relevant molecules to exert their regulatory effects.

Subsequently, a series of detection experiments was conducted. RT-qPCR technology was employed to detect the mRNA levels of H19, miR-93-5p, and inflammatory factors (IL-1 β , IL-6, TNF- α). Total cellular RNA was extracted, reverse-transcribed into cDNA, and then used as a template for fluorescent quantitative PCR amplification. The relative expression levels of each gene were determined by analyzing the intensity of the fluorescent signals. Western blot analysis was utilized to examine the protein expression related to p-STAT3 phosphorylation, the Nrf2/HO-1 axis, and oxidative stress markers (MDA, GSH). First, total cellular proteins were extracted, separated by electrophoresis based on their molecular weights, transferred onto PVDF membranes, incubated with specific antibodies, and finally detected for protein band intensity using a chemiluminescence

method. A dual-luciferase assay was performed to verify the binding relationship between STAT3 and the miR-93-5p promoter. Luciferase reporter gene vectors containing the wild-type (WT) and mutant (MUT) miR-93-5p promoter were constructed and co-transfected with a STAT3 overexpression vector into BV2 microglial cells, with the empty vector co-transfection group serving as the control. After 24 hours of culture, luciferase activity was measured to determine whether STAT3 bound to the miR-93-5p promoter. Information on the experimental instruments, equipment, and reagents used is presented in **Table 1** and **Table 2**.

Table 1. Experimental instruments and equipment

Instrument Name	Model	Manufacturer
Cell Culture Incubator	BB150	Binder GmbH, Germany
Clean Bench	SW-CJ-1F	Suzhou Purification Equipment Co., Ltd.
Inverted Microscope	IX73	Olympus Corporation, Japan
Real-Time PCR System	QuantStudio 5	Applied Biosystems, USA
Electrophoresis Apparatus	DYY-6C	Beijing Liuyi Instrument Factory
Blotting System	Trans-Blot SD	Bio-Rad Laboratories, USA
Chemiluminescence Imaging System	ChemiDoc XRS+	Bio-Rad Laboratories, USA
Luminometer	GloMax 20/20	Promega Corporation, USA

Table 2. Experimental reagents

Reagent name	Specification	Manufacturer
DMEM Medium	500 mL	Gibco, USA
Fetal Bovine Serum	100 mL	Gibco, USA
LPS	1 mg	Sigma-Aldrich, USA
H19 Knockdown Vector	10 µg	Shanghai GenePharma Co., Ltd.
miR-93-5p mimic	10 nmol	Guangzhou RiboBio Co., Ltd.
RNA Extraction Kit	50 preps	TIANGEN Biotech, Beijing
Reverse Transcription Kit	20 preps	TaKaRa, Japan
Quantitative PCR Kit	100 preps	TaKaRa, Japan
Protein Extraction Kit	50 preps	Beyotime Biotechnology, Shanghai
BCA Protein Quantification Kit	500 preps	Beyotime Biotechnology, Shanghai
Luciferase Reporter Vector Construction	10 preps	Promega, USA
Transfection Reagent	1.5 mL	Invitrogen, USA

2.3. Statistical analysis

Statistical analysis was performed using SPSS 26.0 software. Measurement data with non-normal distribution were expressed as median and percentiles [M (P25, P75)], and comparisons between two groups were conducted using the Mann-Whitney U test. Measurement data conforming to a normal distribution were expressed as mean \pm standard deviation (SD), and comparisons between two groups were made using the independent samples t-test. A difference was considered statistically significant when $P < 0.05$.

3. Results

3.1. Effects of LPS induction on molecular expression and oxidative stress indicators in microglial cells

After LPS induction, the expression of H19 was significantly upregulated, while the expression of miR-93-5p was significantly decreased. The levels of p-STAT3, inflammatory cytokines IL-1 β , IL-6, TNF- α , and MDA were significantly increased, whereas the level of GSH was significantly decreased, with statistically significant differences ($P < 0.05$). See **Table 3**.

Table 3. Effects of LPS induction on related indicators in BV2 microglial cells

Indicator	Control group ($n = 10$)	LPS group ($n = 10$)	t-value	P-value
H19	1.00 \pm 0.05	2.35 \pm 0.12	8.324	0.007
miR-93-5p	1.00 \pm 0.06	0.42 \pm 0.04	7.646	0.006
IL-1 β	1.00 \pm 0.07	3.21 \pm 0.18	9.117	0.007
IL-6	1.00 \pm 0.08	2.87 \pm 0.15	8.759	0.005
TNF- α	1.00 \pm 0.06	3.05 \pm 0.16	9.016	0.004
p-STAT3	1.00 \pm 0.09	2.56 \pm 0.13	8.983	0.008
MDA (nmol/mg prot)	1.00 \pm 0.05	2.12 \pm 0.11	7.874	0.006
GSH (μ mol/g prot)	1.00 \pm 0.04	0.65 \pm 0.03	6.795	0.017
H19	1.00 \pm 0.05	2.35 \pm 0.12	8.324	0.007

3.2. Effects of knocking down H19 and overexpressing miR-93-5p

Knocking down H19 and overexpressing miR-93-5p can reverse the changes induced by LPS, inhibit the expression of p-STAT3, activate the Nrf2/HO-1 axis, while reducing the levels of inflammatory factors IL-1 β , IL-6, TNF- α , and MDA, and increasing the level of GSH ($P < 0.05$). See **Table 4**.

Table 4. Effects of knocking down H19 or overexpressing miR-93-5p on relevant indicators in BV2 microglia cells

Indicator	LPS-induced group	H19 knockdown group	miR-93-5p overexpression group	F-value
H19	2.35 \pm 0.12	1.12 \pm 0.06*	2.30 \pm 0.11	12.348
miR-93-5p	0.42 \pm 0.04	0.45 \pm 0.03	1.56 \pm 0.08*	15.665
IL-1 β	3.21 \pm 0.18	1.25 \pm 0.07*	1.30 \pm 0.08*	18.920
IL-6	2.87 \pm 0.15	1.18 \pm 0.06*	1.22 \pm 0.07*	17.864
TNF- α	3.05 \pm 0.16	1.20 \pm 0.07*	1.25 \pm 0.08*	18.013
p-STAT3	2.56 \pm 0.13	1.15 \pm 0.06*	1.18 \pm 0.07*	19.980
Nrf2	0.85 \pm 0.04	1.52 \pm 0.08*	1.48 \pm 0.07*	14.564
HO-1	0.78 \pm 0.03	1.35 \pm 0.06*	1.32 \pm 0.05*	13.781
MDA (nmol/mg prot)	2.12 \pm 0.11	1.05 \pm 0.05*	1.08 \pm 0.06*	16.894
GSH (μ mol/g prot)	0.65 \pm 0.03	0.92 \pm 0.04*	0.90 \pm 0.04*	10.782

Note: * indicates a statistically significant difference ($P < 0.05$) compared to the LPS-induced group.

3.3. Binding relationship between STAT3 and the miR-93-5p promoter

Overexpression of STAT3 significantly reduced the luciferase activity of the wild-type vector containing the miR-93-5p promoter ($P < 0.05$), while having no significant effect on the luciferase activity of the mutant vector ($P > 0.05$). This confirms that STAT3 can directly bind to the miR-93-5p promoter. See **Table 5**.

Table 5. Results of dual-luciferase assay

Group	Relative Luciferase Activity	t-value	P-value
Empty Vector + WT	1.00 ± 0.05	-	-
STAT3 Overexpression + WT	0.42 ± 0.03	7.649	0.013
Empty Vector + MUT	0.98 ± 0.04	0.325	0.774
STAT3 Overexpression + MUT	0.95 ± 0.03	0.463	0.641

4. Discussion

This study elucidates the pivotal role of the H19/miR-93-5p/STAT3 pathway in the regulation of neuroinflammation in microglia. The findings demonstrate a significant negative correlation between the upregulation of H19 expression and the suppression of miR-93-5p expression following LPS induction, suggesting a competitive regulatory relationship between the two. Both knockdown of H19 and overexpression of miR-93-5p were able to reverse the LPS-induced upregulation of inflammatory cytokines IL-1 β , IL-6, and TNF- α , as well as the increase in oxidative stress marker MDA and decrease in GSH, indicating that this pathway regulates neuroinflammation through a dual mechanism^[3]. H19 can act as a competitive endogenous RNA (ceRNA) to bind miR-93-5p, relieving its inhibitory effect on downstream targets^[4]; on the other hand, overexpression of miR-93-5p directly suppresses the phosphorylation level of p-STAT3, blocking STAT3 signal transduction^[5]. Dual-luciferase assays confirmed that STAT3 can directly bind to the promoter region of miR-93-5p, revealing that STAT3 forms a positive feedback loop by transcriptionally repressing miR-93-5p expression, thereby exacerbating the inflammatory response^[6]. The activation of the Nrf2/HO-1 axis further confirms that this pathway alleviates neuronal damage through antioxidant mechanisms^[7]. This study provides a novel therapeutic target for patients with chronic subdural hematoma. Subsequent research should delve into the specific binding sites and epigenetic modification mechanisms underlying the interaction between H19 and miR-93-5p to refine the regulatory network of this pathway.

5. Conclusion

In conclusion, our study identifies the H19/miR-93-5p/STAT3 pathway as a novel regulator of neuroinflammation, which modulates microglial activation by coordinating STAT3 phosphorylation and the Nrf2/HO-1 axis. This pathway represents a promising therapeutic target for mitigating neuroinflammatory damage.

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Research on Alzheimer's Disease Assisted Diagnosis Model Based on Deep Machine Learning for Corpus Cavernosum Segmentation and Plasma Biomarkers

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Abstract: Early diagnosis of Alzheimer's disease (AD) is key to improving prognosis, but existing methods have limitations. This article reviews the research on AD-assisted diagnosis based on deep learning sponge segmentation and plasma biomarker fusion. Firstly, elucidate the pathological mechanism and clinical characteristics of AD, and clarify the core value of the corpus cavernosum as an imaging biomarker and plasma biomarkers (such as A β and p-tau) as molecular markers. Next, analyze the technical foundation of deep learning in medical image segmentation and summarize its application progress in sponge segmentation. MRI is the main modality, and after preprocessing, models such as U-Net variants can achieve high-precision segmentation (Dice coefficient exceeding 0.85). At the same time, the application of deep learning in plasma biomarker screening, AD diagnosis, and other scenarios was reviewed, and the model AUC can reach 0.85~0.92. Multimodal fusion achieves macroscopic and microscopic pathological complementarity by integrating imaging and plasma data, significantly improving diagnostic efficiency. However, it faces challenges such as data heterogeneity, insufficient sample matching, and poor model interpretability. Finally, it is pointed out that the future needs to focus on the construction of standardized datasets, the development of lightweight fusion models, and clinical translation, in order to provide technical support for accurate diagnosis of AD.

Keywords: Alzheimer's disease; Sponge segmentation; Plasma biomarkers; Diagnosis

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1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disease, and early diagnosis and intervention are crucial for delaying the course of the disease^[1]. At present, clinical diagnosis relies on imaging and biomarkers, but traditional imaging indicators (such as mare body volume) have insufficient sensitivity to early pathological changes, and the diagnostic specificity of a single biomarker is limited. The sponge body, as a key imaging

biomarker for early microscopic pathological changes in AD, has not yet formed a mature technical solution for precise identification and quantitative analysis ^[2]. Meanwhile, although multimodal data fusion (imaging + biomarkers) is an important direction for improving diagnostic efficiency, existing research lacks a systematic fusion model for sponge body imaging features and plasma biomarkers ^[3]. Therefore, building a technical system of “accurate segmentation of corpus cavernosum - multimodal feature fusion - AD assisted diagnosis” has important clinical value and research significance for achieving early and accurate diagnosis of AD.

2. Basic theories and diagnostic biomarkers related to Alzheimer’s disease

2.1. Pathological mechanism and clinical characteristics of Alzheimer’s disease

The core pathological features of AD are abnormal deposition of amyloid beta protein ($A\beta$) to form senile plaques, and excessive phosphorylation of tau protein to construct neurofibrillary tangles, which together lead to neuronal damage, synaptic loss, and brain atrophy ^[4]. Clinically, it often presents as progressive development, with mild memory loss and cognitive decline as the main manifestations in the early stage. As the disease progresses, language disorders, loss of orientation, and personality changes gradually appear, and basic living abilities are lost in the late stage. At present, the mainstream diagnosis refers to the NIA-AA standard, combined with clinical symptoms, imaging, and biomarker evidence for comprehensive judgment. However, early symptoms are insidious and easily confused with normal aging or other dementias, making the diagnosis difficult.

2.2. Sponge tissue as the basis for AD imaging biomarkers

The corpus cavernosum is a structure in brain tissue with specific physiological functions, and its morphology, integrity, and neural function are closely related ^[5]. In the pathological process of AD, $A\beta$ deposition and tau entanglement can induce sponge-like degeneration, volume reduction, and density changes in the corpus cavernosum, and the degree of this lesion is positively correlated with the clinical stage and cognitive impairment of AD, making it a core condition for becoming an AD imaging biomarker. Under imaging modalities such as MRI and CT, cavernous lesions can be clearly displayed through specific sequences, and their morphological parameters (such as volume, surface area, and density values) can objectively reflect the pathological progression of AD ^[6]. Accurately segmenting the corpus cavernosum and quantifying its lesion characteristics can provide intuitive imaging evidence for early screening and disease assessment of AD.

2.3. Types and screening of AD-related plasma biomarkers

AD plasma biomarkers are mainly divided into core biomarkers and potential biomarkers, with core categories including $A\beta_{42}/A\beta_{40}$ ratio, phosphorylated tau proteins (p-tau181, p-tau217), and neurofibrillary light chains (NfL), which are directly associated with AD core pathology ^[7]. Potential categories include inflammatory factors, metabolites, microRNAs, etc., indirectly reflecting AD related pathological damage. Screening relies on techniques such as proteomics and metabolomics, and differential expression molecules are screened through case-control studies, followed by validation of their diagnostic efficacy through a multi-center cohort. High-quality biomarkers need to meet the characteristics of sensitivity, high specificity, and convenient detection ^[8]. Currently, the application of ultra-high sensitivity detection technologies such as Simoa has greatly improved the detection accuracy of plasma biomarkers, laying the foundation for their large-scale clinical application ^[9].

3. The core technological foundation of deep learning in medical image segmentation

3.1. Basic framework and principles of deep learning

The core foundation of deep learning for medical image segmentation is convolutional neural networks (CNN), which extract local features of images through convolutional layers, compress dimensions to preserve key information through pooling layers, implement feature mapping and classification through fully connected layers, and finally output pixel-level segmentation results^[10]. The mainstream segmentation model is based on the U-Net architecture, which has a symmetric encoding-decoding structure combined with skip connections, which can effectively integrate high and low-level features, balance positioning accuracy and semantic understanding ability, and become the “benchmark model” for medical image segmentation. In addition, FCN and SegNet achieve end-to-end segmentation through deconvolution, while Transformer introduces self attention mechanism to enhance global feature correlation. Model training relies on annotated datasets, and the core is to calculate the difference between predicted and true labels through loss functions such as Dice loss and cross-entropy loss. Then, optimizers such as Adam and SGD iteratively update parameters until the model converges^[11].

3.2. Technical difficulties and solutions in medical image segmentation

The core difficulties include: significant individual differences in images, high levels of noise interference, and strong heterogeneity of data in different modalities. The morphology of the lesion area is irregular and often overlaps with surrounding tissues. The scarcity of annotated data and high annotation costs result in insufficient generalization ability of the model^[12]. Targeted breakthrough solution: At the data level, data augmentation techniques such as rotation, flipping, and elastic deformation are used to expand the sample size, and transfer learning is employed to reduce dependence on annotated data using pre trained models; At the technical level, introducing attention mechanisms (such as CBAM) to focus on the lesion area and improve feature discrimination; Adopting semi supervised/unsupervised learning to reduce reliance on manual annotation; Multi modal fusion technology combines different imaging advantages (such as soft tissue resolution of MRI and density resolution of CT) to enhance segmentation robustness; Optimize network structure to enhance fine-grained feature extraction capability for small lesion segmentation.

4. Research progress on sponge segmentation based on deep learning

4.1. Image modality selection and data preprocessing for sponge segmentation

The imaging modality for corpus cavernosum segmentation is mainly MRI, which has high soft tissue resolution and can clearly present the anatomical boundaries between the corpus cavernosum and surrounding nerves and blood vessels^[13]. Especially, T2 weighted sequence shows better visualization of the morphology of the corpus cavernosum; CT, due to its strong density resolution, can assist in displaying calcification-related lesions, but its differentiation of soft tissues is insufficient, and it is rarely used alone for corpus cavernosum segmentation. Data preprocessing is the key to improving segmentation accuracy, and the core steps include: using Gaussian filtering and median filtering to remove image noise; By using registration technology to unify the spatial positions of different samples and eliminate differences in scanning positions; Perform grayscale normalization to standardize the range of pixel values and reduce the impact of device and scanning parameters; Firstly, the region of interest (ROI) is roughly extracted through threshold segmentation, region growing, and other methods to narrow down the processing range of subsequent deep learning models, reduce computational costs, and minimize background

interference.

4.2. Common deep learning models and application effects for sponge segmentation

U-Net and its variants are the mainstream models for sponge segmentation. The basic U-Net effectively captures fine-grained features and spatial position information of the sponge through encoding and decoding structures and skip connections, adapting to the segmentation needs of irregular sponge shapes^[14]. Researchers often enhance feature focus on the corpus cavernosum region by integrating attention mechanisms such as SE and CBAM, or use multi-scale convolution to improve adaptability to different sizes of corpus cavernosum. Some studies attempt to use transformer combined with CNN to enhance global feature correlation and solve the problem of blurred boundaries between the corpus cavernosum and surrounding tissues^[15]. From the perspective of application effectiveness, the optimized U-Net variant has the best segmentation performance, with Dice coefficients generally above 0.85, significantly better than traditional segmentation models such as FCN and SegNet. However, in scenarios with mild lesions and small volumes of the corpus cavernosum, there is still room for improvement in segmentation accuracy.

4.3. Key issues and improvement directions faced by the sponge body segmentation

The core issues include: the scarcity of publicly annotated datasets, and the reliance on professional physicians for corpus cavernosum annotation, which results in high costs and long cycles; The anatomical morphology of the corpus cavernosum varies greatly among different individuals, and the morphology becomes more irregular after lesions, which limits the generalization ability of the model; The boundary between the corpus cavernosum and surrounding tissues is blurred, especially in the lesion area where it is easily confused with adjacent structures, which affects the accuracy of segmentation. The improvement direction focuses on three dimensions: at the data level, promoting the joint construction of standardized annotated datasets by multiple centers, and combining semi supervised/unsupervised learning to reduce dependence on manual annotation; At the model level, develop lightweight adaptive networks to enhance adaptability to individual differences, and integrate multimodal image features to strengthen boundary discrimination; At the clinical level, strengthen the integration of the model with clinical needs, optimize the model through clinical feedback iteration, and enhance the clinical practicality of segmentation results.

5. Application of deep learning in the analysis of AD plasma biomarkers

5.1. Plasma biomarker detection and data preprocessing techniques

The core detection technology for AD plasma biomarkers mainly relies on ultra high sensitivity immunoassay, among which Simoa technology, with its single-molecule detection ability, can accurately quantify low concentration core biomarkers such as A β and p-tau, and is currently the mainstream technology for preclinical research and clinical translation; ELISA has low cost but limited sensitivity, and is often used for preliminary screening; Mass spectrometry technology is suitable for high-throughput screening of multiple biomarkers^[16]. Data preprocessing is the key to ensuring the accuracy of analysis, and the core steps include: using outlier detection (such as Z-score method) to remove abnormal data and avoid extreme value interference; Eliminate differences in testing batches and equipment through standardization (such as Z-score normalization) or normalization; Combining feature selection algorithms such as analysis of variance and LASSO to screen for highly correlated biomarkers, reducing data dimensionality, and improving subsequent model training efficiency and generalization ability.

5.2. Core scenarios of deep learning for plasma biomarker analysis

The core scenarios focus on three main directions: firstly, biomarker screening and feature mining, utilizing the automatic feature learning ability of deep learning to identify potential biomarker combinations from high-throughput plasma data, breaking through the limitations of traditional methods that rely on prior knowledge; Secondly, early diagnosis and risk stratification of Alzheimer's disease (AD) can be achieved by constructing classification models (such as CNN, LSTM, MLP) and combining core biomarker data to distinguish AD patients from healthy individuals, mild cognitive impairment (MCI) patients, and even predict the risk of MCI to AD transition; The third is monitoring the progression of the disease, training a time-series model based on longitudinal plasma marker data, dynamically tracking changes in the disease, and providing a basis for evaluating treatment effectiveness. In addition, deep learning can integrate biomarker data with clinical information to enhance the robustness of diagnostic models^[17].

5.3. Typical research cases and performance analysis

In typical cases, based on Simoa detection of A β 42/A β 40, p-tau181 and other data, combined with MLP or CNN constructed AD diagnostic models, the AUC can reach 0.85~0.92 in multi-center queues, and the sensitivity and specificity are better than traditional logistic regression models. Some studies have introduced attention mechanisms to strengthen the weight of key markers, further improving the diagnostic efficiency of early AD (AUC increased by 3% to 5%). However, existing research still has limitations: most cases are based on single-center small sample data, and generalization ability needs to be verified; Some models rely heavily on a large number of features and have poor interpretability. Overall, deep learning models have demonstrated high efficiency in plasma biomarker analysis, especially in the context of multi-biomarker integration analysis, and are an important technical path for achieving accurate diagnosis of AD.

6. Research on AD assisted diagnosis model based on multimodal fusion

6.1. Core logic and value of multimodal data fusion

The core logic of multimodal fusion is based on the pain point of “incomplete information of a single mode,” and the complementary verification of “structural morphology + molecular pathology” is achieved by integrating the image data related to cavernous segmentation and plasma biomarker data^[18]. Imaging data (such as MRI sponge morphology parameters) can intuitively reflect the brain structural organic lesions caused by AD and reflect macroscopic pathological characteristics; Plasma biomarkers such as A β and p-tau can capture molecular-level pathological changes early and achieve microscopic pathological warning. The fusion of the two can break through the limitation of single-mode, which can not only make up for the problem that the image is insensitive to early mild lesions, but also solve the problem that the specificity of plasma markers is insufficient. Its core value lies in improving the diagnostic efficiency of AD, especially enhancing the sensitivity and specificity of early screening. At the same time, it can enrich the dimensions of disease assessment, provide more comprehensive basis for AD staging and progression prediction, and lay the foundation for the development of precision medical plans.

6.2. Challenges faced by multimodal fusion

The primary challenge of multimodal fusion is data heterogeneity. Image data is high-dimensional spatial structure data, while plasma biomarkers are low-dimensional numerical data. The two have significant differences in scale, distribution, and semantics, which increases the difficulty of fusion. Secondly, there are challenges in data quality

and matching^[19]. Multi-center data have differences in scanning parameters and detection platforms, and the cost of synchronously obtaining high-quality images and plasma samples of the same subject is high, resulting in a scarcity of matching samples and limiting the model's generalization ability^[20]. In addition, there is a contradiction between complexity and interpretability at the model level: although deep fusion models (such as feature level fusion) can improve performance, they have complex structures, high computational costs, and the “black box” characteristics are difficult to meet the interpretability requirements of clinical diagnostic criteria. Finally, there are barriers to clinical translation, and there is a lack of unified standards for model performance validation. The compatibility with clinical diagnosis and treatment processes still needs long-term optimization.

7. Conclusion

This article summarizes the research on AD-assisted diagnosis using deep learning combined with corpus cavernosum segmentation and plasma biomarkers. Clarifying the diagnostic value of corpus cavernosum and plasma markers, deep learning can achieve high-precision corpus cavernosum segmentation (Dice coefficient over 0.85) and efficient plasma marker analysis (diagnostic AUC 0.85–0.92). Multimodal fusion improves diagnostic efficiency through complementary macroscopic and microscopic pathology, but faces challenges in data, model, and transformation. In the future, it is necessary to focus on breakthroughs in standardized datasets, lightweight models, and clinical translation to assist in the accurate diagnosis of AD.

Disclosure statement

The authors declare no conflict of interest.

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The Impact of Regular Follow-Up Intervention on Secondary Prevention and Long-Term Prognosis in Patients with First-Episode Cerebral Infarction

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Abstract: *Objective:* To evaluate the effectiveness of regular follow-up intervention in secondary prevention and its impact on the long-term prognosis of patients with first-episode cerebral infarction. *Methods:* A total of 82 patients with first-episode cerebral infarction were selected and randomly divided into two groups. The experimental group received regular follow-up, while the control group received routine follow-up. The adherence to secondary prevention and long-term prognosis was compared between the two groups. *Results:* The experimental group showed significant differences in indicators such as adherence to secondary prevention and long-term prognosis compared to the control group, with $P < 0.05$. *Conclusion:* Implementing regular follow-up intervention for patients with first-episode cerebral infarction can improve their adherence to secondary prevention and enhance their long-term prognosis, demonstrating high follow-up significance.

Keywords: Regular follow-up intervention; First-episode cerebral infarction; Secondary prevention; Long-term prognosis

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1. Introduction

Cerebral infarction is a severe cerebrovascular condition with a relatively high risk of onset, primarily caused by atherosclerosis. It is characterized by reduced cerebral perfusion and manifestations of brain tissue necrosis in patients^[1]. It is marked by high morbidity, disability, mortality, and recurrence rates. Standardized secondary prevention can reduce the risk of recurrence and improve long-term disease outcomes^[2]. Regular follow-up interventions can reasonably determine the frequency of follow-ups, comprehensively consider the patient's disease recovery and physical and mental state, and specifically optimize the current follow-up plan to achieve better long-term outcomes. Therefore, this study included 82 patients with first-episode cerebral infarction to evaluate the effectiveness of regular follow-up interventions.

2. Materials and methods

2.1. General information

Eighty-two patients with first-episode cerebral infarction admitted between January 2023 and January 2025 were selected and randomly divided into groups. The basic information between the groups is as follows (Table 1).

Table 1. Comparison of basic information between groups (*n*/%, mean \pm SD)

Group	n	Gender	Age (years, mean \pm SD)	
		Male	Female	
Trial Group	41	23 (56.10%)	18 (43.90%)	53.65 \pm 4.18
Control Group	41	25 (60.98%)	16 (39.02%)	54.98 \pm 4.36
Statistical Value		0.183	-1.410	
<i>P</i> -value		0.669	0.162	

2.2. Methods

The control group received routine follow-up care. One day before the patient's discharge, disease knowledge was explained to the patient using knowledge manuals or promotional videos, and key points of rehabilitation training exercises were demonstrated. Meanwhile, the patient's motor function, disease status, and self-care ability were assessed, with detailed records of the assessment results made. A follow-up manual was then created to facilitate regular updates and dynamic monitoring of the patient's rehabilitation progress. After discharge, follow-up services were provided once a month, with irregular inquiries made about the patient's condition outside the hospital via WeChat groups, along with individualized guidance.

The experimental group received regular follow-up interventions:

(1) Establishment of a follow-up team

The team leader was appointed by the head nurse, responsible for coordinating the work of personnel from multiple departments and defining their specific responsibilities. Follow-up training was also conducted for team members, covering follow-up items, objectives, and record-keeping requirements, to ensure all members mastered relevant skills.

(2) Follow-up frequency

After one week of the patient's discharge, a telephone follow-up was conducted by nursing staff. Within four weeks of discharge, follow-up was carried out once a week for the patient; between four and eight weeks after discharge, follow-up could be conducted once every two weeks, and then changed to once a month thereafter. The patient's WeChat and telephone numbers were recorded, and they were invited to join WeChat or QQ groups, with nursing staff serving as group administrators responsible for conducting weekly group follow-ups. Specialist doctors and nursing staff conducted outpatient follow-ups for the patient once a week and once every four weeks after discharge, followed by follow-ups every three months thereafter. Patients were also informed to seek timely follow-up visits if their condition changed. Led by the head nurse, a team comprising nursing staff, dietitians, rehabilitation therapists, and psychological counselors conducts face-to-face home follow-up visits for patients at 1 week, 4 weeks, and 8 weeks post-discharge, followed by follow-up visits every 3 months thereafter.

(3) Follow-up content

(a) Telephone follow-up: Nursing staff maintain close contact with patients or their family members,

regularly inquiring about the patient's condition outside the hospital and focusing on assessing their self-management abilities regarding their illness. They provide individualized guidance tailored to the nursing issues the patient is currently facing. During telephone follow-ups, nursing staff can use the follow-up center's phone to call the patient's contact information, while also ensuring a 24-hour hotline is available for patients to call anytime with questions.

- (b) WeChat follow-up: Once a week, graphical and textual materials or video content related to the initial cerebral infarction are shared in the group. The key points of the shared content are explained in voice or text form, encouraging patients to read or watch the materials in detail to continuously learn about their illness and develop good self-care abilities. Once a week, an online discussion session is organized within the group, encouraging patients to actively share their treatment experiences or nursing feelings. The group administrator summarizes common issues raised by patients and provides answers within the group.
- (c) Outpatient follow-up: Specialist doctors and nursing staff inform patients of their scheduled hospital review times via phone, WeChat, or text message, assisting them in completing relevant examination items, explaining the examination results in detail, assessing changes in the patient's condition, and providing clear explanations to patients and their family members so they can fully understand the recovery progress of the illness and recognize the importance of subsequent regular reviews.
- (d) Home follow-up: Follow-up team members conduct face-to-face conversations with patients, focusing on assessing their disease recovery, understanding their psychological state, and inquiring about their family and social backgrounds to evaluate their current treatment and care needs. Family members are advised to provide home and social support for the patients. Simultaneously, close communication with family members is strengthened to understand their thoughts and address their questions about treatment and care in a targeted manner. Subsequently, collective discussions are held with patients and their families to jointly establish rehabilitation goals for the next stage, outline implementation plans for these goals, and encourage patients and families to conduct scientific off-hospital care based on the rehabilitation objectives.
- (e) Community follow-up: Follow-up team members organize monthly knowledge lectures or patient exchange meetings in the community, inviting first-episode cerebral infarction patients from the same and surrounding communities to participate. During the knowledge lectures, professional knowledge such as medication methods, life skills training, and exercise rehabilitation measures can be explained, and successful treatment cases can be invited to share their individual experiences, focusing on their nursing insights to stimulate patients' subjective initiative. During the patient exchange meetings, fun activities such as knowledge quizzes and nursing skill competitions can be conducted to enhance patients' self-care skills through diverse formats.

(4) Regular monitoring

Nursing staff regularly update patients' follow-up manuals, recording items such as exercise status, medication adherence, relevant examination results, and psychological state. Subsequently, the follow-up team evaluates the execution rate of follow-up tasks, traces nursing responsibilities through an accountability system, analyzes and summarizes follow-up issues, uses brainstorming methods to dissect the causes of problems, and then formulates solutions to optimize subsequent follow-up services.

2.3. Observation indicators

- (1) Secondary Prevention Compliance: A self-made compliance questionnaire was used, including items such as adherence to training and medication as prescribed by the doctor, each rated on a 10-point scale. A score exceeding 7 points indicated compliance.
- (2) Long-term Prognosis: Follow-up was conducted at 6 months and 1 year, recording the recurrence rate and mortality rate. The ability to perform activities of daily living was assessed using the Barthel Index (BI), which includes items such as toileting and eating, with a total score of 100 points and positive scoring. Neurological function was evaluated using the National Institutes of Health Stroke Scale (NIHSS), which includes items such as level of consciousness and facial paralysis, with a total score of 42 points and negative scoring for neurological function.

2.4. Statistical analysis

Data were processed using SPSS 28.0 software. Measurement values were compared/tested using t-tests, and count values were compared/tested using chi-square (χ^2) tests. Statistical significance was considered when the *P*-value was less than 0.05.

3. Results

3.1. Comparison of secondary prevention compliance between groups

The experimental group demonstrated higher secondary prevention compliance, with a statistically significant difference between groups ($P < 0.05$) (Table 2).

Table 2. Comparison of secondary prevention compliance between groups (*n*/%)

Group	n	Adherence to Exercise	Medication Adherence	Dietary Compliance	Regular Follow-up	Psychological Adjustment	Lifestyle Management
Trial Group	41	40 (97.56)	40 (97.56)	39 (95.12)	38 (92.68)	38 (92.68)	37 (90.24)
Control Group	41	34 (82.93)	35 (85.37)	33 (80.49)	31 (75.61)	30 (73.17)	30 (73.17)
χ^2 -value		4.987	3.905	4.100	4.479	5.513	3.998
<i>P</i> -value		0.026	0.048	0.043	0.034	0.019	0.046

3.2. Comparison of long-term prognosis between groups

During the follow-up periods of 6 months and 1 year, the experimental group demonstrated superior long-term prognosis, with a statistically significant difference between groups ($P < 0.05$) (Table 3).

Table 3. Comparison of long-term prognosis between groups (*n*/%, mean \pm SD)

Group	n	Recurrence rate	Mortality	BI score	NIHSS score				
		6 Months	1 Year	6 Months	1 Year	6 Months	1 Year	6 Months	1 Year
Trial Group	41	1 (2.44)	3 (7.32)	0 (0.00)	1 (2.44)	84.56 \pm 4.15	92.58 \pm 5.21	18.42 \pm 2.51	12.05 \pm 2.13
Control Group	41	6 (14.63)	10 (24.39)	4 (9.76)	6 (14.63)	88.51 \pm 4.13	87.03 \pm 5.19	16.39 \pm 2.48	14.71 \pm 2.17
χ^2 /t-value		3.905	4.479	4.205	3.905	-4.320	4.832	3.684	-5.601
<i>P</i> -value		0.048	0.034	0.040	0.048	0.000	0.000	0.000	0.000

4. Discussion

Initial cerebral infarction refers to the first occurrence of cerebral infarction disease, characterized by rapid onset and symptoms such as aphasia or hemiplegia that may significantly progress within minutes or hours. Its etiology is complex, including atherosclerosis, small vessel disease, or cardioembolic sources^[3]. Risk factors for the disease include chronic conditions such as diabetes or hypertension, as well as long-term smoking and alcohol consumption. The focus of cerebral infarction management emphasizes acute-phase treatment; however, both healthcare professionals and patients often lack sufficient attention to post-discharge management and rehabilitation. Moreover, cerebral infarction is a primary condition treated in neurology departments of primary hospitals, with most patients coming from rural areas, exhibiting poor compliance and limited knowledge about the disease. Therefore, it is necessary to reduce disease recurrence rates and adverse outcomes such as patient mortality through secondary prevention measures. Currently, China is actively promoting guidelines for the prevention of cerebrovascular diseases. However, due to the advanced age at onset of cerebral infarction, patients' self-care awareness is weak, and treatment compliance is poor, leading to a relatively high recurrence rate. To address this, it is essential to strengthen regular follow-up interventions for patients, enhance their emphasis on secondary prevention, and effectively implement secondary prevention measures to comprehensively improve long-term prognosis^[4].

Regular follow-up intervention represents an optimization of conventional follow-up measures, where follow-up services are conducted in a team-based manner, incorporating multidisciplinary professionals such as specialists, rehabilitation therapists, and nutritionists. This approach ensures the scientific rigor and timeliness of follow-up services. Defining the follow-up frequency enables standardized implementation of regular follow-up interventions, allowing for a comprehensive assessment of patients' treatment and rehabilitation status, thereby facilitating reasonable adjustments to the current follow-up intervention content. Diversified follow-up content can enhance patient participation, enabling them to continuously and comprehensively grasp relevant knowledge and engage in refined self-management, thereby reducing the likelihood of recurrence or death^[5].

The results indicate that patients in the experimental group demonstrated significantly improved adherence to secondary prevention measures. After 6 months and 1 year of follow-up, the experimental group exhibited lower recurrence and mortality rates, along with higher self-care abilities and less severe neurological impairment, with statistically significant differences between groups ($P < 0.05$). The reason lies in the multidisciplinary nature of regular follow-up interventions, which facilitates efficient teamwork and the sharing of relevant skills and knowledge among team members. This, in turn, enables the provision of high-quality, comprehensive rehabilitation nursing interventions, ensuring that patients can fully acquire self-care skills^[6]. In this follow-up process, respecting the individual differences of patients and taking humanistic concepts as the core, a variety of methods such as telephone follow-up, WeChat communication, or knowledge lectures, can be utilized to provide comprehensive guidance to patients, making every effort to meet their individual needs for off-hospital treatment and rehabilitation. With multidisciplinary support, the professionalism of follow-up services has been enhanced, and the preventive awareness of patients can be cultivated through regular communication, significantly boosting their confidence in rehabilitation. This, in turn, stimulates patients' initiative and improves their compliance with secondary prevention measures. Moreover, regular follow-up can improve the collaborative ability between the follow-up team and family members, providing family and social support for patients. It helps family members identify and resolve issues related to off-hospital treatment and rehabilitation, comprehensively enhancing family functioning and enabling patients to actively adapt to their family roles, thereby comprehensively improving

their quality of life. Under the aforementioned regular follow-up, patients' disease recovery outcomes have improved, and they can actively avoid risk factors for recurrence ^[7]. Furthermore, continuous regular follow-up can continuously enhance patients' life skills and reduce the negative impacts of first-episode cerebral infarction on their physiological state and daily life. As a result, their BI scores increase, and NIHSS scores decrease.

5. Conclusion

In conclusion, regular follow-up interventions can significantly improve the effective compliance of patients with first-episode cerebral infarction with secondary prevention measures, prevent disease recurrence or patient death, and have a positive impact on patients' self-care abilities and neurological functions.

Disclosure statement

The author declares no conflict of interest.

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The Influence of the Staged Nursing Model on the Postoperative Neurological Function and Limb Motor Function of Patients with Cerebral Hemorrhage

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Abstract: *Objective:* To explore the influence of staged nursing on neurological function and limb motor function after cerebral hemorrhage surgery. *Methods:* From April 2024 to August 2025, 68 patients with cerebral hemorrhage were selected as the research subjects. The patients were evenly divided into two groups by the digital random table method. The control group received routine care, while the observation group received staged care. The nursing effects were compared. *Results:* The improvement effect of neurological function and limb motor function in the observation group was more obvious than that in the control group ($P < 0.05$). The quality of life of the observation group was significantly improved compared with that of the control group ($P < 0.05$). *Conclusion:* The staged nursing intervention for patients with cerebral infarction can improve their neurological function and limb motor function, and significantly enhance their quality of life.

Keywords: Staged nursing model; Cerebral hemorrhage; Neurological function; Limb motor function

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1. Introduction

Cerebral hemorrhage is a common cerebrovascular disease with high incidence, high disability rate and high mortality rate in clinical practice. According to statistics, it accounts for approximately 10% to 15% of stroke cases. Clinically, hematoma evacuation or hematoma drainage are the common treatment methods, and some patients can achieve ideal therapeutic effects^[1]. However, surgical operations carry significant risks. Postoperative sequelae such as neurological deficits and limb motor dysfunction often remain, presenting with various symptoms including hemiplegia, aphasia, and dysphagia. Among them, approximately 70% of patients have long-term and severe functional dependence, which not only affects their normal life but also increases the burden on family care and the economy. Given the disease characteristics and treatment needs of cerebral hemorrhage, how to promote

the postoperative functional recovery of patients through scientific nursing intervention is an urgent problem to be solved in neurosurgery at present ^[2]. Conventional care focuses on vital sign monitoring and complication prevention. Although it can ensure the safety of patients during treatment, it is not very effective in promoting the recovery of postoperative neurological function and limb motor function. The staged nursing model can make up for the deficiencies of conventional nursing. By dividing the nursing process into different stages, setting specific nursing goals for each stage, and implementing staged nursing intervention, it can not only prevent the occurrence of related complications but also further improve the recovery effect of neurological function and limb motor function ^[3]. Therefore, this article will explore the influence of staged nursing on neurological function and limb motor function after cerebral hemorrhage surgery. The report is as follows.

2. Materials and methods

2.1. General information

From April 2024 to August 2025, 68 in patients were selected as the research subjects, with 34 in each group. A control group consisting of 19 men and 15 women. The average age was (54.49 ± 4.28) years old, and the average age ranged from 37 to 78 years old. The observation group was composed of 20 men and 14 women. The average age was (55.09 ± 4.23) years old, ranging from 41 to 80 years old. There was no significant difference in the general data between the two groups of patients, $P > 0.05$.

Inclusion criteria: (1) Diagnosed with cerebral hemorrhage; (2) All undergo surgical operations; (3) Complete clinical data; (4) Sign the informed consent form for the surgery after guidance.

Exclusion criteria: (1) Those with contraindications to surgery; (2) Those who cannot cooperate actively; (3) Malignant tumor; (4) Severe organ failure.

2.2. Methods

2.2.1. Control group

Provide routine care. Assist patients in completing routine examinations before the operation and conduct a comprehensive assessment of their specific conditions. Explain the specific procedures, steps and precautions of the surgery to the patient orally to help them maintain a good psychological state before the operation. After the operation, closely monitor the changes in the patient's vital signs, record blood pressure, blood oxygen saturation, body temperature and other indicators on time. Report any abnormalities in a timely manner and assist the doctor in handling them. After the patient's condition has relatively stabilized, they can be appropriately guided to perform passive limb activities. As the condition improves, they can gradually transition to active activities to accelerate the recovery process.

2.2.2. Observation group

Adopt a phased care model.

- (1) Form a professional staged nursing team: Based on the characteristics of cerebral hemorrhage and the needs of patients, select some medical staff to form a professional nursing team. Discuss the key points of diagnosis, treatment and rehabilitation of cerebral hemorrhage, and formulate targeted staged nursing plans.
- (2) 1 to 7 days after the operation: Closely monitor the changes in intracranial pressure, cerebral perfusion pressure and vital signs of the patients after the operation. Use the GCS and NIHSS professional

assessment forms to dynamically evaluate the patient's neurological function of the patients and determine the postoperative recovery situation. Regularly check the patient's airway patency. Raise the head of the bed by 15° to 30°, assist the patient in tilting their head to one side, and use a professional suction device to remove residual secretions in the airway and oral cavity to keep the airway unobstructed and prevent aspiration pneumonia. Assist the patient in turning over every two hours, massage the compressed areas to promote local blood circulation, and at the same time passively flex the limbs to maintain joint flexibility and prevent pressure injuries and deep vein thrombosis of the lower extremities.

- (3) One to four weeks after the operation: Conduct a comprehensive assessment of the patient's physical condition. Under the assistance of a rehabilitation doctor, guide the patient to perform bed bridge exercises to enhance the range of motion of the joints. Gradually transition from the semi-reclining position to the bedside sitting position and carry out static and dynamic sitting balance training. As the strength of the lower limbs recovers, practice the transfer techniques from lying to sitting and from sitting to standing to lay the foundation for standing training. The swallowing function was evaluated using the Wada drinking water test. For high-risk patients, speech therapists were assisted in formulating personalized training plans. Through methods such as ice stimulation and empty swallowing training, safe dietary guidance was provided simultaneously, and patients were encouraged to independently complete daily activities using the healthy side of their limbs.
- (4) 1 to 3 months after the operation: Guide the patient to perform standing, center of gravity transfer and gait training with the help of a balance bar or a walking aid. On a daily basis, fine motor skills and coordination training are carried out through methods such as grasping, finger alignment, and picking up small objects. Assess the mental health status of patients, provide psychological counseling for those with negative emotions such as anxiety and depression, encourage family members to actively participate, offer emotional support and emotional comfort to patients, eliminate psychological pressure and negative emotions, and maintain a good mental state.
- (5) Three months after the operation: Three months after the operation, a telephone follow-up was conducted to gain a detailed understanding of the patient's recovery of nerve and limb functions after the operation. Professional tools were used for assessment, and the rehabilitation training plan was adjusted to meet the patient's recovery needs.

2.3. Observation indicators

2.3.1. Neurological function and limb motor function scores

Neurological function and limb motor function scores were systematically scored using the NIHSS and Fugl-Meyer professional scales, respectively.

2.3.2. Quality of life score

The SF-36 was used to score the four aspects of physical, social, emotional and physiological.

2.4. Statistical analysis

Data was entered into SPSS22.0 statistical software for calculation. The measurement data conforming to the normal distribution are expressed as mean \pm standard deviation (SD) and tested by t-test. Count data are expressed as $n(\%)$ and tested by χ^2 . $P < 0.05$, and the comparison was statistically significant.

3. Results

3.1. Compare the scores of neurological function and limb motor function

When comparing the two groups, the improvement effects of neurological function and limb motor function in the observation group were more obvious ($P < 0.05$). Please refer to **Table 1** for details.

Table 1. Comparison of neurological function and limb motor function scores (mean \pm SD, points)

Group	Number of cases	Neural function (NIHSS)		Neural function (FMA)	
		Before nursing	After nursing	Before nursing	After nursing
Observation Group	34	18.92 \pm 4.15	11.02 \pm 2.37	62.14 \pm 7.08	79.68 \pm 5.53
Control group	34	19.05 \pm 4.21	15.72 \pm 2.41	62.08 \pm 7.12	73.63 \pm 5.41
<i>t</i>	-	0.128	8.108	0.035	4.560
<i>P</i>	-	0.898	0.000	0.972	0.000

3.2. Compare the quality of life scores

The comparison between the two groups showed that the quality of life score of the observation group was significantly improved ($P < 0.05$). Please refer to **Table 2** for details.

Table 2. Comparison of quality of life scores (mean \pm SD, points)

Group	Number of cases	Physical function		Social function		Emotional function		Physiological function	
		Before nursing	After nursing	Before nursing	After nursing	Before nursing	After nursing	Before nursing	After nursing
Observation Group	34	62.23 \pm 6.69	79.84 \pm 4.24	65.75 \pm 7.45	82.05 \pm 6.31	92.94 \pm 5.53	85.37 \pm 4.29	61.41 \pm 7.34	82.03 \pm 4.01
Control group	34	62.19 \pm 6.72	73.41 \pm 4.09	65.81 \pm 7.21	76.59 \pm 6.08	92.85 \pm 5.43	78.79 \pm 4.03	62.05 \pm 7.31	75.53 \pm 3.36
<i>t</i>	-	0.025	6.364	0.034	3.633	0.068	6.518	0.360	7.245
<i>P</i>	-	0.981	0.000	0.973	0.001	0.946	0.000	0.720	0.000

4. Discussion

Cerebral hemorrhage refers to the bleeding caused by the rupture of blood vessels in the brain parenchyma without trauma. It is characterized by a sudden onset and rapid progression of the disease, posing a significant threat to the physical health and life safety of patients. Hypertensive cerebral hemorrhage is the main cause of this disease, accounting for approximately 70% to 80%. Additionally, abnormal structure of cerebral blood vessels and head trauma are also common causes of this disease ^[4,5]. Headache, vomiting, consciousness disorders, and elevated blood pressure are all common symptoms of cerebral hemorrhage, and surgical treatment is mostly adopted in clinical practice. The core goals of treating cerebral hemorrhage are to eliminate the hematoma, reduce intracranial pressure, relieve compression on brain tissue, and preserve neurological function. However, the surgical trauma is significant, and various complications such as infection and subcutaneous hematoma are highly likely to occur after the operation. At the same time, it also increases the risk of sequelae such as neurological function damage and limb motor dysfunction ^[6].

The staged nursing model is based on the development laws of diseases, the dynamic changes of patients' conditions or the process of rehabilitation. It divides the entire nursing process into several definite stages, and each stage has targeted nursing goals, contents and measures. Through the implementation of staged care for patients with cerebral hemorrhage, both their neurological function and limb motor function were significantly improved, and their quality of life was also significantly enhanced. There was a significant difference compared with the control group ($P < 0.05$). By analyzing the causes, the staged nursing model can divide the care into different time stages based on the characteristics of the disease and the needs of the patients. The period from 1 to 7 days after the operation belongs to the acute stage. Through posture care, early rehabilitation training, etc., complications such as joint contracture and muscle atrophy can be avoided, thereby providing conditions for subsequent rehabilitation training^[7]. Stepped training is a process from passive bed activities to active standing and walking. Continuous and repetitive training of damaged nerves can promote the reconstruction of synaptic connections to the greatest extent. Compared with conventional care, the staged care model encourages family members to actively participate in the care process, which can provide emotional support for patients, help stabilize their emotions, maintain a good psychological state, and thus actively cooperate with the treatment^[8].

5. Conclusion

In conclusion, implementing staged care for patients with cerebral hemorrhage can significantly improve the neurological function and limb motor function, and has a remarkable nursing effect on their quality of life.

Disclosure statement

The author declares no conflict of interest.

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The Influence of Early Extensor Rehabilitation Therapy on the Functional Recovery of Hemiplegic Upper Limbs During the Recovery Period of Cerebral Infarction

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Abstract: *Objective:* To explore the effect of early extensor rehabilitation therapy in patients with upper limb hemiplegia during the recovery period of cerebral infarction. *Method:* A total of 78 patients with upper limb hemiplegia during the recovery period of cerebral infarction were included as the research subjects and all received treatment in our hospital from January 2024 to December 2024. The groups were grouped by double-blind method, with 39 cases in each group. The control group and the observation group received early flexor rehabilitation treatment and early extensor rehabilitation treatment respectively. The upper limb function and self-care ability of the two groups before and after treatment were compared. *Result:* After the intervention, the upper limb motor function score of the observation group was significantly higher than that of the control group, $P < 0.05$; After treatment, the Barthel index of the observation group was significantly increased compared with that before treatment, and there was a significant difference compared with the control group, $P < 0.05$. *Conclusion:* The implementation of early extensor rehabilitation therapy for patients in the recovery period of cerebral infarction with hemiplegia of the upper limbs can effectively promote the recovery of upper limb function and improve their self-care ability in life, which is worthy of clinical promotion.

Keywords: Upper limb hemiplegia; The recovery period of cerebral infarction; Early extensor rehabilitation treatment; Upper limb function

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1. Introduction

Cerebral infarction is a common clinical disease. Its occurrence is related to insufficient blood supply to the brain, which leads to ischemia, hypoxia and necrosis of the central nervous system tissue, thereby causing functional disorders in the innervated areas^[1]. Hemiplegia is a common complication after cerebral infarction, with upper limb hemiplegia being particularly common, which has a huge impact on patients' daily lives. It is understood that approximately 60% to 80% of patients in the recovery period of cerebral infarction have varying degrees of

upper limb dysfunction. If not treated promptly and effectively, it can affect the recovery of upper limb function and even leave permanent disability^[2,3]. At present, there are many methods for treating hemiplegia after cerebral infarction in clinical practice, including limb function training, acupuncture physiotherapy, neuro-muscle electrical stimulation, etc. However, many of these methods pay more attention to the recovery of flexor muscle function and neglect the training of extensor muscle function, thereby affecting the rehabilitation effect^[4,5]. Therefore, more efficient treatment methods should be actively explored to enhance the effectiveness of rehabilitation. This study selected 78 patients with upper limb hemiplegia after cerebral infarction as samples to explore the clinical value of early extensor rehabilitation therapy.

2. Materials and methods

2.1. Basic information

A total of 78 patients in the recovery period of cerebral infarction were included as the research subjects, all of whom had hemiplegia of the upper limbs. All patients received relevant treatments in our hospital from January 2024 to December 2024. During the research process, the patients were divided into the control group and the observation group by a double-blind method. Among the 39 patients in the control group, there were 23 males and 16 females. The youngest was 45 years old and the oldest was 78 years old, with a median value of (62.35 ± 5.87) years old. Among the 39 patients in the observation group, there were 22 males and 17 females. The youngest was 43 years old and the oldest was 80 years old, with a median value of (63.25 ± 5.16) years old. The comparison of basic data between the two groups of patients showed no statistical significance ($P > 0.05$). This study was approved by the hospital ethics committee.

Inclusion criteria: (1) All patients were confirmed to have cerebral infarction by cranial CT or magnetic resonance imaging. (2) All patients were in the recovery period (14 to 180 days after the onset of the disease). (3) There is unilateral upper limb dysfunction. After Fugl-Meyer assessment of motor function, the functional score of the affected upper limb is between 10 and 45 points. (4) The patient's cognitive function is normal and can cooperate with rehabilitation treatment.

Exclusion criteria: (1) Those with combined dysfunction of important organs; (2) Those with combined upper limb fractures, joint deformities, inflammatory responses or other severe diseases of the musculoskeletal system; (3) Those with abnormal coagulation mechanisms; (4) Others who cannot cooperate with rehabilitation treatment; (5) Those with recurrent conditions or those with other serious complications.

2.2. Methods

All patients received symptomatic and supportive treatments such as blood pressure reduction, blood sugar reduction, lipid regulation, anti-platelet aggregation, improvement of cerebral circulation, and nerve nutrition. On this basis, different rehabilitation treatment measures were given to the two groups of patients.

The control group received early flexor rehabilitation treatment:

- (1) Active flexor training: Guided patients to actively carry out contraction exercises of the flexor muscles of the affected upper limb, including forward flexion of the shoulder joint, flexion of the elbow joint, palmarion of the wrist joint, flexion and grasping of the fingers, etc. During the training process, professional rehabilitation instructors will provide guidance to ensure that each movement is correct and in place. Each movement should be maintained for 5 to 10 seconds, and repeated 10 to 15 times as a set. Each training session lasts for 20 minutes, with 2 repetitions per day.

- (2) Flexor resistance training: Flexor resistance training can only be carried out after the flexor strength of the affected upper limb has recovered to grade 4 or higher. During the training process, elastic bands are used as resistors to guide patients to flex their fingers and forearms while resisting resistance. During the training process, the resistance of the elastic band can be adjusted according to the patient's muscle strength, 20 minutes per session, twice a day.
- (3) Coordination training: Guide the patient to alternately perform flexion and extension training of the wrist joint, finger joint, and elbow joint to improve their coordination ability and movement accuracy gradually. Each session lasts for 15 minutes, twice a day. The above training should be carried out every day for 8 consecutive weeks.

The observation group received early extensor rehabilitation treatment:

- (1) Active extensor training: Guided patients to actively complete the contraction training of the upper limb extensor muscles, including posterior extension of the shoulder joint, extension of the elbow joint, dorsiflexion of the wrist joint, and posterior extension of the fingers, etc. Also guided by a rehabilitation therapist, incorrect movements are corrected in a timely manner to ensure they are in place. Each movement should be maintained for 5 to 10 seconds. Each set consists of 10 to 15 repetitions, with each session lasting 20 minutes, performed twice a day.
- (2) Extensor resistance training: Extensor resistance training should be initiated when the strength of the extensor muscles on the affected upper limb reaches grade 4 or above. During training, patients need to complete extensor muscle training for various parts of the upper limbs, including the shoulder, elbow, wrist, finger and other joints, while resisting resistance. Elasticity should be appropriately adjusted according to the individual's muscle recovery condition to promote the slow recovery of muscle strength.
- (3) Extensor coordination training: Guide patients to alternately perform actions such as dorsal extension of the affected wrist joint and flexion and extension of the elbow joint to enhance the coordination of movements. 10 to 15 times per group, 15 minutes each time, twice a day.
- (4) Homework training: Guide patients to carry out targeted extensor muscle function exercises based on their daily life needs, such as pushing tables, opening doors, lifting heavy objects, and wring out towels with the affected palm, to promote the improvement of their extensor muscle function and self-care ability in daily life. The above training should be carried out every day for 8 consecutive weeks.

2.3. Index observation

2.3.1. Upper limb motor function

The assessment was completed through the upper limb part of the Fugl-Meyer Assessment of Motor Function Scale, including reflex activity, coordinated activity of flexor and extensor muscles, activities with and without coordinated movement, hyperreflexia, wrist stability, elbow extension, and forward flexion at 30°. There were a total of 33 items, with scores ranging from 0 to 66 points, and the scores were negatively correlated with functional disorders. The measurement time was before treatment and after the completion of the 8-week training.

2.3.2. Self-care ability

The assessment of self-care ability is completed through the modified Barthel Index scale, including dressing, eating, washing, walking, using the toilet, going up and down stairs, etc. It is scored out of 100, and the score is positively correlated with self-care ability. The measurement time was before treatment and after the completion of the 8-week training.

2.4. Statistical analysis

SPSS 24.0 software was applied. Measurement data were expressed as mean \pm standard deviation (SD), and count data were expressed as (%). The former was tested by t-test and the latter by chi-square test. When $P < 0.05$, it is statistically significant.

3. Results

3.1. Comparison of upper limb motor functions

Comparison of upper limb motor function scores: After treatment, the values of the observation group were higher, $P < 0.05$. See **Table 1**.

Table 1. Comparison of upper limb motor function (mean \pm SD, points)

Group	Number of cases	Before treatment	After treatment
Control group	39	27.82 \pm 6.51	45.24 \pm 7.65
Observation Group	39	28.35 \pm 6.42	58.76 \pm 8.32
<i>t</i>		0.632	7.470
<i>P</i>		0.718	0.000

3.2. Comparison of self-care ability

The comparison of the Barthel index shows that the value of the observation group is higher, with $P < 0.05$. See **Table 2**.

Table 2. Comparison of Barthel index between the two groups (mean \pm SD, points)

Group	Number of cases	Before treatment	After treatment
Control group	39	41.82 \pm 8.71	62.15 \pm 8.73
Observation Group	39	42.35 \pm 8.62	76.38 \pm 9.51
<i>t</i>		0.270	6.883
<i>P</i>		0.788	0.000

4. Discussion

Cerebral infarction, also known as ischemic stroke, is mainly caused by the narrowing or occlusion of cerebral blood vessels, resulting in ischemia, hypoxia and necrosis of brain tissue, thereby causing neurological dysfunction^[6,7]. Upper limb hemiplegia is one of the most common complications of cerebral infarction. As the upper limb involves the coordinated movement of multiple joints and muscles, and after the onset of the disease, it is prone to conditions such as extensor muscle weakness and flexor muscle spasm in the upper limb, the difficulty of functional recovery is even greater. Studies have shown that the recovery period is a crucial time for the recovery of neurological function in patients with cerebral infarction^[8,9]. Timely and effective rehabilitation treatment can promote brain tissue remodeling and the reorganization of the nervous system, helping patients restore their neurological and motor functions. However, in conventional rehabilitation training, flexor muscle training is the main focus. Although it can improve nerve spasm, extensor muscles cannot be effectively trained, resulting in many patients

still having problems such as extensor muscle weakness and insufficient coordination ability after rehabilitation, thereby affecting the overall recovery of the limbs^[10,11].

In this study, after the observation group received early extensor training, the upper limb motor function score and Barthel index score of the patients in this group were significantly improved compared with those before treatment, and there was a significant difference from the control group ($P < 0.05$), suggesting that this training method is beneficial to the recovery of upper limb motor function and self-care ability of the patients. The main reasons are as follows:

- (1) Through active training, resistance training and coordinated training of extensor muscles, the strength and endurance of the extensor muscles on the affected side can be effectively enhanced, the force balance between extensor and flexor muscles can be improved, muscle spasms can be alleviated, and thus the motor function of the upper limbs can be improved^[12]. For instance, extensor resistance training can gradually increase resistance to promote the proliferation and differentiation of extensor muscle fibers, thereby achieving a gradual improvement in muscle strength. Extensor coordination training can enhance the regulatory effect of the cerebral motor cortex on extensor muscle strength and improve the coordinated cooperation of extensor and flexor muscles^[12].
- (2) The organic combination of extensor function training and occupational training helps patients enhance their self-care ability in practical application, further stimulates their confidence in recovery, and increases their enthusiasm for training, thereby achieving an improvement in their self-care ability in daily life^[13,14]. For instance, practicing actions such as pushing a table and opening a door with the affected hand can help patients skillfully apply extensor muscle strength in their daily lives, achieving a common improvement in extensor muscle and self-care ability.
- (3) The implementation of early extensor rehabilitation training can improve the microcirculation in the area around the lesion after cerebral infarction, enhance local blood supply, promote the repair and regeneration of nerve cells, accelerate the remodeling of nerve function, and thereby facilitate the recovery of motor function in hemiplegic limbs^[15].

5. Conclusion

In conclusion, implementing early extensor rehabilitation treatment for patients in the recovery period of cerebral infarction with hemiplegia of the upper limbs is beneficial to the recovery of their upper limb motor function and self-care ability, and is worthy of promotion.

Disclosure statement

The authors declare no conflict of interest.

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Research Progress on Epidemiological Characteristics, Pathogenesis, and Prevention and Control of Multisystem Complications of Childhood Obesity

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Abstract: Childhood obesity has emerged as a significant global public health issue, with its epidemic trend and the complexity of its pathogenic mechanisms posing formidable challenges to prevention and control efforts. This article systematically reviews the epidemiological characteristics of childhood obesity, focusing on its global and national prevalence status and core risk factors. It delves into the collaborative pathogenic mechanisms involving genetic and epigenetic regulation, intestinal microbiota dysbiosis, and disruptions in the neuro-endocrine-metabolic network. Furthermore, it comprehensively elucidates the clinical features of multisystem complications. Finally, it summarizes research progress in prevention strategies, clinical interventions, and novel technologies, providing references for the standardized prevention and control of childhood obesity.

Keywords: Childhood obesity; Epidemiology; Pathogenesis; Multisystem complications; Prevention and control progress

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1. Introduction

Childhood obesity is a chronic metabolic disease caused by excessive accumulation of body fat, diagnosed based on a Body Mass Index (BMI) \geq the 95th percentile for age and gender^[1]. With dramatic changes in dietary patterns and lifestyles, childhood obesity has exhibited trends of “globalization, younger age of onset, and increasing severity,” and has been identified by the World Health Organization as one of the most urgent public health challenges of the 21st century. Obesity in childhood not only directly hinders growth and development but also increases the risk of chronic diseases in adulthood through the “metabolic memory” effect, while triggering psychological and behavioral issues, resulting in lifelong health impairments^[2]. This paper integrates core evidence from recent years to systematically review research progress in childhood obesity, providing a scientific basis for

clinical practice and public health interventions.

2. Epidemiological characteristics

2.1. Global and domestic prevalence

The incidence of childhood obesity worldwide has exploded over the past half-century, with particularly notable “catch-up growth” in low- and middle-income countries, which have become new engines driving the global obesity epidemic. Developed countries in Europe and North America are at a high plateau of prevalence, while Asia, despite having a lower baseline prevalence, is experiencing a growth rate far exceeding that of other continents.

The prevalence of childhood obesity in China is also severe. According to the “Chinese Guidelines for the Diagnosis and Treatment of Obesity (2024 Edition)”^[3] released by the National Health Commission in 2024, the overweight rate among children and adolescents aged 6 to 17 reached 11.1%, and the obesity rate was 7.9%, with a combined total of nearly 20%. For children under 6 years old, the overweight and obesity rates were 6.8% and 3.6%, respectively, showing a clear trend towards younger ages. In terms of population distribution, the characteristics of “higher prevalence in the north than in the south, in urban areas than in rural areas, and among boys than among girls” remain, but the increase in rural areas has been significantly higher than that in urban areas, and the gap between urban and rural areas continues to narrow. Special groups such as left-behind children and only children face a significantly higher risk of obesity due to differences in lifestyle and care patterns, making them a key focus group.

2.2. Core risk factors

The occurrence of childhood obesity is not the result of a single factor but rather the interaction of genetic and environmental factors, with environmental factors being the primary driving force behind the current epidemic. In terms of diet, excessive intake of high-energy, high-sugar, and high-fat processed foods and sugary beverages, as well as insufficient intake of dietary fiber and high-quality protein, and irregular meal patterns and overeating, directly contribute to energy imbalance^[4]. Among behavioral factors, the “triple threat” of insufficient outdoor activities, prolonged screen time, and sleep deprivation collectively reduces energy expenditure and disrupts metabolic rhythms. At the social environmental level, parental cognitive biases, the lack of health education in schools, insufficient community sports facilities, and misleading food marketing collectively create an “obesogenic environment” that is detrimental to health.

Genetic factors provide a predisposing background for the development of obesity, with the heritability of childhood obesity estimated to be around 40%—70%. Classic gene variants such as FTO and MC4R are closely associated with obesity susceptibility^[5]. It is noteworthy that genetic risks can only fully manifest under the catalysis of environmental factors, and improving lifestyle can effectively reduce the incidence probability among genetically susceptible populations.

3. Pathogenesis

3.1. Genetic and epigenetic regulation

Genetic factors influence obesity susceptibility by regulating pathways related to energy metabolism and fat synthesis. Polymorphisms in genes such as PPARG and ADIPOQ can promote fat accumulation by affecting

adipocyte differentiation and insulin sensitivity, respectively ^[6]. More critically, epigenetic mechanisms play a “bridging role” in the interaction between genetics and the environment. Maternal obesity, malnutrition, or exposure to environmental pollutants during pregnancy can lead to abnormal epigenetic modifications such as methylation in the fetal genome, such as methylation changes in the promoter region of the LEP gene. This “metabolic imprinting” can persist into adulthood, significantly increasing the risk of obesity ^[7]. Additionally, microRNAs such as miR-143 and miR-221 can participate in the pathological process of obesity by targeting and regulating genes involved in adipocyte differentiation.

3.2. Intestinal dysbiosis

Intestinal microbiota imbalance is a significant pathogenic mechanism underlying childhood obesity ^[8]. Overweight/obese children exhibit significantly lower diversity in their intestinal microbiota compared to children of normal weight, along with characteristic alterations in microbial composition: an increase in the abundance of certain Firmicutes genera and a decrease in certain Bacteroidetes genera. This imbalance promotes obesity through three pathways: enhancing intestinal fat absorption efficiency; fermenting dietary fiber to produce short-chain fatty acids that activate intestinal receptors and stimulate appetite; and triggering low-grade inflammation that activates the TLR4/NF- κ B pathway, leading to insulin resistance. Additionally, the intestinal microbiota can regulate central appetite centers via the “gut-brain axis,” forming a closed regulatory loop of “microbiota-metabolism-nerve.” Research has also found that feeding practices, dietary patterns, exercise habits, and sleep behaviors are modifiable factors influencing the intestinal microbiota, providing targets for obesity prevention and control through microbiota intervention ^[9].

3.3. Disruption of the neuro-endocrine-metabolic network

The regulatory network formed by the central nervous system and the endocrine system is central to maintaining energy balance. Dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis is extremely common in obese children, with elevated cortisol levels specifically promoting abdominal fat accumulation ^[10]. Disruption of the leptin-leptin receptor signaling pathway is a critical factor. Obese children often exhibit “leptin resistance,” characterized by elevated leptin levels that fail to effectively suppress appetite or increase energy expenditure, leading to a vicious cycle of metabolic imbalance. Additionally, endocrine abnormalities such as decreased insulin sensitivity and insufficient growth hormone secretion can exacerbate obesity by promoting fat synthesis and reducing fat breakdown, respectively ^[11].

3.4. Mediating role of environmental factors

The aforementioned environmental risk factors do not directly cause obesity but rather facilitate its development by targeting the aforementioned mechanisms. High-sugar diets can activate the hypothalamic reward pathway, leading to appetite addiction, while also causing dramatic fluctuations in blood glucose levels and excessive insulin secretion ^[12]. A lack of physical activity not only reduces energy expenditure but also decreases muscle mass and basal metabolic rate. Sleep deprivation disrupts the function of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in decreased leptin secretion and increased ghrelin levels, as well as reduced insulin sensitivity, forming a pathological chain of “sleep deprivation-metabolic disorder-obesity.”

4. Multisystem complications

Childhood obesity is not merely a matter of excessive body weight; it can cause persistent damage to multiple organ systems, triggering a series of serious complications. Moreover, these damages are characterized by their insidious and progressive nature.

4.1. Metabolic system complications

Metabolic syndrome is the most common complication in obese children, characterized by central obesity, hypertension, hyperglycemia, and dyslipidemia as its core manifestations, significantly increasing the risk of long-term chronic diseases. The age of onset for type 2 diabetes mellitus (T2DM) continues to advance, with obese children facing a more than tenfold higher risk of developing the disease compared to children of normal weight. Moreover, T2DM often has an insidious onset, leading to delays in diagnosis and treatment. Non-alcoholic fatty liver disease is another highly prevalent complication, with approximately half of obese children exhibiting varying degrees of hepatic steatosis. Some cases may progress to hepatitis and fibrosis, becoming the primary cause of liver disease during childhood ^[13].

4.2. Cardiovascular system complications

Childhood obesity is an independent risk factor for cardiovascular diseases in adulthood and can directly cause cardiovascular damage during childhood. The prevalence of hypertension is significantly higher among obese children, often presenting insidiously and going unnoticed ^[14]. Dyslipidemia is characterized by elevated triglycerides and low-density lipoprotein cholesterol, along with reduced high-density lipoprotein cholesterol, accelerating the progression of atherosclerosis. Long-term obesity can also lead to structural and functional changes in the heart, such as left ventricular hypertrophy and myocardial strain, with severe cases potentially resulting in heart failure.

4.3. Complications of the respiratory system and musculoskeletal system

Obstructive sleep apnea syndrome is a characteristic complication in obese children, manifesting as nighttime snoring and apnea, daytime drowsiness, and lack of concentration. Chronic hypoxemia can adversely affect brain development and cardiovascular function ^[15]. Obese children also have a significantly higher prevalence of asthma, with more frequent recurrences and greater difficulty in control. In terms of the musculoskeletal system, excessive body weight can increase pressure on the lower limb bones, leading to premature epiphyseal closure, scoliosis, flat feet, and other deformities. It also accelerates the wear and tear of articular cartilage in the knee and hip joints, accompanied by insufficient muscle strength and decreased motor coordination, creating a vicious cycle of “obesity - reduced physical ability - worsening obesity” ^[16].

4.4. Psychological behavior and social adaptation complications

Obese children often face ridicule and discrimination from their peers due to their body size, leading to a significantly higher incidence of psychological issues such as low self-esteem, anxiety, and depression compared to children of normal weight ^[17]. They also exhibit higher rates of inattention and decreased learning efficiency, with impaired social skills and confidence. Over the long term, this can result in decreased social adaptability, affecting career development and quality of life in adulthood.

5. Prevention and control strategies

The prevention and control of childhood obesity should adhere to the core principle of “prevention first and comprehensive intervention,” establishing a multi-dimensional, full-cycle prevention and control system, while implementing differentiated intervention measures for children with different weight statuses.

5.1. Prevention strategies

The prevention and control of childhood obesity adhere to the core principle of “prevention first” and establish a comprehensive prevention and control model integrating “family-school-community-society.” At the family level, parents should set a healthy example, optimize dietary structure, ensure children’s daily intake of sufficient vegetables, fruits, and high-quality protein, supervise them to engage in at least one hour of moderate-intensity physical exercise, control screen time, and ensure adequate sleep. At the school level, nutrition and health education should be incorporated into the curriculum, the quality of cafeteria meals should be improved, and time for physical activities should be guaranteed. At the community level, sports facilities should be improved, and scientific popularization on obesity prevention and control should be carried out. At the societal level, food advertising should be strictly regulated, the production of healthy foods should be encouraged, and a unified national network for monitoring and intervening in childhood obesity should be established ^[18].

5.2. Clinical intervention measures

For children who have already developed obesity, a comprehensive treatment plan combining “dietary adjustment + exercise intervention + behavioral correction” should be adopted. Dietary adjustment focuses on “energy control and nutritional balance,” reducing the intake of sugary beverages and processed snacks, maintaining regular meals, and avoiding extreme dieting ^[19]. Exercise interventions primarily consist of moderate-intensity aerobic exercises combined with strength training, with personalized plans tailored according to children’s age and interests. Behavioral modification enhances intervention adherence by establishing healthy habits, implementing reward and punishment mechanisms, improving parent-child relationships, and providing psychological counseling.

5.3. Research on novel therapeutic technologies and medications

Currently, multiple breakthroughs have been achieved in the field of pediatric obesity treatment. Digital health interventions have emerged as a new hotspot. For instance, family-oriented online healthy lifestyle programs can significantly reduce BMIz scores, improve dietary quality and exercise habits, and enhance the quality of life in children, offering a feasible pathway for large-scale obesity interventions.

In terms of pharmacological treatment, GLP-1 receptor agonists such as semaglutide have demonstrated clear efficacy in obese children aged 12 and above ^[20]. For example, daily subcutaneous injection of liraglutide 3.0 mg combined with lifestyle interventions can significantly reduce BMI in obese children aged 6 to 12, with good safety profiles, providing a new option for pharmacological treatment in younger obese children ^[21]. Fecal microbiota transplantation remains in the clinical research stage, aiming to achieve weight reduction by improving gut microbiota composition, but its long-term efficacy and safety require further validation. Bariatric surgery is only applicable to a very small number of severely obese children with serious comorbidities, necessitating strict indication control and long-term postoperative management.

6. Conclusion

Childhood obesity is a chronic disease resulting from the combined effects of multiple factors, including genetics, environment, gut microbiota, and disturbances in the neuro-endocrine-metabolic network. Its prevalence is alarming and has emerged as a significant global public health issue. Childhood obesity not only affects growth and development but also triggers complications across multiple systems, such as metabolic, cardiovascular, and respiratory systems, while also causing psychological, behavioral, and social adaptation impairments. The breakthroughs in the 2024 updated clinical guidelines and multiple clinical studies have provided new evidence for prevention and control efforts. Current prevention and control strategies should adhere to a “prevention-first, comprehensive intervention” approach, creating a healthy environment through collaborative efforts from families, schools, communities, and society at large. For children already affected by obesity, individualized comprehensive interventions should be implemented, supplemented by novel drugs or technological treatments when necessary. In the future, with the advancement of precision medicine and digital health technologies, individualized and precise prevention and control will become the mainstream trend, offering stronger guarantees for the effective management of childhood obesity.

Disclosure statement

The authors declare no conflict of interest.

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Exploring the Magnetic Resonance Imaging Manifestations of Hippocampal and Amygdala Structures in Temporal Lobe Epilepsy Based on Voxel-Based Morphological Analysis

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Abstract: Temporal lobe epilepsy (TLE) is the most common refractory subtype of epilepsy in clinical practice, with a complex pathogenesis and a lack of precise biomarkers for diagnosis and prognosis evaluation, seriously affecting the quality of life of patients. The hippocampus and amygdala, as the core structures of the limbic system, play a key role in the pathogenesis of TLE. Structural abnormalities in both are considered important pathological bases for the initiation, spread, and progression of epileptic discharges. Although conventional magnetic resonance imaging can detect obvious hippocampal sclerosis, it is difficult to capture microstructural changes and has limited ability to identify hidden damage in areas such as the amygdala, leading to misdiagnosis or missed diagnosis in some patients with hidden TLE. Voxel-based morphological analysis (VBM) can accurately quantify the volume and density changes of the whole brain gray and white matter, providing technical support for analyzing the microstructural damage of the hippocampus and amygdala in TLE patients. Previous studies have suggested that the amygdala is not only a “susceptible area” for epileptic discharges, but may also serve as a “relay station” involved in discharge diffusion. Its structural abnormalities are closely related to the frequency and prognosis of TLE attacks. However, the synergistic effect and specific pathological mechanisms of structural changes in the hippocampus and amygdala still need to be further clarified. Therefore, this study used VBM technology to systematically analyze the magnetic resonance imaging manifestations of the hippocampus and amygdala in TLE patients, aiming to reveal their structural abnormalities and provide imaging evidence for the accurate diagnosis, mechanism research, and prognosis evaluation of TLE.

Keywords: Morphological analysis of voxels; Temporal lobe epilepsy; Magnetic resonance

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1. Introduction

Temporal lobe epilepsy is one of the most common subtypes of adult epilepsy, accounting for about 40% -50% of all epilepsy cases, and up to 60–70% of refractory epilepsy. Its etiology is complex, mainly including hippocampal sclerosis, traumatic brain injury, central nervous system infection, cerebrovascular disease, etc. ^[1] Among them, hippocampal sclerosis is the most common pathological basis. The disease is characterized by recurrent partial episodes, and long-term episodes not only lead to progressive cognitive decline, especially significant decline in learning and memory abilities, but also trigger emotional disorders such as anxiety and depression, seriously damaging the patient's daily living and social skills, and bringing heavy medical burden and economic pressure to the family and society.

The hippocampus and amygdala, as core components of the limbic system, play crucial roles in physiological processes such as learning, memory encoding, and emotion regulation, and are closely related to the pathogenesis of temporal lobe epilepsy. Clinical studies have confirmed that most patients with temporal lobe epilepsy exhibit sclerosis symptoms such as hippocampal neuron loss and gliosis, accompanied by abnormal morphology of the amygdala ^[2]. These pathological changes have complex causal relationships with the onset and spread of epileptic seizures, which may be the inducer of epileptic seizures or secondary damage caused by recurrent seizures, becoming the core target area for clinical localization of epileptic foci.

Structural magnetic resonance imaging (sMRI) has been widely used for brain structure assessment and lesion localization in temporal lobe epilepsy due to its high spatial resolution advantage ^[3]. It can clearly display morphological changes in key structures such as hippocampus and amygdala, providing important imaging evidence for clinical diagnosis. However, traditional sMRI mainly relies on qualitative observation, which lacks sensitivity to early and subtle structural changes, and cannot achieve accurate quantitative analysis of parameters such as brain volume and density, making it difficult to meet the needs of early disease screening, disease progression monitoring, and personalized treatment evaluation. Therefore, it is urgent to introduce precise quantitative analysis techniques to make up for this deficiency.

2. Research progress of VBM in hippocampal structure analysis of temporal lobe epilepsy

2.1. Core findings of VBM research on changes in hippocampal volume and density

Based on Voxel-based morphological analysis (VBM), with the quantitative advantage of voxel levels, specific changes in the hippocampal structure of patients with temporal lobe epilepsy (TLE) were clearly revealed ^[4]. The core findings focused on the lateral and regional specificity of volume atrophy and density abnormalities. Most studies have confirmed that patients with unilateral TLE have significantly reduced hippocampal volume on the epileptic side, and the degree of atrophy is higher than that on the non epileptic side. This feature is particularly prominent in medial temporal lobe epilepsy. VBM further discovered that hippocampal atrophy is not uniformly distributed, but is more pronounced in subregions such as CA1, CA3, and the dentate gyrus, which may be related to the susceptibility of neurons in these regions to abnormal discharge damage. For patients with bilateral TLE, there is heterogeneity in hippocampal structural changes, with some patients showing symmetrical atrophy on both sides and others showing asymmetrical changes mainly on one side ^[5]. This difference may be related to the pathogenesis and progression of the disease. In addition, the decrease in hippocampal gray matter density detected by VBM often occurs earlier than visible volume atrophy, providing a sensitive indicator for early pathological change identification of TLE. However, the differences in sample size, scanning parameters, and analysis software

among different studies have led to slight discrepancies in some results, which require further validation through large-scale standardized research.

2.2. Correlation study between hippocampal structural abnormalities and clinical features of TLE

The quantitative analysis of VBM provides precise evidence for the association between hippocampal structural abnormalities and clinical features of TLE, with core correlation dimensions covering seizure characteristics, cognitive function, and drug effects. In terms of seizure-related characteristics, research has shown that the degree of hippocampal atrophy is positively correlated with the frequency and duration of epileptic seizures^[6]. Patients with a course of more than 5 years have a significantly higher rate of hippocampal volume reduction than those with short-term seizures, suggesting that long-term abnormal discharges may exacerbate hippocampal neuronal damage. In terms of cognitive function correlation, VBM found that patients with decreased gray matter density in the hippocampal CA1 region and dentate gyrus had significantly lower episodic memory and spatial memory scores than those with normal structure, and the degree of cognitive impairment was positively correlated with the degree of hippocampal structural abnormalities, revealing the key role of hippocampal structural integrity in cognitive function. In terms of drug effects, some studies have found through VBM comparison that patients who regularly take antiepileptic drugs for a long time have a slower progression of hippocampal atrophy than those who do not regularly use drugs. However, there are differences in the protective effects of different drugs on hippocampal structures, and there is a lack of large-scale, long-term follow-up data support. In addition, a few studies suggest that hippocampal structural abnormalities may also be related to seizure types, and patients with complex partial seizures have a wider range of hippocampal abnormalities.

2.3. Differences in VBM research on hippocampal structural changes in different subtypes of TLE

The precise quantitative ability of VBM technology clearly distinguishes the specific differences in hippocampal structural changes among different subtypes of TLE patients, providing an objective basis for TLE subtype classification^[7]. In the comparison between medial temporal lobe epilepsy (mTLE) and lateral temporal lobe epilepsy (lTLE), VBM studies showed that the incidence of hippocampal volume atrophy in mTLE patients was as high as 70% -80%, and it was mostly significant atrophy on the epileptic side. Significant gray matter density reduction was observed in various subregions of the hippocampus; However, the hippocampal structural changes in patients with lTLE are relatively mild, with only some patients showing mild bilateral hippocampal volume reduction, without obvious lateral specificity. This is related to the fact that mTLE has the hippocampus as the core of the epileptic foci, and lTLE's epileptic foci are mostly located in the lateral temporal lobe. In the comparison of TLE subtypes with and without hippocampal sclerosis (HS), the differences are more significant: TLE patients with HS show a significant reduction in hippocampal volume on the epileptic side, a significant decrease in gray matter density, and often accompanied by irregular hippocampal morphology in VBM; For TLE patients without HS, there may not be a significant reduction in hippocampal volume, but some patients can detect subtle gray matter density abnormalities in local subregions (such as CA3) through VBM. In addition, studies have found through VBM that there are differences in the pattern of hippocampal structural changes between patients with familial TLE and those with sporadic TLE, and familial patients are more likely to experience bilateral contralateral neuropathy.

3. Research progress of VBM in amygdala structure analysis of temporal lobe epilepsy

3.1. Core findings of VBM research on changes in amygdala volume and density

The voxel-based morphometric measurement (VBM) technique, with its advantages of automation and whole-brain coverage, has become a core tool for analyzing the microstructural changes in the amygdala of patients with temporal lobe epilepsy (TLE). Its core findings focus on two dimensions: volume atrophy and density abnormalities. Most studies have confirmed that the volume of the amygdala on the affected side of TLE patients is significantly reduced, and the degree of reduction is positively correlated with the course of the disease^[8]. The volume reduction rate in patients with a course of more than 10 years can reach 15–20%. More importantly, VBM can detect a decrease in grayscale values that are difficult to detect with conventional MRI, indicating neuronal loss, gliosis, and reduced synaptic connections in the amygdala. In patients with unilateral TLE, about 30–40% will experience a mild reduction in the volume of the contralateral amygdala, indicating that epileptic discharges may cause bilateral structural damage. In addition, there are differences in amygdala changes among different subtypes of TLE: amygdala atrophy is more pronounced in hippocampal sclerosis-related TLEs, while non-hippocampal sclerosis type TLEs may only exhibit local density abnormalities. These findings provide imaging biomarkers for the objective diagnosis of TLE, especially for occult cases without clear hippocampal lesions, which have important reference value^[9].

3.2. Study on the correlation between abnormal amygdala structure and clinical features of TLE

Existing imaging evidence suggests that some TLE patients exhibit ipsilateral amygdala volume atrophy or contralateral compensatory changes, but the relationship between these morphological changes and clinical symptoms has not been fully elucidated and there are significant individual differences.^[10] Analysis has found that in some patients, the significant reduction in amygdala (especially ipsilateral) volume may be related to longer disease duration or higher frequency of epileptic seizures. This may reflect the cumulative effect of neuronal damage or remodeling caused by repeated epileptic activity. However, this association is not absolutely linear, and other factors such as age of onset and medication history may constitute important confounding variables. Meanwhile, preliminary observations suggest that abnormalities in the amygdala structure may be potentially associated with certain specific symptom dimensions. For example, some TLE patients with obvious anxiety or emotional regulation difficulties have more common signal abnormalities or connectivity changes in the amygdala (often involving both sides). This supports the neurobiological hypothesis that the dysfunction of the amygdala as a hub of the limbic system may be involved in the comorbidity of emotional symptoms in TLE. In addition, studies have reported that the synergistic atrophy of the amygdala and hippocampus may be associated with complaints of memory impairment, but the causal relationship and directionality still need further verification.

3.3. Exploration of the role of the amygdala in the pathogenesis of TLE

Combining VBM research results with neurophysiological mechanisms, the dual role of the amygdala in the pathogenesis of TLE can be indirectly inferred, serving as both a “susceptible area” for epileptic discharges and a “relay station” for discharge diffusion. Firstly, the decrease in grayscale values and neuronal loss detected by VBM in the amygdala may be due to excitotoxic damage caused by long-term epileptic discharges: excessive release of glutamate leads to calcium influx imbalance, which in turn destroys neuronal structure and forms a vicious cycle of “discharge damage easier discharge”. This explains why patients with amygdala structural abnormalities have

more frequent seizures. Secondly, the abnormal structure of the bilateral amygdala in patients with unilateral TLE suggests that the amygdala may serve as a diffusion pathway for epileptic discharges, transmitting discharges to the contralateral hemisphere through the limbic system connection and participating in the formation of global cerebral seizures. In addition, abnormal structural connections between the amygdala and regions such as the hippocampus and temporal pole (confirmed by VBM combined with diffusion tensor imaging) may exacerbate the formation of epileptic networks and enhance the synchronicity of discharges. At the same time, the ion microenvironment disorder caused by amygdala gliosis further reduces the neuronal firing threshold and promotes the maintenance of epileptic foci. This indirect evidence suggests that structural abnormalities in the amygdala are not secondary changes to TLE, but rather a key link involved in its pathogenesis.

4. The value and challenges of VBM technology in the clinical application of temporal lobe epilepsy

4.1. Clinical diagnosis and differential diagnostic value

Voxel-based morphometry (VBM) technology, with its advantages of automation and quantification, has become an important auxiliary tool for clinical diagnosis of temporal lobe epilepsy (TLE). Traditional imaging has low sensitivity to early or mild changes in brain structure, while VBM can accurately detect gray matter volume atrophy in peripheral system structures such as hippocampus and amygdala in TLE patients through whole brain voxel level analysis, and even identify subclinical brain structural abnormalities in patients with atypical clinical symptoms, providing objective imaging evidence for early diagnosis of TLE. In terms of differential diagnosis, TLE often needs to be distinguished from frontal lobe epilepsy, epileptic seizures caused by mental and psychological disorders, etc. The brain structural changes of these diseases have different characteristics. For example, frontal lobe epilepsy is often manifested as abnormal gray matter volume in the frontal lobe, while VBM can significantly improve the accuracy of differential diagnosis by comparing the brain structural morphological characteristics of different diseases, combining clinical symptoms and EEG results. In addition, for cryptogenic TLEs without clear lesions, VBM can detect potential brain structural changes, providing direction for further etiological exploration and compensating for the shortcomings of traditional imaging.

4.2. Classification and prognostic evaluation value

VBM technology may provide a certain reference basis for the classification and prognosis evaluation of temporal lobe epilepsy (TLE), but its conclusions need to be comprehensively judged in combination with other clinical indicators, and it is difficult to use it alone as an absolute classification or prognosis judgment standard. In terms of subtyping assistance, there may be subtle differences in the VBM changes of key structures such as the amygdala and hippocampus in patients with different subtypes of TLE. For patients with TLE related to hippocampal sclerosis, the volume shrinkage of the amygdala and hippocampus on the affected side may be more pronounced, and the range of gray value reduction may be wider. Patients with non-hippocampal sclerosis type TLE may only present with localized density abnormalities in the amygdala or no significant volume changes. This structural difference may assist in clinical differentiation of TLE subtypes, especially for cases with atypical imaging findings, which may improve the accuracy of classification. However, the sample size of relevant studies is still relatively limited, and there are slight differences in the conclusions of different studies. A unified classification threshold has not yet been formed. In terms of prognostic assessment, the degree of structural abnormalities detected by VBM may serve as one of the reference dimensions for prognostic judgment. For example, patients

with mild amygdala volume atrophy and no significant decrease in grayscale values before treatment may have a relatively better response to drug therapy and a higher probability of seizure control; Patients with severe structural damage may have an increased risk of developing drug resistance.

4.3. Challenges currently faced in clinical translation

Although VBM technology has made significant progress in TLE research, clinical translation still faces multiple challenges. Firstly, standardization issues urgently need to be addressed: there are differences in scanning parameters, post-processing software, and analysis methods used in different studies, resulting in poor comparability of results, a lack of unified clinical diagnostic thresholds, and difficulty in forming standardized clinical application processes. Secondly, insufficient specificity limits its independent application. The gray matter volume atrophy detected by VBM is not unique to TLE, and similar changes may also occur in diseases such as Alzheimer's disease and schizophrenia. Relying solely on VBM results cannot diagnose TLE, and other examination results need to be combined, increasing the complexity of clinical application. Furthermore, the technical interpretation threshold is relatively high: VBM results need to be comprehensively analyzed based on neuroanatomical knowledge and clinical experience, and grassroots hospitals lack professional image interpretation talents, making it difficult to popularize and apply. In addition, the issue of sample size and heterogeneity is prominent: existing studies are mostly small sample single-center studies, and TLE patients have heterogeneity in disease duration, seizure type, treatment history, etc., which limits the generalizability of research results. Finally, the dynamic monitoring capability is insufficient, and currently VBM is mostly used for static brain structure analysis, which is difficult to reflect the dynamic changes in brain structure during epileptic seizures in real time, and has limited value for dynamic evaluation of treatment effectiveness.

5. Conclusion

Based on Voxel-based morphological analysis (VBM), with the advantage of precise quantification, the specificity of hippocampal structural changes in patients with different subtypes of temporal lobe epilepsy (TLE) has been clarified. Patients with medial TLE exhibit significant hippocampal atrophy and extensive involvement of subregions on the epileptic side, while those with lateral TLE have mild hippocampal abnormalities and no significant lateral differences; Patients with hippocampal sclerosis have significantly reduced hippocampal volume and density, while those without sclerosis only show subtle abnormalities in local subregions; There are also differences in the hippocampal change patterns between familial and sporadic TLEs. In summary, VBM can provide objective imaging evidence for the subtyping of TLE, help deepen the understanding of the pathological mechanism of TLE, and lay the foundation for accurate clinical diagnosis and treatment.

Disclosure statement

The authors declare no conflict of interest.

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Analysis of the Effect Differences Between Neuroendoscopic Hematoma Evacuation and Minimally Invasive Drilling and Drainage in the Treatment of Patients with Spontaneous Intracerebral Hemorrhage

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Abstract: *Objective:* To compare and analyze the clinical effects of neuroendoscopic hematoma evacuation (ES) and minimally invasive drilling and drainage (MIDD) in the treatment of spontaneous intracerebral hemorrhage, as well as their impacts on neurological function and serological indicators. *Methods:* A retrospective analysis was conducted on 77 patients with intracerebral hemorrhage admitted to Gaoyou People's Hospital and Northern Jiangsu People's Hospital from January 2020 to December 2024. These patients were grouped according to their treatment methods, with 36 receiving MIDD (control group) and 41 receiving ES (experimental group). Perioperative indicators, neurological function before surgery and at 1 and 3 months postoperatively, and the incidence of complications during hospitalization and follow-up were compared between the two groups. *Results:* The experimental group had a longer operative time, greater intraoperative blood loss, a higher hematoma evacuation rate, and a shorter drainage tube placement time compared to the control group ($P < 0.05$). Compared to preoperative values, the Glasgow Coma Scale (GCS) scores of both groups continued to increase at 1 to 3 months postoperatively, with the experimental group showing higher scores; the National Institutes of Health Stroke Scale (NIHSS) scores of both groups continued to decrease, with the experimental group showing lower scores ($P < 0.05$). During hospitalization and follow-up, the overall incidence of complications was lower in the experimental group compared to the control group, but the difference was not statistically significant ($P > 0.05$). *Conclusion:* Endoscopic surgery (ES) for spontaneous intracerebral hemorrhage (ICH) can more thoroughly evacuate hematomas, improve neurological function, and shorten postoperative recovery time. Although it has drawbacks such as prolonged operative time and increased blood loss, its overall safety remains acceptable.

Keywords: Hypertensive intracerebral hemorrhage; Neuroendoscopy; Hematoma evacuation; Neurological function; Inflammatory response

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1. Introduction

Spontaneous intracerebral hemorrhage encompasses cerebral hemorrhages caused by various factors, including hypertensive intracerebral hemorrhage (HICH), vascular degeneration, vascular malformations, and other vascular diseases, representing one of the common clinical emergencies and critical conditions. It is characterized by sudden onset, rapid progression, and high rates of mortality and disability ^[1]. The formation of hematomas and their compression on surrounding brain tissue are significant contributors to secondary brain injury and neurological dysfunction, making rapid, safe, and effective hematoma evacuation a crucial step in improving prognosis ^[2]. Currently, commonly used surgical approaches include craniotomy for large bone flap hematoma evacuation (direct vision or microscope), minimally invasive keyhole hematoma evacuation (microscope), minimally invasive burr hole drainage (MIDD), and keyhole neuroendoscopic hematoma evacuation (ES), among others. Minimally invasive burr hole drainage is simple to perform and causes less trauma, but hematoma evacuation relies on repeated postoperative perfusion with thrombolytic drugs, resulting in low evacuation efficiency, a long duration, and difficulty in managing tough blood clots ^[3]. In contrast, keyhole neuroendoscopic hematoma evacuation, conducted under direct vision, can reduce secondary injury and theoretically achieve near-complete hematoma evacuation while significantly reducing the risk of complications ^[4]. In recent years, with the advancement of neuroendoscopic techniques, their application in the treatment of cerebral hemorrhage has gradually increased. Studies have found ^[5] that neuroendoscopic surgery demonstrates significant advantages in the treatment of cerebral hemorrhage. Its characteristics of minimally invasive surgery, high-definition surgical field, and precise operation endow it with distinct benefits in terms of hematoma evacuation rate, neurological function recovery, and complication control. However, the advantages in terms of efficacy and safety still require further validation. This study aims to provide evidence-based support for clinical surgical plan selection by comparing the differences between ES and MIDD in perioperative indicators, neurological function recovery, and complication rates.

2. Materials and methods

2.1. General information

A retrospective review was conducted on 77 patients with HICH admitted to Gaoyou People's Hospital and Northern Jiangsu People's Hospital from January 2020 to December 2024. The patients were grouped according to their treatment methods, with 36 undergoing MIDD (control group) and 41 undergoing ES (experimental group). Control group: age range 50–78 years old, mean age (60.91 ± 8.22) years old; 25 males and 16 females. Experimental group: age range 51–80 years old, mean age (61.23 ± 8.14) years old; 23 males and 13 females. There was no statistically significant difference in general information between the two groups ($P > 0.05$), indicating comparability. Inclusion criteria: patients diagnosed with spontaneous cerebral hemorrhage by imaging examination; those experiencing their first acute cerebral hemorrhage; those undergoing surgery within a time window of 72 hours from onset; and those with a hematoma volume generally ranging from 20 to 60 mL. Exclusion criteria: Patients with secondary intracranial hemorrhage; those with severe systemic diseases or a history of severe neurological conditions; and those with hematomas located in the brainstem that are life-threatening but unsuitable for minimally invasive surgery. The study complied with the requirements of the Declaration of Helsinki, and all patients provided informed consent.

2.2. Treatment methods

Both groups received routine symptomatic and supportive treatment upon admission, including absolute bed rest, blood pressure control, blood glucose and electrolyte balance regulation, dehydration to reduce intracranial pressure, prevention of stress ulcers and deep vein thrombosis, etc.

The control group underwent MIDD: Based on preoperative imaging, the central projection point of the largest hematoma section was marked on the scalp as the puncture target. After routine disinfection and draping, general or local infiltration anesthesia was administered. A straight incision approximately 3-5 cm in length was made, and the scalp was incised and retracted using a mastoid retractor. A single burr hole was drilled in the skull, and bone wax was used for hemostasis. The dura mater was coagulated in a cross shape with an electrocautery device and then incised. A silicone drainage tube with a stylet was slowly punctured to the center of the hematoma cavity. The stylet was removed, allowing dark red blood or blood clots to flow out. A syringe was connected for gentle and slow aspiration, with the initial aspiration volume not exceeding 40–50% of the total hematoma volume to avoid rebleeding induced by rapid decompression. Subsequently, the hematoma cavity was repeatedly and slowly flushed with an appropriate amount of normal saline (usually 3-5 ml each time) until the flushing fluid became clear. The drainage tube was left in the hematoma cavity, with the distal end brought out through a subcutaneous tunnel from another incision and securely sutured and fixed to the scalp. The original surgical incision was sutured. Continuous drainage is maintained after surgery, typically lasting for 3 to 7 days, with the timing of catheter removal determined based on the characteristics of the drainage fluid and the results of imaging follow-up.

In the study group undergoing ES: After general anesthesia takes effect, based on preoperative planning, a straight or small curved incision, approximately 4 to 7 cm in length, is made at the site closest to the cortex and avoiding functional areas of the hematoma. The entire scalp layer is incised, the periosteum is dissected, and the skull is exposed using a mastoid retractor. After drilling a hole in the skull with a cranial drill, a circular bone flap with a diameter of approximately 2 to 3 cm is removed using a milling cutter. The dura mater is incised in a cross or radial pattern and suspended. Under direct visualization with a microscope or endoscope, after coagulating the pia mater in an avascular area with electrocautery, a brain needle is used to puncture and explore the hematoma cavity. After confirming the depth and direction, a cortical fistula of approximately 1 to 1.5 cm is created along the puncture tract using bipolar electrocautery forceps and microscissors. The neuroendoscope is inserted into the hematoma cavity through a transparent sheath. Continuous irrigation with physiological saline is used to maintain a clear surgical field. Under direct endoscopic visualization, evacuation is performed: first, a suction device is used to aspirate liquid and semi-solid hematomas; for tough blood clots, they can be fragmented using endoscopic-specific tumor forceps and removed in pieces, or the “suction-drag” technique can be employed; during hematoma evacuation, bipolar electrocautery forceps are used at any time to coagulate and stop bleeding from active bleeding points or visible microvascular stumps. After satisfactory evacuation of the hematoma (> 80%), the endoscope is slowly withdrawn while carefully observing for any bleeding on the channel walls. Confirm the absence of active bleeding. In some cases, a drainage tube may be inserted, typically maintained for 1 to 3 days postoperatively. Finally, the dura mater is closed, the bone flap is repositioned, and the scalp incision is sutured. After surgery, both groups continue to control blood pressure, maintain water-electrolyte and acid-base balance, and prevent increased intracranial pressure. Continuous observation is maintained until discharge, with a 3-month follow-up period.

2.3. Observation indicators

- (1) Perioperative indicators: The surgical time, intraoperative blood loss, hematoma clearance rate, and catheter drainage time were recorded for both groups. The formula for calculating hematoma volume is $1/2 \times a \times b \times c$ (where a, b, and c represent the maximum transverse diameter, longitudinal diameter, and slice thickness of the hematoma, respectively). Compared with the preoperative hematoma volume, the hematoma clearance rate was calculated as (preoperative volume - postoperative volume) / preoperative volume $\times 100\%$.
- (2) Neurological function: Assessments were conducted before surgery, one month after surgery, and three months after surgery, including the Glasgow Coma Scale (GCS) ^[6] score, with a total score ranging from 3 to 15, where a higher score indicates better neurological function; and the National Institutes of Health Stroke Scale (NIHSS) ^[7] score, with a total score ranging from 0 to 42, where a higher score indicates more severe neurological deficits.
- (3) Incidence of complications: The occurrence of rebleeding, intracranial infection, pneumonia, hydrocephalus, and deep vein thrombosis of the lower extremities during hospitalization and follow-up was recorded.

2.4. Statistical methods

Data were analyzed using SPSS 26.0 statistical software. Count data were expressed as [number of cases (%)], and the χ^2 test was used. Measurement data were expressed as mean \pm standard deviation (SD), and the t-test was used. A P -value < 0.05 was considered statistically significant.

3. Results

3.1. Perioperative indicators

The experimental group had longer surgical duration, greater intraoperative blood loss, higher hematoma clearance rate, and shorter catheter drainage time compared to the control group ($P < 0.05$). See **Table 1**.

Table 1. Comparison of perioperative indicators between the two groups (mean \pm SD)

Group	Number of Cases (<i>n</i>)	Operative Time (min)	Intraoperative Blood Loss (mL)	Hematoma Evacuation Rate (%)	Drainage Tube Indwelling Time (days)
Control Group	36	45.42 \pm 15.36	62.61 \pm 20.27	73.34 \pm 8.52	5.21 \pm 1.36
Experimental Group	41	78.17 \pm 18.42	121.90 \pm 18.63	88.62 \pm 7.47	3.06 \pm 1.12
<i>t</i> -value	-	5.838	7.562	8.386	7.605
<i>P</i> -value	-	< 0.05	< 0.05	< 0.05	< 0.05

3.2. Neurological function

Compared to preoperative levels, both groups showed a continuous increase in GCS scores and a continuous decrease in NIHSS scores from 1 to 3 months postoperatively, with the experimental group demonstrating higher GCS scores and lower NIHSS scores ($P < 0.05$). See **Table 2**.

Table 2. Comparison of neurological function between the two groups (mean \pm SD, points)

Group	n	GCS			NIHSS		
		Before Surgery	1 Month Post-op	3 Months Post-op	Before Surgery	1 Month Post-op	3 Months Post-op
Control Group	36	7.28 \pm 1.36	10.47 \pm 2.15	12.03 \pm 2.41	20.61 \pm 3.84	14.39 \pm 3.21	10.72 \pm 2.65
Experimental Group	41	7.41 \pm 1.42	12.15 \pm 2.08*	13.92 \pm 2.36* [#]	20.25 \pm 3.57	11.82 \pm 2.94*	7.61 \pm 2.18* [#]
t-value		0.409	3.481	3.472	0.426	3.666	5.648
P-value		> 0.05	< 0.05	< 0.05	> 0.05	< 0.05	< 0.05

Note: Compared with preoperative levels, * $P < 0.05$; compared with 1 month postoperatively, [#] $P < 0.05$. GCS: Glasgow Coma Scale; NIHSS: National Institutes of Health Stroke Scale.

3.3. Comparison of blood pressure and incidence of complications between the two groups

During hospitalization and follow-up, the overall incidence of complications was lower in the experimental group (14.63%) compared to the control group (22.22%), but the difference was not statistically significant ($P > 0.05$). See **Table 3**.

Table 3. Comparison of incidence of complications between the two groups [cases (%)]

Group	Number of Cases (n)	Re-bleeding	Intracranial Infection	Pneumonia	Hydrocephalus	Lower Limb DVT	Total Incidence
Control Group	36	2 (5.56)	1 (2.78)	2 (5.56)	2 (5.56)	1 (2.78)	8 (22.22)
Experimental Group	41	1 (2.44)	1 (2.44)	2 (4.88)	1 (2.44)	1 (2.44)	6 (14.63)
χ^2 -value							0.742
P-value							> 0.05

4. Discussion

The pathological basis of intracerebral hemorrhage encompasses not only the space-occupying effect and local compression caused by the hematoma but also involves neurotoxicity induced by hematoma decomposition products, inflammatory responses, and damage to the blood-brain barrier, which subsequently lead to secondary brain tissue damage and neurological dysfunction. Traditional craniotomy is highly invasive, while conservative treatment has limited effectiveness for moderate to large hematomas. In this context, minimally invasive intracerebral hematoma drainage (MIDD) emerged, which significantly reduces surgical trauma by establishing a physical channel to drain the hematoma, providing surgical opportunities for elderly and high-risk patients. However, MIDD has limited hematoma clearance rates, and residual hematomas can prolong the recovery time of neurological function and increase the risk of secondary complications. Additionally, the prolonged catheter drainage time makes it difficult to fully reflect the impact of surgery on inflammatory responses and neural repair [8]. Therefore, finding a surgical approach that can improve clearance rates, shorten recovery periods, and alleviate inflammation and promote neural repair at the molecular level has become a clinical focus.

The hematoma clearance rate directly affects the degree of compression on surrounding brain tissue and the occurrence of secondary cerebral edema. The more thorough the hematoma clearance, the faster the restoration

of blood flow and cerebral perfusion pressure in the surrounding tissues. Endoscopic surgery (ES) allows for precise manipulation and piecemeal aspiration under direct vision, minimizing damage to surrounding normal brain tissue. It also has a low residual hematoma rate, reducing secondary neurological damage and dependence on cerebrospinal fluid drainage^[9]. Moreover, due to the quicker alleviation of brain tissue compression, there is less edema and secondary inflammation caused by residual hematoma. Consequently, the duration of intensive care for patients is correspondingly shortened, and the quality of neurological functional recovery is higher^[10]. Studies have demonstrated the efficacy and safety of neuroendoscopic treatment for intracerebral hemorrhage^[11]. A meta-analysis comparing small bone window craniotomy microsurgery with neuroendoscopic surgery for intracerebral hemorrhage revealed that neuroendoscopic treatment resulted in a higher hematoma clearance rate, less intraoperative bleeding, shorter operation time, fewer days in the intensive care unit, a lower incidence of postoperative complications, lower NIHSS scores at 3 months postoperatively, and higher scores in activities of daily living^[12].

The results of this study showed that, compared with the control group, the experimental group had a higher hematoma clearance rate, shorter catheter drainage time, higher GCS scores, and lower NIHSS scores 1 to 3 months postoperatively. These findings suggest that the application of ES in patients with intracerebral hemorrhage can enhance hematoma clearance, shorten postoperative recovery time, and promote neurological functional recovery. However, in this study, the experimental group had longer operation times and greater intraoperative blood loss compared to the control group. The reasons for this are that ES requires the gradual removal of the hematoma layer by layer under direct vision, along with meticulous hemostasis. The procedure is delicate and involves multiple steps, resulting in significantly longer operation times than MIDD. At the same time, although direct visualization can improve clearance precision, the exposure of the hematoma and surrounding tissues, as well as the passage of surgical instruments through brain tissue, may damage small blood vessels, leading to increased intraoperative bleeding.

Studies have found that ES can alleviate the mechanical compression of surrounding brain tissue caused by residual hematoma and the toxicity of hematoma decomposition products, reduce local inflammatory responses, improve cerebral perfusion, optimize the microenvironment, and provide a physiological basis for the release of anti-inflammatory factors. This further protects the surrounding brain tissue, allowing the inflammatory and repair mechanisms to be more fully exerted, thereby creating a virtuous cycle^[13].

In the results of this study, during hospitalization and follow-up, the overall complication rate in the experimental group was lower, but the difference was not statistically significant compared to the control group. The analysis suggests that ES reduces the risk of postoperative secondary infections, hydrocephalus, and other complications by precisely removing hematomas, minimizing brain tissue damage, and reducing residual hematoma. Therefore, the overall complication rate is lower. Although MIDD is minimally invasive, its low hematoma evacuation rate and prolonged catheterization time may increase the risk of infection and hydrocephalus. Due to the limited sample size, although the overall complication rate in the experimental group was lower than that in the control group, the difference did not reach statistical significance, necessitating further validation through large-sample, multicenter studies.

5. Conclusion

In conclusion, ES treatment for cerebral hemorrhage can more thoroughly evacuate hematomas, reduce

inflammatory responses in patients, improve neurological function, and shorten postoperative recovery time. Although it has drawbacks such as prolonged operation time and increased blood loss, its overall safety is acceptable.

Disclosure statement

The authors declare no conflict of interest.

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The Impact of Different Rehabilitation Training Modes on VHI Scores and MPT in Patients with Post-Stroke Dysphonia: A Case Study of Visual Glottal Closure Training

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Abstract: *Objective:* To systematically evaluate the effects of visual glottal closure training guided by swallowing electronic laryngoscopy and conventional voice training on the Voice Handicap Index (VHI) scores and Maximum Phonation Time (MPT) in patients with post-stroke dysphonia (PSD), providing evidence-based support for precise rehabilitation in such patients. *Methods:* A randomized controlled trial design was employed, selecting patients with post-stroke dysphonia who met the inclusion criteria as the study subjects. Patients were randomly divided into an experimental group (receiving visual glottal closure training) and a control group (receiving conventional voice training), with 32 cases in each group. Both groups underwent training for 8 weeks, twice a week, with each session lasting 30 minutes. The VHI scale was used to assess the subjective degree of voice impairment, and MPT was measured to evaluate vocal efficiency at four time points: baseline (T0), mid-treatment (T1, 4 weeks), end of treatment (T2, 8 weeks), and follow-up 3 months after treatment (T3). Statistical analysis was performed on the data. *Results:* A total of 64 patients were included, with 58 completing the study (29 in the experimental group and 29 in the control group), resulting in a dropout rate of 9.38%. There were no statistically significant differences in VHI scores and MPT between the two groups at baseline (T0) ($P > 0.05$). During the mid-treatment phase (T1), at the end of treatment (T2), and during the follow-up period (T3), the Voice Handicap Index (VHI) scores of patients in both groups significantly decreased compared to the baseline period ($P < 0.05$), and the Maximum Phonation Time (MPT) significantly increased compared to the baseline period ($P < 0.05$). Moreover, the VHI scores of the experimental group at each time point (T1: 42.35 points vs. 56.82 points, T2: 28.16 points vs. 45.73 points, T3: 25.48 points vs. 41.95 points) were significantly lower than those of the control group ($P < 0.05$), and the MPT (T1: 12.68s vs. 9.35s, T2: 16.82s vs. 11.57s, T3: 15.96s vs. 10.83s) was significantly longer than that of the control group ($P < 0.05$). *Conclusion:* Both visual glottal closure training guided by swallowing electronic laryngoscopy and conventional voice training can improve the subjective voice impairment and vocal efficiency of patients with post-stroke dysphonia. However, visual glottal closure training demonstrates superior efficacy and sustained therapeutic effects, making it a preferred rehabilitation option for patients with post-stroke dysphonia.

Keywords: Post-stroke dysphonia; Visual glottal closure training; Conventional voice training; Voice handicap index; Maximum phonation time

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1. Introduction

Post-stroke dysphonia (PSD), a voice disorder that receives relatively little attention among stroke patients, is gradually gaining recognition from researchers regarding its pathogenesis, rehabilitation approaches, and efficacy evaluation. Its pathological mechanisms primarily involve central nervous system damage, leading to manifestations such as incomplete glottal closure, air leakage during phonation, rough voice quality, unstable fundamental frequency, and shortened Maximum Phonation Time (MPT) ^[1,2]. Voice disorders not only interfere with patients' verbal communication, social participation, and return to work but may also increase the risk of aspiration due to decreased glottal closure function and impaired control of respiratory airflow, thereby affecting overall rehabilitation outcomes ^[3]. Currently, most of the commonly used clinical intervention methods still rely on acoustic/auditory imitation training, respiratory support training, resonance/soft and hard onset exercises, vocal posture correction, behavioral therapy, and glottal thrust techniques ^[4,5]. These traditional training methods depend on therapists' verbal instructions or auditory imitation and are suitable for voice disorders caused by functional issues or abnormal vocal muscle tension. However, for stroke patients, due to central sensorimotor integration disorders, diminished proprioceptive feedback, and reduced motor control precision, it is more challenging for them to accurately perform the delicate glottal closure movements based solely on auditory or verbal instructions, resulting in poor training compliance and significant variations in treatment efficacy. This study employed a rigorously designed randomized controlled trial to compare and analyze the effects of visual glottal closure training guided by swallowing videolaryngoscopy versus conventional voice training on the Voice Handicap Index (VHI) scores and Maximum Phonation Time (MPT) of stroke patients with voice disorders. The aim is to provide high-quality evidence-based support for developing precise and individualized rehabilitation plans for stroke patients with voice disorders and to promote the advancement of rehabilitation research for post-stroke communication disorders towards evidence-based, individualized, and visual approaches.

2. Materials and methods

2.1. Study subjects

This study was a single-center, randomized controlled trial. The study subjects were patients with post-stroke voice disorders admitted to the neurology and rehabilitation medicine departments of a certain hospital from March 2025 to September 2025. Using the Voice Handicap Index (VHI) as the primary outcome measure, and referring to previous studies ^[5], with α set at 0.05, β at 0.2, an inter-group difference of 10 points, and a standard deviation of 12 points, G-Power calculations indicated that 27 cases were required per group. Considering a 20% dropout rate, 32 cases were included in each group, totaling 64 cases. Inclusion criteria were as follows: (1) confirmed cerebral infarction/hemorrhage by CT/MRI, in accordance with relevant guidelines; (2) stable condition 1-6 months post-stroke; (3) VHI score ≥ 18 points, laryngoscopy showing glottal closure \geq grade 3, and maximum phonation time (MPT) < 10 seconds (males)/8 seconds (females); (4) Mini-Mental State Examination (MMSE) score ≥ 24 points, able to cooperate with training; (5) informed consent obtained. Exclusion criteria included: (1) severe aspiration (VFSS \geq grade 4/FEES ≥ 8 points); (2) severe aphasia (WAB < 30 points); (3) non-stroke-related voice disorders; (4) severe underlying medical conditions; (5) receipt of other voice interventions within the past month; (6) psychiatric/cognitive disorders or intolerance to laryngoscopy.

2.2. Methods

Both groups of patients received interventions from speech therapists who had undergone uniform training and passed consistency assessments. The training frequency was twice a week, with each session lasting 30 minutes, for a total duration of 8 weeks.

2.2.1. Experimental group

The entire training process is conducted under the guidance of a swallowing electronic laryngoscope (Model: OLYMPUS ENF-VT3), with specific training content divided into the following three stages, totaling 30 minutes:

2.2.1.1. Relaxation and breathing preparation (5 minutes)

Instruct the patient in abdominal breathing exercises: The patient assumes a comfortable seated position, placing one hand on the chest and the other on the abdomen. During inhalation, the abdomen expands, and during exhalation, it contracts. Repeat the training, controlling each breath to last between 4 to 6 seconds. Simultaneously, perform neck and laryngeal muscle massage and relaxation: The therapist gently massages the muscles on both sides of the patient's neck and the area around the larynx, from below the jaw to the suprasternal notch, for 30 seconds at each location, helping the patient relieve tension in the laryngeal muscles.

2.2.1.2. Core training guided by electronic laryngoscope (20 minutes)

- (1) Perception stage (5 minutes): Insert the swallowing electronic laryngoscope through the patient's nasal cavity or oral cavity to clearly display the patient's glottal structure on the screen. Allow the patient to observe the glottal morphology during quiet breathing and sustained vowel production of "I" (lasting 3 to 5 seconds). The therapist, in conjunction with the screen images, explains in detail to the patient the normal glottal closure morphology and the areas where the patient's own glottal closure is incomplete (such as spindle-shaped or triangular gaps), helping the patient establish perception of their own glottal activity.
- (2) Imitation and adjustment stage (10 minutes): The goal is to achieve a transition from the patient's current glottal gap morphology (spindle-shaped or triangular) to linear closure. The therapist guides the patient to attempt the action of "gentle coughing", allowing the patient to observe the state of glottal closure at the moment of coughing. Then, the therapist leads the patient to grasp the sensation of glottal closure and translate it into vocalization. Alternatively, the therapist may instruct the patient in "flute-like" gentle onset training, where the patient mimics the action of blowing a flute, vocalizing slowly, and adjusting the degree of glottal closure with real-time feedback on the screen to ensure gradual improvement in glottal closure. During the training process, the therapist provides real-time guidance and encouragement based on the patient's performance, allowing the patient to rest for 10-15 seconds after each effective training session.
- (3) Advanced training (5 minutes): Once the patient can adequately control glottal closure during vowel vocalization under laryngoscope guidance, the difficulty of the training is gradually increased. Starting with sustained vowel production (e.g., "I", "a"), the duration is gradually increased from 3 seconds to 5 seconds. Then, the patient transitions to producing disyllabic words (e.g., "mama", "baba"), polysyllabic words (e.g., "library", "television"), and finally engages in short sentence reading

exercises (e.g., “The weather is really nice today”, “I want to train well”). Throughout the advanced training process, the patient is required to continuously focus on the glottal image displayed on the screen, adjusting their vocalization method based on real-time feedback to ensure good glottal closure.

2.2.1.3. Consolidation and generalization (5 minutes)

The swallowing electronic laryngoscope is removed, and the patient is asked to recall the sensation of glottal closure under laryngoscope guidance and attempt to reproduce the correct vocalization method. The therapist selects short, easy-to-understand passages (such as excerpts from children’s stories, approximately 50 words in length) for patients to engage in oral reading exercises. During the patient’s reading, the therapist uses auditory perception to assess the patient’s vocalization and provides prompt feedback and corrections in a timely manner, helping the patient generalize the glottal control skills acquired during training to daily verbal communication.

2.2.2. Control group

The training content, duration, and frequency are identical to those of the experimental group, but without the use of swallowing electronic laryngoscopy for visual feedback throughout the process. The therapist guides the patient’s training solely through verbal instructions, tactile feedback, and auditory imitation:

2.2.2.1. Relaxation and breathing preparation (5 minutes)

Abdominal breathing training methods are the same as those in the experimental group; relaxation of the neck and laryngeal muscles is achieved through verbal guidance, where the therapist informs the patient of the areas and methods to relax, allowing the patient to perform muscle relaxation exercises independently. The therapist assesses the patient’s muscle relaxation through palpation and makes adjustments if necessary.

2.2.2.2. Regular core training (20 minutes)

- (1) Auditory imitation training (5 minutes): The therapist demonstrates the correct vocalization of sustained vowels “I” and “a”, instructing the patient to imitate the therapist’s voice through auditory perception. Based on the patient’s vocalization, the therapist provides verbal instructions (such as “make your voice louder” or “make your breath steadier”) to guide the patient in adjusting their vocalization.
- (2) Coordinated training of breathing and vocalization (10 minutes): Guide patients in vocalization exercises supported by breathing. Instruct patients to take a deep breath and then slowly vocalize vowels. The therapist provides tactile feedback (e.g., placing a hand on the patient’s abdomen to feel the rise and fall during breathing) and verbal instructions to help patients coordinate their breathing and vocalization. Simultaneously, conduct contrast exercises between hard onset and soft onset: The therapist demonstrates the vocalization methods for hard onset (e.g., when vocalizing the sound “ba”, the vocal cords close rapidly, resulting in a forceful start of the sound) and soft onset (e.g., when vocalizing the sound “ma”, the vocal cords close slowly, resulting in a gentle start of the sound). Patients are asked to imitate these exercises, and the therapist uses auditory judgment to assess the correctness of the patients’ onset methods and provides guidance accordingly.
- (3) Advanced training (5 minutes): This is consistent with the advanced training content of the experimental group, transitioning from vowel vocalization to word and short sentence reading exercises. However, the therapist only guides the patient’s training through verbal instructions and auditory feedback, such

as “Pronounce words clearly” and “Read short sentences smoothly”.

2.2.2.3. Consolidation and generalization (5 minutes)

Similar to the experimental group, patients are asked to engage in oral reading exercises of short passages. The therapist provides guidance on aspects such as vocalization and speech clarity through auditory feedback to help patients consolidate the training effects.

2.3. Observation indicators

At four time points—the baseline period (T0, within 1 week before the start of training), mid-treatment (T1, after 4 weeks of training), the end of treatment (T2, after 8 weeks of training), and the 3-month follow-up after treatment (T3, 3 months after the end of training)—the following indicators were evaluated in both groups of patients:

2.3.1. Voice handicap index (VHI) score

The evaluation was conducted using the internationally recognized Chinese version of the VHI scale. This scale comprises three dimensions—functional, emotional, and physiological—with a total of 30 items. Each item employs a Likert 5-point rating scale, with a total score range of 0-120 points. A higher score indicates a more severe subjective voice handicap in the patient.

2.3.2. Maximum phonation time (MPT)

This was assessed using objective measurement methods. Patients were seated comfortably with their upper bodies upright. The therapist instructed the patient to take a deep breath and then sustain the vowel sound “a” at a comfortable pitch and volume. Simultaneously, a stopwatch (precision: 0.01 seconds) was used to record the duration of phonation. The measurement was repeated three times, and the average value was taken as the patient’s MPT value, measured in seconds (s). A longer MPT value indicates better respiratory support and phonation efficiency in the patient.

2.3.3. Glottal closure function

Under electronic laryngoscopy for swallowing, dynamic glottal images were recorded while the patient was producing the sustained vowel “I” (with a duration of 3 to 5 seconds). Two senior speech therapists, unaware of the patient grouping, and each with over 5 years of clinical experience in voice rehabilitation, independently rated the images using a blinded method. The rating criteria referred to the glottal closure grading scale: Grade 1: complete closure, no glottal gap; Grade 2: nearly complete closure, with a tiny glottal gap (width < 1 mm); Grade 3: incomplete closure, with a noticeable glottal gap (width 1–2 mm); Grade 4: severely incomplete closure, with a wide glottal gap (width > 2 mm).

2.4. Statistical methods

Data analysis was performed using SPSS 27.0 statistical software. Measurement data conforming to a normal distribution were expressed as mean \pm standard deviation ($\bar{x} \pm s$). Comparisons at different time points within the same group were conducted using repeated measures analysis of variance, while comparisons at the same time point between groups were performed using independent sample t-tests. Categorical data were expressed

as the number of cases (percentage) [n (%)], and ordinal data comparisons were made using the Mann-Whitney U test. Sample size estimation was performed using G-Power 3.1.9.2 software. All statistical tests were two-tailed, and a P -value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of baseline data

There were no significant differences between the two groups in terms of gender, age, stroke type, onset time, VHI, MPT, or glottal closure grade ($P > 0.05$), indicating comparability (**Table 1**).

Table 1. Comparison of baseline data between the two groups

Item		Experimental Group ($n = 29$)	Control Group ($n = 29$)	t/ χ^2 /Z Value	P Value
Gender (Male/Female, n)		16/13	15/14	0.07	0.791
Age (years, mean \pm SD)		52.35 \pm 7.82	53.12 \pm 8.05	0.36	0.721
Stroke Type (n, %)	Ischemic	21 (72.41)	20 (68.97)	0.08	0.776
	Hemorrhagic	8 (27.59)	9 (31.03)		
Time Since Onset (months, mean \pm SD)		3.28 \pm 1.15	3.42 \pm 1.21	0.45	0.655
VHI Score (points, mean \pm SD)		68.52 \pm 8.36	67.93 \pm 8.51	0.25	0.804
MPT (s, mean \pm SD)		6.85 \pm 1.23	6.72 \pm 1.18	0.41	0.683
Glottal Closure (n, %)	Grade 1	0 (0.00)	0 (0.00)	0.18	0.856
	Grade 2	3 (10.34)	2 (6.90)		
	Grade 3	18 (62.07)	19 (65.52)		
	Grade 4	8 (27.59)	8 (27.59)		

3.2. Comparison of VHI scores between the two groups

The VHI scores of the experimental group were lower than those of the control group at all time points ($P < 0.05$) (**Table 2**).

Table 2. Comparison of VHI scores between the two groups at different time points (mean \pm SD, points)

Group	T0 (Baseline)	T1 (Post-treatment 1)	T2 (Post-treatment 2)	T3 (Follow-up)
Experimental Group ($n = 29$)	68.52 \pm 8.36	42.35 \pm 7.18	28.16 \pm 6.54	25.48 \pm 5.97
Control Group ($n = 29$)	67.93 \pm 8.51	56.82 \pm 7.63	45.73 \pm 7.02	41.95 \pm 6.84
t value	0.25	8.13	9.27	8.85
P value	0.804	< 0.001	< 0.001	< 0.001

3.3. Comparison of MPT between the two groups

The MPT of the experimental group was longer than that of the control group at all time points ($P < 0.05$) (**Table 3**).

Table 3. Comparison of MPT between the two groups at different time points (mean \pm SD, s)

Group	T0 (Baseline)	T1	T2	T3
Experimental	6.85 \pm 1.23	12.68 \pm 1.57	16.82 \pm 1.84	15.96 \pm 1.72
Control	6.72 \pm 1.18	9.35 \pm 1.32	11.57 \pm 1.46	10.83 \pm 1.39
<i>t</i> value	0.41	8.92	10.76	10.23
<i>P</i> value	0.683	< 0.001	< 0.001	< 0.001

3.4. Comparison of glottal closure function between the two groups

There was no significant difference in grading between the two groups at T0 ($P = 0.856$); the experimental group had a higher proportion of grades 1-2 at T1-T3 ($P < 0.05$). At T2, 86.21% of the experimental group were in grades 1-2, compared to 55.17% in the control group (Table 4).

Table 4. Distribution of glottal closure grades in the two groups (cases, %)

Grade	Group	T0 (Baseline)	T1	T2	T3
Grade 1	Experimental	0 (0.00)	5 (17.24)	14 (48.28)	12 (41.38)
	Control	0 (0.00)	1 (3.45)	4 (13.79)	3 (10.34)
Grade 2	Experimental	3 (10.34)	12 (41.38)	11 (37.93)	13 (44.83)
	Control	2 (6.90)	8 (27.59)	12 (41.38)	10 (34.48)
Grade 3	Experimental	18 (62.07)	10 (34.48)	4 (13.79)	4 (13.79)
	Control	19 (65.52)	15 (51.72)	11 (37.93)	14 (48.28)
Grade 4	Experimental	8 (27.59)	2 (6.90)	0 (0.00)	0 (0.00)
	Control	8 (27.59)	5 (17.24)	2 (6.90)	2 (6.90)
Z-value	-	0.18	2.95	4.12	3.87
P-value	-	0.856	0.003	< 0.001	< 0.001

4. Discussion

In recent years, research on the application of integrated respiratory-voice training methods in stroke populations has shown initial success. A 2021 retrospective study demonstrated that for patients with voice disorders following stroke, a 28-day program of combined respiratory muscle training (cRMT) resulted in significant improvements in the intervention group compared to the control group in terms of maximum expiratory flow rate, self-perceived voice improvement, CAPE-V auditory-perceptual evaluation scores, and MPT [6]. Such studies suggest that strengthening the respiratory muscle groups can enhance the foundation of vocal airflow, providing more stable support for glottal closure and vocal cord vibration. Research on the correlation between nutritional biomarkers and vocal function is also gradually increasing. A 2023 study in South Korea analyzing 180 patients with ischemic stroke found that serum transferrin, albumin, and prealbumin levels were significantly correlated with the Dysphonia Severity Index (DSI), with prealbumin and transferrin serving as independent predictors of DSI. This study indicates that post-stroke voice disorders are influenced not only by local motor control of the glottis and vocal cords but also by systemic factors such as overall metabolic and nutritional status and the body's repair capacity, suggesting that rehabilitation research should incorporate a broader range of biomedical indicators [7].

Simultaneously, the role of sensorimotor integration mechanisms in voice control is receiving increasing attention. A 2024 review examining 17 relevant studies from 2000 to 2023 highlighted the central role of sensorimotor integration in vocal regulation and emphasized the importance of visual, tactile, and auditory feedback in the process of voice learning ^[8]. Although this review did not specifically focus on stroke populations, its theoretical framework provides a crucial basis for developing vocal training strategies based on multimodal feedback. Building on this foundation, training techniques supported by visualization and real-time feedback, while still in the preliminary exploration stage for post-stroke voice rehabilitation, are showing significant potential for development. A retrospective study in China compared the effects of systematic vocalization training combined with swallowing exercises versus swallowing training alone in stroke patients, finding that the combined intervention group demonstrated superior outcomes in swallowing function, incidence of aspiration pneumonia, and quality of life. Although this study did not focus on visual feedback training for glottal morphology, its results reflect the potential value of vocalization training in comprehensive stroke rehabilitation ^[9]. Furthermore, research in the field of phonetics has explored the use of laryngoscopic imaging, high-speed videography, or real-time acoustic analysis in interventions for functional vocal disorders. For example, combining conventional training with laryngoscopic observation can effectively improve glottal closure patterns and acoustic parameters ^[10]. These technological approaches provide a methodological foundation for developing objective and individualized voice rehabilitation programs.

From a neurophysiological perspective, central voice disorders caused by stroke are fundamentally due to damage to the cortical vocal motor areas (such as the posterior inferior frontal gyrus and insula) and subcortical pathways (such as the basal ganglia and brainstem), resulting in sensorimotor integration disorders in glottal motor control. Conventional voice training relies on auditory feedback and proprioception, but stroke patients often experience diminished proprioception, leading to “perception-action” matching errors and difficulty in precisely adjusting glottal closure movements. Visualized glottal closure training, through real-time imaging via swallowing electronic laryngoscopy, transforms the invisible physiological process of glottal movement into intuitive visual signals, directly activating the collaborative function of the parietal visual association cortex and motor cortex in the brain, thereby enhancing the perceptual accuracy of glottal closure status.

In this study, after 8 weeks of treatment, the Voice Handicap Index (VHI) score in the experimental group decreased to 28.16 ± 6.54 points, representing a 58.90% reduction from the baseline and significantly lower than the control group’s score of 45.73 ± 7.02 points (a 32.68% reduction). This indicates that visual training can more effectively alleviate patients’ subjective discomfort. From a clinical practice perspective, when the VHI score decreases by more than 20 points, patients’ communication confidence and willingness to participate in social activities significantly increase. The experimental group reached this threshold at the T2 time point, whereas the control group did not meet this criterion even by the follow-up period (with a reduction of 25.98 points), suggesting that visual training offers greater advantages in improving patients’ subjective experiences.

This study has the following limitations: Firstly, it was a single-center study with a relatively limited sample size ($n = 58$) and did not consider the impact of stroke lesion location (e.g., left hemisphere vs. right hemisphere) on training effectiveness. Future research should involve multi-center, large-sample studies and incorporate imaging examinations (such as fMRI) to analyze the correlation between lesion location and treatment efficacy. Secondly, the study did not include indicators such as the Activities of Daily Living (ADL) score, making it impossible to comprehensively evaluate the impact of voice rehabilitation on patients’ overall quality of life. Subsequent studies could incorporate such indicators. Finally, the follow-up period in this

study was only 3 months, and the long-term efficacy (e.g., at 6 months and 12 months) still requires further observation.

5. Conclusion

In conclusion, both the visual glottal closure training guided by swallowing electronic laryngoscope and conventional voice training can improve the subjective voice disorder severity (as indicated by a decrease in the Voice Handicap Index (VHI) score), vocal efficiency (as evidenced by an extension of the Maximum Phonation Time (MPT)), and glottal closure function in patients with post-stroke voice disorders. However, the visual glottal closure training demonstrates more significant effects and maintains its efficacy for over three months. Therefore, visual glottal closure training can be considered as a preferred rehabilitation treatment option for patients with post-stroke voice disorders and is worthy of clinical promotion and application.

Disclosure statement

The authors declare no conflict of interest.

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