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ORIGINAL RESEARCH

Effects of GLP-1 Receptor Agonist on Glycolipid Metabolism and Micro Inflammatory Status in Patients with Abdominal Obesity and Type 2 Diabetes

Wei Shao, BM; Jianli Wu, BM; Meiqin Zhu, BM; Yanqi Wang, BM; Haideng Ci, MM

ABSTRACT

Objective • To explore the impact of Liraglutide, a GLP-1 receptor agonist, on glycolipid metabolism and microinflammatory status in patients with abdominal obesity and type 2 diabetes.

Methods • This study consecutively enrolled 60 patients with abdominal obesity and type 2 diabetes at Jiande Hospital of Traditional Chinese Medicine from October 2020 to December 2021. They were randomly divided into a control group (30 cases) receiving routine treatment and a liraglutide group (30 cases) receiving Liraglutide in addition to routine treatment for 3 months. The control group received routine treatment, which included metformin at a dose of 1g twice daily, along with dietary and exercise guidance. The liraglutide group received an initial dose of 0.6 mg daily for the first week, increased to 1.2 mg daily in the second week, and further increased to 1.8 mg daily in the third week, continuing at this dose until the end of the 12-week treatment period, with adjustments based on tolerance.

Results • Significant improvements were observed in SBP, DBP, BMI, waist-to-hip ratio, and various glycolipid and microinflammatory indexes in the Liraglutide group compared to controls ($P < .05$). Specifically, SBP, DBP, BMI, waist-to-hip ratio, FPG, 2hPG, HbA_{1c}, TG, TC, hs-CRP, TNF-α, and IL-6 levels decreased more significantly in the liraglutide group. Conversely, C-peptide and fasting insulin levels increased more in the liraglutide group. No significant difference in the incidence of adverse reactions was observed between the two groups ($P > .05$).

Conclusion • Liraglutide can improve glycolipid metabolism and microinflammatory status in patients with abdominal obesity and type 2 diabetes, which has high medication safety. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Type 2 diabetes is an endocrine and metabolic disease primarily caused by insulin resistance and obesity. In China, 24.3% of diabetic patients are obese, with 45.4% of this obesity being abdominal.[1,2] Abdominal obesity, defined as excess fat accumulation in the abdominal area and typically measured using the waist-to-hip ratio (WHR) or waist circumference (WC), is prevalent among Chinese patients with type 2 diabetes. Human glucagon-like peptide-1 (GLP-1) ameliorates hepatic lipid deposition in patients with type 2 diabetes.[3,4] While the specific mechanism of GLP-1 action is not fully understood, it is known that GLP-1 receptor agonists, like Liraglutide, promote insulin secretion, improve insulin resistance, delay gastric emptying, and suppress appetite.[5] These mechanisms suggest potential benefits for managing glucose and lipid metabolism, as well as reducing inflammation. Understanding the impact of GLP-1 receptor agonists on glycolipid metabolism and inflammatory status in patients with abdominal obesity and type 2 diabetes is of significant clinical relevance.[6] This study aims to explore these effects to provide insights into improved management strategies for metabolic dysfunction, thereby mitigating complications and enhancing patient outcomes.[7] The specific relevance of this study in a Chinese population is underscored by the high prevalence of abdominal obesity and its implications for type 2 diabetes management. Our hypothesis is that Liraglutide, a GLP-1 receptor agonist, can significantly improve glycolipid metabolism and reduce microinflammatory markers in this demographic, offering a safe and effective therapeutic option. In this study, we analyzed the effects of GLP-1 receptor agonists on glycolipid metabolism and microinflammatory status in patients with abdominal obesity and type 2 diabetes to provide evidence-based guidance for clinical practice.

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MATERIALS AND METHODS

Baseline information

This study consecutively enrolled 60 patients with abdominal obesity and type 2 diabetes at Jiande Hospital of Traditional Chinese Medicine from October 2020 to December 2021. The patients were randomly divided into a control group (30 cases) and a liraglutide group (30 cases) using a random number table. The control group received conventional treatment, while the liraglutide group received liraglutide in addition to conventional treatment. In the control group, there were 17 males and 13 females, aged 19-65 years (mean age 48.53±7.26 years), with a disease duration of 5-13 years (mean duration 8.94±3.17 years). In the liraglutide group, there were 16 males and 14 females, aged 18-65 years (mean age 49.01±7.19 years), with a disease duration of 5-13 years (mean duration 9.02±2.53 years).

Inclusion criteria: (1) All patients met the diagnostic criteria for diabetes mellitus established by the World Health Organization in 1999;[8] (2) All patients met the diagnostic criteria for abdominal obesity with a waist circumference ≥90 cm in males or ≥85 cm in females;[9] (3) All patients had poor glycemic control, with HbA_{1c} >7% and BMI ≥28 kg/m²; (4) Patients had not used lipid-regulating drugs 2 weeks before participating in the treatment; (4) patients did not use lipid-modulating drugs 2 weeks before participating in the treatment.

Exclusion criteria**:** (1) patients with the combined presence of malignant tumors or hematological disorders; (2) increased cortisol; (3) patients with long-term treatment with antipsychotic or (and) antidepressant medications; (4) patients with cognitive dysfunction; (5) patients with the combined presence of infectious diseases; and (6) patients with allergies to therapeutic drugs.

Treatment

Control group: Patients received conventional treatment, which included metformin (Tianjin Pacific Pharmaceutical Co., Ltd; National Drug Code: H12020797) at a dose of 1g twice daily, along with dietary and exercise guidance. Treatment lasted for 12 weeks.

Liraglutide group: Patients received liraglutide (Hangzhou Jiuyuan Genetic Engineering Co., LTD.; Chinese medicine approval: S20233109) in addition to conventional treatment. The initial dose was 0.6 mg once daily for the first week, increased to 1.2 mg daily in the second week, and further increased to 1.8 mg daily in the third week, continuing at this dose until the end of the 12-week treatment period. Adjustments were made based on tolerance, in line with current clinical guidelines and previous research findings.

Observation indicators

Conventional indicators. The diastolic blood pressure (DBP), systolic blood pressure (SBP), body mass index (BMI), and waist-to-hip ratio were measured before and after treatment. SBP and DBP were measured using an electronic sphygmomanometer (Shandong Weibo Medical Equipment Co., Ltd., Jining, China), and BMI was calculated as weight (kg) divided by height squared (m²).

Glycolipid metabolism indicators. Three mL of venous blood was drawn from the patients' fasting vein before and after treatment, centrifuged for 10 minutes at 3000 rpm (Hebei MedZone Medical Instrument Co., Ltd., Langfang, China), and the serum was retained. Fasting blood glucose (FPG), two-hour postprandial blood glucose (2hPG), C-peptide, fasting insulin (Fins), and glycosylated hemoglobin (HbA_{1c}) were measured using glucose oxidase method (Wuhan Elite Bioscience and Technology Co.), and triglyceride (TG) and total cholesterol (TC) concentrations were determined using an automatic biochemical analyzer (Nanjing Beden Medical Co., Ltd., Nanjing, China).

Microinflammatory status

Three mL of venous blood was drawn from the patients' fasting vein before and after treatment, centrifuged for 10 minutes at 3000 rpm using a 10 cm radius centrifuge (Hebei Medical Zong Medical Equipment Co., Ltd., Langfang, China), and the serum was retained. Serum levels of interleukin-6 (IL-6), hypersensitive C-reactive protein (hs-CRP), and tumor necrosis factor-α (TNF-α) were measured using enzyme-linked immunosorbent assay kits (Shanghai Sigma Aldrich Trading Co., Ltd., Shanghai, China).

Adverse reactions

The occurrence of adverse reactions, including nausea and vomiting, hypoglycemia, and diarrhea, was recorded and compared between the two groups during the treatment period.

Statistical analysis

The Statistical Package for Social Science (SPSS) 22.0 was used to process the data. Measurement data (BMI, waist-to-hip ratio, FPG, 2hPG level, etc.) were compared by *t* test ($\bar{x} \pm s$); count data (gender, incidence of adverse reactions, etc.) were compared by χ^2 test, expressed as percentage (%), with $P < .05$ indicating statistical significance. Assumptions of normality and homogeneity of variance were checked to ensure the validity of the *t* tests and chi-square tests.

RESULTS

Statistical analysis was performed using SPSS 22.0. Independent *t* tests were applied to compare the means of continuous variables between the two groups, while chi-square tests were used for categorical data. Assumptions of normality and homogeneity of variance were checked using Shapiro-Wilk and Levene's tests, respectively.

Comparison of conventional indicators

After 12 weeks of treatment, significant improvements were observed in several clinical indicators in the liraglutide group compared to the control group: Blood Pressure: Systolic blood pressure (SBP) decreased from 164.63±19.12 mmHg to 154.42±4.05 mmHg in the control group and from

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Table 1. Comparison of routine indexes between control and liraglutide groups ($\bar{x} \pm s$).

Indexes	Time	Control group (n=30)	Liraglutide group (n=30)	*t*	*P* value
DBP (mmHg)	Pre-treatment	105.04±10.18	102.97±10.26	0.784	.436
	Post-treatment	94.35±5.36	90.91±5.27	2.507	.015
SBP (mmHg)	Pre-treatment	164.63±19.12	166.01±19.26	0.279	.782
	Post-treatment	154.42±4.05	148.07±5.39	5.159	.000
BMI (kg/m²)	Pre-treatment	32.15±2.07	31.91±2.02	0.454	.651
	Post-treatment	30.34±1.58	29.17±1.56	2.886	.006
Waist-to-hip ratio	Pre-treatment	1.019±0.018	1.016±0.015	0.701	.486
	Post-treatment	0.975±0.016	0.967±0.012	2.191	.033

166.01±19.26 mmHg to 148.07±5.39 mmHg in the liraglutide group ($P < .05$). Diastolic blood pressure (DBP) decreased from 105.04±10.18 mmHg to 94.35±5.36 mmHg in the control group and from 102.97±10.26 mmHg to 90.91±5.27 mmHg in the liraglutide group ($P < .05$). BMI and Waist-to-Hip Ratio: BMI reduced from 32.15±2.07 kg/m² to 30.34±1.58 kg/m² in the control group and from 31.91±2.02 kg/m² to 29.17±1.56 kg/m² in the liraglutide group ($P < .05$). Waist-to-hip ratio decreased from 1.019±0.018 to 0.975±0.016 in the control group and from 1.016±0.015 to 0.967±0.012 in the liraglutide group ($P < .05$). See Table 1 and Figure 1.

Comparison of glycolipid metabolism indexes

Fasting blood glucose (FPG) levels decreased from 8.65±0.91 mmol/L to 7.39±0.57 mmol/L in the control group and from 8.73±0.84 mmol/L to 6.12±0.52 mmol/L in the liraglutide group ($P < .05$). Two-hour postprandial blood glucose (2hPG) levels decreased from 13.01±1.03 mmol/L to 9.28±0.63 mmol/L in the control group and from 12.85±0.92 mmol/L to 8.45±0.61 mmol/L in the liraglutide group ($P < .05$). HbA_{1c} levels reduced from 8.74±0.66% to 6.87±0.67% in the control group and from 8.81±0.73% to 6.46±0.42% in the liraglutide group ($P < .05$). Triglycerides (TG) decreased from 4.57±0.36 mmol/L to 3.01±0.16 mmol/L in the control group and from 4.48±0.39 mmol/L to 2.43±0.14 mmol/L in the liraglutide group ($P < .05$). Total cholesterol (TC) decreased from 5.61±0.49 mmol/L to 5.13±0.36 mmol/L in the control group and from 5.53±0.51 mmol/L to 4.81±0.32 mmol/L in the liraglutide group ($P < .05$). C-peptide levels increased from 0.98±0.12 ng/mL to 1.08±0.13 ng/mL in the control group and from 0.96±0.09 ng/mL to 1.15±0.14 ng/mL in the liraglutide group ($P < .05$). Fasting insulin (Fins) levels increased from 12.44±2.28 mU/L to 13.65±2.09 mU/L in the control group and from 12.29±2.46 mU/L to 15.06±2.11 mU/L in the liraglutide group ($P < .05$). See Table 2 and Figure 2.

Comparison of indicators of micro inflammatory state

Reductions in microinflammatory markers such as hs-CRP, TNF-α, and IL-6 are clinically significant because they indicate a decrease in systemic inflammation, which is a critical factor in the progression of type 2 diabetes and its complications. Specifically, hs-CRP levels decreased from 4.15±1.07 mg/L to 2.85±1.03 mg/L in the control group and from 4.24±1.08 mg/L to 2.16±1.01 mg/L in the liraglutide group ($P < .05$). TNF-α levels reduced from 16.54±2.23 ng/L to 14.07±1.22 ng/L in the control group and from 16.76±2.12 ng/L to 12.88±1.31 ng/L in the liraglutide group ($P < .05$). IL-6 levels decreased from 8.08±1.43 μg/L to 6.72±0.69 μg/L in the control group and from 8.25±1.39 μg/L to 6.21±0.65 μg/L in the liraglutide group ($P < .05$).

Figure 1. Comparison of routine indexes between control and liraglutide groups.

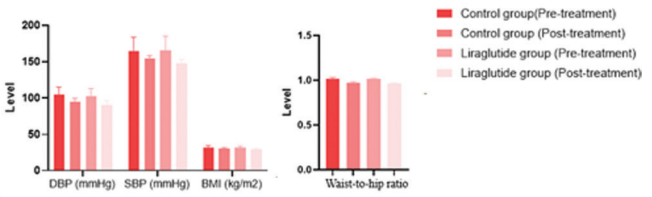


Table 2. Comparison of glycolipid metabolism indexes between control and liraglutide groups ($\bar{x} \pm s$).

Indexes	Time	Control group (n=30)	Liraglutide group (n=30)	*t*	*P* value
FPG (mmol/L)	Pre-treatment	8.65±0.91	8.73±0.84	0.354	.725
	Post-treatment	7.39±0.57	6.12±0.52	9.016	.000
2hPG (mmol/L)	Pre-treatment	13.01±1.03	12.85±0.92	0.635	.528
	Post-treatment	9.28±0.63	8.45±0.61	5.184	.000
C-peptide (ng/mL)	Pre-treatment	0.98±0.12	0.96±0.09	0.730	.468
	Post-treatment	1.08±0.13	1.15±0.14	2.010	.049
Fins (mU/L)	Pre-treatment	12.44±2.28	12.29±2.46	0.245	.807
	Post-treatment	13.65±2.09	15.06±2.11	2.600	.012
HbA1c (%)	Pre-treatment	8.74±0.66	8.81±0.73	0.390	.698
	Post-treatment	6.87±0.67	6.46±0.42	2.840	.010
TG (mmol/L)	Pre-treatment	4.57±0.36	4.48±0.39	0.929	.357
	Post-treatment	3.01±0.16	2.43±0.14	14.942	.000
TC (mmol/L)	Pre-treatment	5.61±0.49	5.53±0.51	0.620	.538
	Post-treatment	5.13±0.36	4.81±0.32	3.639	.001

Figure 2. Comparison of glycolipid metabolism indexes between control and liraglutide groups.

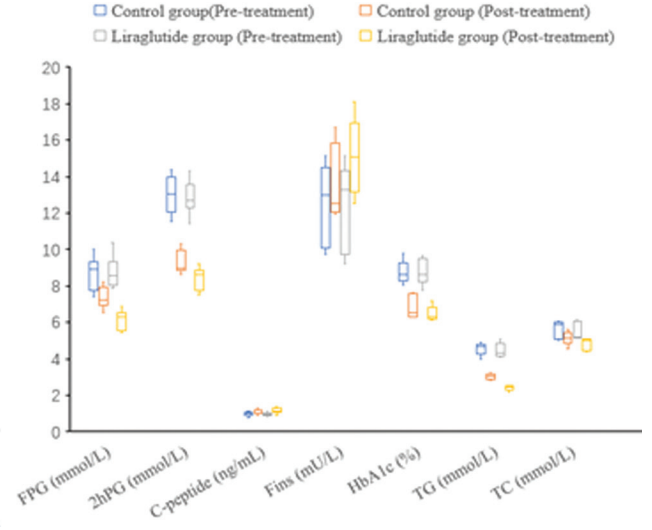


Table 3. Comparison of microinflammatory status indicators between control and liraglutide groups ($\bar{x} \pm s$).

Indicator	Time	Control group (n=30)	Liraglutide group (n=30)	*t*	*P* value
hs-CRP (mg/L)	Pre-treatment	4.15±1.07	4.24±1.08	0.324	.747
	Post-treatment	2.85±1.03	2.16±1.01	0.620	.011
TNF-α (ng/L)	Pre-treatment	16.54±2.23	16.76±2.12	0.392	.697
	Post-treatment	14.07±1.22	12.88±1.31	3.641	.001
IL-6 (μg/L)	Pre-treatment	8.08±1.43	8.25±1.39	0.467	.642
	Post-treatment	6.72±0.69	6.21±0.65	2.947	.005

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Figure 3. Comparison of microinflammatory status indicators between control and liraglutide groups.

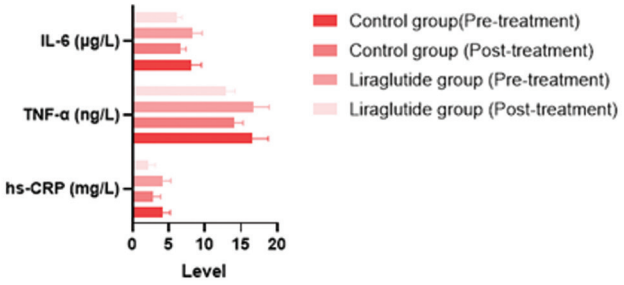


Table 4. Comparison of the occurrence of adverse reactions in the control and liraglutide groups (%)

Groups	n	Nausea and vomiting	Hypoglycemia	Diarrhea	Total incidence
Control subjects	30	0 (0.00)	0 (0.00)	1 (3.33)	1 (3.33)
Liraglutide group	30	1 (3.33)	0 (0.00)	1 (3.33)	2 (6.67)
χ^2					0.351
P value					.554

Comparison of the occurrence of adverse reactions

Adverse reactions, including nausea, vomiting, hypoglycemia, and diarrhea, were monitored throughout the study. The incidence of adverse reactions was low and not significantly different between the groups (3.33% in the control group vs. 6.67% in the liraglutide group, $P > .05$), suggesting a favorable safety profile for liraglutide. Table 4 provides a detailed breakdown of these adverse reactions.

DISCUSSION

Type 2 diabetes is characterized by insulin resistance and impaired pancreatic β-cell function, which is mainly manifested by high blood glucose, and prolonged hyperglycemia is prone to a variety of complications.[10] Human body fat is divided into subcutaneous fat and visceral fat, the accumulation of which will lead to abdominal obesity and insulin resistance, and the occurrence of type 2 diabetes is closely related to it.[11] Obesity not only increases the prevalence of type 2 diabetes but also impairs pancreatic beta cell function, exacerbates insulin resistance, and increases the risk of complications and death.[12,13]

The results of this study showed that at the end of treatment, SBP, DBP, BMI, waist-to-hip ratio, FPG, 2hPG, HbA_{1c}, TG, TC, hs-CRP, TNF-α, and IL-6 were lower than before treatment in both groups and lower than the control group in the liraglutide group; the levels of C-peptide and Fins were higher than before treatment and higher than the control group in the liraglutide group. It is suggested that liraglutide, like metformin, can lower blood pressure, lipids and glucose, and diastole blood vessels, improve endothelial function, reduce ischemia-reperfusion injury, and reduce inflammatory response. This may be due to the fact that although metformin has a certain hypoglycemic effect and improves insulin sensitivity, it has little effect on body mass,[14] while GLP-1 receptor agonists are a kind of cholecystokinin, which is mainly secreted by the pancreatic islet A cells and intestinal mucosal L cells to get GLP-1 receptor agonists that is, intestinal mucosal L cell secretion products, which acts on the pancreatic islet B cells and in the cardiovascular system, the lungs, the brain, the gastrointestinal tract, the kidneys, muscles, the liver, and fat. It acts on pancreatic islet B cells and GLP-1 receptors widely distributed in the cardiovascular system, lungs, brain, gastrointestinal tract, kidneys, muscles, liver, and adipose tissues and organs, which can significantly reduce body mass and waist circumference, and delay the occurrence of diabetes mellitus and cardio-cerebral vascular events.[15] Abdominal obesity is closely related to insulin resistance. It is a risk factor for the occurrence and progression of type 2 diabetes. Liraglutide belongs to a kind of GLP-1 agonist analogs, and its efficacy is highly similar to the natural GLP-1 agonists. Receptor agonist is highly similar to natural GLP-1 agonists, it can act on both pancreatic α and β cells, stimulate insulin secretion in a glucose concentration-dependent manner, and reduce glucagon secretion, thus ensuring that the organism can reduce hypoglycemia without hypoglycemia; not only that, but it also acts on the gastrointestinal tract system, inhibits the gastric emptying rate and gastric acid secretion, and induces a feeling of satiety and reduces the appetite, thus reducing body weight; C-peptide is the C peptide is the homologous peptide of insulin and also a component of proinsulin, which plays a significant role in the folding of proinsulin molecule and the correct pairing of disulfide bonds, so the low level of C peptide may cause insufficient insulin secretion in the body, thus leading to hyperglycemia; the body is in a long-term hyperglycemic environment, which will affect the sensitivity of sympathetic nerves and parasympathetic nerves, and the stimulation of the involuntary nerves will be reduced and the vasculature will gradually change from a state of tension to a state of high glucose. When the patient's blood sugar decreases, the stimulation of the involuntary nerve decreases, and the blood vessels gradually recover from the state of tension, but due to the impaired nerve sensitivity, its recovery cycle increases, and the blood pressure level decreases but is still not as high as the normal range; diabetes itself belongs to a kind of inflammation-responsive disease, and when the condition gradually improves, the inflammatory indexes that the body responds to the degree of inflammation correspondingly also decrease. Previous studies have shown that liraglutide can effectively reduce glycated hemoglobin and body mass, with good glycemic control and weight loss, which is consistent with the results of our study.[16]

The results of this study showed that during the 12 week treatment period, there was no difference in the incidence of adverse reactions in patients in the liraglutide group compared with the control group. It suggests that liraglutide, like metformin, is able to ensure the safety of patients' medication while treating the disease. Liraglutide has a significant therapeutic effect on abdominal obese type 2 diabetes patients, which can improve their glucose lipid metabolism and microinflammatory status and has a high drug safety. However, the clinical application still needs to consider the individual differences of patients and possible

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adverse reactions. The observed improvements in glucose and lipid metabolism and the reduction in microinflammation status among abdominal obese type 2 diabetes patients treated with liraglutide, hold significant clinical implications. Firstly, enhancing glucose and lipid metabolism can mitigate the pathological processes of diabetes, thereby reducing the risk of cardiovascular events. Secondly, alleviating microinflammation status may contribute to lowering systemic inflammation levels, improving organ function, and decreasing the risk of diabetes-related complications. Consequently, these findings provide clinicians with a more comprehensive management strategy, including adjustments to medication regimens and dietary and exercise guidance to achieve better disease management and prevention.

The observed improvements in glycolipid metabolism and microinflammatory status suggest that liraglutide is a valuable therapeutic option for patients with abdominal obesity and type 2 diabetes. Its ability to reduce inflammation and improve metabolic health highlights its potential to reduce the risk of diabetes-related complications. Clinicians should consider incorporating liraglutide into treatment plans, especially for patients struggling with weight management and poor glycemic control. This study has several limitations, including a relatively small sample size and a short duration. Long-term studies with larger populations are necessary to confirm these findings and evaluate the sustained effects of liraglutide. Future research should also explore the mechanisms underlying liraglutide's anti-inflammatory effects and its impact on different patient populations, including those with varying degrees of obesity and metabolic dysfunction.

CONCLUSION

Liraglutide significantly improves glycolipid metabolism and reduces microinflammatory markers in patients with abdominal obesity and type 2 diabetes, suggesting its potential as a safe and effective therapeutic option. Further research is warranted to explore its long-term benefits and optimize its use in clinical practice.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report that are relevant to this article.

FUNDING

This study did not receive any funding in any form.

AUTHOR CONTRIBUTIONS

WS and JW designed the study and performed the experiments, JW and MZ collected the data, YW and HC analyzed the data, and WS prepared the manuscript. All authors read and approved the final manuscript.

ETHICAL COMPLIANCE

This study was approved by the ethics committee of the First People's Hospital of Jiande. Signed written informed consents were required. Signed written informed consent was obtained from the patients and/or guardians.

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