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Integrating Artificial Intelligence into the Diagnosis of Neurological Diseases in Traditional Chinese Medicine

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Abstract: Traditional Chinese medicine (TCM) uses a holistic approach and syndrome differentiation to diagnose neurological disorders. However, traditional diagnostic methods—which rely heavily on subjective clinical experience—lack objective standardization. This paper reviews the transformative application of artificial intelligence (AI) in modernizing TCM diagnostics for neurological diseases. By integrating advanced technologies such as machine learning (ML), deep learning (DL), and natural language processing (NLP), AI provides unprecedented objectivity and precision. Current applications demonstrate significant breakthroughs, notably in the use of deep learning to analyse extensive clinical records for automated syndrome differentiation (e.g., stroke patients) and the use of image recognition for automated tongue diagnosis. These innovations are shifting TCM from an experience-dependent paradigm to a data-driven model. Looking forward, the future of AI in TCM neurology hinges on multimodal data fusion, which integrates imaging, tongue, pulse, and clinical data to digitally reconstruct the TCM diagnostic process. Furthermore, developing explainable AI (XAI) is critical to overcoming the “black box” dilemma, thereby fostering clinician trust. The widespread deployment of these intelligent systems via cloud computing holds immense potential for grassroots healthcare, although it necessitates robust ethical and legal frameworks to ensure data privacy. Ultimately, AI significantly accelerates the scientific validation of TCM, paving the way for personalized and precision medicine in treating neurological conditions.

Keywords: Traditional Chinese medicine; Artificial intelligence; Neurological disorders

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1. Introduction

The rapid advancement of artificial intelligence (AI) and its widespread application in medical diagnostics have demonstrated tremendous potential, particularly in the diagnosis and management of neurological disorders within the framework of traditional Chinese medicine (TCM). As a medical system with a

millennial history, TCM emphasizes a holistic concept and treatment based on syndrome differentiation (Bian Zheng Lun Zhi). In light of modern medical technologies, TCM diagnostics can now achieve unprecedented objectivity and precision. In recent years, the integration of AI technologies—such as machine learning and deep learning—into research on TCM-based neurological disorders has effectively increased disease recognition rates and diagnostic efficiency^[1]. By analysing traditional diagnostic data, such as pulse and tongue manifestations, and coupling them with AI algorithms, it is possible to achieve reliable computer-aided diagnosis for neurological conditions such as stroke and cerebral infarction^[2]. Furthermore, AI plays a pivotal role in TCM data mining, disease prediction, and the formulation of personalized treatment regimens, thereby providing novel technical support for the research of neurological disorders in TCM. This paper aims to review the current application status, key technologies, and future trajectories of AI in the diagnosis of TCM-related neurological diseases, serving as a comprehensive reference for subsequent research.

2. Diagnostic characteristics and current status of TCM

Guided by a holistic philosophy, traditional Chinese medicine (TCM) emphasizes “syndrome differentiation and treatment” (*Bianzheng Lunzhi*). Common neurological disorders such as stroke (termed *Pianku* in TCM), epilepsy (*Xianzheng*), and neurasthenia (associated with *Bumei*, *Xulao*, or *Yuzheng*) are primarily driven by pathological mechanisms, including the internal stirring of liver wind, obstruction of collaterals by phlegm and blood stasis, and deficiency of qi and blood^[3]. These diseases are characterized by complex pathogenic mechanisms, diverse clinical manifestations, an interplay of acute and chronic features, and highly variable pathogenesis^[4]. The diagnostic system of traditional Chinese medicine (TCM) emphasizes the integration of four diagnostic methods: inspection, auscultation and olfaction, inquiry, and palpation. This comprehensive approach incorporates specific diagnostic techniques, such as tongue and pulse diagnosis, as well as facial complexion, body posture, and tongue coating^[5]. The successful application of these methods requires extensive clinical experience. Because the diagnostic process relies deeply on the subjective judgment of the practitioner, it often exhibits substantial subjectivity and a lack of interrater consistency^[6]. Moreover, traditional techniques such as tongue and pulse diagnosis lack objective, quantitative indicators, making their standardization and digitization highly challenging^[7]. Additionally, when complex and variable neurological diseases are confronted, traditional diagnostic modalities struggle to comprehensively reflect underlying pathological changes and are susceptible to external environmental factors and individual variations^[8]. Although the continuous advancement of modern technologies—such as medical imaging and neuroelectrophysiology—can yield objective disease data, seamlessly integrating these modalities into the TCM syndrome differentiation system remains a persistent challenge^[9]. The inherent limitations of traditional diagnostic methods pose notable challenges for the use of TCM in the diagnosis of neurological diseases. Therefore, leveraging modern technology is imperative for enhancing the objectivity and accuracy of diagnosis, ultimately unlocking new diagnostic possibilities for neurological disorders within the TCM framework.

3. Overview of artificial intelligence technologies

The rapid advancement of artificial intelligence (AI) in the medical field has driven profound transformations in disease diagnosis, treatment formulation, and health management. Core AI technologies—primarily machine learning (ML), deep learning (DL), and natural language processing (NLP)—are being integrated into medicine in depth, providing novel technical methodologies for the diagnosis of neurological disorders.

Machine learning is a technology that enables computers to automatically learn models from vast amounts of data to perform predictions and classifications. Through algorithmic optimization, ML can recognize complex patterns and is widely applied in medical image analysis, disease prediction, and risk assessment ^[4]. In the diagnosis of neurological diseases, ML models such as support vector machines (SVMs) and random forests have been utilized for neuroimaging analysis and disease classification ^[10]. Furthermore, deep learning uses multilayered neural networks to simulate the structure of human brain neurons and has a robust capacity for automatic feature extraction. For instance, deep convolutional neural networks (CNNs) can automatically identify minute structural changes in brain MR and CT images, effectively improving the diagnostic accuracy for neurological diseases and demonstrating immense potential in the early diagnosis of conditions such as epilepsy and Alzheimer's disease ^[11–12]. Additionally, NLP technology enables computers to understand, analyse, and generate natural language text. In medicine, NLP is employed for extracting information from electronic medical records, literature mining, and clinical decision support ^[13]. Within the neurological domain, NLP assists in organizing patients' clinical descriptions and extracting key symptom information, thereby providing vital support for computer-aided diagnosis ^[14].

The application of AI in medicine has expanded beyond auxiliary image analysis to encompass multimodal data fusion, personalized prediction, and intelligent decision support ^[4]. Particularly in the diagnosis of neurological diseases, the integration of AI with neuroimaging, genomic information, and clinical data significantly enhances the accuracy of early disease recognition and diagnosis. For example, the application of DL models to brain MRI detection has substantially improved diagnostic precision ^[12]. Moreover, combining NLP techniques with the analysis of electronic health records enables the rapid screening of potential neurological patients, providing a solid evidence base for early intervention ^[13].

4. Application of AI in the diagnosis of TCM-related neurological diseases

With rapid technological advancements, the application of AI in the diagnosis of neurological diseases within traditional Chinese medicine (TCM) has continued to increase, advancing the modernization and scientific validation of the TCM diagnostic framework. A research team from Taiyuan University of Technology collected traditional TCM medical records from 1,134 stroke patients for deep learning analysis ^[14]. The study embedded the diagnostic logic of TCM's "Six-Meridian Syndrome Differentiation" (*Liu Jing Bian Zheng*), encompassing syndrome types, symptoms, treatment modalities, and prescriptions. The results indicated that the diagnostic accuracy for four syndrome types—Taiyang, Yangming, Shaoyin, and Jueyin—exceeded 80%. However, the accuracy for Shaoyang and Taiyin syndromes fell below 80% because their representation accounted for less than 10% of the total sample size. These findings demonstrate that an adequate volume of medical records, coupled with machine deep learning, can effectively increase the diagnostic efficiency of TCM and assist practitioners in the rapid identification of syndrome types. In the long term, by strengthening case databases to include imaging, clinical symptoms, and treatment plans, and by combining these with ML model training, intelligent prediction and risk assessment for the TCM management of neurological diseases can be realized.

Furthermore, AI analytical models for tongue diagnosis are being gradually established that utilize image recognition technology to extract features of the tongue coating to assist in syndrome differentiation and treatment. One study focusing on tongue images of stroke patients aimed to improve the accuracy of automatically extracting and recognizing stroke-related tongue features through image processing and ML techniques ^[15]. Considering that tongue shape, color, and texture reflect the body's physiological and

pathological states in TCM theory, a labelling and recognition system was designed. The model learned to automatically identify key features such as tongue shape, color, and texture, with the results showing an average diagnostic accuracy exceeding 81%.

The current breakthroughs in the use of AI for syndrome differentiation indicate that TCM is transitioning from a traditional “experience-dependent” paradigm to a “data-driven” model. In the future, with the establishment of comprehensive databases and the capture of constitutional features in high-risk populations, AI could issue early warnings during the latent stages of neurological diseases (e.g., Alzheimer’s disease and stroke precursors). This aligns perfectly with the core TCM philosophy of “preventive treatment of disease” (*Zhi Wei Bing*).

5. Future development trends and prospects

With the continuous maturation of artificial intelligence (AI) technology, its application in the diagnosis of neurological diseases within TCMs has broad prospects. Future technological breakthroughs will focus primarily on multimodal data fusion and the optimization and validation of deep learning models. At the data level, a “panoramic” diagnostic approach that integrates multisource information—such as medical imaging, tongue manifestations, and pulse conditions—is essentially a digital reconstruction of TCM clinical reasoning based on the “Four Diagnostic Methods.” The bottleneck for future breakthroughs lies in dynamic feature weight allocation algorithms (e.g., scientifically evaluating the relative importance of pulse conditions versus gait videos in the diagnosis of tremor syndrome, or Chan Zheng), which are essential for comprehensively enhancing diagnostic accuracy and reliability^[16-17]. At the model level, in addition to introducing cutting-edge algorithms such as transfer learning and conducting multicenter, large-sample clinical trials to verify model stability, the development of explainable AI (XAI) is particularly crucial^[18-19]. To prevent clinicians from falling into the dual dilemma of the TCM “experience black box” and the deep learning “algorithm black box”, AI must possess logical traceability. By displaying the derivation basis alongside the final syndrome type conclusions, AI can truly earn the trust of physicians, assist in clinical teaching, and achieve a steady translation from technological innovation to clinical utility.

Building upon these technological breakthroughs, the scalable application of intelligent TCM diagnostic systems and the establishment of related ethical and legal frameworks constitute another core focus of future development. With respect to clinical promotion, the integration of cloud computing and the mobile internet will enable intelligent systems to not only alleviate the burden on medical staff and promote the standardization of TCM diagnostics but also facilitate deployment in grassroots medical institutions^[20]. By accessing top-tier AI expert systems via the cloud, grassroots physicians can effectively construct an integrated “home-community-hospital” network for the screening and chronic disease management of neurological conditions (such as stroke sequelae). However, in the preliminary stages of comprehensive system implementation, paramount importance must be attached to data privacy and medical ethical risks^[21]. Faced with the latent dangers of the use of highly sensitive biometric data (e.g., facial and tongue images), as well as the ambiguous attribution of legal liability in cases of AI misdiagnosis or “doctor-machine opinion conflicts”, the industry urgently needs to formulate strict security standards and establish a liability division mechanism tailored specifically for AI-assisted healthcare. Only by operating within a compliant and transparent legal and ethical framework can a virtuous cycle be ensured for the application of AI technologies in the diagnosis and treatment of TCM-related neurological diseases.

6. Conclusion

The development and maturation of AI technology have demonstrated immense potential and broad prospects for its application in the diagnosis of TCM-based neurological diseases. By integrating advanced technologies such as machine learning, deep learning, and natural language processing, researchers have achieved significant milestones in image recognition, syndrome analysis, case database construction, and the formulation of personalized treatment plans. These innovative applications not only increase the efficiency and accuracy of the diagnosis of TCM-related neurological diseases but also propel the modernization and scientific validation of the TCM diagnostic framework, providing novel technological support for the inheritance and development of traditional medicine. Looking ahead, advancing AI research in this field requires a sustained focus on multimodal data fusion—combining imaging, tongue diagnosis, pulse diagnosis, and genomic information—to construct panoramic and multidimensional diagnostic models^[22]. Concurrently, multicenter, large-sample clinical validations are imperative to ensure the stability and practical utility of these models. Furthermore, promoting legislative development and ethical oversight to safeguard patient privacy and data security will provide the necessary institutional guarantees for the widespread application of AI in TCM neurology. In summary, AI holds tremendous development potential and application value in this domain. Future research will significantly accelerate the modernization of TCM, drive the evolution of personalized and precision medicine, and provide robust technical support for improving therapeutic outcomes in patients with neurological diseases.

Ultimately, the trajectory of AI in diagnosing neurological diseases will pivot toward multisource data fusion, enhanced model explainability, and seamless clinical translation. Multimodal learning involves the synthesis of imaging, genomic, and clinical data to yield a more comprehensive delineation of disease phenotypes. Simultaneously, model explainability will remain a paramount research focus to bolster clinicians' trust and foster broader clinical acceptance. Moreover, catalyzed by the proliferation of edge computing and cloud computing, AI diagnostic tools will become increasingly ubiquitous, vigorously propelling the advancement of personalized healthcare.

Disclosure statement

The author declares no conflict of interest.

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Intellectual Property and Copyright Protection in Grade-A Tertiary Hospitals: Current Status and Challenges

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Abstract: In recent years, amidst an environment where medical promotion systems have heightened requirements for research quality, large domestic hospitals, particularly Grade-A Tertiary hospitals, have faced not only research pressures but also severe challenges regarding intellectual property and copyright protection. Effective intellectual property protection is crucial for the scientific research innovation and achievement transformation of hospitals and medical practitioners, while also influencing medical quality and industry development levels. Despite the formulation of numerous intellectual property-related laws and regulations by the state by 2024, there remains significant confusion in clinical practice regarding how to effectively apply intellectual property protection policies. Furthermore, with the diversification of medical activities, balancing patient privacy rights with intellectual property issues has become an urgent problem to solve. To delve into the importance of intellectual property protection, this article combines examples from relevant hospitals to discuss the vital role of intellectual property in medical innovation, research achievement transformation, and clinical medicine development, proposing corresponding improvement strategies. The article aims to provide references for the sustainable development of Grade-A Tertiary hospitals and promote the advancement of the medical industry.

Keywords: Grade-A Tertiary hospitals; Intellectual property; Copyright protection; Clinical medicine; Medical innovation

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1. Introduction

Intellectual property protection can foster innovation, safeguard research results, and facilitate technology transfer. In Grade-A Tertiary hospitals, where teaching, research, and clinical practice coexist, intellectual property protection holds significant importance. In the context of rapid medical industry development, the emphasis on intellectual property affects hospitals' economic benefits and medical service quality ^[1].

Implementing intellectual property management in the medical field through relevant strategies helps protect various important technological achievements and contributes to creating more beneficial medical innovations and advancements for work ^[2].

Grade-A Tertiary hospitals represent the highest level of hospitals in China, boasting advanced medical technologies and extensive clinical experience, and occupying a pivotal position in the national medical system. These hospitals not only provide high-quality medical services to the general public but also undertake the tasks of cultivating a large number of medical and health personnel and conducting scientific research. However, with fierce competition in the medical market, Grade-A Tertiary hospitals face numerous issues regarding intellectual property protection, including weak awareness, inadequate laws and regulations, and a lack of professional teams ^[3].

The main challenges in intellectual property protection for Grade-A Tertiary hospitals are as follows: Firstly, hospitals have limited awareness of intellectual property and lack experience and methods in intellectual property application and management, resulting in ineffective protection of their research and development achievements ^[4]. Secondly, the development of information technology has led to a contradiction between scientific research and legal protection in the era of big data—while data utilization is prevalent, how to protect individual privacy poses a challenge. Hospitals face the risk of infringement liability during the research process ^[5]. Thirdly, some hospitals have inadequate internal controls, with insufficient recognition of the novel technologies, drugs, and other achievements independently developed by their staff, especially researchers, failing to promptly incorporate them into the intellectual property protection system of relevant departments ^[6]. Therefore, given these challenges, it is imperative to strengthen intellectual property protection within Grade-A Tertiary hospitals.

2. Intellectual property and copyright protection

2.1. Basic concepts and classifications of intellectual property

2.1.1. Definition of intellectual property

Intellectual property is a proprietary right granted by law to individuals for their intellectually creative achievements, aiming to protect their legitimate interests and encourage innovation in intellectual activities ^[7]. The core of intellectual property is to legally protect people's intellectual achievements from being arbitrarily utilized or replicated by others. It encompasses literary, artistic, and scientific works, as well as confidential information, written language, products, designs, patents, and other forms related to industry, commerce, and services. With intellectual property, creators can receive compensation for their inventions and creations, giving rise to the issue of intellectual property protection ^[8]. In today's society, intellectual property has become a significant global asset, and protecting intellectual property is one of the driving forces for promoting social development, cultural prosperity, and technological advancement amidst globalization.

2.1.2. Classification of intellectual property

There are three main types of intellectual property related to clinical medicine: patent rights, copyrights, and trademark rights ^[9].

- (1) Patents: Patents refer to the exclusive rights granted by the state to inventors or rights holders for their inventions. Patents include invention patents, utility model patents, and design patents, where: 1) Invention patents protect new technical solutions, generally with a high technical level and a protection

- period of 20 years; 2) Utility model patents protect new technical solutions applicable to practical use proposed for the shape, structure, or combination of a product, with a protection period of 10 years; 3) Design patents protect new designs formed by designing the shape, pattern, color, or combination thereof of a product suitable for industrial application, with a protection period of 10 years.
- (2) Copyrights: Copyrights refer to the ownership that authors have over the literary, artistic, and scientific works they create, including reproduction rights, distribution rights, exhibition rights, performance rights, etc. Copyrights do not require registration; as long as a work exists, copyright arises. They are unconditional and protected by specific national laws, with a protection period of the author's lifetime plus 50-70 years after their death (varying according to different countries' laws)^[9].
 - (3) Trademarks: A trademark is a symbol used to distinguish goods and services, preventing others from using identical or similar marks to cause confusion among the relevant public. Only registered trademarks are valid for 10 years, but can be renewed indefinitely. The validity of a trademark is determined by its use^[9].

In a legal sense, different types of intellectual property apply to different fields and have distinct protection methods, forming the intellectual property system we are familiar with today, providing legal protection for innovation and entrepreneurship. For Grade-A Tertiary hospitals, patents and copyrights are the most common, with trademarks being used less frequently.

2.2. Maintenance of innovation achievements and copyrights in Grade-A Tertiary hospitals

2.2.1. Characteristics of medical innovation

Medical innovation in Grade-A Tertiary hospitals has the following characteristics: Firstly, medical innovation often arises from the cross-fusion of multidisciplinary knowledge, including medicine, engineering, computer science, and other professional expertise^[10]. Interdisciplinary collaboration enables hospitals to create more advanced medical technologies or treatment methods. For example, the application of artificial intelligence in medical diagnosis and personalized treatment has significantly transformed traditional medical models and is expected to form a new trend of big data + intelligence + medicine in the future^[11]. Secondly, medical innovation achievements are based on clinical data and emphasize practical processes^[12], also valuing patient opinions. Thirdly, the success of medical innovation products relies on clinical trials and extensive data analysis for evaluation, continuously adjusting products and services during the innovation process based on trial and analysis results to ultimately achieve better treatment outcomes or enhance patients' treatment experiences. Medical innovation products have high social value, positively impacting public health and improving overall medical service quality^[13]. Therefore, effectively protecting the intellectual property formed through medical innovation enables hospitals to derive benefits and incentives in this regard in the future.

2.2.2. Applicability analysis of relevant copyright laws and regulations

For the innovation achievements of Grade-A Tertiary hospitals, strengthening copyright protection is crucial. Hospital research achievements, academic papers, medical technologies, and software are works or objects protected by copyright law; they not only protect authors' creative rights but also serve as regulations for hospital intellectual property management^[14]. However, due to the unique characteristics of medical innovation, existing copyright laws and regulations cannot fully protect the intellectual property and research

innovation achievements with copyright attributes of Grade-A Tertiary hospitals. For instance, with the rapid development of medical technology, numerous new technological inventions and creations have emerged in artificial intelligence, big data analysis, and other areas, with corresponding innovation achievements having strong copyright attributes. However, current laws lack relevant provisions, often failing to provide reasonable protection for new technological research and development and computer software^[14]. Moreover, in cases of multi-unit collaboration, issues such as confirming copyright ownership arise. Therefore, Grade-A Tertiary hospitals should strengthen their learning and understanding of copyright-related laws and regulations, formulate and improve relevant rules and regulations, and fully safeguard the legitimate rights and interests of innovation achievements, thereby facilitating the hospital's development and growth^[15].

2.3. Current status of intellectual property protection in Grade-A Tertiary hospitals

2.3.1. Implementation of copyright protection work

Most Grade-A Tertiary hospitals adopt various measures to protect the copyrights of their achieved outcomes or medical literature, such as registering copyrights, using DRM (Digital Rights Management) technology, and signing confidentiality agreements^[16]. Research results indicate that the vast majority of hospitals have recognized the importance of intellectual property and are establishing relevant management systems to combat plagiarism, piracy, and other behaviors that infringe upon researchers' legitimate rights and interests. Simultaneously, they conduct internal training on copyright-related issues, encouraging researchers to comply more with copyright laws and regulations during the writing process. Additionally, hospitals collaborate with in-house legal advisors to improve relevant copyright protection policies, ensuring there are legal bases for addressing plagiarism, piracy, and other behaviors^[17].

However, this protection system still faces numerous challenges in practice. Firstly, some hospitals have not yet established effective systems for copyright registration and management, failing to register important clinical outcomes in a timely manner, resulting in a lack of legal protection. Secondly, with the development of the internet, the phenomenon of "copying and transferring" has become increasingly severe, with rapid dissemination leading to rampant plagiarism, infringement, and even piracy^[18].

2.3.2. Effectiveness evaluation of protection measures

From existing research on the effectiveness of copyright protection measures in Grade-A Tertiary hospitals, although these hospitals have taken some measures to protect their copyrights, they have not fully achieved the desired effects. On the one hand, China's copyright registration rate is low, and some hospital researchers have weak awareness of copyrights, leaving many achievements unprotected. On the other hand, although some hospitals have started adopting digital copyright management-related technologies, the implementation costs are high, and operators of these technologies require certain professional training^[19].

Furthermore, hospitals often find themselves in distress due to infringement disputes, involving cumbersome legal procedures and high time costs in handling these events, leading some hospitals to abandon their rights protection efforts. Moreover, hospitals' investments in copyright protection do not yield reasonable returns, resulting in a lack of motivation among hospital management to increase protection efforts. Therefore, further construction of protection mechanisms is necessary, prompting hospitals to take copyright issues seriously. Simultaneously, achieving better protection of hospitals' research achievements and intellectual property from infringement requires leveraging certain legal and technological means^[20].

2.4. Case analysis

2.4.1. Analysis of successful cases

For Grade-A Tertiary hospitals, a good example of copyright protection involves managing and legally protecting research achievements. One hospital developed a new type of medical device, applying for patents and registering copyrights during the process ^[21]. Through this approach, they protected their innovation achievements and laid a solid foundation for the subsequent commercialization of the product. This hospital transformed research achievements into a product, yielding significant economic benefits while also bringing certain social benefits and enhancing the hospital's academic influence and research capabilities. Secondly, this hospital attached great importance to leveraging its legal department for intellectual property management, ensuring that all staff members complied with relevant laws and regulations during work to prevent infringement. Therefore, hospitals can learn from successful cases based on their actual situations, implementing effective copyright protection and intellectual property management to promote hospital development ^[22].

2.4.2. Analysis of failed cases and lessons learned

In contrast, successful cases provide relevant experience for Grade-A Tertiary hospitals, while failed cases serve as warnings. For instance, a medical institution failed to value the research achievements of a new drug, neglecting to apply for relevant patents in a timely manner during the achievement transformation process. When the institution's research achievements emerged, other companies directly replicated and commercialized them, causing significant economic losses and undermining the institution's clinical academic status ^[23]. Simultaneously, unclear copyright ownership issues existed in research projects, leading to contradictions among some individuals and hindering the progress of the entire research work. Through analyzing such failed cases, it can be concluded that strict adherence to intellectual property management and protection is necessary from both legal and research perspectives, as it constitutes not only rights but also fundamental hospital work. It is hoped that major hospitals will increase their attention, actively establish relevant rules and regulations, and take preventive measures to avoid such outcomes ^[24].

2.5. Future development directions and improvement suggestions

2.5.1. Vigorously cultivating intellectual property awareness

As Grade-A Tertiary hospitals attach great importance to the protection, management, and utilization of intellectual property, the awareness of intellectual property protection among medical staff remains insufficient in reality. Therefore, to strengthen medical staff's awareness of intellectual property protection, relevant training or promotional activities should be conducted to familiarize medical staff with basic knowledge of intellectual property, including what intellectual property is, why it should be protected, and how to effectively protect and manage it ^[25]. Research indicates that strengthening effective management of hospital intellectual property helps protect innovations, inventions, and research achievements, enhancing the hospital's comprehensive competitiveness and research capabilities. Effective hospital intellectual property management also standardizes various management tasks related to intellectual property within the hospital, such as regulating departments' application rights for intellectual property, maintenance, and usage systems, guiding the hospital's intellectual property work towards scientific and standardized development, thereby cultivating medical staff's awareness of intellectual property and promoting the hospital's technological development and innovation to new heights.

2.5.2. Improving relevant laws and regulations to meet the needs of the healthcare industry

Due to the rapid development of the medical industry, existing laws and regulations can no longer fully meet the current requirements for intellectual property protection. Relevant functional departments should conduct a comprehensive and detailed review, evaluation, and revision of existing laws and regulations to meet the special needs of the medical industry. It is recommended to introduce specialized clauses in relevant regulations involving medical technology, intellectual property, and other fields, such as clearly defining the rights and obligations of medical institutions to avoid unnecessary legal disputes. Establish a corresponding intellectual property management system based on the characteristics of the medical industry, guiding hospitals and research institutions to actively carry out technological innovation, achievement transformation, and application in the medical field. Increase efforts in intellectual property protection, assisting medical institutions in addressing intellectual property-related challenges in the medical industry ^[26]. A sound legal system can better safeguard the healthy development of the medical industry.

3. Conclusion

Based on the current state of intellectual property (IP) and copyright protection in tertiary-level grade-A hospitals amidst the evolving landscape of modern medicine, this paper, through literature review and practical work experience, concludes that while there has been some improvement in IP protection in China's tertiary-level grade-A hospitals, significant gaps remain. Intellectual property serves as a crucial indicator of a hospital's innovative capacity and plays a pivotal role in promoting the development of general practice within the healthcare sector. Effective protection of new drug development, the creation of novel medical devices, and the practical application of clinical research findings are essential for hospitals to fully leverage their potential, encouraging medical staff to explore boldly and innovate fearlessly, ultimately better serving patients.

Despite varying conclusions from different studies, certain contradictions persist. Some argue that stringent IP protection can motivate healthcare professionals to engage in more scientific research and drive hospitals to enhance their innovation. Conversely, others contend that overly strict IP protection may hinder information sharing and collaborative exchange among personnel, thereby slowing the pace of medical advancement. The relationship between the two is not always as expected to move in the same direction. Therefore, finding an appropriate balance in incentivizing innovation is crucial, ensuring that the rights and obligations of innovators are properly arranged on the basis of mutual benefit and win-win outcomes for stakeholders, while preventing the adverse effects of excessive IP protection. In addition to specific policy support, hospitals must also foster a culture of inclusivity, cooperation, and resource sharing and refine the operational guidelines for internal processes.

The survey reveals that the paths for improvement in strengthening IP and copyright protection in tertiary-level grade-A hospitals include conducting publicity and education to enhance awareness of IP protection regulations, refining management models to standardize and improve procedures for IP declaration, utilization, and rights defense within medical institutions, and establishing open sharing platforms to facilitate cross-institutional collaboration in IP protection and medical innovation development. It is believed that these improvement measures will facilitate further progress in IP protection work in tertiary-level grade-A hospitals, ultimately benefiting the entire healthcare industry and patients at large.

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Exploration of the Prognosis of Occupational and Recreational Therapy Combined with Psychosocial Intervention for Long-Term Hospitalized Patients with Chronic Schizophrenia

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Abstract: Chronic schizophrenia is a mental illness characterized by long duration and severe functional impairment. Long-term hospitalized patients often exhibit social function deterioration, exacerbation of negative symptoms, and decreased quality of life due to isolation from the social environment and monotonous life. While medication alone can effectively improve positive symptoms, it fails to enhance social function and long-term prognosis. Occupational and recreational therapy promotes the maintenance of cognitive and behavioral abilities through structured activity training, while psychosocial intervention focuses on social adaptation and role function reshaping. The combination of these two approaches offers a new practical direction for comprehensive rehabilitation of long-term hospitalized patients with chronic schizophrenia, holding significant importance for optimizing rehabilitation strategies and improving patients' quality of life.

Keywords: Occupational and recreational therapy; Psychosocial intervention; Long-term hospitalization; Chronic schizophrenia

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1. Introduction

The long-term hospitalization environment has a dual impact on patients with chronic schizophrenia, providing a stable care environment on one hand, but potentially accelerating functional decline due to social isolation on the other. The core objective of rehabilitation intervention is to delay functional deterioration, activate residual abilities, and restore social participation willingness. Occupational and recreational therapy primarily maintains patients' basic cognitive and physical coordination abilities through participation in labor skills and recreational activities^[1-2]. Psychosocial intervention focuses on three main aspects: communication

skills, emotion management, and social role cognition. These two intervention methods complement each other in their dimensions of action, and their combined implementation is expected to produce a synergistic effect, providing a more systematic support framework for the overall rehabilitation of long-term hospitalized patients.

2. Prognostic dilemmas and intervention needs of long-term hospitalized patients with chronic schizophrenia

2.1. Core prognostic dilemmas

The prognostic dilemmas faced by long-term hospitalized patients with chronic schizophrenia are multifaceted, with four core aspects. Among them, the persistent presence of negative symptoms is the most prominent issue, manifesting as emotional indifference, lack of motivation, social withdrawal, and poverty of speech, directly affecting patients' initiative in rehabilitation and becoming a major obstacle to rehabilitation treatment^[3]. Social function deficits are mainly manifested in decreased self-care abilities, impaired social communication, loss of vocational skills, weakened social roles, and complete isolation from the social environment due to long-term hospitalization, further exacerbating social skill decline and social adaptation disorders.

2.2. Core intervention needs

In response to the aforementioned dilemmas, clinical intervention needs to transcend the control of single symptoms and form a comprehensive rehabilitation goal of "symptom improvement-function reshaping-psychological adjustment-social reintegration"^[4]. Intervention needs to focus on four core directions: (1) effectively improving patients' negative emotions and stimulating their intrinsic motivation and behavioral initiative. (2) Reversing cognitive decline, repairing impaired cognitive function, and improving thinking and executive abilities; (3) Reconstructing social functions, mainly including the restoration of self-care and social communication abilities; (4) Adjusting mindset, correcting patients' cognitive biases about the disease, reducing negative emotions, and establishing a stable social support system^[5]. Occupational and recreational therapy can improve patients' emotions and behaviors, enhancing their emotions and motivation, while psychosocial intervention can provide precise support from multiple dimensions such as cognition-emotion-society, synergistically improving patients' physiological, psychological, and social functions, meeting the needs of comprehensive rehabilitation for long-term hospitalized patients with schizophrenia.

3. Theoretical basis for the combined application of occupational and recreational therapy and psychosocial intervention

3.1. Rehabilitation mechanism of occupational and recreational therapy

Occupational and recreational therapy is a novel rehabilitation approach based on behavioral activation, environmental adaptation, and potential development, aiming to provide multidimensional rehabilitation effects for patients. In terms of behavioral activation, regular participation in handicrafts, calligraphy and painting training, sewing training, and agricultural therapy activities can stimulate patients' nervous systems, improve neurotransmitter balance, enhance behavioral initiative and execution, and alleviate negative symptoms such as emotional indifference and lack of motivation. In terms of environmental adaptation, work and leisure activities simulate social situations, helping patients overcome the negative impact of the

hospitalization environment, gradually adapt to group activity patterns and interpersonal interaction methods, thereby reducing social withdrawal behaviors.

In terms of potential development, occupational and recreational therapy focuses on exploring patients' interests and strengths, enhancing their sense of accomplishment and self-worth through painting, calligraphy, handicrafts, and simple agricultural labor, and stimulating patients' intrinsic rehabilitation motivation. Meanwhile, occupational and recreational therapy can also promote patients' physical activities, enhance blood circulation and metabolism, alleviate physiological discomfort caused by long-term bed rest, and provide a physiological basis for patients' physical and mental rehabilitation.

3.2. Rehabilitation Mechanism of Psychosocial Intervention

Cognitive correction intervention helps patients establish objective cognition of the disease, self, and society, correcting negative cognitive biases, thereby reducing negative emotions such as inferiority and despair, and improving treatment compliance. Through methods such as mindfulness-based stress reduction, emotion expression training, and supportive psychotherapy, patients are helped to identify, accept, and adjust negative emotions, improving emotional stability.

Social skill training can improve patients' language expression, interpersonal communication, and conflict resolution abilities through role-playing, group interaction, and communication simulation, reducing social avoidance behaviors. Social support intervention connects families, communities, and medical institutions to establish a "trinity" support system composed of families, peers, and communities, reducing patients' sense of social isolation and enhancing rehabilitation confidence.

3.3. Synergistic mechanism of combined intervention

The comprehensive application of occupational and recreational therapy and psychosocial intervention is not a simple superposition, but achieves a "1+1>2" effect through mechanism and effect complementarity. Occupational and recreational therapy provides behavioral carriers and practical scenarios for psychosocial intervention, breaking patients' behavioral avoidance states and creating conditions for psychological interventions such as cognitive correction and social training. Psychosocial intervention provides psychological support and motivation assurance for occupational and recreational therapy, improving patients' emotional states, enhancing self-efficacy, correcting cognitive biases, and increasing patients' enthusiasm and persistence in participating in occupational and recreational training, preventing activities from becoming mere formalities.

The combination of the two can form a closed-loop rehabilitation model of "behavioral activation-psychological adjustment-function enhancement": occupational and recreational training activates patients' behaviors, improving their physical and emotional states; psychological intervention effectively alleviates patients' negative emotions, corrects their cognitive biases, and enhances their rehabilitation motivation; a good psychological state and motivation further increase participation in occupational and recreational training, thereby consolidating behavioral and functional improvements and forming a virtuous cycle, comprehensively promoting patients' prognosis^[6].

4. The impact of combined intervention on core prognostic indicators in long-term hospitalized patients with chronic schizophrenia

4.1. Improvement of negative symptoms

Negative symptoms represent core manifestations in long-term hospitalized patients with chronic schizophrenia and are significant factors influencing their prognosis. Multiple clinical studies have confirmed that the integration of occupational and recreational therapy with psychosocial interventions can markedly ameliorate negative symptoms, exhibiting superior efficacy compared to single-intervention approaches. Occupational and recreational therapy, through regular activities, enhances patients' behavioral initiative and alleviates demotivation and behavioral withdrawal. Psychosocial interventions and motivational interviewing address negative cognitions such as feelings of worthlessness and hopelessness, stimulate intrinsic rehabilitation motivation, and improve emotional indifference and poverty of speech ^[7]. Clinical data reveal that after 12 weeks of intervention, patients' scores on the Scale for the Assessment of Negative Symptoms (SANS) significantly decreased, with notable improvements in dimensions such as emotional indifference, demotivation, and social withdrawal. These improvements persisted for six months and were significantly superior to those achieved with monotherapy or occupational and recreational therapy alone ^[8]. This suggests that combined intervention can improve negative symptoms, potentially through enhanced prefrontal activity and increased dopamine receptor sensitivity, indicating its role in modulating circuit function.

4.2. Restoration of cognitive function

Cognitive dysfunction is a core impairment in the long-term hospitalization treatment of chronic schizophrenia, directly affecting patients' quality of life and social adaptability. Clinical studies indicate that the combination of occupational and recreational therapy with psychosocial interventions can repair cognitive function across multiple dimensions ^[9]. In occupational and recreational therapy, activities such as handicrafts, board games, and physical exercise stimulate patients' attention and memory, enhancing their information processing capabilities. Research employs a combination of cognitive remediation therapy, group cognitive training, and social cognitive training to correct cognitive biases. Randomized controlled studies have found significant improvements in scores on the Wisconsin Card Sorting Test (WCST) and the Mini-Mental State Examination (MMSE), suggesting shared neural regulatory mechanisms between these interventions ^[10]. Additionally, combined intervention enhances patients' social cognitive abilities, improving emotional recognition and psychological reasoning, thereby providing a cognitive foundation for social function recovery.

4.3. Reconstruction of social function

Social dysfunction is the most prominent symptom in long-term hospitalized patients with chronic schizophrenia and a critical factor hindering their reintegration into society. The integration of occupational and recreational therapy with psychosocial interventions effectively reconstructs patients' social function ^[11]. Occupational and recreational therapy improve patients' self-care and vocational skills through life skills and vocational training. Social skills training and group interaction training enhance social interaction abilities, while family and community support interventions provide environmental support for the application of social functions.

Clinical data show that after 12 weeks of treatment, patients' scores on the Social Disability Screening Schedule (SDSS) and the Nurses' Observation Scale for Inpatient Evaluation (NOSIE) significantly

improved, with marked enhancements in self-care, social communication, and vocational skills. Some patients were able to engage in basic household chores and work ^[12]. Follow-up studies indicate that comprehensive intervention sustains social function recovery for over one year, significantly reduces relapse rates, and improves quality of life ^[13].

4.4. Enhancement of psychological state and quality of life

Long-term hospitalized patients with chronic schizophrenia commonly experience negative emotions such as low self-esteem, anxiety, depression, and hopelessness, leading to low self-identity and poor quality of life. The combination of occupational and recreational therapy with psychosocial interventions improves patients' psychological state and quality of life through emotional regulation, self-cognition enhancement, and social support. Occupational and recreational therapy generate pleasurable activity experiences, reducing anxiety and depression while enhancing achievement and self-worth. Mindfulness-based stress reduction, psychotherapy, and cognitive reconstruction correct negative self-cognitions, alleviate negative emotions, and improve psychological resilience ^[14].

Clinical studies demonstrate significant reductions in Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD) scores, along with notable increases in self-esteem and quality of life scale scores. Patients' negative emotions are significantly relieved, with marked improvements in self-identity and life satisfaction ^[15]. Improving psychological state enhances treatment adherence and rehabilitation initiative, forming a virtuous cycle of "psychological improvement-functional enhancement-quality of life improvement", thereby optimizing long-term prognosis.

5. Conclusion

In summary, exploring the integration of occupational and recreational therapy with psychosocial interventions can enhance the prognosis of hospitalized patients with chronic schizophrenia, providing a vital theoretical basis for expanding psychiatric rehabilitation practices and improving patients' quality of life. Deepening the understanding of the mechanisms and applicability of combined interventions, along with continuous refinement of treatment models and evaluation systems, facilitates the establishment of more scientific and personalized chronic disease rehabilitation plans. In the future, with the cross-fusion of rehabilitation medicine and psychiatry and the enrichment of community rehabilitation resources, rehabilitation pathways for long-term hospitalized patients will become more diversified, and intervention methods more precise, ultimately improving long-term prognosis, promoting social function recovery, and steadily enhancing the level of psychiatric rehabilitation services.

Disclosure statement

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Clinical Study on the Efficacy and Safety of Tirofiban Arterial Thrombolysis Combined with Sequential Intravenous Therapy for Acute Ischemic Stroke

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Abstract: *Objective:* To investigate the clinical efficacy and safety of tirofiban arterial thrombolysis combined with sequential intravenous therapy in patients with acute ischemic stroke (AIS). *Methods:* A total of 85 AIS patients admitted to the hospital from February 2024 to February 2026 were selected as the study subjects. They were divided into a control group (44 cases, treated with tirofiban intravenous therapy alone plus conventional therapy) and an observation group (41 cases, treated with tirofiban arterial thrombolysis combined with sequential intravenous therapy plus conventional therapy) according to the treatment regimen. The National Institutes of Health Stroke Scale (NIHSS) scores and modified Rankin Scale (mRS) scores of the two groups were compared before treatment and at 1 day, 3 days, 7 days, and 90 days after treatment. The occurrence of adverse reactions during treatment was also recorded. *Results:* Compared with the control group, the NIHSS scores of the observation group were lower at all time points (1 day, 3 days, 7 days, and 90 days after treatment) (all $P < 0.001$). At 90 days after treatment, the proportion of patients with an mRS score of 0–2 in the observation group was 78.05%, higher than that in the control group (56.82%). Meanwhile, the proportion of patients with poor prognosis and death in the observation group was 21.95%, lower than that in the control group (43.18%) ($P < 0.05$). During treatment, there was no statistically significant difference in the incidence of adverse reactions between the observation group and the control group ($P > 0.05$). *Conclusion:* Tirofiban arterial thrombolysis combined with sequential intravenous therapy for AIS can effectively improve neurological deficits in patients, enhance long-term prognosis, and does not increase the risk of serious adverse reactions, demonstrating high clinical safety.

Keywords: Acute ischemic stroke; Tirofiban; Arterial thrombolysis; Sequential intravenous therapy; Neurological function; Safety

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1. Introduction

Acute ischemic stroke (AIS) is a common neurological emergency characterized by high morbidity, disability, and mortality, seriously threatening patients' lives, health, and quality of life ^[1]. According to statistics, ischemic stroke accounts for more than 70% of all strokes, and approximately 1/5 to 1/3 of patients have progressive stroke. If not promptly intervened, the neurological deficits will continue to worsen, significantly increasing the risk of poor prognosis ^[2]. Currently, intravenous thrombolysis and endovascular therapy are the mainstream reperfusion treatment options for AIS. However, due to the limited treatment time window, some patients cannot receive standard intravenous thrombolysis within the effective time frame. Moreover, the issues of vascular re-occlusion and poor neurological recovery after intravenous thrombolysis alone remain prominent. Tirofiban, a reversible platelet glycoprotein IIb/IIIa receptor antagonist, exerts an antithrombotic effect by inhibiting platelet aggregation. It is widely used in the treatment of coronary heart disease and acute coronary syndrome and has gradually been applied as an adjuvant therapy for AIS in recent years ^[3]. Although conventional intravenous tirofiban therapy can inhibit platelet aggregation, for patients with severe occlusion of the responsible vessel and a large thrombus burden, it is difficult to rapidly achieve an effective local drug concentration with intravenous administration alone, resulting in limited treatment effects. Arterial thrombolysis can directly deliver the drug to the responsible lesion vessel, rapidly dissolve the thrombus, and restore blood flow perfusion. Combined with sequential intravenous therapy, it can maintain the antiplatelet effect while reducing the risk of vascular re-occlusion ^[4]. Currently, more data are needed to support clinical studies on tirofiban arterial thrombolysis combined with sequential intravenous therapy for AIS. This study retrospectively analyzed the data of 85 AIS patients admitted to the hospital to investigate the clinical efficacy and safety of this combined regimen and provide a reference for optimizing clinical treatment plans.

2. Materials and methods

2.1. General information

A total of 85 AIS patients admitted to the Department of Neurology of the hospital from February 2024 to February 2026 were selected as the study subjects. They were divided into a control group (44 cases) and an observation group (41 cases) according to the treatment regimen. Inclusion criteria: (1) Met the diagnostic criteria for AIS in the "Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2023" and had ischemic lesions confirmed by cranial CT or MRI; (2) First-ever stroke with an onset time ≤ 24 hours and presenting with neurological deficits; (3) NIHSS score ≥ 4 ; (4) Aged 18–90 years; (5) Patients and their families signed informed consent forms. Exclusion criteria: (1) Combined with intracranial hemorrhage, bleeding tendency, or coagulation dysfunction; (2) Severe cardiac, hepatic, or renal insufficiency; (3) Platelet count $< 50 \times 10^9/L$; (4) Allergic to tirofiban or contrast agents; (5) Combined with malignant tumors or severe infections; (6) Previous history of stroke with significant residual neurological deficits.

In the control group, there were 24 males and 20 females, with an average age of (63.45 ± 7.21) years and an average onset time of (11.26 ± 3.45) hours. There were 28 cases of hypertension, 16 cases of diabetes, and 19 cases of hyperlipidemia. In the observation group, there were 22 males and 19 females, with an average age of (64.12 ± 7.53) years and an average onset time of (11.58 ± 3.62) hours. There were 26 cases of hypertension, 14 cases of diabetes, and 17 cases of hyperlipidemia. There was no statistically significant difference in general information between the two groups ($P > 0.05$), indicating comparability.

2.2. Treatment methods

Both groups of patients received conventional AIS treatment, including oxygen inhalation, maintenance of water and electrolyte balance, control of blood pressure and blood sugar, antiplatelet aggregation (aspirin 100 mg/day orally), statin therapy to regulate lipids and stabilize plaques, and symptomatic supportive treatment to improve circulation and nourish nerves.

The control group received tirofiban intravenous therapy alone in addition to conventional treatment. Tirofiban hydrochloride for injection was initially infused intravenously at a rate of 0.4 $\mu\text{g}/(\text{kg}\cdot\text{min})$ for 30 minutes, followed by maintenance intravenous infusion at a rate of 0.1 $\mu\text{g}/(\text{kg}\cdot\text{min})$ for 24–48 hours. During treatment, platelet count and coagulation function were monitored. If the platelet count was $< 90 \times 10^9/\text{L}$, the platelet count was rechecked to exclude pseudothrombocytopenia, and the drug was discontinued if necessary.

The observation group received tirofiban arterial thrombolysis combined with sequential intravenous therapy in addition to conventional treatment. Patients underwent femoral artery puncture for whole-brain angiography to identify the responsible lesion vessel and thrombus location. Tirofiban (0.25–1 mg) was slowly injected into the responsible lesion vessel through a microcatheter at a rate of 1 ml/min. After injection, angiography was repeated to assess vascular recanalization. Immediately after arterial administration, sequential intravenous therapy was initiated, with tirofiban maintained at a rate of 0.1 $\mu\text{g}/(\text{kg}\cdot\text{min})$ for 24–48 hours. The monitoring indicators during treatment were the same as those in the control group.

2.3. Observation indicators

- (1) Degree of neurological deficits: The National Institutes of Health Stroke Scale (NIHSS) was used to assess the degree of neurological deficits in patients before treatment and at 1 day, 3 days, 7 days, and 90 days after treatment. The total score of the scale ranges from 0 to 42, with higher scores indicating more severe neurological deficits.
- (2) Long-term prognosis: At 90 days after treatment, the modified Rankin Scale (mRS) was used to assess the prognosis of patients. An mRS score of 0–2 indicated a good prognosis (no significant disability or mild disability, able to live independently), 3–5 indicated a poor prognosis (moderate to severe disability, dependent on others for care), and 6 indicated death.
- (3) Safety indicators: The occurrence of thrombocytopenia (platelet count $< 100 \times 10^9/\text{L}$), bleeding events (including intracranial hemorrhage, skin and mucous membrane bleeding, gastrointestinal bleeding, etc.), allergic reactions, and abnormal liver and kidney function during treatment in the two groups was recorded.

2.4. Statistical methods

SPSS 27.0 was used for data analysis. The t-test was used for inter-group comparison of measurement data, and the χ^2 test was used for inter-group comparison of count data. $P < 0.05$ indicated a statistically significant difference.

3. Results

3.1. Comparison of NIHSS scores at different time points between the two groups

Compared with the control group, the NIHSS scores of the observation group were lower at 1 day, 3 days, 7

days, and 90 days after treatment (all $P < 0.001$), as shown in **Table 1**.

Table 1. Comparison of NIHSS scores at different time points between the two groups

Group	Before treatment	After treatment 1d	After treatment 3d	After treatment 7d	After treatment 90d
Control group (n=44)	12.35 ± 3.12	10.21 ± 2.87	8.56 ± 2.43	6.89 ± 2.15	4.23 ± 1.87
Observation group (n=41)	12.51 ± 3.08	8.12 ± 2.56	6.34 ± 2.11	4.52 ± 1.98	2.56 ± 1.34
<i>t</i>	0.252	3.549	4.474	5.275	4.717
<i>P</i>	0.802	0.001	<0.001	<0.001	<0.001

3.2. Comparison of mRS scores between the two groups of patients at 90 days after treatment

At 90 days after treatment, the proportion of patients in the observation group with an mRS score of 0-2 was 78.05%, which was higher than that in the control group (56.82%). Meanwhile, the proportion of patients with poor prognosis and death in the observation group was 21.95%, which was lower than that in the control group (43.18%) ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of mRS scores between the two groups of patients at 90 days after treatment [Case (%)]

Group	mRS 0-2 (Good Prognosis)	mRS 3-5 (Poor Prognosis)	mRS 6 (Death)	Poor Prognosis + Death Total
Control Group (n=44)	25 (56.82)	17 (38.64)	2 (4.55)	19 (43.18)
Observation Group (n=41)	32 (78.05)	8 (19.51)	1 (2.44)	9 (21.95)
χ^2	-	-		4.331
<i>P</i>	-	-		0.037

3.3. Comparison of the incidence of adverse reactions between the two groups of patients

During the treatment period, there was no statistically significant difference in the incidence of adverse reactions between the observation group and the control group ($P > 0.05$), as shown in **Table 3**.

Table 3. Comparison of the incidence of adverse reactions between the two groups of patients

Group	Thrombocytopenia	Intracranial Hemorrhage	Skin and Mucosal Hemorrhage	Total Adverse Reactions
Control Group (n=44)	5 (11.36)	3 (6.82)	4 (9.09)	12 (27.27)
Observation Group (n=41)	4 (9.76)	2 (4.88)	3 (7.32)	9 (21.95)
χ^2				0.323
<i>P</i>				0.570

4. Discussion

Acute ischemic stroke (AIS) is the most prevalent type of stroke in clinical practice. Its core pathophysiological mechanism involves the occlusion of the responsible blood vessel, leading to cerebral ischemia and hypoxia. This, in turn, initiates an ischemic cascade reaction, resulting in neuronal cell damage or even necrosis. Therefore, rapidly restoring blood flow perfusion in the ischemic area, inhibiting platelet

aggregation, and preventing vascular re-occlusion are crucial for improving patients' clinical outcomes ^[5]. Tirofiban, as a highly effective glycoprotein IIb/IIIa receptor antagonist, competitively binds to the IIb/IIIa receptors on the platelet membrane, blocking the interaction between fibrinogen and platelets, thereby potently inhibiting platelet aggregation and preventing thrombus formation and further expansion. It holds significant value in the antithrombotic treatment of AIS ^[6]. In clinical practice, although conventional intravenous infusion of tirofiban can exert certain antiplatelet effects, for patients with a heavy thrombus burden and severe vascular occlusion, the intravenous administration method struggles to rapidly achieve effective therapeutic concentrations at the local lesion site. Additionally, some patients may exhibit drug resistance, leading to suboptimal treatment outcomes and difficulty in meeting clinical treatment needs.

This study addressed the aforementioned treatment challenges by applying intra-arterial thrombolysis with tirofiban combined with sequential intravenous therapy to patients in the observation group. This treatment regimen directly delivers the drug to the responsible lesion vessel via the arterial route, enabling rapid thrombolysis and restoration of blood flow perfusion in the ischemic area. Subsequently, sequential intravenous administration maintains a sustained antiplatelet effect, effectively reducing the risk of vascular re-occlusion. Clinical results demonstrated that the NIHSS scores of the observation group were significantly lower than those of the control group at 1 day, 3 days, 7 days, and 90 days post-treatment, indicating that the combined treatment regimen could more rapidly and effectively improve patients' neurological deficit symptoms. Further analysis of its mechanism of action revealed that intra-arterial thrombolysis directly acts on the lesion vessel, rapidly opening the occluded vessel, restoring cerebral blood flow supply, and alleviating neuronal cell damage caused by ischemia and hypoxia. Sequential intravenous tirofiban therapy continuously inhibits platelet aggregation, prevents thrombus reformation, maintains vascular patency, and creates favorable conditions for neurological recovery ^[7].

In terms of long-term prognosis, the proportion of patients with an mRS score of 0–2 in the observation group at 90 days post-treatment was 78.05%, significantly higher than the 56.82% in the control group. This suggests that intra-arterial thrombolysis with tirofiban combined with sequential intravenous therapy can effectively improve patients' long-term prognostic quality and reduce the incidence of disability ^[8]. This outcome is closely related to the combined treatment's ability to rapidly restore blood flow perfusion, alleviate cerebral ischemia-reperfusion injury, and reduce neuronal cell apoptosis, laying a solid foundation for patients' subsequent neurological rehabilitation ^[9]. Furthermore, the incidence of death and poor prognosis in the observation group was lower than that in the control group, further confirming that the combined treatment regimen can effectively reduce the risk of adverse outcomes in AIS patients and improve their long-term quality of life.

Safety assessments showed no statistically significant difference in the incidence of thrombocytopenia and bleeding events between the two groups, and no severe adverse reactions occurred in either group. Tirofiban can potentially induce thrombocytopenia in clinical use, with most such adverse reactions being reversible and gradually returning to normal after drug discontinuation. Bleeding events are a critical adverse reaction requiring close attention during tirofiban treatment, particularly intracranial hemorrhage, which can be life-threatening in severe cases. In this study, the incidence of intracranial hemorrhage was low in both groups, suggesting that intra-arterial thrombolysis with tirofiban combined with sequential intravenous therapy does not increase the risk of severe bleeding. This may be related to strict control of arterial drug dosage, standardized patient screening, and close monitoring of relevant indicators during medication in

clinical practice. In clinical practice, regular monitoring of patients' platelet counts and coagulation function, along with timely adjustment of drug dosage, can effectively reduce the risk of thrombocytopenia and bleeding events, ensuring treatment safety^[10].

This study has certain limitations, as it is a single-center retrospective study with a relatively small sample size and a short follow-up period, which may introduce some bias into the results. Future research should involve multi-center, large-sample prospective clinical studies to further validate the long-term efficacy and safety of intra-arterial thrombolysis with tirofiban combined with sequential intravenous therapy for AIS, providing more reliable evidence-based medical evidence for its clinical application.

5. Conclusion

In conclusion, intra-arterial thrombolysis with tirofiban combined with sequential intravenous therapy for AIS can effectively improve patients' neurological deficits, increase the rate of favorable long-term prognosis, and does not increase the risk of adverse reactions such as thrombocytopenia and severe bleeding. It exhibits high clinical application safety and is worthy of further promotion and application in clinical practice. In clinical practice, it is essential to strictly grasp treatment indications and strengthen monitoring during medication to ensure the safety and effectiveness of treatment.

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Clinical Observation of Tic Disorders and Persistent Replication of Cytomegalovirus Infection

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Abstract: *Objective:* To investigate the causal relationship between tic disorders (TD) and their behavioral problems with persistent replication of cytomegalovirus (CMV) infection (i.e., persistent positivity for CMV-IgM antibodies). *Methods:* 1. A highly specific serological micro-enzyme-linked immunosorbent assay (ELISA) was used for antibody detection, with persistent positivity for CMV-IgM antibodies as an indicator of active CMV infection and replication; 2. Serum CMV-IgM antibody tests were conducted sequentially on 96 patients with TD, their parents, and healthy individuals; 3. Follow-up CMV-IgM antibody tests were performed on children and mothers with a history of abnormal medical conditions during pregnancy and infancy; 4. CMV-IgM antibody tests were conducted on 46 patients at admission, during treatment, and after discharge to observe the relationship between changes in antibody titers and the improvement or disappearance of clinical symptoms; and treatment outcomes were compared among 18 patients with comorbid obsessive-compulsive disorder (OCD) and 16 patients with a positive family history. *Results:* 1. The IgM positivity rate among children was 90.6% (87/96); the IgM positivity rate among healthy children was 17.8% (13/73), with a significant difference between the two groups ($P < 0.01$). The IgM positivity rate among fathers was 72.4% (21/29), while that among healthy males was 11.4% (4/35), showing a significant difference ($P < 0.01$). The IgM positivity rate among mothers was 89.9% (62/69), while that among healthy women was 15.6% (7/45), with a significant difference ($P < 0.01$). There was a significant positive correlation between the IgM positivity rates in the child and parent groups, which differed significantly from the IgM positivity rate in the healthy group. 2. During treatment, as the clinical manifestations of tics and behavioral problems gradually decreased or disappeared, the CMV-IgM antibody titers in patients also decreased synchronously or converted from positive to negative; 3. The cure rates in this group of TD patients, those with comorbid OCD, and those with a positive family history were 58.7% (27/46), 55.6% (10/18), and 53.3% (8/15), respectively, showing a significant positive correlation among the three groups. 4. Patients with a long disease course and complex conditions who adhered to antiviral treatment showed a gradual decrease in antibody titers or conversion from positive to negative, along with significant improvement in clinical symptoms. *Conclusion:* 1. Tic disorders and their behavioral problems are closely associated with active CMV infection and persistent replication; 2. CMV infection in children is closely related to infection in their parents; 3. A positive family history is a manifestation of familial aggregation due to CMV infection; 4. The timing of infection, duration, and differences in the autoimmune

response in children can lead to significant variations in the pathological damage caused by viral replication to patient organs and tissues, as well as in clinical manifestations and outcomes.

Keywords: Tic disorders; Cytomegalovirus; Infection; Replication; Antibodies; Immune response; Mother-to-child transmission

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1. Introduction

At present, the treatment of many patients with tic disorders remains highly challenging, particularly in cases involving self-harm, self-injurious behavior, and compulsive symptoms. The etiology and pathogenesis of tic disorders are still not fully understood. Although family history, twin studies, and genetic research suggest a hereditary component, inconsistencies remain between these findings and clinical observations. For example, some children with tic disorders may experience spontaneous remission without treatment. Likewise, many infectious diseases also demonstrate familial clustering, which may complicate the interpretation of genetic associations. Differences observed following twin infections may, in some cases, produce effects similar to those attributed to genetic factors in twin studies. Since 1995, researchers have investigated the potential relationship between tic disorders, CMV infection, and maternal–fetal transmission through clinical observations and related studies. The findings suggest that some patients with tic disorders show evidence of CMV infection with persistent viral replication (CMV-IgM positivity) and that these infections appear to be closely associated with parental CMV infection^[1–4].

2. Materials and methods

2.1. General information

(1) From April 1996 to 2000, 96 patients (81 males and 15 females) diagnosed with tic disorders according to the ICD-10 or CCMD-2-R criteria by experts from multiple tertiary hospitals across 17 provinces and municipalities were sequentially tested for CMV-IgM antibodies; among them, 52 had chronic tic disorders (TD) and 44 had vocal tics (TS); comorbid conditions included mental retardation in 9 cases, schizophrenia in 5 cases, enuresis in 4 cases, and autism in 2 cases; the age at consultation ranged from 5 to 27 years, with an average age of 11.3 years; the shortest disease history was 3 weeks, and the longest was 21 years. (2) Behavioral problems in 56 patients included learning difficulties (LD) in 35 cases, emotional disorders (ED) in 27 cases, attention deficit hyperactivity disorder (ADHD) in 26 cases, obsessive-compulsive disorder (OCD) in 18 cases, sleep disorders (SD) in 8 cases, and self-injurious behavior (SIB) in 3 cases; LD, ED, and ADHD were the most common comorbid conditions, while SIB posed the greatest harm. (3) Treatment outcomes were compared between TD patients with comorbid OCD and those with a positive family history.

2.2. Serum CMV-IgM antibody detection

A highly specific Chai's micro-ELISA method was used for CMV-IgM antibody detection (1). Five milliliters of venous blood were collected, and the serum was naturally separated in a refrigerator and numbered for testing. The reagents included high-titer antigen prepared from human embryonic lung cells (diploid) infected with the CMV standard strain AD 169 and an enzyme conjugate (1:4000). The dilution factor of the tested

serum ranged from 1:500 to 1:8000. Samples were sent to the Biological Research Laboratory of the Chinese Academy of Military Medical Sciences (CAST) in Beijing for testing.

3. Results

3.1. Reporting of CMV-IgM antibody test results and titers in patients with tic disorders

3.1.1. CMV-IgM antibody test results and antibody titers

The titer of a specimen was determined by the highest dilution factor at which a positive reaction occurred in the serum; the results were reported using a + / - notation to indicate the titer range of the corresponding serum specimen. CMV-IgM antibody test results for 96 patients at the outpatient clinic are shown in **Table 1**.

Table 1. CMV-IgM antibody test results and antibody titers

CMV-IgM Antibody Titer	<1:500 (--)	≥1:500 (±)	≥1:1000 (+)	≥1:2000 (++)	≥1:4000 (+++)	≥1:8000 (++++)	Total Positive Rate
Detected/Total	- 9/96	6/96	7/96	8/96	29/96	37/96	87/96
IgM Antibody Positive Rate	- 9.38%	6.25%	7.29%	8.33%	30.20%	38.54%	90.62%

In this group of 96 patients, the positive rate of CMV-IgM antibodies (titer \geq 1:500) was 90.62%, with 77.08% having IgM antibody titers \geq 1:2000. This indicates that patients with tic disorders not only have a high positive rate of CMV-IgM antibodies but also exhibit high antibody titers. In this group, 9 patients tested negative for CMV-IgM antibodies (all titers < 1:500). Among them, the IgM antibodies of the parents of 7 children were all positive (all antibody titers \geq 1:4000), and the IgM antibodies of the parents of 1 child with autism were strongly positive (titer of 1:8000). In contrast, the CMV-IgM antibodies of the other 2 patients and their parents tested negative in both initial and follow-up tests (titer < 1:500), warranting further investigation.

3.1.2. Comparison of CMV-IgM positivity rates between the children and parents group and the healthy control group

CMV-IgM antibody test results for the group of 96 children and their parents versus the healthy control group are shown in **Table 2**.

Group	Children and Parents Group			Healthy Examination Group		
	Patient Group	Father Group	Mother Group	Examined Children	Examined Males	Examined Females
Number of subjects / Mean age (years)	96 / (11.3)	29 / (41.2)	69 / (38.4.)	73 / (10.8)	35 / (39.3)	45 / (37.6)
IgM positive / Number of subjects	87 / 96	21 / 29	62 / 69	13 / 73	4 / 35	7 / 45
IgM positive rate (%)	90.6%	72.4%	89.9%	17.8%	11.4%	15.6%

The positive rate of CMV-IgM antibodies in the child patient group was 90.6%, while the positive rates of IgM antibodies in their parents were 72.4% and 89.9%, respectively. In the healthy control group, the positive rate among children was 17.8%, the positive rate of IgM antibodies among male participants was 11.24%, and the positive rate among female participants was 15.55%. There was a significant positive

correlation between the positive rates of IgM antibodies in children with tic disorders and their parents. This represents a significant difference compared to the healthy control group.

3.1.3. Follow-up testing of CMV-IgM antibodies during maternal pregnancy, infant period, and at onset of tic and behavioral disorders

Follow-up testing for CMV-IgM antibodies in relation to abnormalities during the mother’s pregnancy and the child’s infancy, as well as tic and behavioral issues, is shown in **Table 3**.

Group	Detection of abnormal CMV-IgM antibodies during mother’s pregnancy/delivery and patient’s infancy					Detection of CMV-IgM antibodies at the onset of tic disorders and behavioral problems						
	Mother	Pregnancy & Delivery	Neonatal Jaundice	Enuresis	Frequent Fever	Tic Disorder	ADHD	LD	ED	OCD	SIB	SD
Examined/Required	34/46	21/56	6/56	3/46	24/56	46/56	26/56	35/56	27/56	14/56	3/56	8/56
Positive/Examined	29/34	21/21	6/6	3/3	23/24	44/46	25/26	34/35	27/27	14/14	3/3	7/8
IgM Positive Rate (%)	85.3%	100%	100%	100%	95.8%	95.7%	96.1%	97.1%	100%	100%	100%	87.5%

The follow-up test results for symptoms and signs such as miscarriage during pregnancy, tocolysis, and neonatal jaundice, as well as CMV-IgM antibodies, suggest intrauterine CMV infection in the affected children [3-5]. Clinical symptoms commonly observed in these children, such as neonatal pneumonia, frequent fevers, and enuresis, are associated with persistent active CMV infection (i.e., continuous replication of CMV infection) [3-5]. The positive rates of CMV-IgM antibodies in various groups with tic disorders and behavioral issues, as shown in the table, all indicate a close association between the onset of these conditions and CMV infection.

3.2. Differences between anti-CMV viral infection treatment and antipsychotic medication for symptomatic treatment of tic disorders (TD) and behavioral issues

3.2.1. CMV-IgM positivity and antiviral treatment outcomes in patients with tic disorders, comorbid obsessive-compulsive disorder (OCD), and positive family history

CMV-IgM antibody testing and antiviral treatment for patients with tic disorders and comorbid obsessive-compulsive disorder (OCD), as well as those with a positive family history, are shown in **Table 4**.

Table 4. CMV-IgM positivity and antiviral treatment outcomes in patients with tic disorders, comorbid obsessive-compulsive disorder (OCD), and positive family history

Group	Tic Disorder				Obsessive-Compulsive Disorder				Positive Family History			
	Indicator	Lgm positive	Cured	Markedly effective	Indicator	Lgm positive	Cured	Markedly effective	Indicator	Lgm positive	Cured	Markedly effective
Number	44/46	27/46	9/46	8/46	16/16	10/18	3/18	3/18	15/16	8/15	3/15	4/15
Result	95.7%	58.7%	19.6%	17.4%	100%	55.6%	16.7%	16.7%	93.8%	53.3%	20%	26.7%

In this group of patients with tic disorders (TD), the IgM positive rate was 95.7%, and the cure rate was 58.7%. Among them, patients with obsessive-compulsive disorder (OCD) and those with a positive family history had IgM positive rates of 100% and 93.8%, respectively, with cure rates of 55.6% and 53.3%. There was a significant positive correlation between their IgM positive rates and cure rates, suggesting that the onset of these conditions is related to CMV infection.

3.2.2 Comparison of psychotropic drug (dopamine/serotonin-based) versus nucleoside antiviral (ganciclovir-based) treatment for TD, OCD, and related conditions

Differences between the treatment of TD and OCD with psychotropic drugs such as dopamine and 5-hydroxytryptamine and antiviral nucleoside drugs are shown in **Table 5**.

Item	Purpose, method, and effects of antipsychotic drugs such as dopamine and serotonin	Purpose, method, and effects of ganciclovir-based nucleoside antiviral drugs
Names of treated conditions	TD, TS, enuresis, OCD, SIB, LD, ED, SD, ADHD	TD, TS, enuresis, OCD, SIB, LD, ED, SD, ADHD
Purpose and method of treatment	Antipsychotic drugs such as dopamine and serotonin: regulate neurotransmitter imbalance, control or alleviate clinical symptoms; select different drugs and dosages based on patient condition.	Nucleoside antiviral drugs: inhibit viral replication, block immunopathological damage to target tissues, eliminate or reduce neurotransmitter metabolic disorders, allowing patient symptoms to naturally resolve; dosage calculated by body weight.
Conditions with rapid response	No clear pattern; treatment is difficult for complex cases such as SIB and OCD, with significant side effects.	SIB and OCD often respond within 1–2 weeks of treatment, with potential for clinical cure, and no side effects associated with antipsychotics.
Duration of treatment required	Controlling and alleviating symptoms involves regulating neurotransmitter imbalance, with no defined time limit; patients may be treated for months or years without certainty, and some cases are difficult to cure.	Anti-CMV treatment generally takes 3–6 months; longer treatment and recovery time is needed for complex cases. Antiviral treatment duration is determined by the decline of CMV-IgM antibody titer to approximately 1:500.
CMV-IgM testing	Antipsychotic treatment with dopamine, serotonin, etc., does not require CMV-IgM antibody testing.	Anti-CMV antiviral treatment requires the biological indicator of positive CMV-IgM antibodies.
Efficacy evaluation criteria	The primary criterion is the degree of improvement in clinical symptoms, with no biological indicator requirement.	The criteria for cure or recurrence are based on both the degree of symptom improvement and the biological indicator of IgM antibody titer levels.

Antipsychotic drugs such as dopamine and serotonin have been used for many years to treat TD (Tic Disorder). However, treating complex conditions and behavioral issues can be challenging, with numerous side effects from the medications. Anti-infective therapy aims to suppress the body’s immune response to persistent CMV (Cytomegalovirus) infection replication, thereby preventing immunopathological damage to target tissues and organs and addressing neurotransmitter metabolic disorders. Its characteristics include significant improvement in antiviral therapy for TD and comorbid conditions like behavioral issues (e.g., SIB - Self-Injurious Behavior) within 1–2 weeks, with the potential for cure. Children who were forced to leave school due to vocal or behavioral issues affecting others or themselves can return to campus. During treatment, common side effects of antipsychotic drugs are absent, allowing most patients to complete treatment successfully.

3.2.3. Evaluation criteria for the efficacy of antiviral therapy in tic disorder and behavioral issues

The primary evaluation criteria are based on the degree of improvement in tic symptoms and behavioral issues after antiviral therapy, treatment duration requirements, the decline in CMV-IgM antibody titers, and whether the condition relapses after discontinuation. Cure: (1) Complete disappearance of tic symptoms, self-injurious behavior, and obsessive-compulsive behavior; (2) CMV-IgM antibody titers decline to around 1:500, with a treatment duration of 3–6 months or more; (3) No relapse after 6 months of discontinuing antiviral therapy, allowing return to school or normal life. The cure rate in this group was 58.69% (27/46). Significant improvement: The patient's tic symptoms, obsessive-compulsive behavior, learning disabilities, and other behavioral issues improve by 70%, with a treatment duration of about 3 months and antibody titers declining to $\leq 1:1000$ (+). This standard was met by 19.56% (9/46). Effective: Significant clinical improvement after more than 3 weeks of antiviral therapy, but withdrawal for some reason. This group accounted for 17.39% (8/46). Ineffective: Withdrawal from treatment for some reason (1 case due to significant pathological changes found in head imaging, another case withdrew for other reasons). This group accounted for 4.34% (2/46).

3.2.4. Insights from antiviral therapy

(1) Immediate effects after 1-2 weeks of treatment are often observed in the last-appearing clinical symptoms, such as self-injurious behavior, obsessive-compulsive behavior, enuresis, and sleep disorders. The efficacy of the first-appearing tics, hyperactivity, and learning difficulties manifests later, fully reflecting the pathological characteristics and repair patterns of infection and immune damage. (2) Patients with complex conditions and longer disease durations need confidence and determination to persist with treatment and rehabilitation to achieve significant progress. (3) Provides new treatment methods and hope for a cure for patients with refractory comorbid conditions. (4) Follow-up after more than 20 years: No cases of impaired fertility due to antiviral therapy have been found, making such concerns unwarranted.

4. Discussion

With the increasing prevalence of chronic and vocal TD, especially comorbid conditions like SIB, Obsessive-Compulsive Disorder (OCD), Learning Disability (LD), Sleep Disorder (SD), and Attention Deficit Hyperactivity Disorder (ADHD), they have become severe chronic diseases harming children's physical and mental health. The etiology of TD remains unclear, with research primarily focusing on biological factors such as genetics, immunity, and neurobiochemistry.

CMV is one of the most common congenital infectious pathogens in humans, infecting fetuses and children through vertical and horizontal transmission during intrauterine, perinatal, and growth periods, causing various infectious syndromes ^[1, 3-4]. Wu Shengling used PCR to examine organ tissue samples from congenitally malformed fetuses and found the highest positivity rates for CMV-DNA in the thymus, brain, and liver, with a brain positivity rate of 53.9%. Liu Lanqing et al. used virus isolation, serum antibody determination, and molecular biology methods to find a 51.4% (36/70) positivity rate for CMV infection-induced nervous system damage in children, indicating CMV infection as a significant pathogen causing severe central nervous system damage in infants and children. Yow et al. found a 59% positivity rate for urinary CMV isolation in children within 5 years of birth ^[6]. Hou Zhifu et al. detected urinary CMV-DNA in

160 children, with a positivity rate of 18.8%, the highest in children aged 1-5 years ^[7]. The high incidence age of CMV infection in children is similar to the age characteristics of TD onset.

Based on the theory of viral maternal-fetal transmission, combined with family aggregation phenomena and twin studies related to genetic factors, the authors believe that family aggregation phenomena and twin effects can also occur in the occurrence and development of infectious diseases. Therefore, the authors initiated clinical research and observation on the relationship between CMV infection and TD onset in 1996 ^[8].

To clarify the causal role and exact criteria of infectious agents in diseases, infectious agents can be isolated from patients, and antibodies against these pathogens, especially recent IgM antibodies, can be monitored to determine the role of single infectious agents in the development of autoimmune diseases ^[2]. IgM antibodies are specific antibodies produced by the infected body during the active or latent phases of viral infection ^[2, 9]. Accordingly, this article selects CMV-IgM antibody positivity as an observational indicator for clinical research.

In this group of 96 TD patients, the CMV-IgM antibody positivity rate was 90.6% (87/96), with parent antibody positivity rates of 72.4% and 89.9%, respectively, significantly different from the healthy control group. The results also showed a significant positive correlation between CMV infection in children and their parents ^[1, 3, 4-5].

Among the 46 patients treated for anti-CMV infection, the IgM antibody positivity rate was 97.7%, with a cure rate of 58.7%. The cure rates for patients with comorbid OCD and positive family history were 55.6% and 53.3%, respectively, showing a significant positive correlation between infection rates and cure rates, all closely associated with CMV infection. Treatment revealed that behavioral issues like SIB, SD, and OCD, appearing later in the disease course, showed the earliest treatment effects. For example, two children with chronic TD who developed severe self-injurious behaviors like eye-gouging and tongue-biting stopped these behaviors after one week of antiviral therapy, with immediate improvement in anxiety and depression. Antiviral therapy not only brings hope for a cure to patients with complex and refractory TD and behavioral issues but also lacks the side effects of antipsychotic drugs. Based on the medical history of some children during maternal pregnancy and growth and the curable results of patients with positive family history, it suggests the etiological role of CMV maternal-fetal transmission in the disease's occurrence and development, providing new insights for etiological research on related neuropsychiatric diseases in children.

During treatment, to clarify the relationship between CMV infection and TD and comorbid conditions, excluding interference from other factors, early treatment only used nucleoside antiviral drugs for observation. For patients unable to stop taking large amounts of antipsychotic drugs, during antiviral therapy, antipsychotic medications should not be arbitrarily increased, decreased, adjusted, or suddenly stopped to avoid interfering with the treatment process and clinical observation. After symptoms are basically controlled, the dosage of psychiatric drugs should be gradually reduced under the guidance of a professional physician, and rehabilitation treatment time should be extended. Antiviral therapy has strict treatment duration requirements, not only requiring symptom reduction and disappearance but also needing CMV-IgM antibody titers to meet standards (generally 3–6 months). Treatment for patients with complex conditions may take about a year. Treatment is difficult for patients with clear pathological changes in brain tissue. During more than 20 years of follow-up, no cases of impaired fertility in male or female patients due to antiviral therapy have been found, making premature withdrawal from treatment unnecessary.

5. Conclusion

This clinical observation suggests that TD and its comorbid behavioral issues are primarily chronic infectious autoimmune diseases that gradually develop through CMV maternal-fetal transmission. It is likely the result of CMV infection and persistent replication, where blood antibodies penetrate the damaged blood-brain barrier and bind to similar antigens in neural tissue, affecting neurotransmitter metabolism.

Disclosure statement

The authors declare no conflict of interest.

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Study on the Correlation between Retinal Ganglion Cell Layer Thickness Measured by OCT and the Severity of White Matter Hyperintensities in Cerebral Small Vessel Disease

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Abstract: *Objective:* To investigate the correlation between the thickness of the retinal ganglion cell layer (GCL) measured by optical coherence tomography (OCT) and the severity of white matter hyperintensities (WMH) in cerebral small vessel disease (CSVD). *Methods:* Thirty-one patients with CSVD were selected and divided into a mild group (21 cases) and a moderate-to-severe group (10 cases) based on the severity of WMH. Additionally, 30 healthy individuals were selected as the control group. All subjects underwent 3.0T cranial MRI and OCT examinations. The severity of WMH was assessed using the Fazekas scale, and the thickness of the GCL in each quadrant, as well as the average and minimum thickness, was measured to analyze their correlation with WMH and their predictive value. *Results:* Statistically significant differences were observed among the three groups in terms of GCL thickness in the superior nasal, inferior nasal, inferior, and inferior temporal quadrants, as well as the average and minimum thickness ($P < 0.05$). The average GCL thickness showed a significant negative correlation with the Fazekas score ($P < 0.05$). Multiple linear regression analysis revealed that the average GCL thickness in the moderate-to-severe WMH group was significantly lower than that in the mild group ($P < 0.05$), and type 2 diabetes mellitus enhanced this negative correlation. The ROC curve demonstrated that after adjusting for clinical factors, the area under the curve (AUC) for predicting moderate-to-severe WMH using the average GCL thickness reached 0.83. *Conclusion:* The thickness of the GCL in patients with CSVD is negatively correlated with the severity of WMH, and the average GCL thickness has good predictive value for moderate-to-severe WMH. Meanwhile, OCT, as a non-invasive fundus imaging technique, can provide a new method for the early identification of CSVD and the assessment of white matter lesions.

Keywords: Cerebral small vessel disease; White matter hyperintensities; Retinal ganglion cell layer; Optical coherence tomography

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1. Introduction

Cerebral small vessel disease (CSVD) refers to a series of clinical, imaging, and pathological syndromes caused by various etiologies affecting the small arteries and their distal branches, arterioles, capillaries, venules, and small veins in the brain. It has become a common disease that seriously endangers the health of the population ^[1]. White matter hyperintensities (WMHs) are important imaging indicators reflecting brain parenchymal damage in CSVD and are associated with an increased risk of dementia ^[2]. Studies on the pathogenesis of CSVD have shown that microvascular damage often occurs significantly earlier than brain parenchymal damage ^[3]. However, current clinical assessment methods for CSVD are limited. Conventional CT and MRI can only display organic lesions in the brain parenchyma, while techniques such as MR perfusion imaging, arterial spin labeling, and PET are difficult to promote routinely in clinical practice due to their high cost, complex operation, and partial invasiveness ^[4].

Optical coherence tomography (OCT), as an emerging retinal vascular imaging technique, has become a highly promising non-invasive screening and assessment tool for CSVD due to its advantages of being non-invasive, having high resolution, being convenient and economical, allowing for continuous tracking, and enabling three-dimensional imaging ^[5]. However, most existing OCT-related studies have focused on the analysis of fundus lesions and fundus vascular morphological parameters, and there is a lack of research using OCT to assess CSVD ^[6]. Moreover, most domestic-related studies are single-center and small-sample studies, and their conclusions still need to be verified. This study aimed to detect the thickness of the retinal ganglion cell layer (GCL) in patients with CSVD using OCT and explore its correlation with the severity of WMHs, in order to find non-invasive biomarkers for white matter lesions in CSVD and provide new methods for early screening and disease assessment.

2. Materials and methods

2.1. General information

Thirty-one patients with cerebral small vessel disease (CSVD) who were hospitalized in the neurology department of the hospital from January 2023 to June 2025 were selected. Based on the results of 3.0T cranial MRI examinations, the patients were divided into two groups according to the severity of white matter hyperintensities (WMH): a mild WMH group with 21 cases and a moderate-to-severe WMH group with 10 cases. Meanwhile, 30 healthy individuals who underwent physical examinations during the same period were selected as the healthy control group. This study was approved by the hospital's ethics committee, and all subjects signed informed consent forms.

Inclusion criteria: (1) Age between 50 and 80 years old; (2) CSVD patients met the diagnostic criteria for sporadic cerebral small vessel disease outlined in the "Chinese Expert Consensus on the Diagnosis and Treatment of Cerebral Small Vessel Disease 2021"; (3) Voluntarily participated in this study and signed an informed consent form.

Exclusion criteria: (1) Patients in the acute symptomatic phase of CSVD or non-sporadic CSVD caused by metabolic, toxic, infectious, genetic, or other factors; (2) Intracranial or extracranial arterial stenosis > 50%, or non-acute cortical/subcortical cerebral infarction with a diameter > 1.5 cm; (3) A history of intracranial hemorrhage or concurrent other neurological diseases; (4) Concurrent ocular diseases that affect fundus observation; (5) Presence of contraindications for magnetic resonance imaging or inability to undergo OCT examinations and neuropsychological scale assessments.

There were no statistically significant differences among the three groups in terms of age, gender, body mass index (BMI), history of smoking and alcohol consumption, and comorbidities ($P > 0.05$), indicating comparability (**Table 1**).

Table 1. Comparison of basic information among the three groups

Item	Healthy Control Group (<i>n</i> = 30)	Mild WMH Group (<i>n</i> = 21)	Moderate-to-Severe WMH Group(<i>n</i> = 10)	<i>P</i> value
Age (years, mean ± SD)	57.87 ± 7.78	59.43 ± 8.39	64.30 ± 6.95	0.091
Gender [n(%)]	Male	12 (57.14)	5 (50.00)	0.869
	Female	15 (50.00)	9 (42.86)	
BMI [kg/m ² , M (Q ₁ , Q ₃)]	23.70 (22.23, 25.86)	23.88 (22.09, 25.54)	24.49 (23.56, 25.56)	0.464
Smoking [n(%)]	No	26 (86.67)	17 (80.95)	0.891
	Yes	4 (13.33)	4 (19.05)	
Alcohol consumption [n(%)]	No	27 (90.00)	19 (90.48)	0.846
	Yes	3 (10.00)	2 (9.52)	
Hypertension [n(%)]	No	15 (50.00)	10 (47.62)	0.806
	Yes	15 (50.00)	11 (52.38)	
Type 2 diabetes mellitus [n(%)]	No	25 (83.33)	18 (85.71)	0.260
	Yes	5 (16.67)	3 (14.29)	

2.2. Methods

- (1) Cranial MRI Examination and Imaging Assessment: A 3.0T magnetic resonance scanner from GE (USA) was used to perform cranial MRI + MRA + Flair + SWI sequence scans on all subjects. Without knowledge of the patients' clinical information and grouping, two experienced senior neurologists evaluated the MRI images with reference to the "Chinese Expert Consensus on the Diagnosis and Treatment of Cerebral Small Vessel Disease 2021." The images were required to be clear, with good contrast and no significant artifacts.
- (2) OCT Examination: Subjects were prohibited from smoking and consuming alcoholic beverages for 3 hours prior to the examination, and a light diet was required for at least 1.5 hours before the examination. Visual acuity testing, automatic refraction, intraocular pressure measurement, slit-lamp examination, and fundus photography were performed first to exclude ocular diseases that affect fundus observation. Using OCT equipment, the subject's mandible was placed on the chin rest, and the forehead was pressed forward against the forehead support. The height of the chin rest was adjusted so that the lateral canthus of the subject's eye was at the level of the eye position marker line. The subject was instructed to fixate on the internal fixation light inside the equipment lens, and the scanning head was aligned with the center of the subject's pupil. It was then gradually advanced until a clear fundus image appeared on the display screen, and the fundus image was adjusted to be as clear as possible. Scans were performed in 3mm×3mm and 6mm×6mm areas centered on the macular fovea and optic disc, respectively, with 4 B-scans performed at each position. If motion artifacts were present or the image quality was poor, the scan was repeated. After completing scans on both eyes, eyes with an image quality score > 5 and a signal strength index > 40 were selected for analysis. If both eyes met the criteria, the eye with better image quality was chosen.

2.3. Observation indicators

- (1) The severity of WMHs was assessed using the Fazekas scale, with scores assigned separately for periventricular and deep white matter hyperintensities (0–3 points each), resulting in a total score ranging from 0–6 points. Scores of 1–3 points indicated mild WMH, while scores of 4–6 points indicated moderate-to-severe WMH.
- (2) GCL Thickness Indicators: The thickness of the GCL in the superior temporal, inferior temporal, superior nasal, inferior nasal, superior, and inferior quadrants, as well as the average and minimum thickness of the GCL.

2.4. Statistical Methods

Data analysis was performed using SPSS 26.0 and R 4.4.1 software packages. Normally distributed measurement data were expressed as mean \pm standard deviation (Mean \pm SD), non-normally distributed data were expressed as median (Q₁, Q₃), and count data were expressed as number of cases (percentage) [n (%)]. Comparisons of measurement data among multiple groups were performed using one-way ANOVA or Kruskal-Wallis tests, while comparisons of count data were performed using Pearson chi-square tests, continuity-corrected chi-square tests, or Fisher’s exact tests. Correlation analysis was performed using Spearman’s method, with $P < 0.05$ considered statistically significant.

3. Results

3.1. Comparison of GCL thickness indicators among the three groups

There were statistically significant differences among the three groups in terms of GCL thickness in the superior nasal, inferior nasal, inferior, and inferior temporal quadrants, as well as the average and minimum thickness ($P < 0.05$). There were no statistically significant differences among the three groups in terms of GCL thickness in the superior temporal and superior quadrants ($P > 0.05$) (**Table 2**).

Table 2. Comparison of GCL thickness indicators among the three groups

Item	Healthy Control Group (n=30)	Mild WMH Group (n=21)	Moderate-to-Severe WMH Group (n=10)	P value
GCL TS	81.5 (79.3, 85.0)	84.0 (82.0, 87.0)	80.5 (72.3, 84.0)	0.097
GCL S	85.5 (81.3, 89.0)	86.0 (84.0, 90.0)	80.5 (70.3, 83.8)	0.053
GCL NS	87.0 (83.3, 90.8)	87.0 (85.0, 90.0)	81.0 (76.0, 84.8)	0.027
GCL NI	83.0 (79.3, 88.3)	85.0 (83.0, 90.0)	77.0 (74.0, 82.0)	0.015
GCL I	80.5 (75.3, 85.8)	83.0 (79.0, 87.0)	73.0 (68.0, 79.0)	0.020
GCL TI	82.5 (77.3, 86.0)	85.0 (80.0, 90.0)	75.0 (70.0, 78.8)	0.016
GCL average	84.0 (79.0, 86.0)	85.0 (82.0, 90.0)	78.5 (71.5, 81.0)	0.020
GCL min	80.0 (76.0, 82.0)	83.0 (79.0, 85.0)	72.5 (67.3, 77.0)	0.003

Note: GCL: Ganglion Cell Layer; TS: Superior Temporal; S: Superior; NS: Superior Nasal; NI: Inferior Nasal; I: Inferior; TI: Inferior Temporal; average: Average Thickness; min: Minimum Thickness

3.2. Correlation between average GCL thickness and Fazekas score

Spearman’s rank correlation analysis revealed a significant negative correlation between the average GCL thickness and the Fazekas score in the overall study cohort ($R = -0.299$, $P < 0.05$) (**Figure 1**).

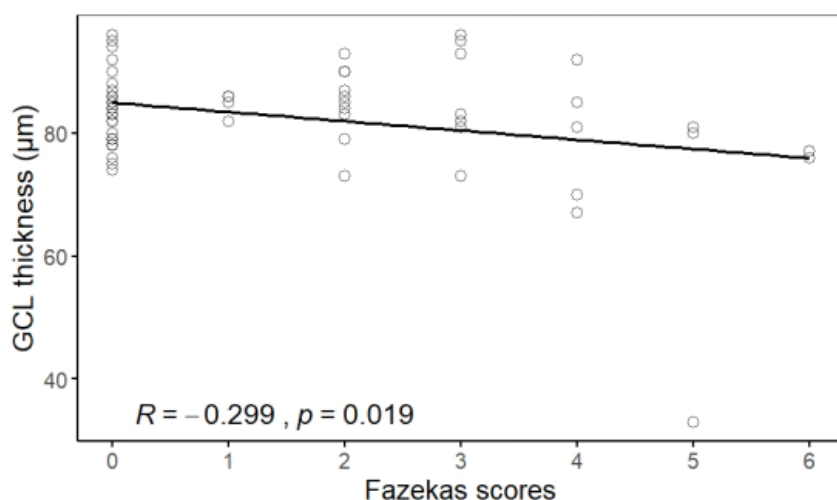


Figure 1. Spearman’s rank correlation analysis between GCL thickness and Fazekas score

3.3. Regression analysis of GCL thickness and WMH severity

Using CSVD patients as the study subjects, a multiple linear regression model was constructed with the average GCL thickness as the dependent variable and WMH severity as the independent variable. The results showed that in the unadjusted model (Model 1), the average GCL thickness in the moderate-to-severe WMH group was lower than that in the mild WMH group (95% CI: -18.93 to -3.34, $P < 0.05$). After adjusting for age and gender (Model 2), the effect size changed slightly (95% CI: -19.62 to -3.11, $P < 0.05$). After further adjusting for hypertension and type 2 diabetes (Model 3), a significant negative correlation was observed between moderate-to-severe WMH and the average GCL thickness (95% CI: -18.17 to -0.87, $P < 0.05$) (Table 3).

Table 3. Linear regression analysis of WMH and GCL thickness in patients with cerebral small vessel disease

Variable	Model 1		Model 2		Model 3	
	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>
Mild (WMH)	0.00 (Reference)		0.00 (Reference)		0.00 (Reference)	
Moderate-to-severe (WMH)	-11.13 (-18.93 to -3.34)	0.009	-11.36 (-19.62 to -3.11)	0.012	-9.52 (-18.17 to -0.87)	0.041

3.4. The impact of subgroup variables on the relationship between average GCL thickness and WMH severity

Stratified analysis was conducted to assess the impact of age, gender, BMI, hypertension, and diabetes on the relationship between GCL thickness and WMH severity. The results revealed a significant interaction effect for age ($P < 0.05$), indicating that the reducing effect of moderate-to-severe WMH on average GCL thickness varied across different age groups. In the subgroup of patients with type 2 diabetes, the correlation between moderate-to-severe WMH and reduced average GCL thickness was significantly enhanced ($\beta = -39.00$, 95% CI: -44.54 to -33.46, $P < 0.05$). No statistically significant interactions were observed in the subgroups stratified by gender, BMI, and hypertension ($P > 0.05$) (Figure 2).

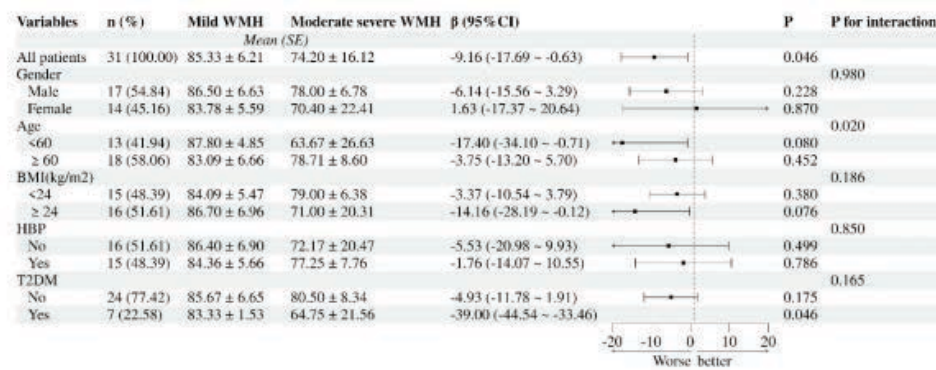


Figure 2. The impact of subgroup variables on the relationship between average GCL thickness and WMH severity

3.5. Predictive value of average GCL thickness for moderate-to-severe WMH

ROC curve analysis demonstrated that the area under the curve (AUC) for predicting moderate-to-severe WMH using average GCL thickness alone was 0.80 (95% CI: 0.62–0.99). After adjusting for age and gender, the AUC was 0.80 (95% CI: 0.63–0.98). Further adjustment for hypertension and diabetes increased the AUC to 0.83 (95% CI: 0.67–0.99), suggesting that average GCL thickness has good predictive value for moderate-to-severe WMH, and combining it with clinical factors can enhance predictive ability (**Figure 3**).

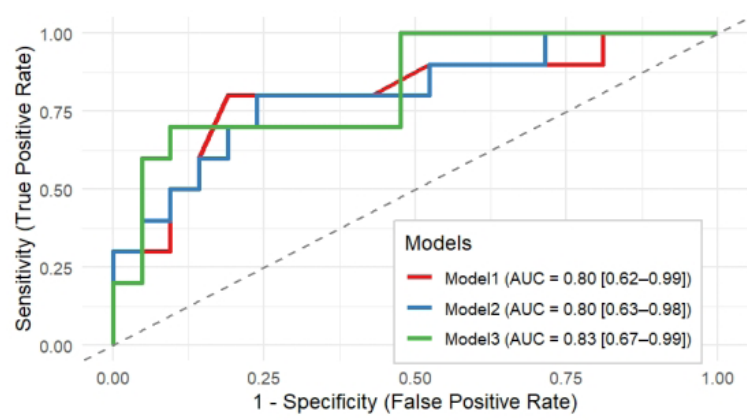


Figure 3. ROC curve for predicting moderate-to-severe WMH based on average GCL thickness

4. Discussion

Cerebral small vessel disease (CSVD) is a series of pathological, clinical, and imaging syndromes caused by multiple etiologies, affecting small cerebral vessels and brain parenchyma. CSVD often has an insidious onset with subtle clinical manifestations, frequently going unnoticed. Moreover, common clinical assessment and examination methods struggle to reflect the pathological state of intracranial vessels [7]. Therefore, this study employed OCT to analyze the correlation between GCL thickness and WMH severity in CSVD patients. The results revealed a significant negative correlation between WMH severity and average GCL thickness in CSVD patients. As the Fazekas score increased, indicating worsening WMH, GCL thickness progressively thinned. Furthermore, the average GCL thickness demonstrated good predictive value for moderate-to-severe WMH, consistent with the findings of Song et al. [8]. The underlying reason is that the

retina and cerebral vessels share a common embryological origin from the mesoderm, and both microvascular systems lack collateral circulation from choroidal vessels, making them highly sensitive to ischemic and hypoxic injuries^[9]. Cerebral microcirculation hypoperfusion, a key pathological mechanism of CSVD, leads to ischemic injury of the cerebral white matter, manifesting as the onset and progression of WMH. Simultaneously, systemic microcirculation pathological changes concurrently affect the retina, resulting in insufficient retinal microvascular perfusion, triggering apoptosis and degeneration of retinal ganglion cells, and ultimately leading to a reduction in GCL thickness^[10].

In this study, the association between GCL thickness and WMH varied across different regions. Significant intergroup differences were observed in the average thickness and the thickness in the inferior nasal, inferior, and inferior temporal regions, while the difference in the superior temporal region did not reach statistical significance. This may be related to variations in blood supply distribution and sensitivity to ischemia across different retinal regions^[11-12]. Additionally, subgroup analysis revealed that type 2 diabetes significantly enhanced the negative correlation between moderate-to-severe WMH and GCL thickness. Diabetic patients exhibit microcirculation disorders, leading to thickening of the microvascular basement membrane, narrowing of the lumen, and decreased blood flow perfusion. This not only exacerbates ischemic injury to the cerebral white matter, worsening WMH severity, but also further intensifies ischemic apoptosis of retinal ganglion cells, further reducing GCL thickness. Huang et al. demonstrated that CSVD patients with diabetes had more pronounced WMH, particularly deep WMH, and more significant reductions in retinal vessel density, corroborating the findings of this study^[13]. Multivariate linear regression analysis showed a negative correlation between WMH severity and average GCL thickness. ROC curve analysis indicated that the corrected model had an AUC of 0.83 for predicting moderate-to-severe WMH, suggesting that average GCL thickness can serve as an effective predictor of moderate-to-severe WMH. As a non-invasive, convenient, and quantifiable detection technique, OCT offers advantages over expensive imaging examinations like cranial MRI, including ease of operation, low cost, absence of radiation, and the ability for repeated testing^[14-15]. Clinically, OCT can be used to detect the average GCL thickness, indirectly assessing WMH severity in CSVD patients, stratifying patients based on imaging burden, reducing unnecessary cranial MRI examinations, and lowering medical costs.

5. Conclusion

In summary, GCL thickness in CSVD patients is negatively correlated with WMH severity, and average GCL thickness has good predictive value for moderate-to-severe WMH. Meanwhile, OCT, as a non-invasive retinal imaging technique, provides a new means for early identification of CSVD and assessment of cerebral white matter lesions. However, this study has certain limitations: (1) It is a single-center study with a relatively small sample size, which may affect the stability of the results; (2) The study population consisted of middle-aged and elderly individuals, and some subjects were excluded from analysis due to poor OCTA image quality caused by cataracts or other ocular diseases, potentially influencing the study results. Future research will involve multi-center, large-sample, prospective follow-up studies to further validate the correlation between GCL thickness and WMH progression in CSVD patients and clarify its value as a disease assessment biomarker.

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Disclosure statement

The authors declare no conflict of interest.

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Summary of the Best Evidence for Discharge Preparation Services in Patients with Myasthenia Gravis

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Abstract: Based on the “6S” pyramid evidence model, this study systematically searched and integrated high-quality evidence such as relevant guidelines, expert consensus, systematic reviews, and clinical studies on discharge preparation services for patients with myasthenia gravis (MG) worldwide up to March 27, 2024. A total of 12 literatures were finally included, and 14 best practice recommendations were summarized, covering six key links: assessment within 24 hours of admission, in-hospital services, pre-discharge preparation, discharge-day services, post-discharge follow-up, and effect evaluation. Evidence indicates that a comprehensive assessment should be completed within 24 hours of the patient's admission, and a multidisciplinary collaborative discharge plan should be initiated. Personalized health education and rehabilitation training should be carried out during hospitalization. Before discharge, patients' self-management capabilities should be confirmed, and structured discharge guidance should be provided. Post-discharge continuous care should be strengthened through regular follow-up. This can effectively improve patients' discharge readiness, reduce readmission rates, and provide an evidence-based basis for medical staff to systematically implement discharge preparation services for MG patients and ensure the safety of the transition period.

Keywords: Myasthenia gravis; Discharge preparation services; Evidence-based nursing; Evidence summary

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1. Introduction

Myasthenia gravis (MG) is an autoimmune disease related to neuromuscular junction transmission disorders. Its global incidence is 0.6–2.8 per 100,000 people, while in China, it reaches 2.19–11.07 per 100,000 people^[1–3]. Discharge preparation services originated from the continuous care system in the United States, aiming to ensure that patients receive appropriate follow-up care after discharge through systematic planning during hospitalization, thereby improving their health status and quality of life^[4–5]. Currently, discharge decisions for MG patients are mainly based on clinical symptoms and examination results, with subsequent precautions

simply informed in the form of discharge summaries, lacking systematicness and continuity. To optimize this process, this study systematically searched, evaluated, and integrated relevant evidence on discharge preparation services for MG patients, aiming to provide an evidence-based basis for clinical practice.

2. Materials and methods

2.1. Establishment of the research question

This study adopted the PIPOST model proposed by the Evidence-Based Nursing Center of Fudan University to construct the evidence-based question, clearly defining the following elements: Population (P) = patients with myasthenia gravis; Intervention (I) = discharge preparation services; Professionals (P) = medical staff; Outcomes (O) = improvement of discharge readiness, self-management ability, and quality of life, etc.; Setting (S) = hospitals; Type of evidence (T) = guidelines, expert consensus, evidence summaries, best practices, clinical decisions, and systematic reviews.

2.2. Literature search

Based on the “6S” pyramid evidence model, this study systematically searched relevant literature from multiple domestic and foreign guideline websites, databases, and professional society websites up to March 27, 2024, including UpToDate, JBI, PubMed, Embase, CNKI, and other Chinese and English resources. Search terms included various names of myasthenia gravis and keywords related to discharge planning and continuous care. Chinese and English search terms were combined according to disease names, intervention measures, and literature types, respectively. The specific search strategy using PubMed as an example is shown in **Figure 1**.

```
# 1( ( Myasthenia Gravis, Generalized[Title/Abstract] OR Generalized Myasthenia Gravis[Title/Abstract] OR Myasthenia Gravis, Ocular[Title/Abstract] OR Ocular Myasthenia Gravis[Title/Abstract] OR MuSK Myasthenia Gravis[Title/Abstract] OR Myasthenia Gravis, MuSK[Title/Abstract] OR Anti-MuSK Myasthenia Gravis[Title/Abstract] OR Myasthenia Gravis, Anti-MuSK[Title/Abstract] OR MuSK MG[Title/Abstract]) )
AND
# 2( (discharge planning[Title/Abstract] OR discharge plan[Title/Abstract] OR patient transfer[Title/Abstract] OR post discharge[Title/Abstract] OR continuing care[Title/Abstract] OR transitional nursing[Title/Abstract] OR patient discharge[Title/Abstract] OR transitional care[Title/Abstract]) )
AND
# 3( (systematic review[Publication Type] OR meta-analysis[Publication Type] OR guideline[Publication Type] OR best practice[Title/Abstract] OR evidence summary[Title/Abstract] OR recommended practice[Title/Abstract]) )
)
# 4 # 1and # 2and # 3
```

Figure 1. Search strategy example

2.3. Inclusion and exclusion criteria

2.3.1. Inclusion criteria

Research subjects were patients with myasthenia gravis; research content involved discharge preparation services; literature types included clinical decisions, best practices, guidelines, evidence summaries, expert consensus, and systematic reviews; languages were limited to Chinese and English.

2.3.2. Exclusion criteria

Full text unavailable, duplicate publications, and literature with low methodological quality.

2.4. Literature quality evaluation

Corresponding tools were used to evaluate the quality of included literature: AGREE II (2017 version) [8] for guidelines; the 2016 version of corresponding evaluation tools from the JBI Evidence-Based Healthcare Center of Australia for expert consensus and systematic reviews [6, 9]; clinical decisions were directly included as high-quality evidence. Three systematically trained researchers independently completed the evaluation and cross-checked. Disagreements were resolved through team discussions. Evidence inclusion followed the principles of prioritizing high quality, authority, and timeliness.

2.5. Evidence grading

This study adopted the JBI Evidence Pre-grading and Recommendation Level System (2014 version) to grade the included evidence [7]. This system classifies evidence levels into 1–5 (Level 1 is the highest, Level 5 is the lowest), and recommendation intensity is divided into Grade A (strong recommendation) and Grade B (weak recommendation) based on the feasibility, applicability, clinical significance, and effectiveness of the evidence [10].

3. Results

3.1. Literature search results and basic characteristics of included literatures

A total of 268 literatures were retrieved. After removing duplicates, 207 literatures remained. Through title and abstract reading, 20 literatures were initially screened. After full-text reading and quality evaluation, 12 literatures were finally included, including 1 clinical decision, 3 guidelines, 3 expert consensus, 2 evidence summaries, 1 systematic review, and 2 randomized controlled trials [11–22]. The general characteristics of the included literature are shown in **Table 1**.

Table 1. General characteristics of the included literatures ($n=12$)

Included Literature	Publication Year	Literature Source	Literature Type	Research Theme
China Geriatric Nursing Alliance [11]	2020	Yimaotong	Expert Consensus	Expert Consensus on Discharge Preparation Services for Elderly Patients
Xu Yafang et al. [12]	2024	Yimaotong	Expert Consensus	Expert Consensus on Whole-Course Management of Adult Generalized Myasthenia Gravis Patients
Sheng Zhaoyuan et al. [13]	2024	CNKI	Expert Consensus	Expert Consensus on Traditional Chinese Medicine Rehabilitation Self-Management for Patients with Myasthenia Gravis

Scott ^[14]	2010	PubMed	Systematic Review	Preventing Readmission: Improving Referral Care in Discharge Processes
RONO ^[15]	2023	RONO	Guideline	Best Practice Guideline for Transitions in Care and Services (2nd Edition)
Narayanaswami P, Sanders DB et al. ^[16]	2020	PubMed	Guideline	International Consensus Guidance for the Management of Myasthenia Gravis
Li Zhuyi et al. ^[17]	2020	Yimaotong	Guideline	Chinese Guidelines for the Diagnosis and Treatment of Myasthenia Gravis
Wang Hui et al. ^[18]	2020	CNKI	Evidence Summary	Evidence Summary of Key Tasks in Hospital Discharge Planning for Inpatients
Whitehorn et al. ^[19]	2019	JBI	Evidence Summary	Discharge Planning: Key Principles
Alper et al. ^[20]	2023	UpToDate	Clinical Decision	Hospital Discharge and Readmission
Yang Ruolan et al. ^[21]	2021	CNKI	Randomized Controlled Trial	The Impact of Nursing Intervention Based on the Knowledge-Attitude-Behavior Theory on Self-Efficacy and Self-Burden of MG Patients
Zhao Feng et al. ^[22]	2020	Chinese Medical Association	Randomized Controlled Trial	The Impact of Self-Efficacy Intervention on Self-Care Ability and Quality of Life of MG Patients

3.2. Results of literature quality evaluation

The results of the literature quality evaluation showed that among the 12 included literatures, 3 guidelines were evaluated by AGREE II ^[15-17]. Only the RONO guideline was recommended as Grade A and adopted, while the other 2 guidelines were not recommended due to their recommendation levels of Grade B and Grade C. 3 expert consensuses, 1 systematic review, 1 clinical decision from UpToDate, and 2 randomized controlled trials were all evaluated as high-quality evidence and included in the final analysis, as shown in **Table 2** ^[11-17, 21-22].

Table 2. Methodological Quality Evaluation Results of Included Guidelines (*n*=3)

Included Guidelines	Scope and Purpose	Standardized Score (%)					Editorial Independence	Number of Domains with $\geq 60\%$ Scores	Number of Domains with $\geq 30\%$ Scores	Recommendation Level
		Stakeholder Involvement	Rigor of Development	Clarity of Presentation	Applicability	Applicability				
RONO ^[15]	100.00	92.59	90.28	100.00	83.33	61.61	6	6	Grade A	
Narayana ^[16]	85.7	57.1	47.6	85.7	42.9	85.7	3	6	Grade B	
Li Zhuyi et al. ^[17]	64.3	35.7	50.0	78.6	21.4	42.9	2	5	Grade C	

3.3. Summary of the best evidence

The best evidence for discharge preparation services in MG patients was extracted from the 12 included literatures, and finally, an evidence summary consisting of 14 items under 6 themes was formed: assessment within 24 hours of admission, in-hospital services, pre-discharge preparation, discharge-day services, post-discharge follow-up, and effect evaluation (**Table 3**).

Table 3. Summary of the best evidence for discharge preparation services in patients with myasthenia gravis

Evidence Category	Evidence Content	Evidence Level
Assessment within 24 Hours of Admission	<p>1. Complete the initial needs assessment within 24 hours of the patient's admission, identify high-risk groups, assess the patient's condition, promote effective communication among patients, family members, and medical staff, and immediately initiate personalized discharge preparation services.^[11, 18-19] 2. The assessment content should comprehensively cover multiple dimensions such as the patient's age, MG classification, activities of daily living, swallowing and respiratory function, motor ability, psychological status, medication status (e.g., immunosuppressants, biological agents, glucocorticoids), as well as mastery of medication knowledge, medication adherence, caregiver ability, family economic support, readmission risk, and accessibility of post-discharge services.^[11-12, 18] 3. Establish a multidisciplinary team to jointly formulate and initially implement the discharge plan.^[18]</p>	Grade A
In-Hospital Services	<p>4. Conduct health education through various methods such as bedside one-on-one education and disease health manuals to help patients and caregivers master self-care skills.^[11, 18, 21] 5. Health education content should cover MG disease knowledge, medication guidance, predisposing factors, and crisis identification to improve patients' treatment adherence.^[11-12, 18] 6. Develop personalized education plans based on different manifestations of skeletal muscle involvement (e.g., diplopia, dysphagia, walking difficulties, dyspnea) and the patient's cultural background, focusing on preventing complications such as falls, aspiration, and deep vein thrombosis.^[11-12, 18] 7. Guide patients and caregivers to familiarize themselves with the precautions for commonly used medications, monitor adverse drug reactions, and ensure standardized medication in accordance with medical advice.^[11-12, 18] 8. Encourage patients with stable conditions to perform respiratory muscle training, swallowing function exercises, and aerobic exercise to enhance muscle strength and improve functional status.^[12-13, 22]</p>	Grade A
Pre-Discharge Preparation	<p>9. Assess the patient's discharge readiness to ensure that the patient, with the assistance of caregivers, has the ability to manage common symptoms, master rehabilitation knowledge (diet, exercise, sleep), identify crisis triggers, and conduct emergency handling.^[12, 18] 10. Check the patient's self-prepared medications before discharge and remove expired or discontinued drugs.^[12, 18]</p>	Grade A
Discharge-Day Services	<p>11. Confirm that the patient meets the discharge criteria 1 hour before discharge. +12. Provide the patient with a discharge summary, which should include key information such as basic condition, medication guidance, precautions, follow-up arrangements, and self-management plans.^[11-12, 18]</p>	Grade A
Post-Discharge Follow-Up	<p>13. Complete the first telephone follow-up within 3-7 days after the patient's discharge, and the second follow-up 2 weeks or 1 month after discharge, with each follow-up lasting 15-20 minutes. Follow-up content should include physical recovery status, existing problems, medication management, progress of rehabilitation training, and follow-up visit arrangements.^[14-15, 20]</p>	Grade A
Effect Evaluation	<p>14. Effect evaluation indicators should include patient satisfaction, self-care ability, quality of life, average length of hospital stay, and incidence of adverse events outside the hospital.^[11]</p>	Grade B

4. Discussion

4.1. Early screening and assessment provide a basis for subsequent care needs of MG patients

Evidence 1 points out that discharge preparation services are time-sensitive, and patient screening and assessment should be completed within 24 hours of admission to identify high-need groups and provide a basis for formulating personalized discharge plans. Evidence 2 further clarifies the assessment content and timing, covering multiple dimensions such as the patient's basic status, disease characteristics, self-

management ability, and social support ^[11,18–19].

4.2. Multidisciplinary cooperation in the formulation and implementation of discharge plans

Evidence 3 emphasizes the importance of multidisciplinary collaboration in the formulation and implementation of discharge plans, but its feasibility in current clinical practice still faces challenges. Future research can focus on constructing an efficient multidisciplinary collaboration mechanism and corresponding talent training system to improve the overall quality of discharge preparation services ^[18]. Evidences 4–10 point out that during discharge preparation services, close observation should be paid to the positive signs of MG patients caused by systemic skeletal muscle involvement, such as fluctuating muscle weakness, fatigue, and corresponding symptoms caused by involvement of facial muscles, masticatory muscles, pharyngeal muscles, cervical muscles, and respiratory muscles ^[3, 12–13, 22]. Based on these clinical manifestations, the multidisciplinary team should collaborate to carry out precise health guidance and skill training to help patients master the key points of home self-care, thereby improving their discharge readiness, promoting a smooth transition of patients to home or community, and enhancing their self-management ability.

4.3. Implementation of precise discharge plans

Evidences 11 and 13 indicate that MG patients should meet relevant criteria when discharged from the hospital, and the hospital should provide systematic guidance on safe medication and follow-up arrangements in accordance with the discharge plan to ensure the continuity and safety of treatment for patients in different care settings. Currently, discharge summaries are mostly in text form, and the education methods are single. More diverse guidance forms should be promoted in the future. Evidence 14 suggests that follow-up conducted by medical staff and pharmacists familiar with the patient's condition through telephone, home visits, remote monitoring, etc., can effectively reduce the incidence of adverse events outside the hospital and unplanned readmissions and improve the patient's quality of life ^[14].

5. Conclusion

This study provides a systematic, evidence-based basis for discharge preparation services in patients with myasthenia gravis. Scientific and effective discharge preparation services can ensure the continuity of patient treatment and improve their quality of life. It is recommended that clinical nurses attach importance to the assessment of patients' discharge readiness and scientifically apply relevant evidence to guide practice in combination with individual differences.

Disclosure statement

The authors declare no conflict of interest.

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Microaspiration Risk Management in Neurocritical Care Patients with Artificial Airways: Clinical Practice and Outcomes

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Abstract: *Objective:* To explore the clinical application effects of constructing and implementing a microaspiration risk management protocol for neurocritical care patients with artificial airways, providing a reference for reducing microaspiration and aspiration pneumonia incidence. *Methods:* Patients with artificial airways admitted to neurocritical care-related departments of a hospital from July 2024 to March 2025 were selected as study subjects. A multidisciplinary collaborative team was established to construct a microaspiration risk management system based on evidence-based medicine. Through current situation investigation and analysis of major barrier factors, comprehensive intervention strategies were implemented, including development of a microaspiration risk assessment scale, modified suction depth guidelines, intelligent cuff pressure monitoring, and gastrointestinal management protocols. The volume of subglottic secretion clearance, microaspiration incidence, and aspiration pneumonia incidence were compared before and after the intervention. *Results:* After implementing the risk management protocol, the volume of subglottic secretion clearance increased from (85.26±13.58) ml to (146.82±21.33) ml; microaspiration incidence decreased from 58.89% to 31.17%; and aspiration pneumonia incidence decreased from 40.77% to 14.72%. All differences were statistically significant ($P<0.001$). *Conclusion:* The evidence-based microaspiration risk management protocol for neurocritical care patients with artificial airways can effectively clear airway secretions, reduce microaspiration and aspiration pneumonia incidence, improve patient prognosis, and has high clinical application value.

Keywords: Neurocritical care; Artificial airway; Microaspiration; Aspiration pneumonia

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1. Introduction

Aspiration refers to the process of liquid or solid substances entering the subglottic airway during eating or non-eating periods, which is divided into overt aspiration and silent aspiration. Microaspiration, as the most common and dangerous form of silent aspiration, refers to the micro-leakage of oropharyngeal secretions

and gastric contents into the lower respiratory tract through the small gap between the tracheal tube cuff and the respiratory tract wall ^[1]. Studies have shown that the incidence of microaspiration in mechanically ventilated patients abroad ranges from 58.2% to 89.0%, and 58.3% to 77.1% domestically. Due to the lack of typical clinical symptoms, approximately 57% of microaspiration events are missed clinically ^[2]. Neurocritical care patients, due to consciousness disorders, impaired swallowing function, weakened cough reflex, and the establishment of artificial airways that disrupt natural airway defense barriers, become a high-risk population for microaspiration ^[3]. Microaspiration not only increases the risk of aspiration pneumonia and ventilator-associated pneumonia (VAP) but also prolongs mechanical ventilation time and hospital stay, increasing mortality and medical costs. Currently, clinical nursing focuses more on the prevention of overt aspiration, lacking microaspiration risk assessment tools and systematic management protocols tailored to the characteristics of neurocritical care patients ^[4-5]. Therefore, this study aims to construct a scientific and systematic microaspiration risk management protocol for neurocritical care patients with artificial airways and evaluate its clinical application effects.

2. Materials and methods

2.1. General information

Patients with artificial airways admitted to the neurocritical care unit, cerebrovascular disease diagnosis and treatment center, and other departments of a hospital from July 2024 to March 2025 were selected as study subjects.

Inclusion criteria: (1) Indwelling artificial airway; (2) Stable vital signs without severe internal environment disorders; (3) ICU stay >3 days.

Exclusion criteria: (1) Hemodynamic instability; (2) Combined mental disorders; (3) Combined tracheoesophageal fistula, gastroesophageal reflux, etc.

A total of 287 patients were included in this study.

2.2. Research methods

2.2.1. Establishment of multidisciplinary team (MDT) management group

In July 2024, a microaspiration risk management group was established, led by the nursing department and composed of multidisciplinary members including neurocritical care medicine, respiratory medicine, nutrition, and rehabilitation. The group consisted of 12 members, with 1 team leader (the director of nursing) responsible for overall coordination; deputy leaders and members included critical care physicians, specialized nurses, nutritionists, and rehabilitation therapists. Members had a clear division of labor, covering protocol development, risk identification, protocol implementation, and quality control.

2.2.2. Current situation investigation and problem analysis

Through retrospective analysis and cross-sectional survey, the incidence of microaspiration in the department before the improvement was investigated. The results showed a microaspiration incidence of 58.89%. Using Pareto analysis, four core problems causing microaspiration were identified: lack of microaspiration risk assessment and screening (26.63%), non-standard artificial airway cuff management (21.89%), lack of dynamic adjustment of enteral nutrition management strategies (16.57%), and incomplete airway secretion management (15.98%).

2.2.3. Evidence retrieval and summary

Computer searches were conducted in BMJ Best Practice, UpToDate, CINAHL, JBI, Cochrane Library, PubMed, CNKI, and Wanfang databases. Search terms included “Microaspiration/Silent aspiration”, “Neurocritical care”, “Artificial airway/Endotracheal tube cuff”, etc. The search timeframe was from database establishment to September 2025. Clinical practice guidelines, systematic reviews, and expert consensus documents were included. After FAME attribute evaluation (Feasibility, Appropriateness, Meaningfulness, Effectiveness), 19 best evidence items were finally included to provide a theoretical basis for protocol development.

2.2.4. Construction and implementation of microaspiration risk management protocol

- (1) Establishment of a risk assessment system and implementation of graded early warning: Based on evidence-based evidence, the “Microaspiration Risk Assessment Scale for Neurocritical Care Patients with Artificial Airways” was developed. Patients were classified into three risk levels: low risk, moderate risk, and high risk, with stratified nursing intervention strategies developed for each level. Risk alerts were set on bedside display screens and nursing station electronic screens, with focused attention on high-risk periods such as before airway procedures and before enteral nutrition initiation.
- (2) Innovation in secretion management technology to block aspiration sources: To address the downward flow of oropharyngeal secretions, a “continuous saliva collector” was designed, combined with a high lateral position (80°–135°), using an “H-type anti-slip adjustable back support” to maintain position, allowing oral secretions to accumulate in the lateral buccal region and be continuously suctioned. This solved the problems of incomplete clearance and mucosal damage associated with traditional wiping methods. For intratracheal suctioning, modified suction depth guidelines were developed for different tracheal tube sizes, and a “five-color suction depth scale” was developed to achieve precise quantification of suction depth, avoiding coughing and microaspiration caused by deep stimulation.
- (3) Optimization of cuff management strategy and clearance of subglottic secretions: Subglottic suction graded pressure control technology was implemented. Different negative pressure ranges were set based on secretion viscosity, and a “subglottic secretion collector” and “subglottic suction pressure prompt card” were developed to achieve dynamic switching of negative pressure and accurate statistics. An intelligent cuff pressure monitoring system was introduced, connecting the cuff tail end with a pressure sensor to achieve real-time monitoring and alarm through the monitor, solving the problems of pressure loss and human resource consumption associated with traditional pressure measurement methods.
- (4) Standardization of gastrointestinal nutrition management to prevent reflux and aspiration: For central hiccups and gastrointestinal tolerance issues, nurse-led multidisciplinary collaborative treatment was implemented, using diaphragmatic pacing physical therapy combined with ginger antiemetic and acupoint plastering and other traditional Chinese medicine techniques. A comprehensive gastrointestinal management protocol was developed, implementing post-pyloric feeding for high-risk patients, using ultrasound measurement of gastric residual volume (GRV) combined with gastric antrum motility index (MI) for assessment, and dynamically regulating enteral nutrition speed.

2.3. Evaluation indicators

- (1) Volume of subglottic secretion clearance in artificial airway: The total volume of subglottic secretions accumulated in the indwelling artificial airway was recorded.

- (2) Microaspiration incidence: Gastric pepsin content in airway secretions was measured by enzyme-linked immunosorbent assay, with >200ng/ml defined as microaspiration occurrence [6]. (3) Aspiration pneumonia incidence: Diagnosed based on clinical manifestations, imaging changes, and pathological examination.

2.4. Statistical methods

SPSS 26.0 statistical software was used for data analysis. Measurement data were expressed as mean \pm standard deviation (Mean \pm SD), and inter-group comparison was performed using *t*-test; count data were expressed as frequency and percentage, and inter-group comparison was performed using χ^2 test. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of subglottic secretion clearance volume before and after intervention

After implementing the risk management protocol, the volume of subglottic secretion clearance in the artificial airway significantly increased, from (85.26 \pm 13.58) ml before improvement to (146.82 \pm 21.33) ml after improvement, with a statistically significant difference ($t=38.052$, $P < 0.001$).

3.2. Comparison of microaspiration and aspiration pneumonia incidence before and after intervention

After improvement, the microaspiration incidence was 31.17%, lower than 58.89% before improvement ($\chi^2=42.168$, $P < 0.001$); the aspiration pneumonia incidence was 14.72%, lower than 40.77% before improvement ($\chi^2=61.909$, $P < 0.001$) (Table 1).

Table 1. Comparison of Microaspiration and Aspiration Pneumonia Incidence Before and After Intervention [n(%)]

Groups	Microaspiration incidence (%)	Aspiration pneumonia incidence (%)
before improvement	169 (56.33)	126 (42)
After improvement	92 (30.67)	45 (15)
χ^2 Value	40.206	53.662
<i>P</i> Value	< 0.001	< 0.001

4. Discussion

4.1. Innovation in oropharyngeal secretion management strategy to block the microaspiration pathway from the source

The accumulation and downward flow of oropharyngeal secretions is the primary cause of microaspiration in neurocritical care patients. Studies have shown that oropharyngeal colonizing bacteria are the main source of pathogens causing aspiration pneumonia [7]. In traditional nursing, tissue wiping or routine suctioning often fails to thoroughly clear deep pharyngeal retained secretions, and frequent operations easily damage oral mucosa and increase patient discomfort. This study developed a continuous saliva collector combined with a high lateral position (80°–135°), achieving significant results. The mechanism lies in: on one hand, the

high lateral position uses gravity to make oropharyngeal secretions accumulate in the lateral buccal region, avoiding accumulation in the pharynx; on the other hand, the continuous saliva collector achieves continuous, low-negative-pressure suctioning of secretions, solving the “time window” omission problem of traditional intermittent suctioning. Similar to Mraovic et al.’s study indicating that subglottic secretion drainage can significantly reduce microaspiration risk, this study effectively blocked the pathway of oropharyngeal secretions leaking to the lower respiratory tract through the cuff wall through external continuous drainage^[8]. Results showed that the volume of subglottic secretion clearance significantly increased after improvement ($P<0.001$), confirming the high efficiency of this technology in clearing secretion sources.

4.2. Standardization of airway suction depth and cuff management to construct a closed airway defense system

Improper artificial airway cuff management and non-standard airway suctioning operations are important iatrogenic factors causing microaspiration. Addressing clinical pain points, this study implemented dual improvements. First, in airway suctioning, guidelines recommend using modified suctioning methods to reduce airway mucosal damage, but clinical practice often lacks clear scale markings on suction catheters, leading to inaccurate insertion depth^[9–10]. This study developed a “suction depth color scale”, transforming abstract measurement data into visual color guidance, ensuring the suction catheter tip is precisely located 1–2 cm below the tracheal tube tip. This improvement avoided severe coughing and airway mucosal damage caused by deep suctioning, while also preventing secretion retention due to insufficient suction depth. Consistent with Deng et al.’s evidence summary on microaspiration prevention in ICU patients with artificial airways, precise suctioning operations can effectively reduce microaspiration risk around the cuff^[11].

Second, in cuff management, traditional intermittent manual pressure measurement has drawbacks such as large pressure fluctuations and air leakage during measurement. This study introduced an intelligent cuff pressure monitoring system, achieving real-time constant pressure and automatic early warning. Shu et al.’s evidence-based practice pointed out that maintaining cuff pressure in the ideal range of 25–30 cmH₂O is key to preventing microaspiration^[8]. The application of intelligent monitoring systems effectively avoided “micro-leakage” caused by low cuff pressure and mucosal ischemia caused by high pressure, thereby constructing a relatively closed airway defense system and significantly reducing the risk of bacterial translocation and microaspiration.

4.3. Integration of multidisciplinary nutritional intervention strategies for dynamic prevention and control of gastric content reflux

Neurocritical care patients often have gastrointestinal motility disorders and impaired swallowing function, and gastric content reflux is another important source of microaspiration^[12]. This study changed the previous model of single reliance on nurse experience to adjust nutrition protocols, establishing a nurse-led multidisciplinary collaborative mechanism and implementing a comprehensive gastrointestinal management protocol. Through ultrasound monitoring of gastric residual volume (GRV) combined with gastric antrum motility index (MI) to assess gastrointestinal tolerance, dynamic graded regulation of enteral nutrition speed was achieved. Liu et al.’s study emphasized that dynamic assessment of gastrointestinal function and adjustment of feeding strategies are important measures to prevent aspiration^[13]. This study not only standardized post-pyloric feeding pathways but also innovatively introduced diaphragmatic pacing combined with traditional Chinese medicine acupoint plastering for central hiccups, effectively solving the problem

of sudden increase in intra-abdominal pressure and gastric content reflux caused by hiccups. This “dynamic monitoring-early warning-multidimensional intervention” nutritional management model compensates for the shortcomings of traditional nursing in gastrointestinal function management, cutting off the risk source of microaspiration from the digestive tract pathway.

4.4. Construction of a stratified risk assessment system to achieve precision nursing intervention

Microaspiration is occult, and traditional nursing often lacks targeted screening tools^[4]. This study developed the “Microaspiration Risk Assessment Scale for Neurocritical Care Patients with Artificial Airways” based on evidence-based evidence, achieving the transformation from “empirical nursing” to “precision nursing.” By classifying patients into low, moderate, and high-risk levels and implementing intensive interventions during high-risk periods, rational allocation of nursing resources was ensured. Millot et al.’s study pointed out that microaspiration is closely related to ventilator-associated events, and early identification of high-risk populations is key to improving prognosis^[5]. The practice of this study proves that establishing standardized risk assessment and screening mechanisms can significantly enhance nurses’ ability to identify microaspiration risks, thereby taking proactive preventive measures and effectively reducing the incidence of aspiration pneumonia.

5. Conclusion

The microaspiration risk management protocol for neurocritical care patients with artificial airways constructed in this study is scientific, innovative, and practical. Through the establishment of risk assessment systems, innovative improvement of nursing equipment, and operation of multidisciplinary collaborative models, airway subglottic secretions were effectively cleared, and the incidence of microaspiration and aspiration pneumonia was significantly reduced, improving patient clinical outcomes. This protocol has formed a set of replicable and promotable standardized operation norms, which can provide a reference for clinical nursing practice.

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Disclosure statement

The authors declare no conflict of interest.

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Depression Prediction Based on Graph Neural Networks

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Abstract: Depression, as a highly prevalent mental disorder, is traditionally diagnosed using subjective scale-based assessments, which suffer from limitations such as insufficient objectivity and delayed early warning. With the widespread adoption of electronic health records and the rapid advancement of artificial intelligence technologies, data-driven approaches for depression prediction have become a major research focus. This paper systematically reviews the evolution of depression prediction methods, spanning from traditional assessment scales to machine learning and further to deep learning techniques. The paper places particular emphasis on the current applications and unique advantages of graph neural networks (GNNs) in this domain. Existing studies indicate that GNNs can effectively model complex relationships among patient features, thereby improving predictive performance while enhancing model interpretability and offering a novel technical pathway for early detection of depression. However, several challenges remain, including the lack of standardized graph construction methods, issues related to data privacy and quality, and insufficient model generalizability. Future research is expected to focus on constructing multi-center graph datasets, developing interpretable GNN models, and promoting their practical application in public health screening, ultimately advancing mental health services toward a “data-driven and proactive prevention” paradigm.

Keywords: Depression prediction; Graph neural networks; Deep learning; Graph attention networks

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1. Introduction

According to statistics from the World Health Organization (WHO), approximately 1 billion people worldwide are affected by mental disorders. During the COVID-19 pandemic, the prevalence of depression increased by 27.6% ^[1]. Depression has become one of the leading causes of disability in China, ranking second among all causes ^[2]. In recent years, a series of policies have been introduced to promote mental health initiatives, indicating that the early identification and intervention of depression have become critical public health priorities ^[3].

Depression Spectrum Disorder (DSD) is a class of neurological disorders characterized by significant

heterogeneity^[4]. Its core symptoms include persistent low mood, diminished interest, and reduced energy, often accompanied by cognitive and physiological dysfunctions^[5]. Current clinical diagnosis primarily relies on clinician interviews and standardized scales (e.g., PHQ-9, HAMD). However, these approaches suffer from limitations such as strong subjectivity, reporting bias from patients, and difficulty in early detection. Delayed diagnosis may result in missed opportunities for optimal intervention, underscoring the importance of early identification. Automated prediction methods hold the potential to improve screening efficiency, optimize the allocation of medical resources, and support research into disease mechanisms.

Advances in machine learning and deep learning have driven the transition of depression prediction from subjective assessment to data-driven approaches^[6]. In recent years, these methods have achieved promising results in early detection tasks. Graph Neural Networks (GNNs) are capable of learning representations from graph-structured data by jointly modeling node attributes and relational information to perform classification tasks. In the context of depression prediction, leveraging GNNs to capture inter-patient relational features can enhance the discriminative power of predictive models.

2. Related work

In the early stages of depression prediction research, psychological assessment scales were the primary tools, such as the Hamilton Depression Rating Scale (HAMD), Beck Depression Inventory (BDI), and Center for Epidemiologic Studies Depression Scale (CES-D). However, these scales exhibit notable limitations: different instruments cover inconsistent symptom domains, assessments for the same individual may vary substantially across scales, and they are generally characterized by latency and subjectivity, making them inadequate for early warning purposes.

With the advancement of data mining techniques, machine learning methods have been increasingly applied to depression prediction. Models such as Support Vector Machines (SVM), decision trees, and random forests have achieved promising results. For instance, random forest models have reached an AUC of 0.943 in postpartum depression prediction, while ensemble learning approaches have reported accuracies ranging from approximately 88.6% to 89.7%^[7-8]. A related review indicates that the AUC of such models spans from 0.6030 to 0.9976^[6]. Nevertheless, traditional machine learning methods remain limited in handling complex clinical data and multimodal information.

In recent years, deep learning has been widely adopted due to its capability for automatic feature extraction. Convolutional Neural Networks (CNNs) and Recurrent Neural Networks (RNNs) are commonly employed to capture spatial and temporal features, respectively. Numerous studies have demonstrated strong performance on electroencephalogram (EEG) and multimodal datasets. For example, an improved Temporal Convolutional Network (TCN) model achieved an accuracy of 91.3% on the DAIC-WOZ dataset, while a CNN-LSTM-based model (DDNet) attained an accuracy of 96.21% on social media data^[9-10]. In addition, Graph Neural Network (GNN)-based methods have been introduced; by constructing brain networks and integrating ensemble strategies, these approaches achieved an accuracy of 77% on the MODMA dataset^[11].

3. Dataset and data preprocessing

3.1. Dataset

In depression prediction studies based on the DBIDE dataset, preprocessed data can be accessed via publicly

available Amazon S3 storage. The derived data for each subject and different processing pipelines are stored as independent files, enabling on-demand download.

To construct a population graph that integrates both imaging and non-imaging information, this study utilizes rs-fMRI, sMRI, and phenotypic data from the DBIDE dataset. The sample selection is consistent with that of Parisot et al., comprising a total of 871 subjects, including 403 patients with DSD and 468 healthy controls^[8].

For fair comparison, the fMRI data are preprocessed using the same C-PAC pipeline^[9], which includes temporal and motion correction, normalization, band-pass filtering (0.01–0.1 Hz), registration, and the construction of functional connectivity matrices ((S₁, ..., S_N)). The sMRI data are processed using the CIVET pipeline, including denoising, registration, and segmentation. Finally, phenotypic information such as age, sex, full-scale IQ (FIQ), acquisition site, and diagnosis is incorporated jointly for depression prediction modeling.

This study employs two distinct graph construction strategies—P-Edge and PF-Edge—to build the population graph edge structures required for depression research. These two methods differ in construction logic, data sources, and the aspects of topological characteristics they emphasize, making them suitable for modeling subject relationships from different perspectives.

3.2. Data preprocessing

The P-Edge method defines graph node connectivity primarily based on subjects' clinical phenotypic data. It selects key phenotypic attributes, such as age and sex, as the basis for graph construction and determines inter-node relationships through differentiated rules. For continuous phenotypic variables, such as age and full-scale IQ (FIQ), a connection is established if the numerical difference is below a predefined threshold. For categorical variables, such as sex, nodes are connected if the values are identical. Edge label matrices are generated by aggregating the association results of individual phenotypic attributes, and a binary adjacency matrix is subsequently derived through logical rules to complete the population graph construction. This method relies on basic demographic and clinical indicators, offering simplicity, interpretability, and low computational complexity. However, it yields limited variability in edge weights and has a relatively weak capacity to capture deeper associations among subjects.

In contrast, the PF-Edge method measures inter-node correlations (i.e., edge weights) by integrating both phenotypic similarities and the Pearson correlation coefficients between fMRI data of different subjects. By jointly considering phenotypic and imaging features, this approach computes comprehensive inter-subject correlations based on both clinical attribute relationships and functional imaging similarities, thereby defining edge weights and connectivity. This method leverages the complementary strengths of phenotypic clinical attributes and brain network characteristics derived from functional imaging data. It not only preserves the foundational constraints imposed by demographic and clinical features but also incorporates deeper similarity information from functional neuroimaging. Compared with the single P-Edge approach, PF-Edge provides a more comprehensive and multidimensional characterization of inter-subject topological relationships, thereby offering a higher-quality graph structure for graph neural network modeling.

4. Design and implementation of a graph neural network-based depression prediction model

4.1. Implementation of model components

The proposed model consists of four modules: a graph construction module, a feature processing module, a Graph Attention Network (GAT) module, and a classification output module. The implementation details of each module are described as follows.

4.2. Graph structure construction module

All subjects are treated as graph nodes, and brain functional connectivity features are used as node feature vectors. An undirected weighted graph is constructed based on similarity computation. The Pearson correlation distance between subject features is calculated:

$$dist = pdist(features, metric=correlation) \quad (1)$$

A similarity adjacency matrix is then generated using a Gaussian kernel function:

$$adj = \exp\left(-\frac{dist^2}{2\sigma^2}\right) \quad (2)$$

where σ represents the mean distance. A threshold ($h_x = 0.8$) is applied to filter valid edges, and the resulting graph structure is represented as `edge_index` for use in PyTorch Geometric. Functional connectivity matrices from the DBIDE dataset are used as the original fMRI features. Feature selection is performed using analysis of variance (ANOVA), retaining the top 2000 most significant features. These features are subsequently standardized to ensure training stability.

4.3. Graph Attention Network (GAT) Module

A two-layer Graph Attention Network (GAT) architecture is adopted, with the following core design:

- (1) First Layer: The input node features are projected into a hidden representation space with a dimensionality of ($hid_c = 12$). In this stage, attention weights are learned to capture the relative importance of neighboring nodes.
- (2) Second Layer: The learned hidden representations are further transformed to produce the final output for binary classification.

To enhance feature representation, a multi-head attention mechanism is employed (**Figure 1**). This mechanism aggregates information from neighboring nodes by assigning attention coefficients, enabling the model to capture diverse structural patterns. The Exponential Linear Unit (ELU) activation function is applied to introduce nonlinearity and improve the model's expressive capacity. In the final layer, a LogSoftmax function is used to generate class probability distributions. The output dimension is set to 2, corresponding to the two categories: depression (DSD) and healthy control (TC).

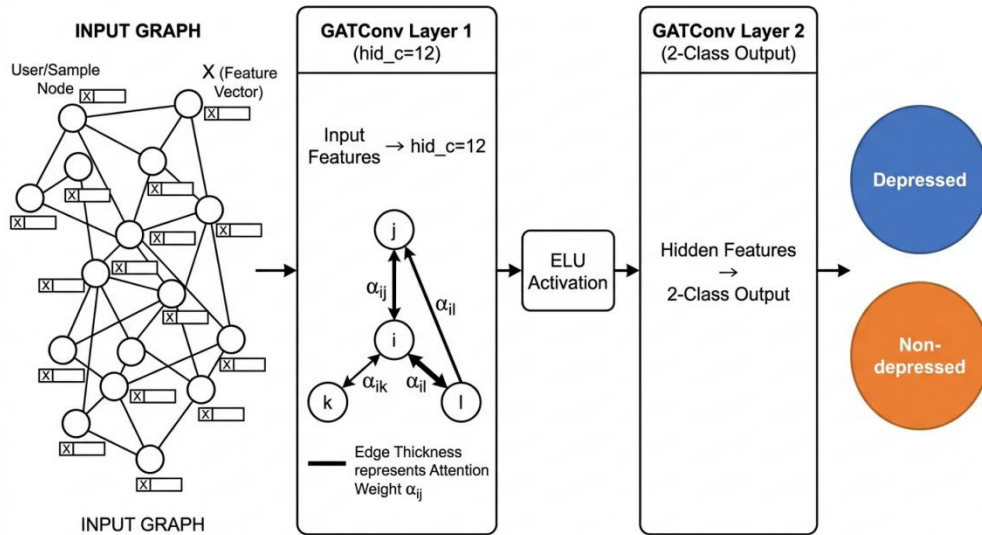


Figure 1. Schematic of attention network structure

5. Experimental results

5.1. Model performance evaluation

The model training process demonstrates stable convergence, achieving a final classification accuracy of 69.32% and an AUC value of 0.6863 on the test set. These results indicate that the proposed depression classification model, based on population graph structures and a Graph Attention Network (GAT), can effectively capture both brain functional connectivity features and topological relationships among subjects, thereby exhibiting a certain capability for assisting in depression identification.

The training loss curve shows a continuous downward trend with gradual convergence, decreasing from an initial value of 0.7935 to 0.0957 at the 200th epoch. This indicates that the model is capable of effectively learning feature representations without exhibiting significant overfitting, and the overall training process is stable and reliable.

5.2. Confusion matrix analysis

The visualization of the confusion matrix is shown in **Figure 2**. In the matrix, rows represent the true labels of samples, while columns represent the predicted labels. Class 0 and Class 1 correspond to healthy controls and depression spectrum disorder (DSD), respectively. The key values in the matrix are as follows: among healthy control samples, 25 cases are correctly classified as Class 0, while 16 cases are misclassified as Class 1; among depression samples, 37 cases are correctly classified as Class 1, while 10 cases are misclassified as Class 0.

From the distribution, the model demonstrates relatively strong recognition capability for depression samples, with the number of true positives significantly exceeding false negatives, indicating that the model effectively captures brain imaging features associated with depression. Meanwhile, the classification accuracy for healthy controls remains at a reasonable level, with a relatively low false positive rate. This is of particular importance in clinical decision-support scenarios, as it helps reduce unnecessary interventions and misdiagnoses.

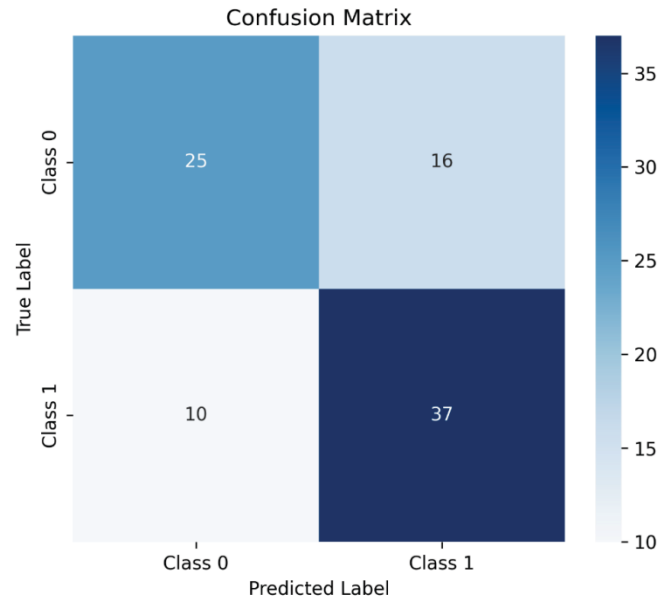


Figure 2. Confusion matrix

6. Conclusion

This study focuses on resting-state functional magnetic resonance imaging (rs-fMRI) data from the DBIDE dataset and addresses the task of automatic identification of depression spectrum disorder by constructing and implementing a classification model based on a Graph Attention Network (GAT).

Multi-center data from DBIDE were preprocessed through cleaning, normalization, and feature selection to extract brain functional connectivity features. To address the limitation of traditional machine learning methods in capturing inter-sample relationships, this study constructs a population graph based on inter-subject feature similarity, transforming tabular data into graph-structured data that incorporates both node features and topological relationships, thereby providing a solid foundation for graph neural network modeling.

The GAT model is implemented using the PyTorch Geometric framework, leveraging the attention mechanism to adaptively learn the importance weights of different subject nodes, enabling deep feature representation and classification of brain imaging data. The model is trained using a stratified cross-validation strategy, optimized with the Adam optimizer and a negative log-likelihood loss function. Over 200 training epochs, the loss converges steadily without significant overfitting.

The model achieves a classification accuracy of 69.32% and an AUC value of 0.6863 on the test set. The confusion matrix analysis indicates that the model performs well in identifying healthy control samples while maintaining a relatively low false positive rate, demonstrating its potential value in clinical decision support. Furthermore, visualization of GAT attention weights confirms that the model can adaptively focus on key inter-subject relationships, thereby enhancing the interpretability of the decision-making process.

Disclosure statement

The author declares no conflict of interest.

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Study on the Correlation between the Levels of LPS and LBP in Feces and Plasma and Neurological Function in Patients with Parkinson's Disease

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Abstract: *Objective:* To analyze the correlation between the levels of LPS (Lipopolysaccharide) and LBP (Lipopolysaccharide-binding protein) in feces and plasma and neurological function in patients with Parkinson's disease (PD). *Methods:* Thirty patients with PD (PD group) who met the inclusion and exclusion criteria and were treated at the neurology outpatient clinic/inpatient department of Heilongjiang Provincial Hospital from March 2025 to December 2025 were selected. Thirty age- and gender-matched healthy individuals who underwent health screenings during the same period were selected as the healthy control group (HC group). The levels of LPS and LBP in feces and plasma were compared between the two groups. *Results:* After testing, the levels of LPS and LBP in feces and plasma of the PD group were significantly higher than those of the HC group. Among PD patients, the levels of LPS in feces of patients in stages III-V were significantly higher than those in stages I-II. The levels of LPS in the plasma of patients in stages III-V were significantly higher than those in stages I-II. The levels of LBP in feces and plasma of patients in stages III-V were significantly higher than those in stages I-II. There was a positive correlation between the levels of LPS in feces and the UPDRS (Unified Parkinson's Disease Rating Scale) scores in PD patients ($r=0.68$, $P<0.01$). There was a positive correlation between the levels of LPS in plasma and the UPDRS scores ($r=0.72$, $P<0.01$). There was a positive correlation between the levels of LBP in feces and the UPDRS scores in PD patients ($r=0.65$, $P<0.01$). There was a positive correlation between the levels of LBP in plasma and the UPDRS scores ($r=0.70$, $P<0.01$). *Conclusion:* The levels of LPS and LBP in feces and plasma can serve as important indicators for evaluating patients with PD, and there is a positive correlation between these levels and neurological function in PD patients.

Keywords: Feces; Plasma LPS; LBP level; Parkinson's disease; Neurological function; Impact

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1. Introduction

Parkinson's disease (PD) is primarily characterized by a decrease in the number of dopaminergic neurons in the substantia nigra. Its clinical symptoms include resting tremor, bradykinesia, muscular rigidity, and abnormal gait and posture ^[1]. In the classification of PD, Jankovic et al. divided PD into tremor-dominant type, mixed type, and gait disorder based on the Unified Parkinson's Disease Rating Scale (UPDRS) score, but its mechanism remains unclear ^[2]. Regarding cognitive impairment, PD is characterized by impairments in planning, organization, thinking, judgment, problem-solving, and visual-spatial abilities, which can ultimately progress to comprehensive dementia, severely affecting patients' daily lives ^[3]. Currently, there are no ideal molecular markers for the early diagnosis and treatment of PD in clinical practice. Research hotspots include the early diagnosis of Parkinson's disease, the discovery of early diagnostic markers, the prediction of disease progression, the sensitivity of drugs, the prognosis judgment, and the differentiation from other Parkinsonian syndromes. This research involves clinical, imaging, genetic, and other approaches, combined with clinical samples such as blood, cerebrospinal fluid, urine, feces, and skin ^[4]. Most clinical studies on PD currently focus on single-omics or dual-omics research using single biological samples, and there is still a scarcity of combined research on gut microbiota, blood metabolomics, and urine metabolomics ^[5]. To better analyze the impact of fecal and plasma levels of LPS and LBP on neurological function in patients with PD, this study selected 30 patients admitted to our hospital as the research subjects and 30 healthy patients who underwent physical examinations during the same period as controls. The aim is to provide a reference for clinical diagnosis and treatment. The report is as follows.

2. Materials and methods

2.1. General information

Thirty patients with Parkinson's disease (PD group) who met the inclusion and exclusion criteria and visited/were hospitalized in the neurology outpatient clinic/inpatient department of Heilongjiang Provincial Hospital from March 2025 to December 2025 were selected. Additionally, 30 age- and gender-matched healthy individuals who underwent health screenings during the same period were chosen as the healthy control group (HC group). The PD group consisted of 17 males and 13 females, with an average age of (65.36±6.83) years. The HC group comprised 16 males and 14 females, with an average age of (65.45±7.22) years. There were no significant differences in general information between the two groups, making them comparable ($P > 0.05$).

Inclusion criteria: All PD patients met the MDS diagnostic criteria for PD established in 2015.

Exclusion criteria: (1) Secondary Parkinson's syndrome, such as that caused by various drugs, poisons, trauma, cerebrovascular diseases, neurodegenerative Parkinson's, and Parkinsonism. (2) Suffering from poisoning, metabolic diseases, immune diseases, infectious diseases, etc. (3) History of gastrointestinal disorders. (4) Unknown primary olfactory abnormalities caused by other factors such as oral or nasal issues. (5) Use of gastrointestinal motility drugs, laxatives, antibiotics, probiotics, or prebiotics within the past month. (6) Dietary biases, such as only eating meat or being vegetarian. (7) Smoking or drinking alcohol within the past month. (8) Patients who cannot cooperate with collecting medical history, evaluations, or retaining fecal samples.

2.2. Methods

All participants in the study were required to provide 5ml of venous blood collected on an empty stomach in the morning. Specific cytokine detection kits were used to measure the levels of tumor necrosis factor- α , IL-

1 β , IL-8, IL-9, MIP-1 β , and MIP-1 α . This project employed an immunoassay “double-antibody sandwich” method based on fluorescent microsphere technology. Statistical analysis was performed using SPSS 25.0 software.

Study subjects were provided with sterile urine collection tubes and instructed on the standard process for urine collection. The samples were returned to the laboratory on the same day and stored frozen at -80°C. Amino acid levels were later measured using targeted metabolomics techniques after thawing.

Patients were given sterile feces collection tubes and instructed to follow a standardized collection process. Using matching sterile scoops, two clean feces samples were placed into the sterile collection tubes containing preservation solution. The preservation solution in the collection tubes ensured no microbial growth at room temperature, stabilized DNA, and preserved the intestinal microbiota’s integrity in its original state upon sampling. The samples were transported back to the laboratory on the same day and stored at -80°C. High-throughput sequencing technology was employed to sequence the 16SrRNA V3+V4 variable regions, referencing the Greengenes database for functional annotation.

2.3. Statistical methods

Quantitative data were tested for normal distribution using the Shapiro-Wilk test and expressed as mean \pm standard deviation (Mean \pm SD). Comparisons between two groups were made using the *t*-test. Non-normally distributed continuous variables were expressed as median and interquartile range (M, P25, P75) and compared using the Mann-Whitney U test. Categorical data were expressed as counts and percentages, and comparisons between groups were made using the chi-square test. Differences in intestinal microbiota composition and diversity among different age groups were studied. LEfSe analysis was used to identify gut microbial markers. Correlation analysis of clinical features in PD patients was performed using methods such as Spearman correlation and RDA. Additionally, PICRUST2 software was utilized to predict gut microbiota-related functional pathways based on metagenomic data.

3. Results

3.1. Comparison of LPS and LBP levels in feces and plasma between the two groups

After testing, the levels of LPS and LBP in feces and plasma of the PD group were significantly higher than those of the HC group, and the difference between the two groups was statistically significant ($P < 0.05$) (Table 1).

Table 1. Comparison of LPS and LBP levels in feces and plasma between the two groups (Mean \pm SD)

Indicator	PD Group(<i>n</i> =30)	HC Group(<i>n</i> =30)	<i>t</i>	<i>P</i>
Fecal LPS (EU/g)	2.85 \pm 0.75	1.22 \pm 0.45	10.207	0.001
Plasma LPS (EU/ml)	0.69 \pm 0.23	0.22 \pm 0.11	10.097	0.001
Fecal LPB (μ g/g)	35.53 \pm 8.36	18.23 \pm 5.63	9.401	0.001
Plasma LPB (μ g/ml)	65.38 \pm 12.45	32.16 \pm 8.72	11.971	0.001

3.2. Comparison of fecal and plasma LPS and LBP levels in PD patients at different H-Y stages

After testing, the fecal LPS levels of patients in stage III-V of the PD group were significantly higher than

those of patients in stage I-II. The plasma LPS levels of patients in stage III-V were significantly higher than those of patients in stage I-II. The fecal LBP levels of patients in stage III-V were significantly higher than those of patients in stage I-II, and the plasma LBP levels of patients in stage III-V were significantly higher than those of patients in stage I-II (**Table 2**).

Table 2. Comparison of fecal and plasma LPS and LBP levels in PD patients at different H-Y stages (Mean \pm SD)

Indicator	Stage I-II(<i>n</i> =17)	Stage III-V(<i>n</i> =13)	<i>t</i>	<i>P</i>
Fecal LPS (EU/g)	2.19 \pm 0.63	3.53 \pm 0.81	5.103	0.001
Plasma LPS (EU/ml)	0.52 \pm 0.18	0.86 \pm 0.22	4.568	0.001
Fecal LBP (μ g/g)	28.86 \pm 7.25	42.35 \pm 9.13	4.515	0.001
Plasma LBP (μ g/ml)	52.14 \pm 10.33	78.53 \pm 13.66	6.033	0.001

3.3. Correlation analysis between fecal and plasma LPS and LBP levels and UPDRS scores in PD patients

There was a positive correlation between fecal LPS levels and UPDRS scores in PD patients ($r=0.68$, $P<0.01$). There was a positive correlation between plasma LPS levels and UPDRS scores ($r=0.72$, $P<0.01$). There was a positive correlation between fecal LBP levels and UPDRS scores in PD patients ($r=0.65$, $P<0.01$). There was a positive correlation between plasma LBP levels and UPDRS scores ($r=0.70$, $P<0.01$) (**Table 3**).

Table 3. Correlation analysis between fecal and plasma LPS and LBP levels and UPDRS scores in PD patients

Indicator	Correlation Coefficient (<i>r</i>)	<i>P</i>
Fecal LPS vs. UPDRS Score	0.69	0.001
Plasma LPS vs. UPDRS Score	0.73	0.001
Fecal LBP vs. UPDRS Score	0.66	0.001
Plasma LBP vs. UPDRS Score	0.71	0.001

4. Discussion

Parkinson's disease is the most common neurodegenerative disease after Alzheimer's disease. There is no cure for Parkinson's disease, and its pathogenesis remains unclear. Clinically, there is also a lack of effective molecular markers for early diagnosis and treatment of Parkinson's disease. Autonomic nervous system dysfunction is the most common non-motor symptom of Parkinson's disease, and its pathogenesis is closely related to the progression of the disease^[6]. Therefore, seeking a biomarker that can effectively evaluate the damage to autonomic nerves in PD is of great significance for improving the prognosis of PD patients.

The results of this study show that the levels of fecal and plasma LPS and LBP in PD patients are significantly higher than those in healthy controls, which is consistent with the results obtained from multiple previous studies^[7]. By constructing an MPTP-induced PD mouse model, Bhattarai et al. found that the LPS content in the colonic tissue of the model group mice increased by 3.2 times compared with the control group, and the plasma LBP concentration increased to 2.1 times that of the control group. Moreover, the number of activated microglia in the substantia nigra was positively correlated with LPS levels ($r=0.63$, $P<0.01$)^[8].

This is highly consistent with the phenomenon observed in this study, where PD patients had elevated LPS and LBP levels and concomitant neurological impairment, indicating that peripheral inflammation caused by LPS may affect the central nervous system through the blood circulation or vagus nerve pathways. A cohort study published by Sampson's team in "Cell" in 2016 showed that among 128 fecal samples from PD patients, the abundance of LPS-encoding genes was 2.7 times higher than that of healthy controls, and the plasma LBP concentration was significantly elevated^[9]. This is similar to the detection result of plasma LBP (65.38±12.5 µg/ml) in the PD group in this study. More importantly, the study used fecal microbiota transplantation experiments to confirm that transplanting the fecal flora from PD patients into germ-free mice not only increased the intestinal barrier permeability of the recipient mice but also reduced the number of dopaminergic neurons in the substantia nigra by 19.3%. This directly demonstrates a causal relationship between gut microbiota metabolites (including LPS) and the onset of PD. A study published by Wang et al. in "Neurobiology of Disease" stated that LBP can form a complex with CD14, enhancing the efficiency of LPS activation of TLR4/MD-2 receptors and increasing the activation level of the downstream NF-κB pathway by 2.3 times, thereby promoting the release of proinflammatory factors IL-1β and TNF-α^[10]. This study showed a strong correlation between LBP levels and UPDRS scores in PD patients ($r=0.71$, $P<0.01$). This mechanism is clinically manifested by LBP acting as an inflammatory amplifier, potentially exacerbating the damage of neuroinflammation to dopaminergic neurons. Studies have shown that gut microbiota imbalance may cause damage to the intestinal barrier function, allowing LPS to easily enter the bloodstream and trigger a systemic inflammatory response. Most PD patients have gut microbiota disorders, which may be a reason for their elevated LPS levels^[11]. As a protein that can bind to LPS, LBP plays a critical role in the inflammatory response triggered by LPS. When LPS levels rise, LBP levels also increase to enhance the recognition and clearance of LPS. This explains the phenomenon observed in this study, where LBP levels were elevated in PD patients. The results of this study showed that as the H-Y stage increased, the levels of LPS and LBP in both feces and plasma of PD patients gradually increased, and there was a positive correlation with the UPDRS score. This suggests that LPS and LBP levels may be associated with the severity of PD. The H-Y stage and UPDRS score are commonly used indicators to evaluate the severity and neurological function of PD patients. These findings imply that LPS and LBP may be involved in the progression of PD. LPS can trigger an inflammatory response by activating the toll-like receptor 4 (TLR4) signaling pathway, releasing a large number of inflammatory factors such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6)^[12]. These inflammatory factors can damage dopaminergic neurons and exacerbate the symptoms of Parkinson's disease. When LBP binds to LPS, it can enhance the activation of TLR4 by LPS, further promoting the intensification of the inflammatory response and subsequently aggravating neurological damage. Comparing the results of fecal samples, it was found that plasma samples are easier to obtain and detect and can more directly reflect systemic inflammatory status. Detecting LPS and LBP levels in plasma may provide critical references for assessing the condition and prognosis of PD patients. However, the specific mechanism of action of LPS and LBP in PD is not yet fully understood and requires further investigation. Questions such as how LPS influences the occurrence and development of PD through the gut-brain axis, and how to improve the neurological function of PD patients by regulating LPS and LBP levels, need to be further explored.

5. Conclusion

In summary, the levels of LPS and LBP in feces and plasma can serve as important indicators for evaluating

Parkinson's disease patients, and there is a positive correlation between these levels and the neurological function of Parkinson's disease patients.

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Clinical Study on the Treatment of Dysarthria After Stroke Using Tongguan Liqiao Acupuncture Combined with Neuromuscular Electrical Stimulation

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Abstract: *Objective:* To explore the clinical efficacy and advantages of Tongguan Liqiao acupuncture combined with neuromuscular electrical stimulation in the treatment of dysarthria after stroke. *Methods:* A randomized, single-blind, controlled clinical trial design was adopted, involving 60 patients with dysarthria after stroke who were randomly divided into a control group (neuromuscular electrical stimulation treatment, 30 cases) and a treatment group (Tongguan Liqiao acupuncture added to the control group treatment, 30 cases). Both groups received treatment once daily, five times a week, for four consecutive weeks. The primary efficacy indicators were the Modified Frenchay Dysarthria Assessment Scale score and speech intelligibility, while the secondary indicator was the Activity of Daily Living (ADL) score. Evaluations were conducted before treatment, at 2 weeks of treatment, at 4 weeks of treatment, and during a follow-up visit 3 months after treatment. *Results:* After treatment, both groups showed significant improvements in the Modified Frenchay score, speech intelligibility, and ADL score compared to before treatment ($P<0.05$). At 4 weeks of treatment, the Modified Frenchay score in the treatment group was (24.3 ± 2.1) points, significantly higher than that in the control group (20.5 ± 2.4) points ($P<0.01$); speech intelligibility in the treatment group was $(82.6\pm 5.3)\%$, significantly higher than that in the control group $(71.4\pm 6.1)\%$ ($P<0.01$). The total effective rate in the treatment group was 86.7%, higher than that in the control group (60.0%) ($P<0.05$). During the 3-month follow-up, the efficacy in the treatment group remained stably superior to that in the control group. No serious adverse reactions occurred in either group. *Conclusion:* Tongguan Liqiao acupuncture combined with neuromuscular electrical stimulation can significantly improve speech function and quality of life in patients with dysarthria after stroke, with superior efficacy to neuromuscular electrical stimulation alone and good safety, demonstrating good clinical application and promotion value.

Keywords: Stroke; Dysarthria; Tongguan Liqiao acupuncture; Neuromuscular electrical stimulation; Clinical study

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1. Introduction

Stroke is the leading cause of death and disability among adults in China, characterized by high incidence, high recurrence rate, and high disability rate^[1]. Dysarthria after stroke is one of the common complications, with an acute-phase incidence rate of 25% to 70%. Some patients may continue to experience it, severely affecting their speech communication abilities, leading to emotional distress, social barriers, and a reduced quality of life^[2]. Currently, there are no specific therapeutic drugs for dysarthria after stroke. Modern medicine primarily relies on physical therapies such as speech rehabilitation training, neuromuscular electrical stimulation, and hyperbaric oxygen therapy, but these methods have slow onset, long treatment courses, and high costs. Traditional medicine mainly employs methods such as acupuncture, herbal medicine, and tuina (Chinese therapeutic massage), among which acupuncture has become one of the ideal clinical choices due to its safety, effectiveness, and low cost. “Tongguan Liqiao Acupuncture” is a special acupuncture method proposed by Academician Shi Xuemin based on the “Xingnao Kaiqiao Acupuncture” method, targeting dysarthria, dysphagia, and other conditions. It follows the treatment principles of “regulating the spirit and guiding qi, nourishing the three yin, and unblocking the orifices,” emphasizing standardized acupuncture techniques and dosages, with clear acupoint selection criteria and operational norms. This study aims to evaluate the clinical efficacy of Tongguan Liqiao Acupuncture combined with neuromuscular electrical stimulation in the treatment of dysarthria after stroke through a randomized controlled trial and to explore optimized treatment plans.

2. Materials and methods

2.1. General information

Sixty patients with dysarthria after stroke who visited the outpatient and inpatient departments of the Brain Disease and Acupuncture-Moxibustion-Tuina Departments at Qinghai Provincial Hospital of Traditional Chinese Medicine from January 2025 to December 2026 were collected and randomly divided into a control group and a treatment group using a random number table method, with 30 cases in each group. There were no statistically significant differences between the two groups in terms of gender, age, disease duration, and stroke type ($P>0.05$), indicating comparability (**Table 1**).

Table 1. Comparison of basic information between the two groups [cases (%), Mean \pm SD]

Group	Number of Cases	Gender (Male/Female)	Age (years)	Disease Duration (days)	Stroke Type (Cerebral Infarction/Cerebral Hemorrhage)
Treatment Group	30	18/12	58.45 \pm 7.21	45.35 \pm 12.41	22/8
Control Group	30	17/13	59.13 \pm 6.84	46.26 \pm 11.91	21/9
χ^2/t value		0.069	0.375	0.290	0.821
P value		0.793	0.709	0.773	0.775

2.2. Diagnostic criteria

Western Medicine Diagnostic Criteria: Refer to the “Guidelines for the Prevention and Treatment of Cerebrovascular Diseases (2024 Edition)”, with cerebral hemorrhage or cerebral infarction confirmed by cranial CT or MRI^[3].

Traditional Chinese Medicine Diagnostic Criteria: Refer to “Internal Medicine of Traditional Chinese

Medicine”, diagnosed as stroke with tongue stiffness and speech difficulties ^[4].

Dysarthria Diagnostic Criteria: Refer to “Practical Neurology”, with a history of stroke, difficulty in forming spoken sounds, manifested as unclear pronunciation, abnormal pitch, etc. ^[5].

2.3. Inclusion and exclusion criteria

Inclusion Criteria: Disease duration ≤ 6 months; age between 30 and 80 years; conscious and stable vital signs; able to cooperate with treatment; signed informed consent form.

Exclusion Criteria: Recurrent stroke episodes with intervals < 6 months; dysarthria caused by other reasons; concurrent severe organ diseases, coagulopathy, severe cognitive impairment, etc.; skin infection or damage at acupuncture points.

2.4. Treatment methods

Basic Treatment: Refer to the “China Guidelines for the Prevention and Treatment of Cerebrovascular Diseases” to control blood pressure, blood sugar, etc. ^[6].

Control Group: Basic treatment + neuromuscular electrical stimulation. Use a swallowing dysfunction treatment device (Yasi YS1002 model), with electrodes placed on both sides of the midline of the neck for 20 minutes each time, once daily.

Treatment Group: Tongguan Liqiao acupuncture was added on the basis of the control group. Acupoint selection: Neiguan, Renzhong, Sanyinjiao, Fengchi, Wangu, Yifeng, Lianquan, Jinjin, Yuye, and the posterior pharyngeal wall. The operation strictly followed standardized techniques once daily.

Both groups received continuous treatment for 5 days followed by a 2-day rest, for a total of 4 weeks.

2.5. Observation indicators

Primary Efficacy Indicators: Modified Frenchay Dysarthria Assessment Scale score (including 8 dimensions such as tongue movement, lip movement, speech comprehension, breathing and laryngeal control, with a total of 28 items, each scored from 1–5 points, with higher scores indicating more severe dysarthria), speech intelligibility (using the Chinese Speech Intelligibility Test Word List to assess the patient’s pronunciation clarity, speech intelligibility = number of correctly pronounced words / total number of words in the word list $\times 100\%$).

Secondary Efficacy Indicators: Activity of Daily Living (ADL) Scale, including eating, bathing, dressing, climbing stairs, etc., with a total of 100 points, with scores positively correlated with living ability.

Safety: Record adverse events such as acupuncture syncope, bleeding, and infection.

Efficacy Evaluation Criteria: Cured: Frenchay score of 27–28 points; markedly effective: score improvement by ≥ 2 grades; effective: score improvement by 1 grade; ineffective: no significant change. Total effective rate = (cured + markedly effective + effective) / total number of cases $\times 100\%$.

2.6. Statistical methods

SPSS 26.0 software was used. Measurement data were expressed as (Mean \pm SD), with paired *t*-tests used for comparisons within groups and independent sample *t*-tests for comparisons between groups; count data were analyzed using the χ^2 test. A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of Frenchay scores before and after treatment in both groups

After treatment, the Frenchay scores in both groups significantly improved ($P < 0.05$), with more pronounced improvement in the treatment group ($P < 0.01$) (Table 2).

Table 2. Comparison of Frenchay scores before and after treatment in both groups [Mean \pm SD, points]

Group	Number of Cases	Before Treatment	After 2 Weeks of Treatment	After 4 Weeks of Treatment	Follow-up at 3 Months
Treatment Group	30	12.55 \pm 2.31	18.71 \pm 2.64	24.33 \pm 2.14	23.92 \pm 2.23
Control Group	30	12.32 \pm 2.50	16.15 \pm 2.42	20.52 \pm 2.44	19.84 \pm 2.61
χ^2/t value		0.370	3.915	6.430	6.510
P value		0.713	0.000	0.000	0.000

3.2. Comparison of speech intelligibility before and after treatment between the two groups

The speech intelligibility in the treatment group was significantly higher than that in the control group ($P < 0.01$) (Table 3).

Table 3. Comparison of speech intelligibility before and after treatment between the two groups [Mean \pm SD, points]

Group	Number of Cases	Before Treatment	After 2 Weeks of Treatment	After 4 Weeks of Treatment	3-Month Follow-up
Treatment Group	30	45.29 \pm 6.32	64.55 \pm 5.81	82.61 \pm 5.33	81.94 \pm 5.43
Control Group	30	44.84 \pm 6.15	56.36 \pm 6.20	71.40 \pm 6.15	70.25 \pm 6.04
χ^2/t value		0.279	5.279	7.545	7.883
P value		0.781	<0.001	<0.001	<0.001

3.3. Comparison of clinical efficacy between the two groups

The total effective rate in the treatment group was significantly higher than that in the control group ($P < 0.05$) (Table 4).

Table 4. Comparison of clinical efficacy between the two groups [cases (%)]

Group	Number of Cases	Recovered	Markedly Effective	Effective	Ineffective	Total Effective Rate
Treatment Group	30	6 (20.00)	12 (40.00)	8 (26.67)	4 (13.33)	86.67% (26/30)
Control Group	30	2 (6.67)	7 (23.33)	9 (30.00)	12 (40.00)	60.00% (18/30)
χ^2/t value						5.455
P value						0.020

3.4. Safety evaluation of the two groups

In the treatment group, two cases experienced minor local bleeding after acupuncture, which stopped spontaneously after compression, with an adverse event rate of 6.67% (2/30); the control group had no adverse reactions. No serious adverse events occurred in either group.

4. Discussion

Dysarthria after stroke is characterized by motor imbalances and muscle paralysis in the articulatory muscle groups caused by stroke, leading to abnormal muscle tone and resulting in speech disorders such as unclear articulation or pronunciation. Most patients also exhibit abnormalities in pitch or speaking speed and may experience symptoms such as coughing when drinking water and difficulty swallowing. There is currently no specific medication for this condition, and modern medical treatments primarily focus on physical therapy and speech rehabilitation training, which can improve the degree of dysarthria in patients. However, the overall effectiveness of these treatments is suboptimal and has certain limitations. Traditional Chinese medicine posits that the locus of dysarthria after stroke is in the brain, manifesting as abnormal function of the tongue, larynx, and pharynx, with the core pathogenesis being obstruction of the orifices by wind, fire, phlegm, and blood stasis, and the spirit failing to guide qi^[7]. The Tongguan Liqiao acupuncture method utilizes Neiguan and Renzhong to regulate the spirit and guide qi, Sanyinjiao to nourish the three yin, Fengchi, Wangu, and Yifeng to unblock the orifices, and Lianquan, Jinjin, Yuye, and the posterior pharyngeal wall for local pricking to activate meridians and benefit the throat, reflecting a “spirit-regulating, yin-nourishing, orifice-unblocking” trinity treatment approach.

This study found that Tongguan Liqiao acupuncture combined with neuromuscular electrical stimulation significantly improved Frenchay scores and speech intelligibility, with superior efficacy to electrical stimulation alone, consistent with previous research^[8]. The reasons for this may include: acupuncture improving blood supply to the vertebrobasilar arteries and promoting neural functional remodeling; local stimulation enhancing coordination of the articulatory muscle groups and improving movement of the tongue, pharynx, and larynx; and the synergistic effect of acupuncture and electrical stimulation exerting dual “central-peripheral” regulatory actions. The Tongguan Liqiao acupuncture method, innovated by Academician Shi Xuemin based on fundamental mechanisms and extensive research, is theoretically grounded in the “Xingnao Kaiqiao acupuncture method” and creates a special acupuncture therapy based on the principles of syndrome differentiation and disease differentiation. Its treatment principles are “nourishing the three yin, regulating the spirit and guiding qi, and unblocking the orifices.” While selecting acupoints along the meridians, it also chooses local acupoints and specific points, adhering to the principle of “one acupoint with multiple functions” to treat both the symptoms and the root cause. Among the acupoint selections, pricking the main acupoints for awakening the brain and unblocking the orifices, as well as acupoints in the tongue, pharynx, and neck regions, where pricking Renzhong and Neiguan regulates the spirit and guides qi; pricking Fengchi, Yifeng, and Wangu unblocks the orifices; pricking Sanyinjiao nourishes the three yin; pricking Lianquan soothes the throat and benefits the tongue; pricking Yuye and Jinjin activates meridians and benefits the tongue; and pricking the posterior pharyngeal wall benefits the throat and activates meridians^[9]. Incorporating specific techniques during treatment can improve cerebral blood circulation, restore the qi and blood circulation status of the tongue and pharynx, thereby alleviating dysarthria, expanding tongue mobility, and significantly improving speech intelligibility in patients. The Tongguan Liqiao acupuncture method adopts the acupuncture excitation technique created by Zhu Lian, using either the piercing-twisting or slow-twisting method for needle insertion, followed by short, rapid needling manipulations and superficial needling, which can induce sensations of soreness, numbness, distension, and pain in the acupuncture area, accompanied by electric shock-like sensations^[10]. Selecting acupoints in the neck region can stimulate the muscles of the pharynx and larynx, increasing their excitability and thereby enhancing the flexibility of the

articulatory muscle groups, significantly boosting nervous system excitability and restoring muscle group coordination. More importantly, acupuncture treatment techniques are mature, easy to operate, and less likely to cause adverse events in patients, who have high tolerance throughout the treatment process, ensuring both treatment effectiveness and safety, thereby achieving long-term clinical efficacy^[11]. This study further confirms the advantages of acupuncture combined with rehabilitation techniques in treating dysarthria after stroke, and the Tongguan Liqiao acupuncture method, characterized by standardized prescriptions, unified techniques, and strong reproducibility, is convenient for clinical promotion.

5. Conclusion

Tongguan Liqiao acupuncture combined with neuromuscular electrical stimulation significantly improves articulatory function and speech intelligibility in patients with dysarthria after stroke, enhancing their ability to perform activities of daily living. This treatment is superior to neuromuscular electrical stimulation alone and demonstrates good safety. With standardized operations and strong reproducibility, it can serve as one of the optimized early rehabilitation protocols for dysarthria after stroke.

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Disclosure statement

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Research Progress on the Antioxidative Stress Effects of Astragalus Active Components and DJ-1 in Multiple Sclerosis

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Abstract: Multiple sclerosis (MS) is an autoimmune disease primarily affecting the white matter of the central nervous system (CNS), characterized by pathological changes of chronic multiple inflammatory demyelination. Its clinical manifestations alternate between relapses and remissions, showing a stepwise progressive development, which can lead to oligodendrocyte death, axonal disintegration, and ultimately neuronal loss, resulting in irreversible damage to neurological functions. In the early stage of onset, inflammatory responses cause excessive accumulation of reactive oxygen species (ROS), disrupting the dynamic balance of intracellular oxidative-antioxidative systems and triggering reactions in the central nervous system. The experimental autoimmune encephalomyelitis (EAE) mouse model is a classic animal model for multiple sclerosis. In traditional Chinese medicine (TCM), MS falls into the categories of “flaccidity syndrome” and “arthralgia syndrome.” During the acute phase, the therapeutic principle focuses on eliminating pathogenic factors while supporting healthy qi; in the remission phase, the treatment emphasizes tonifying healthy qi and replenishing qi. *Astragalus membranaceus*, a commonly used and popular qi-tonifying herb in TCM clinical practice, possesses the effects of tonifying qi to consolidate healthy qi, replenishing qi and lifting yang, strengthening the defensive exterior to consolidate the superficial resistance, and promoting tissue regeneration to heal ulcers. The DJ-1 protein has antioxidative stress ability and potential crosstalk and synergistic relationships with *Astragalus membranaceus* in antioxidative stress and immune regulation. Therefore, both may become new targets for the prevention and treatment of multiple sclerosis in clinical practice. By consulting relevant literatures published from 2013 to 2025 in databases such as China National Knowledge Infrastructure (CNKI), Wanfang, VIP, and PubMed, this paper reviews the research progress of *Astragalus membranaceus* and its active components in the treatment of multiple sclerosis.

Keywords: *Astragalus membranaceus*; Multiple sclerosis (MS); DJ-1; Reactive oxygen species (ROS); Experimental autoimmune encephalomyelitis (EAE); Research progress

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1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system. Lesions can involve brain tissue, spinal cord, optic nerve, etc., with multiple inflammatory demyelination, axonal degeneration, and gliosis as the main pathological characteristics^[1]. It has a high incidence rate, recurrence rate, and disability rate, which can lead to various sequelae such as blindness, sensory disturbance, cognitive impairment, and even paralysis in patients, seriously affecting the quality of life and bringing a huge impact on patients, their families, and the entire society. Western medicine treatment of MS often uses hormones, immunosuppressants, etc., which impose a heavy economic burden and are associated with common adverse reactions. TCM treatment achieves therapeutic effects through overall regulation and coordination of yin and yang. Cluster analysis shows that *Astragalus membranaceus* is the most frequently used TCM in the treatment of multiple sclerosis^[2].

By searching databases such as CNKI, Wanfang, VIP, and PubMed for relevant literatures from 2013 to 2025 with keywords including “*Astragalus membranaceus*”, “active components”, “multiple sclerosis”, “EAE”, “autoimmune encephalomyelitis”, “DJ-1”, and “ROS”, more than 100 literatures were obtained. A total of 44 important relevant literatures were included in this paper to comprehensively discuss the related mechanisms and research progress of the active components of *Astragalus membranaceus* in the treatment of MS.

2. Pathogenesis of multiple sclerosis

The main pathological changes of MS include myelin destruction, blood-brain barrier (BBB) dysfunction, axonal injury, and neuronal loss. It is characterized by the formation of multiple demyelinating plaques in the white matter of the central nervous system, leading to neuroconductive dysfunction and neurodegeneration. Clinical classifications include relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS), among which RRMS is the most common^[3]. There are multi-dimensional interactions between the nervous system and the immune system^[4]. In diseases such as MS or when the BBB is damaged, a large number of peripheral adaptive immune cells such as T cells and B cells enter the central nervous system (CNS), leading to abnormal central immune responses and triggering inflammatory cascades. The specific cause of immune disorders remains unclear^[5].

The pathogenesis of MS is also related to the imbalance of T cells and macrophages. The progression of MS is associated with the secretion of pro-inflammatory cytokines such as IL-12, TNF- α , IL-1 β , and IFN- γ ; the improvement of symptoms is associated with the secretion of anti-inflammatory cytokines such as IL-4 and IL-10. In addition, activated CD4+T cells can mediate and amplify inflammatory responses by producing pro-inflammatory factors such as IL-12 and TNF- α , and enter the central nervous system through the blood-brain barrier, thereby causing nerve damage^[6]. B cells and other B cell subsets can affect the onset and outcome of MS through various different pathways. Its pathogenesis covers multiple aspects, including antibody production, cytokine release, formation of ectopic lymphoid tissue, and migration of B cells to the central nervous system^[7].

Among them, a typical pathological feature of MS is the appearance of oligoclonal band antibodies^[8]. Studies have shown that these oligoclonal band antibodies are not directed against CNS antibodies, and the target antigens generally include Myelin Oligodendrocyte Glycoprotein (MOG), Myelin Basic Protein (MBP), proteolipid protein, myelin-derived lipids, or other specific CNS antigens^[9]. However, the increase

in antibody titers, such as MBP and MOG, also indicates the occurrence of specific immunity. In addition to the above target antigens, many other candidate antigens remain to be studied^[10].

Activated B cells in the blood of MS patients can produce excessive pro-inflammatory cytokines. In 2017, Okada Y et al. found that B cells from MS patients produced insufficient IL-10 compared with healthy controls under CD40L stimulation.

The stable interaction between B cells and T cells is also an important factor driving MS. In addition, the degree of increased permeability of the BBB is positively correlated with the severity of the disease. In the MS animal model, experimental autoimmune encephalomyelitis (EAE), the expression of MMP-9, NADPH, ICAM-1, VCAM-1, etc., in mice is upregulated, leading to increased BBB permeability. Adhesion molecules and chemokines secreted by immune cells promote Th1/M1 macrophages to secrete pro-inflammatory factors into the central nervous system, thereby causing nerve damage.

3. Current status of multiple sclerosis treatment

At present, the global incidence of MS is increasing year by year, with significant differences in global distribution. The incidence and prevalence vary in different countries and regions. According to statistics, the global median prevalence of MS is 33 per 100,000 people, with the highest prevalence in North America and Europe, and the lowest in Asia and sub-Saharan African countries. The incidence rate in women is 2–3 times that in men. MS is characterized by multiple episodes, recurrence, and a high disability rate. With the continuous progression of the disease, it often leads to permanent disability in the end. This not only affects the quality of life of patients, brings a heavy care burden to their families, but also imposes a huge economic burden on the social medical system, including the consumption of medical resources and the increase in long-term care costs. Due to the complex etiology and pathogenesis of MS, there is still no effective cure for the disease so far. According to the 2023 guidelines, glucocorticoid therapy remains the first-line treatment for acute MS, while disease-modifying therapy (DMT) in the remission phase mainly includes immunosuppressants, immunomodulators, and antioxidants. However, due to individual differences among patients, for patients with poor response to hormone therapy, prolonged treatment does not benefit neurological recovery in the long run, but may trigger a series of serious adverse reactions. Moreover, MS is a lifelong disease. The remission phase mainly adopts DMT for immunomodulation and immunosuppressive therapy, but long-term use of immunosuppressants increases the risk of infection and cancer. Long-term use of hormone therapy is likely to lead to drug tolerance in patients, reduce their immunity, and cause relatively many side effects. In addition, due to the high price of hormone drugs, it increases the economic burden on patients, which is not conducive to the long-term treatment of patients. In this case, the combined use of traditional Chinese and Western medicine has a better curative effect, fewer side effects, and saves patients' medical costs. Multiple sclerosis belongs to the categories of “flaccidity syndrome” and “arthralgia syndrome” mentioned in *Huangdi Neijing·Suwen* (Yellow Emperor's Internal Classic·Plain Questions). In the remission phase, it advocates tonifying healthy qi and replenishing qi. *Astragalus membranaceus* has excellent effects of tonifying healthy qi and replenishing qi, enhancing patients' immunity and anti-inflammatory effects. It is used in the combined treatment of multiple sclerosis with traditional Chinese and Western medicine in clinical practice. Relevant literature shows that through the analysis of the medication rules of nationally famous TCM doctors in the treatment of MS, it is found that *Astragalus membranaceus* is included in the high-frequency drugs. When combined with other medicinal

materials into compound prescriptions, *Astragalus membranaceus* can exert a therapeutic effect on MS through mechanisms such as regulating immunity and anti-inflammation. These compound prescriptions include *Astragalus membranaceus-Cuscuta chinensis-Epimedium brevicornum*, *Astragalus membranaceus-Epimedium brevicornum-Codonopsis pilosula*, etc. The clustering of core drugs reflects the compatibility ideas of invigorating the spleen and eliminating dampness, tonifying the liver and kidney, resolving phlegm and promoting blood circulation, regulating qi and removing blood stasis, which embodies the characteristics of TCM in treating MS following “tonifying the kidney, resolving turbidity, detoxifying, and dredging collaterals.”

4. Intervention effects of active components of *Astragalus membranaceus* on multiple sclerosis

Astragalus membranaceus is one of the commonly used qi-tonifying drugs in TCM clinical practice. It is the dried root of *Astragalus mongholicus* or *Astragalus membranaceus* of the Fabaceae family. It is warm in nature, sweet in taste, and belongs to the spleen and lung meridians. It has the effects of tonifying the middle and replenishing qi, promoting qi circulation to relieve bi syndrome, consolidating the exterior to stop sweating, inducing diuresis to reduce edema, promoting fluid production to nourish blood, and promoting tissue regeneration to heal ulcers. Fan Yongping, Shang Xiaoling, and others have used compound prescriptions containing *Astragalus membranaceus* in clinical applications, which have played a certain role in improving the symptoms of MS patients. The chemical components of *Astragalus membranaceus* mainly include three categories: polysaccharides, saponins, and flavonoids, which can exert multiple effects such as inhibiting inflammation, resisting oxidation, preventing cell apoptosis, regulating immune function, and maintaining cardiovascular health.

Astragalus membranaceus is known to contain 25 amino acids, including methionine, glutamic acid, leucine, γ -aminobutyric acid, etc., more than 20 trace elements such as selenium, zinc, iron, copper, etc., as well as other chemical components such as palmitic acid, palmitic acid glyceride, linoleic acid, linolenic acid, betaine, and bitter base. However, these are not the main components of the pharmacological effects of *Astragalus membranaceus*.

The flavonoids and polysaccharides in *Astragalus membranaceus* have the effects of scavenging free radicals and inhibiting oxidative stress. These components may indirectly regulate their antioxidative functions by enhancing the stability or activity of DJ-1, but the specific molecular mechanisms still need further research. Next, the intervention effects of the three main types of pharmacologically active compounds of *Astragalus membranaceus* in multiple sclerosis will be elaborated.

4.1. Astragalus polysaccharides

Astragalus polysaccharides can participate in the treatment of multiple sclerosis through antioxidative stress and anti-inflammatory responses. In the early stage of multiple sclerosis, inflammatory responses cause excessive accumulation of reactive oxygen species (ROS), which further disrupts the dynamic balance of the intracellular oxidative-antioxidative system and ultimately triggers chronic neuronal demyelination in the central nervous system through oxidative stress-mediated neurotoxic mechanisms. Experiments by Zhang Jingfang et al. have proved that Astragalus polysaccharides can increase the activity of superoxide dismutase and total antioxidant capacity. Zhong Ling et al. found that Astragalus polysaccharides can

reduce the malondialdehyde content and increase the peroxidase activity in mice, indicating that Astragalus polysaccharides have good antioxidative effects.

4.2. Astragalus saponins

Studies on the molecular mechanism of Astragaloside IV in regulating CD4⁺T cell differentiation have shown that this active component can significantly downregulate the secretion levels of pro-inflammatory cytokines IFN- γ , TNF- α , and IL-6, as well as the mRNA expression of ROR γ t transcription factor, while significantly upregulating the gene transcription levels of T-bet and Foxp3, thereby remodeling the differentiation pattern of CD4⁺T cell subsets. It inhibits the infiltration of autoreactive T cells into the central nervous system and effectively reduces neuroinflammatory damage. In vitro experiments have shown that Astragaloside IV can regulate the differentiation of Th17 cells and Treg cells. Treg cells are important regulatory T cells in the body that can inhibit T cells. In multiple sclerosis, they reduce the attack of T cells on normal autologous cells, indicating that Astragalus saponins can play an immunomodulatory role by regulating the differentiation of T cells, thereby fundamentally addressing the causes of multiple sclerosis. Phosphorylated myosin phosphatase target subunit 1 (p-MYPT1) is a substrate of Rho-associated protein kinase (ROCK), and its expression level is positively correlated with ROCK activity. After administration of Astragaloside IV, the phosphorylation level of MYPT1 in the spinal cord of EAE mice is significantly decreased, ROCK activation is inhibited, and neurons are protected, indicating that Astragalus saponins have a certain neuroprotective effect. Studies have shown that Astragaloside IV reduces neuroinflammation in EAE mice by inhibiting blood-brain barrier leakage. The mechanism involves reducing the levels of ROS and iNOS in the central nervous system, enhancing the activities of SOD and GSH-Px; in addition, Astragaloside IV can significantly inhibit the activation of microglia in the central nervous system in the EAE model, downregulate the transcription levels of pro-inflammatory cytokines IFN- γ , TNF- α , and IL-6, coordinately regulate the differentiation of CD4⁺T cell subsets, and inhibit their pathological infiltration into the central nervous system. Astragaloside IV can alleviate the clinical symptoms of EAE mice by inhibiting the proportion of CD4⁺T cell subsets expressing interferon- γ and interleukin-17, upregulating the percentage of CD4⁺T cell subsets expressing interleukin-10 and transforming growth factor- β , downregulating the expression of interferon- γ , interleukin-17, and interleukin-6 in the spinal cord and spleen, and upregulating the expression of the anti-inflammatory factor interleukin-4 in the spleen. Its mechanism is related to regulating the immune cell subsets in the spleen, thereby inhibiting the infiltration of inflammatory cells into the central nervous system and reducing myelin loss.

4.3. Astragalus flavonoids

Astragalus flavonoids have anti-inflammatory, antioxidative, immunomodulatory, and skeletal system protective effects. A large number of experiments have proved that Astragalus flavonoids have good anti-inflammatory effects. For example, Gu Minhua et al. found that formononetin can significantly inhibit the abnormal expression of inducible nitric oxide synthase, interleukin-6, and tumor necrosis factor- α , effectively reduce the inflammatory damage of the blood-brain barrier, and inhibit the transcription of MMPs. Xu Feng et al. found that calycosin-7-glucoside can significantly inhibit the proliferation of T lymphocytes and reduce macrophage toxicity, confirming that calycosin-7-glucoside has anti-inflammatory and immunosuppressive effects and can be used to prepare anti-inflammatory drugs and immunosuppressants. It is proven that Astragalus flavonoids have good anti-inflammatory effects. Based on antioxidative stress, Hu Zhiping et

al. found that formononetin can activate the Nrf2/HO-1 pathway, thereby reducing the water content and malondialdehyde level of brain tissue and increasing the superoxide dismutase level in a mouse model of traumatic brain injury, indicating that *Astragalus* flavonoids have a certain antioxidative effect. Yu Yifan et al. proved that total flavonoids of *Astragalus membranaceus* can promote the secretion of cytokines IL-6, IL-1 β , IFN- γ , TNF- α , and cellular mediators NO and PGE2 in the supernatant of macrophage RAW264.7, and upregulate the expression of iNOS and COX-2 proteins, indicating that it has an immunomodulatory effect.

In summary, the three main types of pharmacologically active compounds of *Astragalus membranaceus* all have immunomodulatory and antioxidative stress effects, thereby achieving the prevention and treatment of multiple sclerosis. This includes symptomatic treatment of multiple sclerosis by inhibiting overactive T cells and reducing neuronal demyelination caused by oxidative stress. At the same time, *Astragalus membranaceus* also has anti-inflammatory effects, which can reduce inflammatory responses, thereby reducing damage to neurons, and has a certain protective and preventive effect on osteoporosis, which can reduce bone damage during hormone therapy, reduce the side effects of patients' medication, and improve the quality of life of patients.

5. Antioxidative stress mechanism of DJ-1

DJ-1 is a multifunctional protein widely distributed in organisms. It participates in many cellular life activities such as cell growth, antioxidative stress responses, and gene transcription. However, it has attracted increasing attention in enhancing cellular antioxidative stress, so it is also known as an antioxidative stress protein. Studies have found that DJ-1 may activate the Nrf2-ARE signaling pathway to resist myocardial cell oxidative stress injury induced by hypoxia/reoxygenation (H/R) in H9c2 cardiomyocytes.

DJ-1 can scavenge intracellular reactive oxygen species (ROS) through autoxidation; regulate the morphology and function of intracellular mitochondria to reduce intracellular ROS production; DJ-1 can also activate various molecular signaling pathways in cells, enhance the expression of cellular antioxidant enzymes, promote ROS scavenging, thereby restoring the cellular redox balance, and ultimately enhancing cellular antioxidation, promoting proliferation, and inhibiting cell apoptosis.

Studies have shown that during osteonecrosis of the femoral head (ONFH), through oxidative stress pre-experiments on bone marrow mesenchymal stem cells, it is found that DJ-1 protein exhibits significant antioxidative stress ability: DJ-1 exerts its effects through regulating the Keap1-Nrf2-ARE signaling pathway, phosphatidylinositol-3-kinase/protein kinase B (PI3K/Akt) signaling pathway, ERK1/2 signaling pathway, and mitochondrial antioxidative stress.

5.1. Antioxidative stress mechanism by regulating the Keap1-Nrf2-ARE signaling pathway

Under the induction of cellular reactive oxygen species, DJ-1, as a new antioxidative stress gene, can bind to the Keap1/Nrf2 complex and promote its dissociation. DJ-1 can bind to the inhibitory protein Keap1 to inhibit its interaction with Nrf2, thereby stabilizing the expression of Nrf2. Activated Nrf2 enters the nucleus and binds to Maf proteins to form dimers that recognize the corresponding ARE sequences, thereby initiating the transcription of antioxidant genes and promoting the expression of antioxidant proteins (**Figure 1**). At the same time, when DJ-1 is deficient, the stability of Nrf2 decreases, preventing the activation of the Nrf2/ARE signaling pathway and the expression of downstream antioxidant genes, leading to a significant increase in ROS levels and accumulation of ROS.

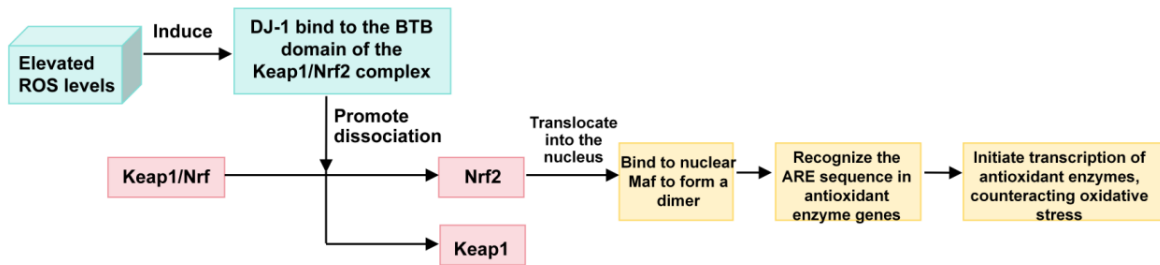


Figure 1. Mechanism of DJ-1 exerting antioxidative stress by regulating the Keap1-Nrf2-ARE signaling pathway. ROS: Reactive Oxygen Species; DJ-1: Parkinsonism Associated Degrees 7; Keap1: Kelch-Like ECH-Associated Protein 1; BTB: Bric-a-brac/Tramtrack/Broad complex; Maf: Small Maf Proteins; ARE: Antioxidant Response Element.

5.2. Antioxidative stress mechanism by regulating the PI3K/Akt signaling pathway

Overexpression of DJ-1 can significantly upregulate Thr308 in the PI3K/Akt signaling pathway to promote Akt phosphorylation. Phosphorylation modification at the Thr308 site is a key regulatory node for the activation of the Akt signaling pathway. The Thr308 site can mediate the phosphorylation activation of Akt through specific binding to phosphoinositide-dependent protein kinase 1 (PDK1). The Thr308 site of the Akt protein can bind to phosphoinositide-dependent protein kinase 1 to activate Akt, thereby promoting the phosphorylation of downstream target proteins to inhibit cell apoptosis and play a role in protecting nerve cells (Figure 2).

In addition, DJ-1 activates the PI3K/Akt pathway, thereby phosphorylating Nrf2 and promoting its nuclear translocation, further enhancing the antioxidant defense. Studies have shown that overexpression of DJ-1 can reduce the production of ROS through this pathway.

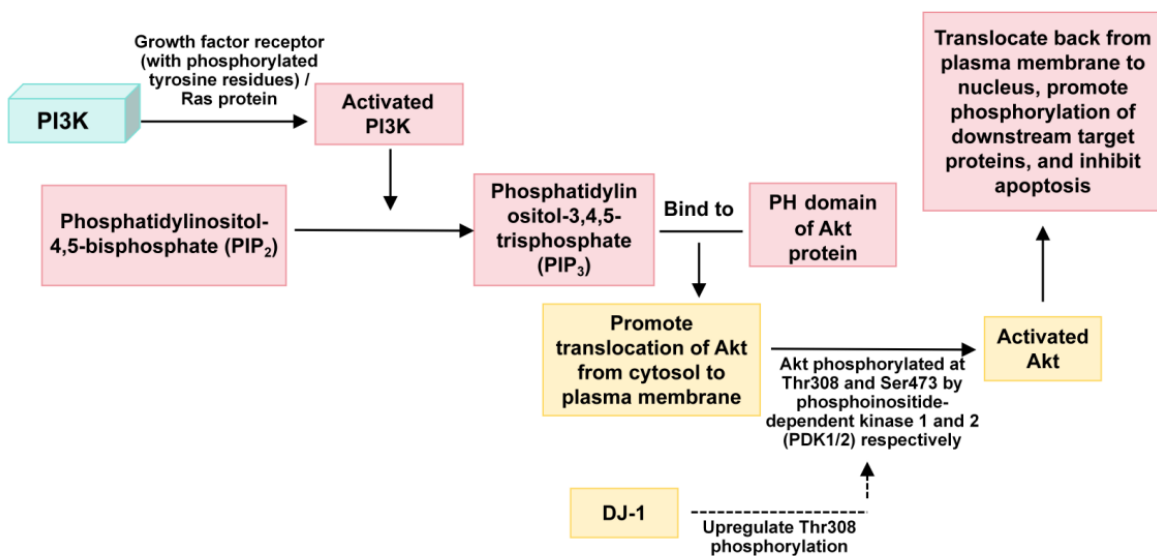


Figure 2. Antioxidative stress mechanism by regulating the PI3K/Akt signaling pathway. PI3K: Phosphatidylinositol-3-Kinase; Ras: Rat Sarcoma GTPase; Akt: Protein Kinase B; DJ-1: Parkinsonism Associated Degrees 7.

5.3. Antioxidative stress mechanism by regulating the extracellular signal-regulated kinase 1/2 (ERK1/2) signaling pathway

This protein can effectively mediate the nuclear translocation of ERK1/2 through direct interaction with ERK1/2. ERK1/2 entering the nucleus further activates members of the ETS oncogene transcription factor family and ultimately enhances ERK1/2 activity through regulating the gene transcription level of manganese superoxide dismutase (MnSOD) or binding to the C-Raf gene to promote the phosphorylation of C-Raf at Ser-338, thereby activating the MEK1 and ERK1/2 molecular signaling pathways. It can also bind to P53 under oxidative stress regulation to inhibit its transcriptional activity and reduce the inhibitory effect of P53 on ERK1/2 activity in the nucleus. Through the above direct or indirect ways, it enhances ERK1/2 activity, promotes the expression of downstream targets, and thus plays an antioxidative role (Figure 3).

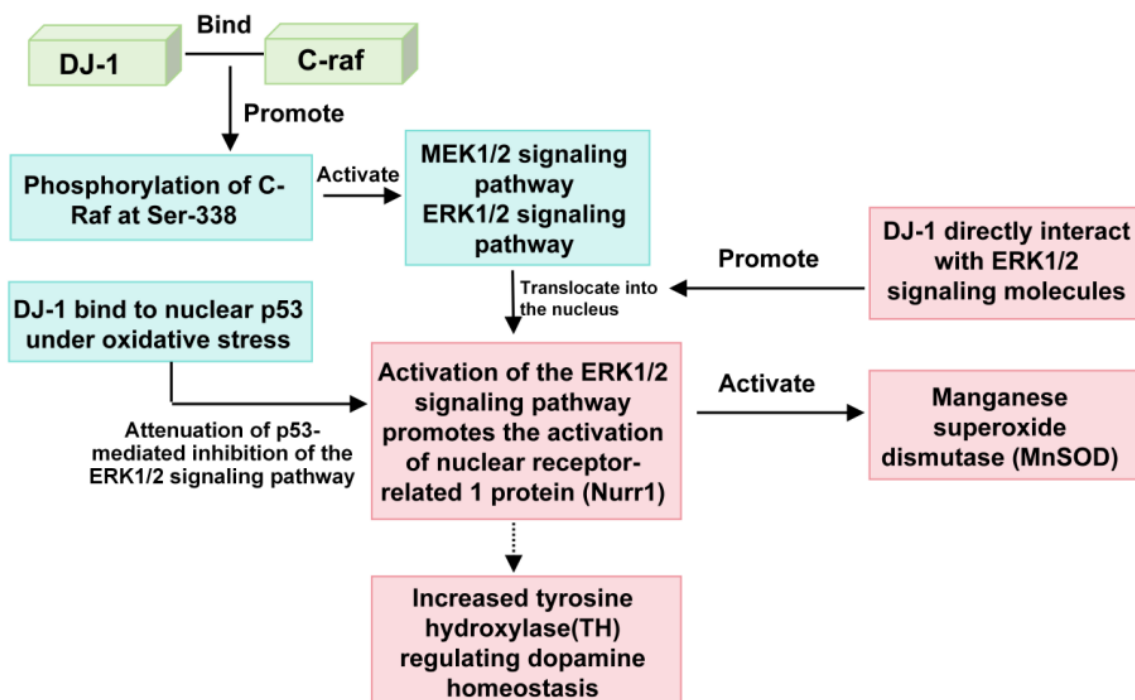


Figure 3. Mechanism of DJ-1 regulating the extracellular signal-regulated kinase 1/2 (ERK1/2) signaling pathway for antioxidative stress. DJ-1: Parkinsonism Associated Degrees 7; C-raf: v-Raf-1 Murine Leukemia Virus Oncogene Homolog 1 Gene; MEK1/2: Mitogen-Activated Protein Kinase Kinase 1/2; ERK1/2: Extracellular Signal-Regulated Kinase 1/2; P53: Tumor Protein 53.

5.4. Mechanism of DJ-1 regulating mitochondrial antioxidative stress

Studies have shown that when cells are stimulated by external factors, this protein can directly bind to Complex I by targeting the inner mitochondrial membrane and participate in regulating its enzyme activity. The protective effect of DJ-1 on Complex I can significantly improve mitochondrial function. Under oxidative stress conditions, the decrease in mitochondrial membrane potential and changes in membrane permeability may serve as key inducers for the mitochondrial translocation and localization of DJ-1 in the inner membrane system. DJ-1 also participates in mitochondrial regulation, which can phosphorylate mitochondrial dynamin-related protein 1 and avoid mitochondrial autophagic degradation.

6. Conclusion and prospect

Multiple sclerosis is a common, non-traumatic, disabling disease that can present various neurological symptoms, seriously affecting the quality of life of patients. Due to the incomplete clarification of its etiology and pathogenesis, the current clinical treatment methods are still relatively limited. Over the past two decades, with the progress of immunotherapy technology, Western medicine mainly inhibits inflammatory responses in clinical practice, while TCM commonly uses methods such as tonifying the middle and replenishing qi and inhibiting oxidative stress to reduce disease recurrence. As a traditional Chinese medicine, *Astragalus membranaceus* has gradually attracted attention in the prevention and treatment of MS. The authors believe that *Astragalus membranaceus* has broad application prospects in the treatment of multiple sclerosis. At the same time, the DJ-1 protein also has antioxidative stress effects. Whether there are potential cross and synergistic relationships between DJ-1 and *Astragalus membranaceus* in antioxidative stress and immune regulation, such as whether *Astragalus membranaceus* and DJ-1 can be combined to jointly intervene in the recurrence of multiple sclerosis? This can be used as a research direction for the authors to further study its mechanism of action, explore combined applications, develop innovative drugs, and carry out large-scale clinical trials, which is expected to provide safer and more effective treatment and recurrence prevention methods for patients with multiple sclerosis.

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Disclosure statement

The authors declare no conflict of interest.

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Subthalamic Nucleus Subdivision-Targeted DBS for Brainstem Neural Remodeling and Long-Term Rehabilitation Follow-up in Parkinson's Disease with Refractory Dysphagia

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Abstract: *Objective:* To investigate the differential efficacy of deep brain stimulation (DBS) targeting distinct subthalamic nucleus (STN) subdivisions on Parkinson's disease (PD) patients with refractory dysphagia, and to elucidate the potential remodeling mechanisms of brainstem swallowing-related nuclei. *Methods:* Seventy-six PD patients with dysphagia admitted between March 2020 and March 2023 were enrolled and randomly assigned to the sensorimotor subdivision group ($n=38$) or the limbic-associative subdivision group ($n=38$). Swallowing function was assessed preoperatively and at 12 and 24 months postoperatively using videofluoroscopic swallowing study (VFSS), high-resolution manometry, and the Penetration-Aspiration Scale (PAS). Tongue pressure and superior laryngeal nerve evoked potentials were also recorded. *Results:* At 24 months postoperatively, the PAS score in the sensorimotor group decreased from 5.89 ± 1.12 preoperatively to 2.34 ± 0.78 ($P<0.01$), which was significantly better than that in the limbic-associative group (4.12 ± 0.95). VFSS revealed a 42.3% increase in laryngeal elevation amplitude and a 38.6% reduction in pharyngeal transit time following sensorimotor subdivision stimulation. Evoked potentials showed a 29.4% shortening of latency in the nucleus tractus solitarius, indicating enhanced excitability of brainstem swallowing inter neurons. *Conclusion:* Precise targeting of the STN sensorimotor subdivision via DBS achieves long-term swallowing function remodeling by upregulating brainstem swallowing center excitability, offering a novel surgical strategy for PD-related dysphagia.

Keywords: Parkinson's disease; Dysphagia; Subthalamic nucleus; Subdivision; Deep brain stimulation; Brainstem remodeling

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1. Introduction

Parkinson's disease is the second most common neurodegenerative disorder worldwide, with its incidence continuously rising due to population aging. It is estimated that by 2030, the number of PD patients in China will exceed five million. Dysphagia, one of the most frequent axial symptoms in PD, occurs in 30%–50% of patients in the early stages and up to 80%–95% in advanced stages. Dysphagia not only leads to severe complications such as malnutrition, dehydration, and aspiration pneumonia but also represents a major independent risk factor for mortality in PD patients ^[1].

STN deep-brain stimulation (STN-DBS) is the gold standard surgery for motor impairment for mid-advanced PD patients. Nevertheless, the influence of STN-DBS on swallowing function still remains controversial. In recent years, STN functional subdivisions have been receiving increasing attention. From an anatomical perspective, there are three functional divisions within the STN: the sensorimotor (ventrolateral), limbic-associative (dorsomedial), and cognitive subdivisions ^[2]. Studies indicate that the sensorimotor subdivision maintains strong axon connections with the thalamo-cortical motor loop and brainstem descending systems. Nevertheless, research directly addressing the differential regulation effect of STN-DBS targeting different STN divisions on swallowing-related brain stem nuclei (nucleus tractus solitarius, nucleus ambiguus, reticular formation, etc.) is rare ^[3–4].

In this study, the author creatively put forward the “targeted modulation” hypothesis, which suggests that specific targeting of the sensorimotor subdivision can increase brainstem swallowing nuclei neuron excitability by regulating the descending system, thereby remodeling the “deparkinsonian” swallowing pattern through modulating the cortico-basal ganglia-brainstem connection. For testing this hypothesis, we conducted a novel prospective randomized controlled study with the integration of neurophysiology and neuroimaging approaches to assess brainstem swallowing nuclei plasticity change following DBS surgery, followed by a 2-year rehabilitation intervention.

2. Materials and methods

2.1. Study participants

PD patients who underwent STN-DBS surgery in the Neurosurgery Department of our hospital between March 2020 and March 2023 were enrolled. Inclusion criteria: (1) Meeting the Chinese diagnostic criteria for PD (2016 version); (2) Hoehn-Yahr stage 2.5–4; (3) Presence of definite dysphagia with a Penetration-Aspiration Scale (PAS) score ≥ 3 ; (4) Refractory to optimized medical therapy (levodopa equivalent dose ≥ 600 mg/day); (5) Signed informed consent ^[5].

Exclusion criteria: (1) Severe cognitive impairment (MoCA < 18); (2) Other neurodegenerative diseases; (3) History of stroke or traumatic brain injury; (4) Contraindications for VFSS (e.g., pregnancy, severe cardiopulmonary insufficiency); (5) Inability to complete the 24-month follow-up ^[6].

A total of 76 patients were enrolled and randomly assigned using a random number table to two groups: the sensorimotor subdivision group ($n=38$) and the limbic-associative subdivision group ($n=38$). No statistically significant differences were observed in baseline characteristics (age, sex, disease duration, H-Y stage, levodopa equivalent dose, preoperative PAS score) between the two groups ($P>0.05$).

2.2. DBS surgery and targeting

One day before surgery, 1.5T or 3.0T MRI scanning was performed to acquire 3D-T1, T2, and SWI

sequences. The Leksell stereotactic frame (Elekta, Sweden) and the StealthStation S7 surgical planning system (Medtronic, USA) were used for STN target coordinate calculation ^[7]. Reference coordinates for the STN sensorimotor subdivision: 3–4 mm below the AC-PC plane, 11–13 mm lateral, and 2–3 mm posterior to the midpoint of the anteroposterior plane. Reference coordinates for the limbic-associative subdivision: 2–3 mm below the AC-PC plane, 9–11 mm lateral, and 1–2 mm posterior to the midpoint of the anteroposterior plane. Intraoperative microelectrode recording (MicroGuide Pro, Alpha Omega, Israel) was used to verify electrode placement. Typical discharge patterns (sensorimotor subdivision: limb movement-related discharge; limbic-associative subdivision: limbic system-related discharge) confirmed target accuracy. The 3389 quadripolar electrode (Medtronic, USA) was implanted.

2.3. Stimulation parameters

The device was activated four weeks postoperatively using continuous constant-frequency stimulation (130 Hz, pulse width 60 μ s). The initial voltage was 1.5 V for the sensorimotor group and 2.0 V for the limbic-associative group. Parameters were individualized based on motor symptom improvement and adverse effects. Stable stimulation parameters were maintained within six months post-surgery (mean voltage between groups: 2.3 ± 0.4 V vs. 2.5 ± 0.5 V, $P > 0.05$). All patients continued their preoperative doses of anti-Parkinsonian medication, which were not adjusted during the follow-up period.

2.4. Swallowing function assessment

Assessments were conducted preoperatively and at 12 and 24 months postoperatively:

- (1) Videofluoroscopic Swallowing Study (VFSS): Performed using a GE Precision MD/RT X-ray system. Patients swallowed contrast media of various viscosities (thin liquid, thick liquid, paste, solid) in anteroposterior and lateral views. Oral transit time, laryngeal elevation amplitude, pharyngeal transit time, and cricopharyngeal opening duration were recorded. Two trained rehabilitation physicians independently scored the results, and the average was taken ^[8].
- (2) Penetration-Aspiration Scale (PAS): An 8-point scale (1 = no penetration, 8 = silent aspiration), with a score ≥ 3 considered abnormal.
- (3) Tongue Pressure Measurement: Maximum isometric tongue pressure (MIP) and tongue-palate swallowing pressure (LSPs) were measured using the Iowa Oral Performance Instrument (IOPI Medical, USA). Each measure was repeated three times, and the average was taken ^[9].
- (4) Superior Laryngeal Nerve Evoked Potentials: Transcutaneous stimulation of the cervical branch (cathode placed lateral to the thyrohyoid membrane) was performed. Evoked potential latency and amplitude were recorded using electromyographic electrodes placed on the cricothyroid muscle ^[10].

2.5. Statistical analysis

SPSS 26.0 was used for statistical analysis. Continuous data were expressed as mean \pm standard deviation. Intergroup comparisons were performed using an independent samples *t*-test or a Mann-Whitney U test. Intragroup pre-post comparisons used a paired *t*-test. Repeated measures data were analyzed using generalized estimating equations (GEE). Categorical data were analyzed using the χ^2 test. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of clinical efficacy between groups

All 76 patients completed the 24-month follow-up with no dropouts. At 24 months postoperatively, the PAS score in the sensorimotor group decreased from 5.89 ± 1.12 preoperatively to 2.34 ± 0.78 ($P < 0.01$), while in the limbic-associative group it decreased from 5.76 ± 1.08 to 4.12 ± 0.95 ($P < 0.05$). Intergroup comparison showed that the improvement in the sensorimotor group was significantly superior to that in the limbic-associative group (difference: 1.78 points, 95% CI: 1.21–2.35, $P < 0.01$).

Regarding swallowing safety indicators, the incidence of aspiration events ($PAS \geq 6$) in the sensorimotor group decreased from 47.4% (18/38) preoperatively to 5.3% (2/38) postoperatively ($P < 0.01$); in the limbic-associative group, it decreased from 44.7% (17/38) to 21.1% (8/38) ($P = 0.07$). The annual incidence of pneumonia decreased from 0.32 episodes/person-year preoperatively to 0.08 episodes/person-year postoperatively in the sensorimotor group ($P < 0.05$); in the limbic-associative group, it decreased from 0.29 to 0.21 episodes/person-year ($P = 0.31$).

3.2. Changes in kinematic parameters

Quantitative VFSS analysis (Table 1) showed that in the sensorimotor group, the postoperative laryngeal elevation amplitude increased by 42.3% compared to preoperative values ($10.2 \pm 2.1\text{mm} \rightarrow 14.5 \pm 2.8\text{mm}$, $P < 0.01$), and the pharyngeal transit time shortened by 38.6% ($1.32 \pm 0.25\text{s} \rightarrow 0.81 \pm 0.18\text{s}$, $P < 0.01$). The limbic-associative group showed improvements of 12.7% and 8.9% in these two indicators, respectively, with significant intergroup differences ($P < 0.01$). Oral transit time and cricopharyngeal opening duration did not change significantly in either group ($P > 0.05$).

Tongue pressure measurement: In the sensorimotor group, postoperative MIP increased from 35.2 ± 8.4 kPa to 52.6 ± 10.3 kPa ($P < 0.01$), and LSPs increased from 28.6 ± 7.2 kPa to 44.1 ± 9.5 kPa ($P < 0.01$). No statistically significant changes in these two indicators were observed in the limbic-associative group ($P > 0.05$).

Table 1. Comparison of VFSS kinematic parameters between groups (Mean \pm SD)

Parameter	Sensorimotor Group (n=38)	Limbic-Associative Group (n=38)
Laryngeal Elevation Amplitude (mm)		
Preoperative	10.2 \pm 2.1	10.5 \pm 2.3
Postoperative 24m	14.5 \pm 2.8*#	11.8 \pm 2.5
Pharyngeal Transit Time (s)		
Preoperative	1.32 \pm 0.25	1.28 \pm 0.22
Postoperative 24m	0.81 \pm 0.18*#	1.16 \pm 0.24
Oral Transit Time (s)		
Preoperative	0.78 \pm 0.15	0.75 \pm 0.14
Postoperative 24m	0.72 \pm 0.13	0.73 \pm 0.15

Note: * $P < 0.01$ compared to preoperative value within the same group; # $P < 0.01$ compared to the limbic-associative group at the same time point

3.3. Electrophysiological remodeling of brainstem nuclei

The evoked potential latency was reduced by 29.4% ($3.74 \pm 0.52\text{ms} \rightarrow 2.64 \pm 0.38\text{ms}$, $P < 0.01$), while the amplitude was increased by 86.7% ($0.98 \pm 0.21\text{mV} \rightarrow 1.83 \pm 0.35\text{mV}$, $P < 0.01$) in the sensorimotor group after

24 months postoperatively in comparison with preoperative data. No statistically significant changes in latency and amplitude were found in the limbic-associative group ($P>0.05$).

This indicates that the application of high-frequency stimulation in the sensorimotor subdivision of the STN markedly increased the excitability of neurons in the brainstem swallowing centers, such as the nucleus tractus solitarius and nucleus ambiguus, indicated by increased efficiency of synaptic transmission (short latency) and increased number of recruited neurons (longer amplitude). In particular, a negative correlation was found between the reduction in latency and improvement of PAS score ($r=-0.72$, $P<0.01$), indicating that the remodeled excitability of the brainstem is the electrophysiological basis of improved swallowing ability.

3.4. Long-term follow-up and safety

During the 24-month follow-up period, there were no serious adverse events such as electrode migration or intracranial infection in the sensorimotor group. In the limbic-associative group, one patient developed stimulation-related worsening of sialorrhea (PAS increased from 4 to 6 at 6 months postoperatively), which improved after parameter adjustment. No DBS-related deaths occurred in either group.

4. Discussion

4.1. Differential modulation of swallowing by STN subdivision DBS

It is evident that DBS to the motor-sensorimotor STN subdivision could enhance the safety and efficacy of swallowing in PD patients with treatment-resistant dysphagia; however, there were no significant changes when targeting the limbic-associative STN subdivision. The current study provides, for the first time, in a randomized design, strong evidence that different functional subdivisions within STN regulate swallowing differently. It therefore explains the previously described heterogeneity of STN-DBS effects on swallowing.

The effect size (improvement of 3.55 points in PAS) identified in the current study was much larger than that found in previous reports on the effects of conventional STN-DBS (improvement of 0.5–2.0 points). Such a large effect size is mainly due to the high targeting precision in the current study. Traditional DBS always selects the whole STN area as the target. During the process, the electrode will inevitably pass through several STN functional subdivisions, which will produce a dissociation phenomenon where “motor improvement” occurs while “swallowing worsening.” In the current study, functional imaging localization prior to surgery and intraoperative microelectrode recording led to millimeter-level accuracy targeting.

4.2. Neural remodeling mechanism of brainstem swallowing centers

A new aspect in this study is the first experimental demonstration in PD patients of the remote regulatory influence of DBS on swallowing nuclei of the brainstem. The latency reduction by 29.4% and amplitude increase by 86.7% of SLN EPs indicate a marked increase in the efficiency of synaptic transmission in the nuclei tractus solitarius and ambiguous.

Animal experiments have shown that the nucleus tractus solitarius is the central component of the “central pattern generator” of the swallowing reflex, and its excitability is critical for determining the initiation threshold and temporal synchronization of the swallowing reflex. Specific modifications in EP responses due to stimulation of the sensorimotor part of the STN suggest the reduction of inhibitory influences of the basal ganglia on brainstem swallowing centers via the pallidothalamic pathway, thus releasing their “hyperinhibition” typical for Parkinson’s disease. This “disinhibition” paradigm is similar to the classic

explanation of therapeutic effects of STN-DBS on limbic motor disorders; however, this study expands the scope of action of this mechanism to autonomic brainstem functions, which can be viewed as a theoretical breakthrough.

Interestingly, the marked improvement in tongue pressure (49.5% increase in MIP) indicates that there is a positive impact on the oral phase of swallowing, which might be through the increased excitability of the hypoglossal nucleus (CN XII). The hypoglossal nucleus is known to have rich innervation from the reticular formation. This implies that the stimulation of the subthalamic region can help improve tongue motor activity through increased excitability of the parvocellular reticular nucleus.

5. Conclusion

Precise deep-brain stimulation targeting the sensorimotor subdivision of the subthalamic nucleus achieves structural and functional remodeling of swallowing function in Parkinson's disease patients with refractory dysphagia by upregulating the synaptic excitability of brainstem swallowing centers, including the nucleus tractus solitarius and nucleus ambiguus. The 24-month postoperative follow-up demonstrates significantly improved swallowing safety, reduced risk of aspiration pneumonia, and an effect size markedly superior to conventional non-selective STN stimulation. This study provides a novel theoretical basis and clinical strategy for the neuromodulatory treatment of PD-related dysphagia.

Disclosure statement

The author declares no conflict of interest.

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Alzheimer's Disease: The Pathogenic Mechanism of β -amyloid Protein Deposition and Plaque Formation

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Abstract: Alzheimer's disease (AD) is a common chronic neurodegenerative disorder with a complex pathogenesis. The progression of AD is closely related to the dysregulation of gene expressions such as β -amyloid precursor protein, presenilin 1, and presenilin 2. The core pathogenic mechanisms mainly involve two key pathways: abnormal deposition of β -amyloid protein ($A\beta$) in the brain, forming senile plaques, and excessive phosphorylation of Tau protein, inducing neurofibrillary tangles. Together, these two factors lead to neuronal damage and necrosis, as well as atrophy of brain tissue structure, ultimately resulting in cognitive decline in patients. This article focuses on the core dimension of β -amyloid deposition and plaque formation in the core pathogenic mechanism of AD and systematically elaborates on it, while also considering the pathogenic role of abnormal Tau protein. Firstly, $A\beta$ is a peptide fragment composed of 39 to 43 amino acid residues produced by the hydrolysis of amyloid precursor protein by β -secretase, which is the main component of senile plaques in AD. $A\beta_{42}$ is prone to form neuronal plaques, while $A\beta_{40}$ tends to deposit in the cerebral vessels. Abnormal accumulation can cause significant neurotoxicity. Secondly, the pathogenic mechanism is analyzed. Due to the imbalance between $A\beta$ production and its clearance, it accumulates abnormally in brain regions related to memory and cognition, such as the cerebral cortex and hippocampus, forming plaques. This disrupts neuronal signal transmission, damages synaptic functions, and triggers inflammatory responses, accelerating nerve damage. Moreover, insufficient sleep reduces the efficiency of $A\beta$ clearance and increases the risk of deposition. Additionally, treatment directions such as inhibiting ubiquitin-binding enzyme UBE2N and applying $A\beta$ -targeted clearance drugs, as well as the application value of serum $A\beta$ as an early peripheral biomarker, are discussed. The principles, classifications, and application scenarios of two core detection techniques, namely enzyme-linked immunosorbent assay and APOE genotyping, are elaborated. At the same time, the pathogenic mechanism of Tau protein over-phosphorylation, losing normal function, aggregating to form neurofibrillary tangles, and subsequently destroying the neuronal transport system, leading to cell death, is also explained. This provides theoretical support and practical references for the early risk assessment of AD, deepening exploration of its pathological mechanism, and the development of targeted treatment plans.

1. Introduction

Alzheimer's disease (AD) is a chronic neurodegenerative disorder. Its onset may be related to dysregulation of genes such as β -amyloid precursor protein (β -APP), presenilin 1 (PSEN1), and presenilin 2 (PSEN2). The core mechanism of this disease involves abnormal deposition of β -amyloid protein in the brain, forming plaques, excessive phosphorylation of Tau protein leading to neurofibrillary tangles, and ultimately causing neuronal death and brain atrophy. In summary, the basic approach to treating AD is to activate certain purine receptors to improve AD cognitive impairment by protecting neurons, clearing A β plaques, and participating in inflammatory responses; inhibiting certain purine receptors can reverse AD memory deficits by reducing neuronal synaptic plasticity damage, A β deposition, accelerating amyloid precursor protein hydrolysis, and participating in inflammatory responses^[1]. This article mainly discusses the pathogenic mechanism of Alzheimer's disease caused by the deposition of β -amyloid protein and the formation of plaques. The deposition of β -amyloid protein is a key step and early change in the onset of Alzheimer's disease. Active and passive immunization to remove A β is an important strategy for preventing and treating AD^[2]. Multiple genetic studies, biochemical data, and animal models have shown that the aggregation of β -amyloid protein (A β) forms oligomers, protofilaments (PFs), and mature fibers. Due to the instability, structural heterogeneity of the fibers, and the misfolding and aggregation of A β , various structures and morphologically diverse aggregates are formed. These aggregates are associated with neurodegenerative diseases^[3].

2. Deposition and plaque formation of β -amyloid protein

2.1. Basic introduction of the protein

β -amyloid protein (A β) is a peptide fragment produced by the hydrolysis of the amyloid precursor protein (APP). It consists of 39 to 43 amino acid residues and is the main component of senile plaques in patients with Alzheimer's disease. The β -secretase plays a crucial role in the formation of A β , and its level or activity directly affects the synthesis of A β . Abnormal deposition of A β leads to neuronal damage and cognitive decline. When it accumulates both within and outside neurons, it causes toxic effects. Specifically, A β 42 is more likely to form neuronal plaques, while A β 40 tends to deposit in cerebral blood vessels. Exploring the pathogenic mechanism of β -amyloid protein deposition and plaque formation is to clarify the molecular mechanism of the core pathological process of Alzheimer's disease, fill the key gap in the research on the pathogenesis of AD, and provide a scientific basis for the development of early screening and targeted treatment. At the same time, clarifying the pathogenic pathway of β -amyloid protein deposition can not only improve the pathological theoretical system of Alzheimer's disease, but also provide core experimental and theoretical support for developing A β -targeted clearance drugs and formulating sleep intervention and other prevention strategies.

2.2. Pathogenesis

β -amyloid protein (A β) is formed through the cleavage of amyloid precursor protein (APP) and is cleared

through metabolic pathways. In patients with Alzheimer's disease (AD), the imbalance between A β production and clearance leads to its abnormal accumulation in regions of the brain related to memory and cognition (such as the cerebral cortex and hippocampus), forming "senile plaques." These plaques disrupt the signal transmission between neurons, damage synaptic function, trigger inflammation, and further accelerate neuronal damage. Lack of sleep reduces the efficiency of clearing A β and increases the risk of its deposition in the brain.

2.3. Treatment principles

Inhibiting the ubiquitin-binding enzyme UBE2N can reduce A β accumulation and improve the pathological features of Alzheimer's disease. The level of UBE2N in the hippocampus of Alzheimer's disease patients is significantly elevated (If using lenvatinib monoclonal antibody)^[4]. The progression of the disease can be slowed down by specifically removing the plaques in the brain. For instance, there are cases where the use of Denamarin has shown that after 6 Denamarin treatments, the load of A β protein in the brain decreased to 7.02 CL, reaching the withdrawal criteria. Denamarin can achieve deep A β clearance in real-world conditions and maintain good safety^[5].

The concentration of A β in the serum of healthy individuals varies by age group: the serum A β concentration in the elderly is significantly higher, while in patients with pre-dementia Alzheimer's disease, the serum A β is significantly lower, showing a strong negative correlation with the brain A β load and the severity of overall cognitive impairment. Moreover, the circadian rhythm fluctuation of serum A β is extremely small, making it a non-daily rhythm-dependent early peripheral biomarker and a practical tool for early detection of Alzheimer's disease^[6].

2.4. Detection methods

There are mainly two methods for detecting the markers related to A β : enzyme-linked immunosorbent assay (ELISA) and APOE genotyping.

2.4.1. Enzyme-linked immunosorbent assay (ELISA)

ELISA immunoassay technology relies on the specific binding of antigens and antibodies, and is mainly used for detecting biomolecules (such as proteins, hormones, and antibodies) in biological fluids. Its core principle is to fix the antigen or antibody on a solid-phase support (such as a microplate), while maintaining its immunological activity. The antibody/antigen is labeled with an enzyme (such as peroxidase), and then a substrate (such as TMB) is used to induce a color reaction. The detectable color change (or optical density) produced by the enzymatic catalytic reaction of the substrate allows for quantitative or qualitative analysis of the target substance.

ELISA is mainly divided into four types: The direct method involves allowing the enzyme-labeled primary antibody to directly bind to the antigen, which is simple but has lower sensitivity. For example, ELISA versus PCR for the diagnosis of chronic Chagas disease: systematic review and meta-analysis^[7]. The indirect method involves first allowing the primary antibody to bind to the solid-phase carrier, and then amplifying the signal through the enzyme-labeled secondary antibody. This method is suitable for antibody detection. For example, the preliminary establishment of the prokaryotic expression method of the A4L protein of bovine nodular dermatitis virus and the indirect ELISA antibody detection method^[8]. This experiment successfully expressed and obtained high-purity recombinant A4L protein using *Escherichia coli*; the rabbit-derived A4L protein

polyclonal antibody prepared can specifically bind to the eukaryotic-expressed A4L protein, and an LSDV ELISA antibody detection method based on the A4L protein was established. The sandwich method involves using double antibodies to capture the antigen, which has strong specificity and is often used for hormone or tumor marker detection. For example, the double antigen sandwich ELISA antibody detection method for swine fever virus ^[9]. This experiment utilized the BioEdit software to compare the complete sequences of the E2 proteins of swine fever virus and bovine viral diarrhea virus, screened the specific sequences of the E2 protein of swine fever virus, constructed the pCDNA3.1-2×rE2-His recombinant expression vector, and established a double-antigen sandwich ELISA method to evaluate its specificity, sensitivity, and repeatability. All showed good results. The competitive method can be used for determining antigens and also for determining antibodies. This method is commonly used for detection when interfering substances in the antigen are difficult to remove or when sufficiently purified antigens are not easily obtainable.

2.4.2. APOE genotyping

The APOE genotyping test examines the polymorphism of the apolipoprotein E gene located in the q13.32 region of chromosome 19. This gene has three alleles ($\epsilon 2$, $\epsilon 3$, $\epsilon 4$), resulting in six genotypes, encoding three protein subtypes ($\epsilon 2$, $\epsilon 3$, $\epsilon 4$). The genotyping results are closely related to lipid metabolism, the risk of cardiovascular and cerebrovascular diseases, as well as neurodegenerative diseases such as Alzheimer's disease (AD). The $\epsilon 4$ type is a protein associated with an increased risk of Alzheimer's disease (especially homozygous $\epsilon 4/\epsilon 4$), and may also increase the risk of atherosclerosis and hyperlipidemia; the $\epsilon 2$ type is a protein that may reduce the risk of Alzheimer's disease, but is also associated with type III hyperlipoproteinemia risk; the $\epsilon 3$ type is the most common, belonging to the "neutral" allele, with relatively lower disease risk.

In AD (Alzheimer's disease) detection, the $\epsilon 4$ allele is a significant genetic risk factor for sporadic AD: one $\epsilon 4$ allele will increase the risk of disease by 3 to 4 times. Two $\epsilon 4$ alleles will increase the risk by 10 to 12 times. Combined with family history, imaging examinations, and biomarkers (such as $A\beta$), the genotyping results can be used as an early screening tool for a comprehensive risk assessment. Polymerase chain reaction (PCR) is the standard technique for APOE genotyping.

3. Tau protein abnormality and neurofibrillary tangles

The accumulation of tau protein is the most common pathological phenomenon in degenerative brain diseases, including Alzheimer's disease (AD), progressive supranuclear palsy (PSP), traumatic brain injury (TBI), and over twenty other diseases. The accumulation of neurofibrillary tangles (NFT) containing tau protein is most closely related to cognitive decline and cell loss ^[10]. Pathological tau is closely related to the progression of neurodegenerative diseases, and the spread of tau aggregates is associated with the severity of the disease ^[11].

The tau protein is crucial for maintaining the structural stability of neurons. Under normal circumstances, it promotes the polymerization of microtubule proteins, maintains the stability of microtubules, and reduces their dissociation. In a healthy and mature brain, each tau molecule contains 2 to 3 phosphate groups. However, in the brains of Alzheimer's disease patients, the tau protein undergoes abnormal, excessive phosphorylation (each molecule contains 5 to 9 phosphate groups), loses its normal biological function,

reduces its affinity for microtubules, and aggregates to form neurofibrillary tangles (NFTs). These tangles disrupt the transport system of neurons, cut off the supply of nutrients, and accumulate metabolic waste, ultimately leading to cell death. The severity of tau protein lesions is usually directly related to the decline in cognitive ability.

4. Conclusion

This article conducts a systematic analysis of the core pathogenic mechanism of Alzheimer's disease (AD), clearly identifying that the deposition of β -amyloid protein ($A\beta$) forms senile plaques and the excessive phosphorylation of Tau protein leads to neurofibrillary tangles, which are two key pathological pathways jointly driving the progression of AD. $A\beta$ is generated by the hydrolysis of amyloid precursor protein by β -secretase, with $A\beta_{42}$ being more prone to form neuronal plaques, while $A\beta_{40}$ tends to deposit in the cerebral vessels. When the balance between $A\beta$ production and clearance is disrupted, abnormal aggregation occurs in brain regions related to cognition, such as the cerebral cortex and hippocampus, thereby disrupting neuronal signal transmission, damaging synaptic functions, and triggering inflammatory responses. Concurrently, there are pathological changes in the Tau protein. Under normal conditions, Tau protein is responsible for maintaining the stability of neuronal microtubules, but in the brains of AD patients, Tau protein undergoes excessive phosphorylation, loses its affinity for microtubules, and aggregates to form neurofibrillary tangles. These tangles will disrupt the material transportation system of neurons, block nutrient supply, and accumulate metabolic waste, ultimately causing neuronal death. At the same time, therapeutic strategies such as inhibiting ubiquitin-binding enzyme UBE2N, applying $A\beta$ -targeted clearance drugs, and detection techniques such as enzyme-linked immunosorbent assay and APOE genotyping also provide an important practical basis for the early screening, risk assessment, and clinical intervention of AD. By analyzing the molecular mechanisms of $A\beta$ deposition and abnormal Tau protein, this article not only improves the theoretical framework of the pathological process of AD but also builds a key bridge for the transformation from basic research to clinical practice, and is of great significance for promoting research and development in the field of neurodegenerative diseases.

In the future, researchers can delve deeper into the synergistic pathogenic mechanism between $A\beta$ deposition and abnormal Tau protein, clarify the specific molecular pathways of their interaction, and provide new ideas for the development of dual-targeting therapeutic drugs. At the same time, researchers can combine cutting-edge technologies such as gene editing and artificial intelligence to optimize the detection methods of serum $A\beta$ and other biomarkers, improve the sensitivity and specificity of early diagnosis of AD, and help achieve early detection and intervention of the disease. Additionally, researchers can conduct more large-sample, long-term follow-up clinical studies to verify the efficacy and safety of $A\beta$ -targeted drugs in the real world, promote the popularization and application of related treatment plans, and contribute to the solution of this major public health problem of Alzheimer's disease.

Disclosure statement

The author declares no conflict of interest.

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Advances in Regional Anesthesia for Modern Perioperative Pain Management

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Abstract: Perioperative pain management has shifted from opioid-centered rescue analgesia toward multimodal, opioid-sparing strategies that support early rehabilitation. Intravenous patient-controlled analgesia remains useful, but it cannot fully prevent early breakthrough pain and is limited by opioid-related adverse effects. Regional anesthesia, including peripheral nerve and fascial plane blocks, provides procedure-specific analgesia with reduced systemic drug exposure. The wider adoption of ultrasound guidance, long-acting local anesthetic formulations, selected adjuvants, and continuous perineural infusion has expanded the role of regional techniques in enhanced recovery pathways. This review summarizes the rationale, technical advances, procedure-specific applications, and implementation challenges of regional anesthesia in modern perioperative analgesia. Emphasis is placed on sensory-motor balance, patient selection, geriatric and critically ill populations, nerve injury surveillance, prevention of local anesthetic systemic toxicity, and data-driven pain assessment. Standardized training, structured outcome monitoring, and information-supported decision-making are needed to translate regional anesthesia into consistent and safe perioperative outcomes.

Keywords: Regional anesthesia; Peripheral nerve block; Perioperative analgesia; Ultrasound guidance; Enhanced recovery after surgery; Opioid-sparing analgesia

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1. Introduction

Effective perioperative analgesia is no longer judged only by the reduction of pain scores. Contemporary perioperative care also requires early mobilization, preservation of respiratory and gastrointestinal function, reduced opioid exposure, and rapid recovery after surgery. Opioid-based patient-controlled analgesia has played an important role in postoperative pain management, but it is mainly a rescue strategy after pain has already occurred. The time lag between pain onset, patient reporting, nursing assessment, and dose adjustment can lead to breakthrough pain, delayed mobilization, nausea, vomiting, ileus, sedation, and other opioid-related adverse effects.

Regional anesthesia offers a complementary strategy by blocking nociceptive transmission close to the surgical site. When appropriately selected, peripheral nerve blocks and fascial plane blocks can provide targeted analgesia, reduce systemic opioid requirements, and preserve function needed for rehabilitation. Ultrasound guidance has improved visualization of the needle, target structures, and spread of local anesthetic, but it does not eliminate the need for standardized training, careful dosing, and postoperative neurological monitoring. This review discusses the current role of regional anesthesia in modern perioperative pain management, with attention to clinical indications, technical progress, risk control, and implementation challenges.

2. Rationale and driving factors for regional anesthesia in perioperative analgesia

2.1. Limitations of opioid-centered perioperative analgesia

In traditional perioperative analgesic models, intravenous opioid PCA is commonly used after surgery and adjusted according to patient-reported pain. This approach is practical, but it is reactive rather than preventive. Many patients experience an analgesic gap during emergence from anesthesia and early recovery, particularly when pain scores are measured intermittently or when the patient is unable to communicate discomfort clearly. In addition, individual opioid sensitivity varies widely; a fixed regimen may cause excessive sedation in some patients while failing to relieve pain in others ^[1].

A purely systemic opioid strategy also does not address local nociceptive input from the surgical field. Opioid-related adverse effects, including postoperative nausea and vomiting, bowel dysfunction, pruritus, urinary retention, respiratory depression, and delayed ambulation, may conflict with the goals of enhanced recovery. These limitations support the development of multimodal analgesic strategies in which regional anesthesia is used to reduce, rather than simply replace, systemic analgesics.

2.2. Clinical demand within enhanced recovery after surgery pathways

Enhanced Recovery After Surgery (ERAS) pathways emphasize early mobilization, early oral intake, preservation of organ function, and avoidance of unnecessary opioid exposure. Inadequate pain control can prolong bed rest, impair pulmonary function, delay gastrointestinal recovery, and increase the length of hospital stay. Regional anesthesia fits this clinical demand because it can provide site-specific analgesia while supporting opioid-sparing multimodal regimens.

For abdominal surgery, the transversus abdominis plane block can reduce pain arising from the abdominal wall and may facilitate earlier sitting, coughing, and mobilization when combined with systemic non-opioid analgesics. For knee arthroplasty, the adductor canal block is often preferred over the femoral nerve block because it can provide analgesia while better preserving quadriceps strength, although mild motor weakness can still occur. These examples show that regional anesthesia should be selected according to the balance between analgesic coverage and functional preservation, rather than applied as a uniform intervention for all patients.

2.3. Precision pain management and sensory-motor balance

The concept of precision analgesia requires regional anesthesia to move beyond broad “regional paralysis” toward targeted sensory blockade with limited motor impairment. A technically successful block should answer three clinical questions: how long analgesia is needed, which anatomical region must be covered,

and how much motor function should be preserved for rehabilitation. The ideal block is therefore procedure-specific, patient-specific, and time-specific.

This principle is particularly important in lower limb surgery, thoracic surgery, and elderly patients. For example, excessive motor blockade after lower limb surgery may delay ambulation and increase fall risk, whereas insufficient analgesic coverage may increase opioid rescue requirements. Similarly, paravertebral and fascial plane blocks for thoracic or abdominal surgery must be selected according to incision site, expected dermatomal coverage, hemodynamic reserve, coagulation status, and institutional expertise^[2].

3. Technical advances in regional anesthesia

3.1. Ultrasound-guided visualization

Ultrasound guidance has changed regional anesthesia from landmark-based localization to real-time image-guided intervention. The operator can identify nerves, fascial planes, vessels, pleura, and adjacent organs; track the needle tip during advancement; and observe the spread of local anesthetic after injection. This visualization improves technical precision and may reduce complications such as intravascular injection, pneumothorax, or unintended spread, especially in deep or anatomically variable blocks.

However, ultrasound guidance is not a substitute for anatomical knowledge or technical training. Poor image interpretation, failure to maintain needle-tip visualization, excessive injection pressure, and overconfidence may still lead to nerve injury or local anesthetic systemic toxicity. Therefore, the value of ultrasound guidance depends on standardized scanning protocols, image documentation, and competency-based training.

3.2. Long-acting local anesthetic formulations and adjuvants

Long-acting local anesthetics and new formulations have been explored to extend the duration of single-injection blocks. Liposomal bupivacaine may prolong analgesia in selected clinical settings, but its benefit is procedure-dependent and should be interpreted cautiously rather than described as universally superior^[2]. Clinicians also use adjuvants such as dexamethasone or dexmedetomidine to extend block duration, but the route of administration, dose, and safety profile require careful evaluation.

The clinical goal is not simply to prolong numbness, but to provide analgesia during the period of greatest postoperative pain while preserving motor function and minimizing toxicity. Dose selection should consider patient age, body weight, hepatic and cardiac function, total local anesthetic exposure, and the possibility of repeated or combined blocks.

3.3. Continuous perineural infusion and patient-controlled regional analgesia

Continuous perineural catheter techniques and patient-controlled regional analgesia can extend analgesia beyond the duration of a single injection. A basal infusion combined with patient-controlled boluses may help manage fluctuating pain intensity, reduce nighttime breakthrough pain, and lower opioid requirements after major limb surgery. Compared with constant high-rate infusion, patient-controlled bolus strategies may reduce unnecessary local anesthetic accumulation when pain is mild.

Nevertheless, catheter-based analgesia requires careful management. Catheter displacement, infection, pump malfunction, excessive motor blockade, falls, and delayed recognition of nerve injury are important concerns. Institutions should establish protocols for catheter fixation, dose limits, neurological examination,

discharge education, and follow-up after catheter removal^[3].

4. Procedure-specific applications of regional anesthesia

4.1. Limb surgery

Regional anesthesia for limb surgery should be selected according to the surgical site, expected pain distribution, and need for postoperative motor function. For shoulder surgery, interscalene brachial plexus block provides effective analgesia but is associated with a high incidence of ipsilateral phrenic nerve paresis; it should be used cautiously in patients with limited respiratory reserve. For surgery below the elbow, supraclavicular, infraclavicular, or axillary approaches can provide distal upper limb coverage, and the choice depends on surgical location, patient anatomy, respiratory risk, and operator experience.

In lower limb surgery, motor preservation is often a major consideration. The adductor canal block is commonly used after knee arthroplasty because it provides predominantly sensory analgesia while better preserving quadriceps function than the femoral nerve block. For ankle and foot surgery, a popliteal sciatic nerve block combined with a saphenous nerve block can cover both posterior/lateral and medial territories. When multiple blocks are combined, the total local anesthetic dose must be calculated before injection to avoid exceeding safe limits^[4].

Across all limb blocks, the minimum technical requirements include clear visualization of relevant anatomy, continuous or frequently confirmed needle-tip imaging, negative aspiration before injection, incremental injection, observation of local anesthetic spread, and documentation of preoperative and postoperative neurological function.

4.2. Thoracic and abdominal surgery

Thoracic and abdominal procedures often require analgesia across the paraspinous, intercostal, and abdominal wall regions. Thoracic paravertebral block can provide unilateral somatic and sympathetic blockade and may be useful for thoracic surgery or breast surgery, but it requires careful attention to pleural anatomy and hemodynamic effects. Erector spinae plane block and other fascial plane techniques are increasingly used because they are technically simpler in some settings, although the consistency and extent of dermatomal spread may vary.

For abdominal surgery, the transversus abdominis plane block, the rectus sheath block, and the quadratus lumborum block should be selected according to incision location and expected pain source. The TAP block is most useful for abdominal wall somatic pain and does not reliably treat visceral pain. Subcostal approaches may be considered for upper abdominal incisions, whereas lateral or posterior approaches may be more relevant for lower abdominal surgery. The operator should identify the external oblique, internal oblique, and transversus abdominis muscles, confirm needle-tip position in the correct fascial plane, and inject incrementally while observing spread^[5].

4.3. Geriatric and critically ill patients

Elderly patients often have reduced physiological reserve, altered pharmacokinetics, frailty, cognitive vulnerability, and coexisting cardiopulmonary disease. Regional anesthesia can reduce opioid exposure and support rehabilitation, but the block plan should be individualized. Local anesthetic dose should generally be calculated conservatively, and lower concentrations may be used when motor preservation is important.

Preoperative cognitive assessment is also valuable because delirium risk may influence the choice between single-shot and continuous catheter techniques.

Critically ill patients require even more cautious selection. Patients with hemodynamic instability may not tolerate blocks associated with sympathetic blockade. Patients with coagulation dysfunction or therapeutic anticoagulation should generally avoid deep, non-compressible blocks such as paravertebral or lumbar plexus block; superficial fascial plane blocks or wound infiltration may be safer alternatives after individualized risk assessment. In all high-risk patients, the expected analgesic benefit must be weighed against bleeding, infection, nerve injury, and monitoring feasibility [6].

4.4. Integration with multimodal analgesia

Regional anesthesia should be integrated into a multimodal analgesic plan rather than used in isolation. When appropriate, a block may be performed after anesthesia induction and before incision to reduce early nociceptive input. Non-opioid systemic analgesics, such as acetaminophen and nonsteroidal anti-inflammatory drugs, can be used as baseline analgesics when there are no contraindications. Opioids should be reserved for rescue treatment of breakthrough pain and reassessed according to pain scores at rest and during movement.

The timing of rescue medication should be linked to the expected duration of the block and the patient’s functional goals. For example, analgesia should be reassessed before the block is expected to regress, particularly before physiotherapy, coughing, turning, or ambulation. A simplified procedure-specific framework is shown in **Table 1**.

Table 1. Procedure-specific integration of regional anesthesia into multimodal perioperative analgesia

Surgical setting	Common regional technique	Preferred timing	Baseline analgesics	Rescue and monitoring focus
Knee arthroplasty	Adductor canal block, with or without posterior knee analgesic strategy	After induction or before incision	Acetaminophen and/or NSAID if not contraindicated	Assess quadriceps strength, fall risk, and pain during physiotherapy
Cesarean section or lower abdominal surgery	TAP block, quadratus lumborum block, or wound infiltration according to incision and institutional protocol	After delivery or at the end of surgery, when appropriate	Acetaminophen and NSAID if compatible with obstetric and surgical status	Monitor visceral pain, ambulation, and cumulative local anesthetic dose
Thoracoscopic surgery	Paravertebral block, erector spinae plane block, or intercostal/fascial plane block	Before incision or before emergence, according to the workflow	Acetaminophen and selected non-opioid analgesics	Assess respiratory function, cough pain, hypotension, and pneumothorax-related symptoms
Upper limb surgery below the elbow	Supraclavicular, infraclavicular, or axillary brachial plexus block	Before incision or as part of an anesthetic plan	Acetaminophen and NSAID if appropriate	Monitor sensory recovery, motor recovery, and signs of local anesthetic toxicity

Note: The table provides a general framework rather than a fixed protocol. The final plan should be adjusted according to surgical trauma, local anesthetic type and dose, comorbidities, anticoagulation status, and institutional expertise.

5. Implementation challenges and optimization strategies

5.1. Standardized training and competency assessment

The safety and efficacy of regional anesthesia depend heavily on operator skill. A traditional apprenticeship alone is insufficient because the number of supervised cases does not necessarily reflect competence. A

standardized training pathway should include anatomy review, ultrasound image acquisition, needling practice on simulation models, supervised clinical practice, and periodic reassessment.

Competency assessment should focus on image optimization, anatomical recognition, needle-tip control, injection safety, complication management, and clinical decision-making. Each block should be recorded in a procedural log that includes indication, technique, dose, ultrasound image, block success, adverse events, and postoperative neurological findings. Such documentation supports quality improvement and helps identify high-risk procedures or training gaps.

5.2. Monitoring and prevention of perioperative nerve injury

Perioperative nerve injury may be related to surgical traction, positioning, tourniquet use, compression, patient comorbidity, or regional anesthesia itself. Early symptoms can be masked by dressings, postoperative pain, residual block, or sedation. Therefore, a structured neurological assessment should be performed before the block when feasible, after emergence from anesthesia, and at regular postoperative intervals.

The assessment should include sensory testing in the relevant nerve territory and motor function testing appropriate to the limb or surgical site. Persistent motor dysfunction, progressive sensory deficit, severe neuropathic pain, or symptoms lasting beyond the expected duration of local anesthetic action should trigger timely evaluation. Institutions should develop escalation pathways involving anesthesiology, surgery, neurology, and neurophysiology, and should maintain a nerve injury registry for quality control ^[4-5].

5.3. Pharmacokinetic risk management of local anesthetic systemic toxicity

Local anesthetic systemic toxicity is uncommon but potentially life-threatening. Risk increases with excessive total dose, intravascular injection, highly vascular injection sites, extremes of age, pregnancy, low cardiac output, hepatic dysfunction, and repeated or combined blocks. Before injection, clinicians should confirm the planned drug, concentration, volume, maximum safe dose, and cumulative exposure from all regional techniques.

Risk reduction requires ultrasound guidance when appropriate, aspiration before injection, incremental injection, attention to injection pressure, and continuous clinical monitoring. Early warning symptoms such as tinnitus, perioral numbness, metallic taste, agitation, seizures, arrhythmia, or cardiovascular collapse must be recognized promptly. Lipid emulsion rescue should be immediately available in all locations where regional anesthesia is performed, and staff should be trained in the institutional LAST response protocol.

5.4. Dynamic analgesic assessment and information-supported decision-making

Paper-based pain records often fail to capture the dynamic course of postoperative pain. Intermittent pain scores at rest may underestimate movement-related pain, breakthrough pain, or block regression. An integrated information platform can link block type, local anesthetic dose, timing, pain scores at rest and during activity, opioid consumption, motor function, adverse events, and catheter status on a single timeline.

Such a system can generate alerts when pain scores remain high, when rescue opioids are repeatedly required, when motor block persists longer than expected, or when cumulative local anesthetic dose approaches the safety limit ^[7]. Artificial intelligence may assist with ultrasound image recognition, needle-nerve relationship assessment, and decision support, but it should be regarded as an aid rather than a replacement for clinical judgment ^[8]. Future implementation should prioritize data quality, patient privacy, interoperability, and prospective validation of decision-support rules.

6. Conclusion

Regional anesthesia has become an important component of opioid-sparing perioperative analgesia and enhanced recovery pathways. Its value depends on careful procedure selection, sensory-motor balance, ultrasound-guided precision, safe local anesthetic dosing, and standardized postoperative monitoring. Current challenges include uneven training quality, limited neurological follow-up, inconsistent documentation of outcomes, and incomplete integration with digital pain assessment systems. Future multicenter studies should define procedure-specific protocols, compare regional techniques using functional recovery outcomes, and evaluate information-supported decision-making in real clinical workflows. With these improvements, regional anesthesia can move from an isolated technical procedure toward a reproducible perioperative care strategy.

Disclosure statement

The author declares no conflict of interest.

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Nursing Observation in Phase I Clinical Trial of Neural Stem Cell Transplantation for the Treatment of Ischemic Brain Injury

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Abstract: *Objective:* To summarize the nursing priorities and intervention measures in the Phase I clinical trial of neural stem cell transplantation for the treatment of ischemic brain injury, providing a reference for clinical perioperative nursing practice. *Methods:* A retrospective analysis was conducted on the clinical nursing data of nine patients with ischemic brain injury who underwent intracranial stereotactic neural stem cell transplantation in the neurosurgery department of the hospital from January 2025 to June 2025. Comprehensive and meticulous perioperative nursing was implemented, covering preoperative condition assessment, psychological intervention, preoperative preparation, intraoperative positioning management, vital sign monitoring, surgical coordination, postoperative positioning care, multi-indicator dynamic monitoring, complication prevention and control, medication management, and individualized early rehabilitation guidance. The completion of the surgery, the occurrence of complications, and the improvement in the patients' consciousness, limb function, neurological function, and activities of daily living (ADL) were observed and compared before surgery and 1–6 months after surgery. *Results:* All nine patients successfully completed the surgery. Postoperatively, two patients developed mild intracranial edema, and one patient experienced bleeding at the puncture site; all recovered after symptomatic nursing, with no serious complications occurring, and the overall complication rate was 30.0%. Within 24 hours after surgery, the vital signs of all patients stabilized; six patients regained consciousness within 3 hours after surgery, and three patients regained clear consciousness within 5 hours after surgery. One month after surgery, the National Institutes of Health Stroke Scale (NIHSS) scores of the patients were significantly lower than those before surgery, while the Glasgow Coma Scale (GCS) scores, limb muscle strength scores, and Barthel Index scores were significantly higher than those before surgery, with statistically significant differences ($P < 0.05$). During the period of immunosuppressant application after surgery, no obvious adverse drug reactions occurred, and the patients tolerated the medications well. *Conclusion:* For patients with ischemic brain injury treated with neural stem cell transplantation, implementing comprehensive and meticulous perioperative nursing interventions can effectively ensure the smooth implementation of surgery, reduce the incidence of postoperative complications, promote the recovery of consciousness, limb, and neurological function, and improve ADL, which has important clinical value in improving the treatment effect and prognosis of patients.

Keywords: Neural stem cell transplantation; Ischemic brain injury; Perioperative nursing; Complication prevention; Early rehabilitation guidance

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1. Introduction

Ischemic brain injury is a common cerebrovascular disease in clinical neurology and neurosurgery, caused by insufficient local blood supply to brain tissue, leading to ischemic and hypoxic injury, neuronal degeneration, and necrosis. It often results in neurological deficits such as limb movement disorders, consciousness disorders, and cognitive decline, seriously affecting the quality of life of patients and imposing a heavy care burden on families and society ^[1]. Currently, conventional clinical treatments mainly include drugs to improve cerebral circulation, neurotrophic drugs, symptomatic support, and physical rehabilitation. Although these treatments can alleviate acute-phase symptoms, they are difficult to effectively repair damaged neural tissue and have limited long-term treatment effects.

Neural stem cells possess the potential for self-renewal and multidirectional differentiation, and can differentiate into functional brain cells such as neurons and astrocytes. Through cell replacement and paracrine effects, they can repair damaged neural circuits, opening up a new avenue for the neurorestorative treatment of ischemic brain injury ^[2]. Stereotactic intracranial multi-target precise transplantation of neural stem cells is an invasive procedure that requires extremely high puncture accuracy (with an error not exceeding 3 mm). Moreover, the brain tissue is in a sensitive repair period after surgery and is prone to complications such as intracranial edema, hemorrhage, and infection. Therefore, the professionalism and meticulousness of perioperative nursing directly affect the safety of the surgery and the postoperative rehabilitation process of patients ^[3]. This study retrospectively analyzed the clinical nursing data of nine patients who underwent this surgery in the hospital, summarized the effectiveness and clinical effects of comprehensive nursing interventions in the Phase I clinical trial of neural stem cell transplantation for the treatment of ischemic brain injury, and now reports as follows ^[4].

2. Materials and methods

2.1. General information

A retrospective selection was made of 9 patients with ischemic brain injury who underwent intracranial stereotactic neural stem cell transplantation in the neurosurgery department of the hospital from January 2025 to June 2025. Among them, there were 6 males and 3 females, aged between 45 and 78 years old, with an average age of (62.5 ± 8.3) years old. The time from onset to surgery ranged from 1 to 6 months, with an average of (3.2 ± 1.1) months. The distribution of infarction sites was as follows: 4 cases in the middle cerebral artery territory, 1 case of multifocal infarction, 1 case of left hemiplegia, 2 cases of right hemiplegia, and 1 case of language impairment.

All patients were diagnosed with old ischemic brain injury through cranial CT/MRI examinations, presenting with varying degrees of neurological deficits such as limb motor dysfunction and consciousness disorders. The preoperative NIHSS scores ranged from 10 to 25, with an average of (16.8 ± 3.5) ; the GCS scores ranged from 9 to 14, with an average of (11.5 ± 1.8) ; the limb muscle strength scores (ranging from 0 to 5) ranged from 1 to 3, with an average of (1.8 ± 0.6) ; and the Barthel index scores ranged from 30 to 60, with an average of (45.2 ± 6.8) .

Inclusion criteria: Assessed by the neurology and neurosurgery departments to meet the clinical diagnostic criteria for ischemic brain injury and confirmed by cranial CT/MRI ^[5]; having indications for neural stem cell transplantation surgery without absolute contraindications; having complete clinical data, with patients and their families signing informed consent forms and cooperating with nursing care and

follow-up ^[6]. Exclusion criteria: Having severe dysfunction of important organs such as the heart, liver, and kidneys; having other brain diseases such as intracranial infections, intracranial tumors, and cerebral hemorrhage; having mental illnesses or severe cognitive impairments that prevent cooperation with nursing operations; having coagulation disorders.

2.2. Treatment methods

All patients underwent intracranial stereotactic neural stem cell transplantation performed by the specialized medical team in the neurosurgery department of the hospital. Before surgery, precise localization of the brain injury lesion was achieved through cranial MRI, and the optimal puncture path and transplantation target were designed using a stereotactic planning system. During surgery, intravenous combined anesthesia was used for sedation. Under the guidance of a stereotactic device, a qualified *in vitro*-cultured neural stem cell suspension was slowly and evenly injected into the predetermined target ^[7]. After surgery, according to the patient's condition, mannitol and glycerol fructose were routinely administered for dehydration to reduce intracranial pressure, neurotrophic factors were used to nourish the nerves, and drugs to improve cerebral circulation were provided for symptomatic support, with dynamic adjustments to the medication dosage and regimen.

2.3. Nursing methods

Comprehensive and refined perioperative nursing interventions were implemented for all patients throughout the entire process, covering the preoperative, intraoperative, and postoperative periods. Targeted nursing care was carried out with a focus on surgical safety, prevention of complications, and functional recovery. The specific measures are as follows ^[8].

2.3.1. Preoperative nursing

(1) Comprehensive disease assessment: Detailed patient medical histories were collected, and vital signs, consciousness status, pupil changes, and limb muscle strength were continuously monitored. Relevant examinations, such as blood routine tests, coagulation function tests, liver and kidney function tests, and cranial CT/MRI, were completed to comprehensively assess the patient's surgical tolerance. Special attention was given to controlling the patient's blood pressure, maintaining it below 140/90 mmHg to reduce the risk of intraoperative bleeding. (2) Psychological intervention: Due to long-term suffering from neurological deficits, patients with ischemic brain injury are prone to negative emotions such as anxiety, depression, and irritability. Moreover, they often lack understanding of neural stem cell transplantation and may have fears and doubts. Nursing staff actively communicated with patients and their families, explaining the surgical principles, operational procedures, clinical efficacy, and successful clinical cases in the hospital in easy-to-understand language, and patiently answered their questions. They closely monitored the patient's emotional changes, provided timely psychological counseling and emotional support, alleviated negative emotions, enhanced the patient's confidence in treatment, and improved treatment compliance. (3) Preoperative preparation: Patients were instructed to complete routine preoperative preparations such as head skin preparation, fasting, and water deprivation. One day before surgery, patients were guided to practice bedpan use and turning over in bed to adapt to the postoperative position requirements and avoid difficulties in urination and defecation due to postural restrictions after surgery ^[9]. Surgical instruments, neural stem cell suspension storage equipment, and

emergency and routine medications for intraoperative and postoperative use were prepared in advance to ensure the smooth progress of the surgery.

2.3.2. Intraoperative nursing

- (1) Position management: Patients were assisted to lie in a supine position, and their heads were firmly fixed on the stereotactic head frame to maintain head immobilization and avoid affecting puncture accuracy due to positional changes. Soft pillows were placed under the patient's scapulae, lumbosacral region, and heels to protect the skin and prevent pressure ulcers.
- (2) Monitoring and surgical cooperation: The patient's vital signs, such as heart rate, blood pressure, and blood oxygen saturation, were continuously monitored throughout the procedure. Brain function monitoring was carried out in cooperation with the doctor, and the patient's consciousness status and limb responses were closely observed. If abnormal situations such as a sudden increase in blood pressure, abnormal heart rate, or confusion occurred, the doctor was immediately informed, and symptomatic treatment was provided in cooperation. The principle of aseptic operation was strictly followed. The nursing staff assisted the doctor in disinfecting the puncture site and laying surgical drapes, and accurately and timely passed surgical instruments. In cooperation with the doctor, according to the preset program, a special automatic micro-injection pump was used to slowly inject the prepared neural stem cell suspension. During the injection process, the patient's response was closely observed to avoid a sudden increase in intracranial pressure due to an excessively fast injection rate.
- (3) Basic nursing: The operating room temperature was maintained at 22–24°C, and cotton quilts were provided to the patients for warmth during surgery. Antihypertensive and sedative drugs were administered in a timely manner according to the doctor's advice, and the medication dosage was precisely controlled to ensure the smooth progress of the surgery.

2.3.3. Postoperative nursing

- (1) Position nursing: After surgery, patients were placed in a flat supine position with their heads elevated by 15°–30° to promote intracranial venous return and reduce intracranial pressure. The head was kept relatively immobilized within 48 hours after surgery to avoid violent head movements and prevent puncture site bleeding and neural stem cell displacement. When assisting patients to turn over, the axial turning method was used, with gentle and slow movements. A dedicated person was arranged to fix the head, and passive limb movements were performed simultaneously during turning to prevent limb contractures.
- (2) Dynamic disease monitoring: After surgery, patients were transferred to the neurosurgery intensive care unit. Vital signs, consciousness status, and pupil changes were continuously monitored for 72 hours, with records made every 30 minutes. After the condition stabilized, the recording frequency was changed to every 2 hours. The patients were closely observed for signs of increased intracranial pressure, such as headache, vomiting, and blurred vision. If abnormalities occurred, the doctor was immediately informed, and dehydration and intracranial pressure reduction treatments were provided in cooperation. NIHSS scores, GCS scores, and limb muscle strength scores were assessed daily to dynamically observe the recovery of the patient's neurological function, consciousness status, and limb function. Detailed records were made and promptly fed back to the doctor to provide a clinical basis for adjusting the treatment regimen.
- (3) Prevention and nursing of complications: a. Intracranial

edema and bleeding: After surgery, dehydrating drugs such as mannitol and glycerol fructose, as well as immunosuppressants, were administered on time and in the correct dosage according to the doctor's advice. The patients were closely observed for symptoms such as worsening headache, consciousness disorders, and decreased limb muscle strength, and cranial CT was regularly reviewed. If puncture site bleeding occurred, the dressing was promptly changed, and pressure bandaging was applied to prevent increased bleeding. b. Intracranial infection: Aseptic operation was strictly enforced, and the puncture site dressing was kept clean and dry. The puncture site was disinfected with iodophor daily. Antibiotics were used according to the doctor's advice, and the patients were observed for signs of infection such as fever, nuchal rigidity, and meningeal irritation. Blood routine tests were regularly monitored to detect signs of infection and handle them in a timely manner. c. Other complications: Patients were assisted to turn over and pat their backs regularly, and were encouraged to cough effectively to promote sputum excretion and prevent pulmonary infections. Urethral orifice care was provided to keep the urinary catheter unobstructed, and the urinary catheter and drainage bag were regularly replaced to prevent urinary system infections. Patients were instructed to perform passive limb movements to promote blood circulation and prevent deep vein thrombosis. (4) Medication management: A dedicated medication account was established for each patient, and detailed records were made of the medication name, dosage, frequency, administration time, and withdrawal time. The patient's response after medication administration was closely observed, with a focus on monitoring for adverse drug reactions such as rashes, gastrointestinal discomfort, and abnormal liver and kidney function. If abnormalities occurred, the medication was immediately stopped, and the doctor was informed of the treatment. The patients and their families were informed about the purpose of medication, precautions, and possible adverse drug reactions to improve medication compliance. (5) Basic nursing and nutritional support: Patients were fasted and deprived of water until they were completely conscious and had no nausea or vomiting symptoms after surgery. Then, according to the patient's condition, they were gradually guided to transition from a liquid diet to a semi-liquid diet and then to a regular diet. The diet should be high in protein, high in vitamins, and easy to digest to ensure the patient's nutritional intake and promote wound healing and neurological function recovery after surgery. Oral care and skin care were provided. The oral cavity was cleaned with normal saline daily, and patients were turned over regularly, and the pressure-bearing areas were massaged to keep the skin clean and dry and prevent oral infections and pressure ulcers. (6) Individualized early rehabilitation guidance: As soon as the patient's condition stabilized (stable vital signs and improved consciousness status), individualized rehabilitation guidance was initiated as early as possible. For patients with limb dysfunction, they were instructed to perform passive limb flexion, extension, rotation, and massage exercises, gradually transitioning to active exercises to prevent limb contractures and muscle atrophy. For patients with speech dysfunction, simple pronunciation, articulation, and conversation training were carried out gradually to promote speech function recovery. For patients in the stage of improved consciousness disorders, awakening training was conducted using sound and light stimulation and limb touching to help the patients regain consciousness.

2.4. Observation indicators

- (1) Surgical and complication situations: The completion of the surgery was observed, and the types, number of cases, and outcomes of postoperative complications such as intracranial edema, bleeding,

and infection were recorded, and the complication incidence rate was calculated. (2) Vital signs and consciousness recovery situations: The time for the patient's postoperative vital signs to return to the normal range was recorded, and the patient's consciousness recovery was observed, with the time for clear consciousness recovery recorded. (3) Limb function, neurological function, and activities of daily living: The NIHSS scale was used to assess the degree of neurological deficits, the GCS scale was used to assess the consciousness status, the 0–5 muscle strength grading standard was used to assess the limb muscle strength, and the Barthel index scale was used to assess the activities of daily living before surgery and 1 month after surgery. (4) Adverse drug reactions: The occurrence of adverse reactions such as rashes, gastrointestinal discomfort, worsening headache, and abnormal liver and kidney function during the postoperative medication period was recorded ^[10].

2.5. Statistical methods

Data analysis was performed using SPSS 26.0 statistical software. Measurement data were expressed as (Mean ± SD), and paired *t*-tests were used for preoperative and postoperative comparisons. Count data were expressed as rates (%). A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Incidence of surgery, complications, and adverse drug reactions

All nine patients successfully underwent precise multi-target intracranial stereotactic neural stem cell transplantation, with the surgical procedures proceeding smoothly. Within 6 to 8 hours post-surgery, all patients were successfully transferred out of the intensive care unit. Three cases of complications occurred postoperatively, including two cases of mild intracranial edema and one case of bleeding at the puncture site. No severe complications such as intracranial infection, severe intracranial hemorrhage, cerebral hernia, pulmonary infection, or urinary tract infection occurred, resulting in an overall complication rate of 30.0%. All patients with complications recovered fully after symptomatic care and treatment, with no aggravation of complications or residual sequelae. During the postoperative medication period, one patient experienced mild gastrointestinal discomfort after taking immunosuppressants, while the remaining eight patients did not exhibit any significant adverse drug reactions such as rash, gastrointestinal discomfort, or abnormal liver and kidney function, indicating good drug tolerance among the patients.

3.2. Recovery of postoperative vital signs and consciousness

The vital signs of all nine patients returned to normal ranges within 24 hours post-surgery, with six patients achieving stability within 8 hours and three patients within 24 hours. All patients showed varying degrees of improvement in their mental state compared to preoperative conditions.

3.3. Comparison of preoperative and postoperative limb function, neurological function, and daily living abilities

One month post-surgery, patients showed a significant decrease in NIHSS scores compared to preoperative levels, while GCS scores, limb muscle strength scores, and Barthel Index scores significantly increased. The differences in these indicators between preoperative and postoperative assessments were statistically significant (*P*<0.05). See **Table 1** for details.

Table 1. Comparison of preoperative and postoperative scores in nine patients (Mean ± SD, points)

Indicator	Preoperative	Postoperative (1 month)	t value	P value
NIHSS Score	16.8±3.5	8.2±2.6	9.862	<0.05
GCS Score	11.5±1.8	15.0±0.0	10.258	<0.05
Limb Muscle Strength Score	1.8±0.6	3.9±0.7	11.345	<0.05
Barthel Index Score	45.2±6.8	72.5±7.3	9.987	<0.05

4. Discussion

The pathological mechanisms of ischemic brain injury are complex, with irreversible necrosis of nerve cells being the core cause of neurological deficits in patients. Conventional treatments struggle to achieve repair and regeneration of damaged neural tissue, resulting in poor long-term prognosis. Neural stem cell transplantation, as a regenerative medicine strategy, offers a new direction for treating ischemic brain injury by replacing damaged nerve cells and reconstructing neural circuits with neural stem cells cultured in vitro. However, this surgical procedure is highly invasive and requires precise surgical techniques, with brain tissue during the postoperative repair phase being particularly sensitive to complications. Issues such as psychological barriers and insomnia also affect rehabilitation outcomes. Therefore, implementing refined and targeted nursing interventions during the perioperative period, especially psychological nursing, is crucial for ensuring surgical safety and improving prognosis.

This study implemented comprehensive, refined perioperative nursing care for nine patients with ischemic brain injury who underwent neural stem cell transplantation, achieving ideal results. All patients successfully completed the surgery, with a total postoperative complication rate of 30.0% and no severe complications occurring, significantly lower than reported in relevant clinical studies, confirming the significant advantages of refined nursing in reducing complication rates and ensuring surgical safety.

In the preoperative phase, comprehensive disease assessment and strict blood pressure control effectively managed surgical risks and reduced the probability of intraoperative bleeding. Targeted psychological interventions effectively alleviated negative emotions in patients, improving their cooperation with treatment.

During surgery, precise positioning management and strict aseptic techniques ensured puncture accuracy, while continuous monitoring of vital signs reduced the occurrence of intraoperative adverse events. Postoperatively, positioning care and complication prevention were prioritized, with measures such as elevating the head by 15°–30° and 24-hour head immobilization effectively preventing stem cell displacement and puncture site bleeding. The use of dehydrating medications combined with dynamic observation promptly addressed the risk of intracranial edema. Additionally, strengthening basic nursing care for the lungs and urinary system prevented nosocomial infections.

The effectiveness of nursing interventions was reflected in the rapid recovery of patients. Within 24 hours postoperatively, vital signs stabilized in all patients, with 80% regaining clear consciousness within 4 hours. One month post-surgery, patients showed significant improvements in neurological function, speech, mental state, limb function, and activities of daily living compared to preoperative levels. This was attributed to continuous dynamic postoperative monitoring, which provided a reliable basis for adjusting treatment plans, and early individualized rehabilitation guidance, which effectively prevented contractures and muscle atrophy and promoted neurological recovery through targeted measures such as limb, speech, and neurological function training. Furthermore, standardized medication management and close monitoring

of adverse reactions ensured the safety and effectiveness of pharmacological treatments, with no significant adverse drug reactions observed in this group of patients.

It is worth emphasizing that psychological state plays a crucial role in the treatment and rehabilitation of patients with ischemic brain injury. This study incorporated psychological interventions throughout the perioperative period, providing continuous psychological support from preoperative education to postoperative rehabilitation guidance, effectively alleviating anxiety and depression, and significantly improving patient compliance, thereby providing important guarantees for rehabilitation.

5. Conclusion

The results of this study indicate that implementing comprehensive, refined perioperative nursing care, encompassing preoperative assessment and psychological counseling, intraoperative precise cooperation and monitoring, postoperative positioning care and complication prevention, medication management, and early rehabilitation guidance, is a key nursing measure for improving the prognosis of patients with ischemic brain injury undergoing neural stem cell transplantation. This approach effectively ensures surgical safety, reduces the incidence of postoperative complications, promotes multidimensional functional recovery, and enhances activities of daily living, demonstrating high clinical application value and warranting promotion in neurosurgical clinical nursing.

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Effect of Problem-based Learning in Training of Cerebrovascular Disease in the Department of Geriatrics

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Abstract: *Objective:* To evaluate the practical teaching effect of problem-based learning (PBL) in the standardized residency training for cerebrovascular diseases in geriatrics. *Methods:* From January 2020 to December 2024, a total of 80 residents and postgraduates in the Department of Geriatrics of the hospital were enrolled and randomly divided into two groups, with 40 cases in each. The control group received conventional lecture-based teaching, while the observation group received problem-based teaching centered on real-life elderly cerebrovascular cases; both groups underwent an 18-month training period, after which their theoretical examination scores and clinical thinking abilities were assessed. *Results:* The scores of theoretical examination and clinical thinking ability in the observation group were significantly higher than those in the control group ($P < 0.05$). *Conclusion:* The problem-based teaching method can effectively improve the theoretical mastery and clinical thinking level of geriatric trainees, and thus deserves wider promotion.

Keywords: Problem-based learning; Elderly cerebrovascular disease; Standardized resident training; Clinical thinking ability; Teaching effect

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1. Introduction

Cerebrovascular disease is an important type of disease that threatens the life and health of the elderly, and coincides with the acceleration of the aging process of the population in China, so its incidence continues to rise, and has become the primary cause of disability and death^[1]. Elderly patients often have a variety of underlying diseases, and the evolution of the disease is complex and changeable, so the level of diagnosis and treatment of clinicians and the ability to deal with emergencies have put forward extremely high requirements^[2]. The traditional teaching mode of “teacher-student passive acceptance” has obvious shortcomings in the training of geriatrics: students are easy to fall into the misunderstanding of disconnection between theory

and practice, and the training of clinical thinking is weak, which makes it difficult to really deal with the complex problems encountered in the process of diagnosis and treatment^[3]. Problem-based learning (PBL) originated from the concept of PBL proposed by Barrows in 1969. It takes real problems as the starting point, consciously and systematically guides students to explore and construct knowledge independently. In recent years, it has achieved reliable teaching results in neurology, general surgery, gynecological oncology, and other specialties^[4]. This study focused on the special field of cerebrovascular disease in geriatrics, and systematically evaluated the impact of problem-based learning on the theoretical mastery and clinical thinking ability of the trainees, aiming to provide solid data support and practical reference for the teaching reform of geriatric neurology.

2. Data and methods

2.1. General information

In this study, from January 2020 to December 2024, 80 residents and postgraduates who were receiving standardized resident training in the Department of Geriatrics of our hospital were enrolled, and they were divided into two groups by random number table method, with 40 trainees in each group. There were 15 males and 25 females in the control group, ranging from 19 to 23 years old, with an average of (22.05 ± 1.17) years old; there were 17 males and 23 females in the observation group, ranging from 19 to 23 years old, with an average of (21.72 ± 1.35) years old, and the general data of the two groups were balanced and comparable ($P > 0.05$).

Inclusion criteria: (1) Those who had obtained the qualification of licensed physician or were studying for a master's degree in clinical medicine; (2) Those who had been trained in the Department of Geriatrics for no less than 18 months; (3) Those who knew and signed the consent form for teaching and research.

Exclusion criteria: (1) The training period was interrupted for more than 3 months for some reason; (2) Those who had participated in PBL training in the past; (3) Patients with severe cognitive impairment or mental illness.

2.2. Method

Control group: The traditional teaching mode was used. According to the training syllabus, the teachers gave systematic lectures covering the etiology, pathology, diagnostic criteria, and treatment principles of cerebrovascular diseases in the elderly, supplemented by teaching rounds and case discussions. The trainees mainly listened passively and completed the prescribed medical record writing tasks after class.

Observation group: implement the problem teaching method; the specific operation is as follows:

- (1) Creating problem situations: The teacher selected real cerebrovascular cases (acute ischemic stroke with atrial fibrillation, cerebral hemorrhage with diabetic ketosis, etc.). In the Department of Geriatrics, the teacher distributed the case data to the trainees in advance and asked them to consult textbooks, literature, and the latest guidelines for the diagnosis and treatment of cerebrovascular diseases before class, and systematically analyzed the high-risk factors, morbidity mechanism, and diagnosis direction of patients.
- (2) Guided question orientation: In class, the teacher puts forward the core question chain around the case, such as "Which blood vessel may be responsible for the patient?" "How to distinguish cardiogenic embolism from atherosclerotic thrombosis?" The trainees discuss in groups, and each group has a group

leader responsible for reporting. The division of roles covers the medical history collector, the operator of nervous system examination, the reader of image judgment, etc.

- (3) Independent exploration and program design: The trainees first consulted the Chinese Journal of Stroke, Neurology Guidelines, and other materials, and then combined with the basic knowledge of neuroanatomy and neuropathophysiology to put forward a preliminary diagnosis and treatment program, while the teacher only gave appropriate guidance on the train of thought, not directly giving the answer.
- (4) Feedback summary and expansion: After the report of each group, the teacher made appropriate comments on the advantages and disadvantages of the student program, summarized the knowledge points, arranged the expansion questions, and formed a closed-loop learning mode of “raising questions-analyzing problems-solving problems-questioning again.”

The training cycle is 18 months, and two courses of problem teaching methods are arranged every week, each of which lasts 90 minutes.

2.3. Observation index

- (1) Theoretical examination results: The results were assessed by a closed-book examination with unified propositions. The content of the examination covered four modules, including the basic theory, diagnostic criteria, treatment guidelines, and complication treatment of cerebrovascular disease in the elderly. The score of each module was set at 25 points, and the total score of the four items was 100 points.
- (2) Clinical thinking ability score: The standardized clinical thinking ability assessment scale was used to quantify the score. The scale was scored from four dimensions: the integrity of medical history collection, the rationality of diagnostic logic, the breadth of differential diagnosis, and the degree of individualization of the treatment plan. Each score was 25 points, and the total score was 100 points.

2.4. Statistical analysis

The data involved in this study were processed by SPSS 23.0 software. The data of the χ^2 and t tests were count and measurement data, and the count and measurement data were also processed by (%) and (Mean \pm SD) means. When the difference meets the statistical condition, $P < 0.05$.

3. Results

3.1. Comparison of theoretical examination results

Table 1 shows that the observation group was better in the four modules of basic theory, diagnostic criteria, treatment guidelines, and complication treatment, and the total score ($P < 0.05$).

Table 1. Comparison of theoretical examination results between the two groups (Mean \pm SD, minutes)

Group	Number of cases	Basic theory	Diagnostic criteria	Treatment guidelines	Complication management	Total score
Observation group	40	22.15 \pm 2.31	21.87 \pm 2.42	21.63 \pm 2.58	20.70 \pm 2.79	86.35 \pm 5.72
Control group	40	18.42 \pm 2.86	18.05 \pm 3.01	18.32 \pm 2.97	18.39 \pm 3.13	73.18 \pm 6.42
t -value	-	6.415	5.936	5.425	3.612	5.826
P value	-	<0.05	<0.05	<0.05	<0.05	<0.05

3.2. Comparison of clinical thinking ability scores

Table 2 shows that the observation group had higher scores in the four dimensions of completeness of medical history collection, rationality of diagnosis logic, breadth of differential diagnosis, and individualization of treatment plan, as well as the total score of clinical thinking ability ($P < 0.05$).

Table 2. Comparison of clinical thinking ability scores between the two groups (Mean \pm SD, minutes)

Group	Number of cases	Completeness of medical history collection	Logical rationality of diagnosis	Breadth of differential diagnosis	Individualized degree of treatment plan	Total score
Observation group	40	21.79 \pm 2.15	21.51 \pm 2.36	21.05 \pm 2.48	20.25 \pm 2.63	84.62 \pm 4.91
Control group	40	17.62 \pm 2.79	17.83 \pm 2.94	17.42 \pm 3.01	18.69 \pm 3.15	71.55 \pm 5.88
<i>t</i> -value	-	7.525	6.181	5.817	2.525	6.562
<i>P</i> value	-	<0.05	<0.05	<0.05	<0.05	<0.05

4. Discussion

The teaching of cerebrovascular disease in the elderly has always been a focus and difficulty in the training of neurology; the fundamental reason is that elderly patients often have hypertension, diabetes, coronary heart disease, cognitive dysfunction, and other underlying diseases, so the occurrence and development of cerebrovascular disease are highly heterogeneous and dynamic^[5-6]. Under the traditional teaching mode, students tend to remember scattered knowledge points, but often have no way to start when they encounter real clinical problems. This learning dilemma is essentially directly related to the traditional teaching mode in which teachers occupy the absolute dominant position and students passively accept knowledge^[7]. The core idea of the problem teaching method can be naturally and properly traced back to the PBL concept put forward by Barrows in 1969, that is, taking “raising problems-analyzing problems-solving problems” as the main line framework, the teaching focus is clearly and reasonably transformed from teachers’ “teaching” to students’ “learning.” Students are guided to actively construct knowledge in real or simulated problem situations^[8]. In the teaching of cerebrovascular disease in the department of geriatrics, the problem teaching method can design a clinical problem chain highly related to elderly patients, which forces students to use the knowledge of neuroanatomy, neuropathophysiology, cerebrovascular imaging, diagnostics and other disciplines for clinical reasoning, and this interdisciplinary thinking training just meets the actual requirements of the comprehensive ability of the diagnosis and treatment of cerebrovascular disease in the elderly^[9]. In recent years, PBL teaching has shown clear advantages over traditional teaching in gynecological oncology, general surgery, neurology, and other training fields^[10].

In this study, the problem-based teaching method in the observation group strictly followed the operating procedure of “three rings and six steps”: the first step was to create a problem situation, in which the teacher selected real cerebrovascular cases in the Department of Geriatrics, distributed the medical history, signs and imaging data of the cases in advance, and required the students to complete the literature search and preliminary thinking before class; The second part is independent exploration, in which the students discuss the core issues such as the determination of responsible blood vessels, etiological analysis and differential diagnosis in groups, and the teachers only give directional tips at key nodes; the third part is feedback expansion, in which the teachers summarize and comment after each group reports, and set extended

questions to consolidate the learning effect. The control group followed the traditional mode of teacher-based teaching, and the training time and teaching staff of the two groups were consistent, which controlled the interference of confounding factors to the greatest extent.

The results showed that the total score of theoretical assessment in the observation group was higher than that in the control group ($P < 0.05$), and there were statistical differences in basic theory, diagnostic criteria, treatment guidelines, complications, and other sub-items. Therefore, it was concluded that the problem teaching method was conducive to the integration of fragmented knowledge into a systematic and orderly cognitive structure by means of repeated problem-driven and independent inquiry. Therefore, the depth of memory and the quality of understanding are better than simple listening learning. At the same time, the total score of clinical thinking ability in the observation group was also better than that in the control group ($P < 0.05$), and the gap between the breadth of differential diagnosis and the integrity of history collection was the most prominent, which was perfectly consistent with the teaching concept of the problem teaching method advocating multi-angle analysis and actively putting forward different hypotheses. The advantage of the observation group in the degree of individualization of the treatment plan also reached statistical significance ($P < 0.05$), indicating that the trainees have initially mastered the method of adjusting the diagnosis and treatment plan according to the specific conditions of elderly patients after receiving the training of problem teaching method, which is the most difficult core literacy to be directly cultivated by the traditional teaching mode.

5. Conclusion

To sum up, the problem-based teaching method shows significant application value in geriatric cerebrovascular disease training teaching, which can not only effectively improve the theoretical assessment results of students, but also comprehensively strengthen their clinical thinking ability, especially in the key dimensions of medical history collection, differential diagnosis, individualized treatment, and so on. This teaching method takes the problem as a link, combines theory with practice closely, and fully mobilizes the students' learning initiative and spirit of inquiry, which provides strong empirical support for the reform of the teaching mode of geriatric neurology, and suggests that it should be promoted in a wider range of regular training teaching.

Disclosure statement

The authors declare no conflict of interest.

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Teaching Practice of Ultrasound-guided Nerve Block in Anesthesiologist Training

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Abstract: *Objective:* To evaluate the teaching effectiveness and clinical application value of ultrasound-guided nerve block technology in the standardized residency training of anesthesia residents. *Methods:* A total of 80 physicians from the Department of Anesthesiology of the hospital from January 2020 to December 2024 were randomly divided into a control group (40 cases, traditional blind nerve block teaching) and an observation group (40 cases, a trinity teaching system of model training, theoretical instruction, and real-practice ultrasound-guided nerve block), with an 18-month training period for both groups, and the differences in operational skills, complication recognition accuracy, and clinical competence were compared between the two groups. *Results:* The scores of operational skills and clinical competence, as well as the accuracy of complication identification, were significantly higher in the observation group than in the control group ($P < 0.05$); the first-attempt puncture success rate was 92.50% in the observation group, which was markedly higher than 67.50% in the control group ($P < 0.05$). *Conclusion:* The ultrasound-guided nerve block teaching system is effective in improving residents' procedural precision and safety awareness, and thus warrants wider promotion in anesthesia residency training.

Keywords: Ultrasound-guided nerve block; Anesthesia training; Teaching practice; Standardized resident training; Visualization technology

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1. Introduction

Anesthesiology, as the core support of perioperative medicine, faces rapid technological iteration, making practitioners feel urgent. In the past five years, the transformation of ultrasound-guided nerve block technology from “experience art” to “precision science” has become an irreversible trend ^[1]. The traditional blind method, which relies on body surface anatomical landmarks and paresthesia localization, is gradually being replaced by visualization technology because of the high failure rate of puncture and the high risk of neurovascular injury ^[2]. The emergence of ultrasound-guided technology has transformed this operation,

which relies on the “art of experience”, into a visual, accurate, and repeatable “scientific operation”, which has been praised by the industry as a major upgrade of anesthesia technology ^[3]. From 2020 to 2024, the National Health Commission continued to promote the improvement of the quality of standardized resident training, and the skill training of anesthesiologists is facing higher requirements. How to systematically implant ultrasound-guided technology into the teaching chain has become an urgent issue for training bases ^[4]. The purpose of this study is to verify the actual effect of ultrasound-guided nerve block integrated into the training system through comparative teaching, and to provide an evidence-based basis for the optimization of anesthesia teaching mode.

2. Data and methods

2.1. General information

In this study, from January 2020 to December 2024, a total of 80 postgraduates and trainees who were receiving standardized training in the Department of Anesthesiology of our hospital were enrolled, and they were divided into the control group and the observation group by means of the random number table method, with 40 trainees in each group. There were 15 male students and 25 female students in the control group, ranging from 19 to 23 years old, with an average of (22.05 ± 1.17) years old. There were 17 males and 23 females in the observation group, ranging from 19 to 23 years old, with an average of (21.72 ± 1.35) years old. The general data of the two groups were balanced and comparable ($P > 0.05$).

Inclusion criteria: (1) Those who had obtained the qualification of medical practitioners or were in the second year or above of training; (2) Those who signed the informed consent and voluntarily participated in the study; (3) The attendance rate during the training period shall not be less than 90%.

Exclusion criteria: (1) those who did not complete the basic anesthesia rotation in the first year of regular training; (2) those who had more than 30 cases of previous experience in ultrasound operation; (3) those who withdrew for more than 2 weeks during the training period.

2.2. Method

In the control group, the traditional teaching mode was adopted, with the body surface anatomical landmark positioning method as the main line, the teacher taught the blind puncture operation through demonstration, and the students practiced repeatedly on the simulation model to find “abnormal sensation”, the theory course was mainly taught by classical anatomical atlas, and the clinical observation was arranged every two weeks, without involving the systematic training of ultrasound equipment.

Observation group: The trinity teaching system of “model training-theoretical teaching-real person practice” was implemented. In the first stage (the first three months), the puncture training of six common blocking paths, such as interscalene brachial plexus, femoral nerve and sciatic nerve, was completed on the ultrasound simulation model. The trainees were required to complete the needle insertion under the ultrasound in-plane imaging technology, and the teacher corrected the needle insertion angle and depth in real time. In the second stage (4 to 9 months), combined with the flipped classroom mode, the theory preview was completed through online video before class, and the clinical cases were analyzed in the form of group discussion, focusing on the identification points of nerves, blood vessels, and fascia in ultrasound images, and the practical examination was organized weekly. In the third stage (10 to 18 months), under the supervision of the instructor, the real-person ultrasound-guided nerve block operation was completed, from

various approaches of TAP (transversus abdominis plane block) to paravertebral block step by step. After each operation, the patient was reviewed and summarized. At the same time, the patient participated in daily VPU (virtual pain ward) rounds, and the ERAS (accelerated rehabilitation surgery) concept was run through the whole process.

2.3. Observation index

- (1) Examination results of operation skills: With the help of a unified standardized scoring table, three physicians with the title of associate senior or above carried out blind scoring, with a total score of 100 points, covering puncture accuracy (30 points), drug diffusion observation ability (25 points), aseptic operation standardization (25 points), and emergency handling ability (20 points). A score of ≥ 85 is judged as excellent, a score of 60 to 84 is judged as qualified, and a score of < 60 is judged as unqualified.
- (2) Complication identification accuracy: self-compiled situational test papers covering 12 common complications such as nerve injury, vascular puncture by mistake, local anesthetic poisoning, pneumothorax, etc., with 5 points for a single question, a total of 60 points, and a score ≥ 48 points as a standard.
- (3) Success rate of the first puncture: The proportion of the first needle reaching the target nerve was recorded in the real clinical operation, and the position of the needle tip was confirmed by ultrasound image as the gold standard.

2.4. Statistical analysis

The data involved in this study were processed by SPSS 23.0 software. The data of χ^2 and t tests were count and measurement data, and the count and measurement data were also processed by (%) and (Mean \pm SD) means. When the difference meets the statistical condition, $P < 0.05$.

3. Results

3.1. Comparison of examination results of operation skills between the two groups

The operation skill examination results of the observation group were better than those of the control group ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of examination results of operation skills between the two groups of trained physicians (Mean \pm SD, minutes)

Group	Number of cases	Puncture accuracy	Drug diffusion observation	Sterile Operation Specification	Emergency handling capability	Total score
Observation group	40	27.35 \pm 1.82	23.10 \pm 1.47	23.80 \pm 1.20	18.65 \pm 1.30	92.90 \pm 4.15
Control group	40	22.40 \pm 2.15	18.75 \pm 1.88	20.30 \pm 1.61	15.20 \pm 1.72	76.65 \pm 5.84
t -value	-	11.282	12.036	10.561	9.726	11.652
P value	-	<0.05	<0.05	<0.05	<0.05	<0.05

3.2. Comparison of complication identification accuracy between the two groups

The accuracy of complication identification in the observation group was higher ($P < 0.05$), as shown in

Table 2.

Table 2. Comparison of complication recognition accuracy between the two groups of training physicians (Mean \pm SD, minutes)

Group	Number of cases	Identification of nerve injury	Vascular mispuncture identification	Identification of local anesthetic poisoning	Identification of pneumothorax	Identification of other complications	Total score
Observation group	40	4.65 \pm 0.48	4.70 \pm 0.45	4.55 \pm 0.50	4.80 \pm 0.40	38.71 \pm 2.11	55.20 \pm 2.85
Control group	40	3.20 \pm 0.72	3.45 \pm 0.68	3.10 \pm 0.82	3.60 \pm 0.65	27.25 \pm 2.93	39.35 \pm 4.73
<i>t</i> -value	-	11.08	10.95	10.12	10.38	16.837	15.247
<i>P</i> value	-	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

3.3. Comparison of the first puncture success rate between the two groups

The success rate of the first puncture in the observation group was higher ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of the success rate of the first puncture between the two groups (cases, %)

Group	Number of cases	Successful first puncture	Failure of the first puncture
Observation group	40	37(92.50)	3(7.50)
Control group	40	27(67.50)	13(32.50)
χ^2 value	-	6.315	6.315
<i>P</i> value	-	<0.05	<0.05

4. Discussion

As the core means of anesthesia and pain medicine, the teaching quality of nerve block technology is directly related to the future clinical competence of trained physicians [5]. The traditional teaching mode has long relied on the experience transmission of “master with apprentice.” In the absence of intuitive image feedback, students can only judge the position of the needle tip by hand feeling and body feeling. This kind of “closed-eye archery” training is not only inefficient, but also buries potential safety hazards [6]. Data from the Mayo Atlas of Regional Anesthesia and Ultrasound-Guided Nerve Blocks have already revealed that although the incidence of serious complications associated with peripheral nerve blocks is only 0.04%, once nerve damage occurs, patients may face months or even permanent dysfunction [7]. However, due to the lack of real-time visualization in the traditional blind puncture method, puncture needle injury and local anesthetic toxicity are recognized as the two main causes of neurological complications, which fundamentally illustrates the necessity of teaching reform [8].

The introduction of ultrasound-guided technology is essentially a paradigm shift from “experience-dependent” to “image-driven” anesthesia operation. High-frequency ultrasound can clearly present the cross-sectional and longitudinal sections of the target nerve, while displaying key structures such as peripheral blood vessels, muscles, and bones. The puncture needle can be seen in the whole process under the ultrasound in-plane imaging technology, and the direction and depth of the needle can be adjusted at any time. The process of drug diffusion can also be observed in real time, which means that the training doctor can establish the operation logic of “what you see is what you get” in the learning stage [9–10]. In this study,

the three-stage progressive mode of “model training-theory teaching-real person practice” adopted by the observation group is based on the mature experience of many training bases in China, such as the virtual pain ward (VPU) management system constructed by the Department of Anesthesia and Perioperative Medicine of Zhengzhou Central Hospital Affiliated to Zhengzhou University. As well as the trinity teaching system of “model training, theory teaching and real person practice”, all confirm the remarkable effect of this mode in shortening the learning curve.

The results showed that the total score of operation skills in the observation group was much higher than that in the control group ($P < 0.05$), especially in the observation ability of drug diffusion, which was closely related to the training characteristics that students could directly see the diffusion of liquid medicine along the nerve sheath under the guidance of ultrasound, which was totally dependent on the traditional teaching. Students are always in the state of “knowing what it is and not knowing why it is”. In terms of complication recognition accuracy, the total score of the observation group was higher than that of the control group ($P < 0.05$), which reflected that the visualization training allowed the trained doctors to repeatedly witness the ultrasound manifestations of dangerous scenes such as blood vessel puncture and nerve injury in the simulation stage, and formed a profound visual memory. The comparison of the success rate of the first puncture between 92.50% and 67.50% has put the teaching effect on the most clinically significant endpoint index.

It is worth noting that ultrasound-guided teaching is not a simple superposition of technology, but the deep penetration of the ERAS concept in anesthesia teaching. The students in the observation group participated in the individualized adjustment of the analgesia program in VPU rounds, and communicated directly with patients in daily education. These experiences make them grow from simple “operators” to “decision-makers” of perioperative pain management, which is the core goal of modern anesthesia training. Of course, the sample size of this study is limited, and it is a single-center study, which still needs to be further verified by multi-center large sample data in the future, but it is certain that ultrasound-guided nerve block technology is no longer an “elective course” in anesthesia teaching, but a “compulsory course” that every trained physician must master.

5. Conclusion

To sum up, the integration of ultrasound-guided nerve block technology into the training teaching system can effectively improve the operation accuracy and safety awareness of training physicians, which is worthy of vigorous promotion and application in anesthesia teaching.

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Disclosure statement

The authors declare no conflict of interest.

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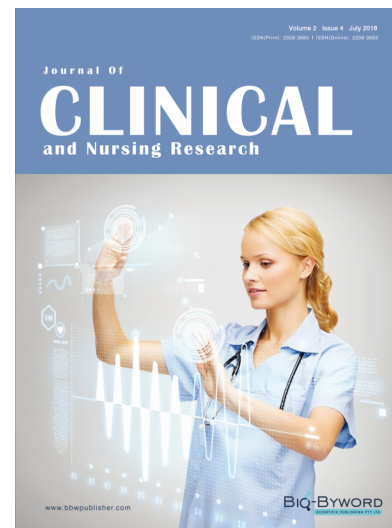
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