# <u>Original Research</u>

# Assessing the Clinical Efficacy of Stereotactic Puncture in Combination with Postoperative Rehabilitation Training for Hypertensive Cerebral Hemorrhage

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## ABSTRACT

**Objective** • This study aims to investigate the clinical efficacy of stereotactic puncture for intracerebral hematoma removal, combined with postoperative individualized health education and rehabilitation training concerning hypertensive cerebral hemorrhage. We also assessed its impact on rebleeding prevention and neurological function recovery.

**Methods** • A retrospective study was conducted, including 90 patients diagnosed with hypertensive cerebral hemorrhage in our hospital between March 2020 and June 2022. The inclusion criteria were patients with an episcleral hematoma volume exceeding 30 ml. The control group underwent minimally invasive removal using neuroendoscopy (45 patients), while the observation group received stereotactic puncture for intracerebral hematoma removal (45 patients). After surgery, both groups received individualized health education and rehabilitation training. The assessment included: (1) determination of clinical efficacy, (2) monitoring for rebleeding within 72 hours after surgery, (3) evaluation of daily living ability using the Barthel index, (4) assessment

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#### INTRODUCTION

Hypertensive intracerebral hemorrhage (HICH) constitutes over 70% of all spontaneous cerebral hemorrhages in humans, making it a prevalent and critical condition frequently encountered in emergency departments.<sup>1</sup> The onset of hypertensive cerebral hemorrhage is marked by its rapidity. Patients present with critical symptoms, and treatment is challenging due to the brain's complex structure and dense vascular network. Tragically, those cases often result in fatal

of motor function using the Fugl-Meyer Assessment (FMA) scale, and (5) monitoring for adverse reactions.

**Results** • The observation group, which underwent stereotactic puncture for intracerebral hematoma removal combined with postoperative individualized health education and rehabilitation training, exhibited significantly better clinical efficacy, Barthel index scores, and FMA scores compared to the control group that underwent neuroendoscopic minimally invasive removal (P < .05). Notably, no complications were observed in either group, and there was no significant difference in the postoperative bleeding rate within 72 hours.

**Conclusions** • The combined treatment approach of stereotactic puncture for intracerebral hematoma removal and postoperative individualized health education and rehabilitation training demonstrates promising therapeutic effects in managing hypertensive cerebral hemorrhage. This approach also contributes significantly to the rehabilitation of patients with hypertensive cerebral hemorrhage, warranting widespread clinical adoption. (*Altern Ther Health Med.* 2024;30(6):122-127).

cerebral hemorrhages. Even in cases of survival, patients commonly experience severe complications, significantly diminishing their expected quality of life with disabilities.<sup>2</sup>

Failure to detect and promptly treat the disease during its early stages leads to more than half of the deaths at this phase. Even in cases where the disease is diagnosed at a later stage, the consequences remain profound.<sup>3</sup> The prognosis of patients remains poor despite active treatment, with more than 50% achieving complete recovery.<sup>2</sup> The literature indicates a substantial impact of hypertensive cerebral hemorrhage on mortality, contributing to approximately 20% to 50% of all deaths related to hemorrhagic diseases.<sup>1-2</sup>

The morbidity and mortality rates are significantly elevated during the first 30 days after the onset, ranging from 33% to 50%.<sup>3</sup> The most common long-term consequences of hypertensive cerebral hemorrhage encompass hemiplegia and aphasia.<sup>4</sup> Notably, only about 30% of patients demonstrate

the capability to independently manage their daily activities 90 days after the disease is diagnosed.<sup>3-4</sup>

Current treatment options for HICH are categorized into medical and surgical approaches. Medical treatment encompasses blood pressure regulation, intracranial pressure management, and hemostasis. On the other hand, surgical interventions are classified into various techniques such as large bone flap craniotomy, small bone window craniotomy, stereotactic hematoma drainage, neuro-endoscopic intracranial hematoma removal, and minimally invasive surgery with navigation assistance.<sup>1-3</sup>

Recent studies have indicated that large bone flap craniotomy is associated with a substantial incision, lengthy operation time, significant intraoperative bleeding, greater damage to the patient's surrounding brain tissue, and a higher likelihood of postoperative complications. This approach may not be helpful to patient recovery. Conversely, small bone window craniotomy may not be suitable for patients with severe cerebral edema.<sup>4,5</sup>

Traditional open hematoma removal surgery is highly traumatic, often leading to many surgical complications. Furthermore, it can aggravate brain tissue edema and cause damage while removing the hematoma. In contrast, minimally invasive surgery offers a less invasive approach characterized by a shorter operating time, rapid hematoma removal, minimal systemic and brain tissue damage, and substantial advantages in treating cerebral hemorrhage.<sup>5</sup>

Minimally invasive surgery encompasses various techniques, such as minimally invasive hematoma puncture, stereotactic drainage, microsurgical techniques, and endoscopic procedures. The crucial factor in protecting patient safety and diminishing disability rates is carefully selecting the appropriate surgical method.<sup>6</sup>

Hypertensive cerebral hemorrhage presents a significant concern in many countries, capturing the attention of various segments of society. Despite global efforts to intervene and manage hypertensive cerebral hemorrhage, the severe consequences of this condition remain challenging to mitigate completely. It is imperative to implement proactive prevention measures, rational health education, and policy initiatives to effectively control and gradually reduce the impact of hypertensive cerebral hemorrhage.

This study assessed the clinical efficacy of combined treatments for hypertensive cerebral hemorrhage. It aimed to provide insights into the effectiveness of different approaches, aiding in better treatment decisions and potentially improving patient outcomes.

# METHODS

#### Study Design

The clinical data of patients treated for hypertensive cerebral hemorrhage via neurosurgical procedures at the Ninth People's Hospital of Hangzhou from March 2020 to June 2022 were retrospectively analyzed. Based on the surgical method, the patients were categorized into either a control group or an observation group.

#### Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) a documented history of hypertension with confirmation of cerebral hemorrhage via cranial CT examination; (2) age under 75 years; (3) initiation of treatment within 48 hours of symptom onset; (4) provision of informed consent.

Exclusion criteria were as follows: (1) abnormal cardiopulmonary function; (2) coagulation dysfunction; (3) bleeding tendencies; (4) any relevant treatment that could influence the study. Finally, 90 participants were enrolled following these criteria, with 45 individuals in each group.

## Control Group Surgical Procedure: Minimally Invasive Neuro-Endoscopic Debulking

The control group underwent a minimally invasive neuro-endoscopic debulking procedure. Initially, the hematoma was identified via cranial CT, and after determining its location, volume, central distance, and angle, the center point was marked. After these measurements, a 1 cm bone hole was drilled in the skull using an electric drill. Subsequently, a puncture cannula was inserted to establish a surgical channel, and the hematoma was removed with the assistance of neuroendoscopy.

#### **Observation Group: Stereotactic Puncture Surgery**

A stereotactic puncture was performed in the observation group to remove the intracerebral hematoma. This procedure involved several key steps.

**Stereotactic Head Frame Installation.** Installing the stereotactic head frame in the observation group began with the administration of local anesthesia. Subsequently, CT data was integrated into the computerized surgical planning system. Additionally, manual calculations were performed following a comprehensive review of the head CT to precisely determine the frame coordinates corresponding to the predefined target point.

**Arch Frame Installation.** The arch frame was installed in the operating room, and sterile towels were routinely disinfected.

**Puncture Procedure.** The optimal entry trajectory was established based on the target point, with the cranial cone penetrating the scalp, skull, and dura mater. A puncture needle was introduced to aspirate 1/2-1/3 of the hematoma.

Hematoma Treatment and Drainage. The hematoma cavity was infused with 30 000 units of urokinase, and a fine silicone drainage tube was inserted and securely positioned. During the puncture, care was taken to avoid cortical vessels and vital functional areas. The presence of any residual hematoma was assessed by considering drainage flow and CT review results. The drainage tube was removed once no residual hematoma was detected.

#### **Rehabilitation Training Procedure**

After surgery, patients received individualized health education and rehabilitation training, encompassing tailored exercise instructions, including limb positioning, passive massage, and active exercises. Limb Positioning. In the first stage, limb positioning was emphasized, involving the following key points: (1) When the patient assumed a supine position, a soft pillow was placed under the affected-side upper limb, supporting it under the scapula to maintain an extended position. The elbow and wrist were extended, with the palm facing upward. A similar soft pillow was positioned at the waist and hip of the affected lower limb, internally rotating the hip joint and slightly bending the legs. (2) For patients lying on their healthy side, adequate support was provided to the upper extremity on the affected side, ensuring the extension of the scapula, elbow, and wrist while keeping the palm facing the healthy side. Simultaneously, the lower extremity on the healthy side was positioned behind the affected side of the lower limb.

Massage and Passive Movements. The second stage involves massage and passive movements. The healthcare provider administers a gentle massage to the hemiplegic patient, adhering to slow and gentle techniques. It includes kneading and gently pressing the paralyzed muscles while soothing and massaging the antagonistic muscles to induce relaxation.

Once the patient's vital signs have gradually stabilized, the healthcare worker guides the patient's family in performing passive exercises for the knee, hip, elbow, and shoulder joints. Passive exercises should be executed gradually and at a moderate pace, with a frequency of two to three times a day, each session lasting no more than half an hour.

Active Movement. The third stage involves active movement exercises, focusing on transitioning from passive to active movements. This stage includes a range of exercises: (1) Bed-assisted exercises: Patients begin with bed-assisted exercises, which encompass lower limb and upper limb functional training. (2) Sitting position exercises: once the muscle strength of the affected limb meets the required standards, patients progress to a sitting position. In this phase, they performed self-assisted exercises in bed to prepare for future activities.

(3) Trunk pitching and lateral flexion: patients supported by family members were encouraged to gradually perform trunk and lateral flexion exercises. These exercises were designed to restore balance function and enhance upper limb coordination. (4) Standing exercises: as the muscle strength of the affected lower limb improved, standing exercises were initiated. These exercises began with bed-supported standing exercises, where patients placed their hands on the bed for support, focusing on balance and coordination. This phase was characterized by gradual and sustained progress. (5) Walk training: Patients progressed to walk training, starting within parallel bars, with healthcare professionals and family members providing appropriate support. As the patient gained confidence and stability over time, the level of support was gradually reduced.

# **Outcome Indicators**

Assessment of Clinical Efficacy. (1) Significant effect: this category indicates cases where the intracerebral hematoma was completely cleared, the patient achieved full self-care capability, and neurological function showed substantial recovery; (2) Effective: this category refers to cases where the intracerebral hematoma was successfully cleared, the patient regained self-care abilities, and neurological function demonstrated recovery; (3) Ineffective: this category denotes cases where the intracerebral hematoma remained uncleared, the patient was unable to resume selfcare, and neurological function remained impaired.

Total Effective Rate. The total effective rate was calculated to provide a comprehensive measure of treatment outcomes in this study using the formula: (Number of significant effect cases + Number of effective cases) / Total cases  $\times$  100%.

**Postoperative Rebleeding.** Postoperative rebleeding was recorded, indicating any instances of rebleeding within 72 hours following surgery.

**Evaluation of Daily Living Ability.** The Barthel index score was used to evaluate daily living ability before and after the intervention. A higher score indicated better independence and more effective rehabilitation intervention.

**Evaluation of Motor Function.** The Fugl-Meyer (FMA) scale score was employed to assess motor function before and after the intervention.

Adverse Reactions. All instances of adverse reactions were carefully recorded and subjected to thorough analysis to assess their impact. These events included any unexpected or unwanted side effects, complications related to the surgery or treatment, allergic reactions, infections, changes in vital signs, or any other health-related concerns. This careful documentation and analysis contribute to a more thorough understanding of potential disadvantages associated with the treatment approach.

#### **Statistical Analysis**

**Sample Size Estimation.** We calculated the required sample size using a two-sided test with  $\alpha = 0.05$  and  $\beta = 0.1$ . The incidence rate P1=10% for the test group sample and P2=25% for the control group sample were considered.

$$n_{1} = n_{2} = 1641.6 \left( \frac{U_{\alpha} + U_{2\beta}}{\sin^{-1}\sqrt{P_{1}} - \sin^{-1}\sqrt{P_{2}}} \right)^{2}$$

The sample size for each study group was provisionally set at 45 cases.

**Randomized Allocation.** Random allocation was achieved using the PEMS 3.1 for Windows "Completely Randomized (Two and Multiple Group) Design Program." This program generated random numbers for a total of 90 subjects, divided into 2 treatment groups, with an equal number of cases in each group. Patients who met the inclusion criteria were assigned to the treatment or control group based on the enrollment order.

**Data Analysis.** The experimental data were analyzed using SPSS 22.0. Measurement data conformed to a normal distribution were presented as mean  $\pm$  standard deviation

**Table 1.** Comparison of Clinical Efficacy Between TwoGroups of Patients [Cases (%)]

| Groups      | n  | Significant Effect (%) | Effective (%) | Ineffective (%) | Total Efficiency Rate (%) |
|-------------|----|------------------------|---------------|-----------------|---------------------------|
| Control     | 45 | 2(4.44)                | 39(86.67)     | 4(8.89)         | 41 (91.1)                 |
| Observation | 45 | 19(42.22)              | 26(57.78)     | 0(0.0)          | 45(100.0) <sup>a</sup>    |
| $x^2$       |    |                        |               |                 | 4.19                      |
| P value     |    |                        |               |                 | .041                      |

<sup>a</sup>Comparison with the control group (P < .05)

#### Table 2. Barthel Index of Patients In Both Groups

| Groups           | Pre-Treatment | Post-Treatment | t     | P value            |
|------------------|---------------|----------------|-------|--------------------|
| Control (45)     | 22.89±16.46   | 60.11±23.12    | 20.42 | <.001 <sup>b</sup> |
| Observation (45) | 22.67±16.97   | 68.78±12.80    | 36.02 | <.001°             |
| t                | 0.06          | 2.20           |       |                    |
| P value          | .95           | .01ª           |       |                    |

<sup>a</sup>Statistically significant difference compared with the control group (P < .05) <sup>b</sup>The statistically significant difference compared with the control group before and after treatment (P < .05);

<sup>c</sup>The statistically significant difference compared with the two groups before and after treatment in the observation group (P < .05).

#### Table 3. FMA Scale For Both Groups of Patients

| Groups           | Pre-Treatment | Post-Treatment | t     | P value            |  |
|------------------|---------------|----------------|-------|--------------------|--|
| Control (45)     | 14.58±16.45   | 58.38±25.65    | 15.97 | <.001 <sup>b</sup> |  |
| Observation (45) | 14.33±12.91   | 68.96±10.86    | 31.80 | <.001°             |  |
| t                | 0.078         | 2.548          |       |                    |  |
| P value          | .94           | <.001ª         |       |                    |  |

<sup>a</sup>Statistically significant difference compared with the control group (P < .05) <sup>b</sup>The statistically significant difference compared with the control group before and after treatment (P < .05)

<sup>c</sup>The statistically significant difference compared with the two groups before and after treatment in the observation group (P < .05)

**Table 4.** Rate of Rebleeding Within 72 h After Surgery in

 Both Groups

| Groups      | n  | Post-Operative Rebleeding (%) |
|-------------|----|-------------------------------|
| Control     | 45 | 1(2.22)                       |
| Observation | 45 | 0 (0.00)                      |
| $\chi^2$    |    | 1.01                          |
| P value     |    | .315                          |

Note: There was no statistically significant difference between the two groups (P > .05).

 $(\overline{x \pm s})$ . The two groups were compared using an independent sample *t* test, and the results were expressed as cases or rates. The  $\chi^2$  test was employed for comparing two groups, and for multiple group comparisons, the Kruskal-Wallis's rank sum test was applied. A significance level of *P* < .05 was considered statistically significant.

#### RESULTS

#### **Comparison of Clinical Efficacy**

In the observation group, 19 cases demonstrated a significant effect, whereas the control group had only 2 such cases. The observation group had 0 invalid cases, while the control group had 4. The total effective rate in the control group was 91.1%, notably lower than the 100% rate observed in the observation group. This difference in efficacy between the two groups was statistically significant (P < .05). Based on the evaluation of the patient's neurological function and self-care abilities (refer to Table 1), we conclude that the group

employing stereotactic puncture intracerebral hematoma removal exhibited superior efficacy compared to the group utilizing minimally invasive neuro-endoscopic removal.

# **Barthel Index Before and After Treatment**

Both groups showed significantly higher Barthel index scores after treatment than before, with statistically significant differences (P < .05). Furthermore, the group that underwent stereotactic puncture for intracerebral hematoma removal demonstrated significantly higher Barthel index scores compared to the group that underwent neuro-endoscopic minimally invasive removal. Post-treatment Barthel index scores in the two groups exhibited statistical differences (P < .05).

Based on the assessment of the patient's ability to perform daily living activities, as reflected by the Barthel index scores (refer to Table 2), we conclude that the stereotactic puncture intracerebral hematoma removal group achieved higher scores than the neuro-endoscopic minimally invasive removal group. It implies better independence and more effective rehabilitation interventions.

#### **Operational Function Score Before and After Treatment**

After treatment, the Fugl-Meyer (FMA) scale scores for both groups exhibited a significant increase compared to scores before treatment, with all showing statistical differences. Notably, the scores of the observation group were significantly higher than those of the control group. When comparing the post-treatment FMA scale scores between the two groups, these differences remained statistically significant (P < .05).

Therefore, we conclude that the motor function of the group undergoing stereotactic puncture for intracerebral hematoma removal surpasses that of the group undergoing neuro-endoscopic minimally invasive removal, as indicated by FMA scale scores for motor function; refer to Table 3.

#### **Comparison of Postoperative Rebleeding**

In the control group undergoing minimally invasive neuro-endoscopic debridement, one patient (2.22%) experienced postoperative rebleeding. However, in the observation group undergoing stereotactic puncture for intracerebral hematoma debridement, there were no instances of postoperative rebleeding. Notably, there was no statistically significant difference in the incidence of postoperative rebleeding between the two groups (P > .05), refer to Table 4.

#### DISCUSSION

HICH is a critical medical condition resulting from the complications of chronic hypertension. It occurs when persistently high blood pressure leads to weakened arteries in the brain, ultimately resulting in spontaneous bleeding within the brain tissue.<sup>7</sup> HICH is a prevalent subtype of intracranial hemorrhage, accounting for a substantial portion of these cases and carrying a heavy burden of morbidity and mortality.<sup>7-8</sup> Survivors often struggle with varying degrees of disability, posing challenges for individuals, families, and healthcare systems.

Hypertensive cerebral hemorrhage is responsible for approximately 50%-70% of all cases of spontaneous intracranial hemorrhage, making it the most prevalent type of such hemorrhage. It is noteworthy that over 30% of individuals who survive hypertensive cerebral hemorrhage must contend with varying degrees of disability, leading to a substantial economic burden on both families and society.<sup>8</sup>

In the early stages of the disease, prompt removal of intracranial hematoma is essential to mitigate cerebral edema and stabilize intracranial pressure. This proactive approach can effectively minimize neuronal damage, lower patient mortality rates, and enhance overall patient survival prospects.<sup>9,10</sup> Consequently, the quest for safer and more efficient techniques, whether novel or combined, remains a pressing challenge for physicians engaged in relevant research.

Stereotactic hematoma drainage involves the precise placement of a catheter under image guidance into the hematoma. This catheter allows for the aspiration of blood, and it remains in place within the hematoma. Through this catheter, small doses of thrombolytic agents are intermittently administered to the brain, facilitating the gradual removal of the residual hematoma.<sup>11</sup> In contrast to endoscopic aspiration, which results in a rapid reduction of hematoma volume, stereotactic aspiration is a more gradual process of volume reduction.

Postoperative rehabilitation plays a pivotal role in the treatment of hypertensive cerebral hemorrhage patients. Supported by evidence-based medicine, effective rehabilitation has been shown to reduce the disability rate in these patients, elevate patient satisfaction, expedite the rehabilitation process, curtail medical expenses, and conserve valuable social resources.<sup>12-13</sup> The core of this rehabilitation approach is individualized exercise, which is a patient-driven process consisting of a personalized regimen of both active and passive physical exercises. The primary objective of these exercises is to restore patients' ability for daily life activities and active participation in society.<sup>12-14</sup>

Our research revealed that, among patients with hypertensive cerebral hemorrhage, those who underwent stereotactic puncture combined with postoperative rehabilitation experienced significantly greater clinical effectiveness compared to those who underwent minimally invasive neuro-endoscopic debridement. The clinical outcomes observed in patients treated with stereotactic hematoma drainage in our study align with findings reported in earlier studies.<sup>15</sup>

In this study, both the Barthel index and FMA scores showed significant improvements before and after treatment in patients who received combined treatment with minimally invasive neuro-endoscopic debridement. Notably, no complications were observed in either group, and there was no significant difference in the rate of postoperative bleeding within 72 hours between the two groups.

Previous studies have suggested that patients with hypertensive cerebral hemorrhage treated with stereotactic hematoma drainage had a significantly better prognosis compared to those undergoing open hematoma removal.<sup>16</sup> Moreover, these studies found no significant difference in the quality of life among patients with hypertensive cerebral hemorrhage,<sup>17</sup> and there was also no substantial improvement in the quality of life when comparing early surgery to conservative treatment.<sup>18</sup>

Consistent with findings from previous studies, the use of stereotactic puncture for intracerebral hematoma removal in patients with hypertensive cerebral hemorrhage has proven to be effective in enhancing the recovery of neurological function post-surgery.<sup>19</sup> Improved neurological recovery can significantly alleviate the burden of therapeutic care throughout the rehabilitation process, expedite the recovery timeline, and reduce the duration of hospitalization.

These findings suggest that the combination of stereotactic puncture intracerebral hematoma removal with postoperative individualized health education and rehabilitation training is highly effective in the treatment of hypertensive cerebral hemorrhage and contributes to the recovery of patients with this condition. Several factors may account for the significantly improved clinical outcomes in HICH patients who undergo stereotactic puncture combined with individualized rehabilitation training after surgery.

Stereotactic puncture is a minimally invasive surgical technique that enables precise guidance of surgical instruments into the intracranial space for the accurate removal of hematoma. When compared to minimally invasive neuroendoscopic clearance, stereotactic puncture offers superior surgical accuracy and control, allowing for maximum hematoma removal while minimizing the impact on surrounding healthy tissue. Individual rehabilitation training after surgery involves a customized plan tailored to each patient's unique circumstances.

Individual rehabilitation training can be customized to address specific needs such as physical therapy, speech rehabilitation, cognitive training, and more based on the patient's neurological damage. This tailored rehabilitation approach maximizes nerve recovery and functional reconstruction, ultimately enhancing the patient's quality of life. Combining stereotactic puncture with individualized postoperative rehabilitation training offers a comprehensive treatment strategy that can address various stages of cerebral hemorrhage simultaneously.

Surgical removal of hematoma mitigates nerve damage, while rehabilitation training fosters functional recovery and neuroplastic development. This comprehensive treatment approach significantly enhances clinical outcomes. Early individualized health education and rehabilitation training following stereotactic puncture for intracerebral hematoma removal can minimize central nerve damage, positively impact nerve cell repair, and contribute to improved central nerve function through functional training. It further promotes neuroplasticity and the recovery of lost functions in patients with cerebral hemorrhage.

Studies have indicated that stereotactic puncture for intracerebral hematoma removal might expedite neurological

recovery in a subset of hypertensive cerebral hemorrhage patients by lowering levels of serum soluble interleukin 2 receptor (sIL-2R) and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL).<sup>20</sup> However, the exact molecular mechanism of this effect requires further comprehensive investigation and confirmation, primarily due to the difficulties in collecting data on inflammatory factors, oxidative stress markers, and neuro-factor-related indicators both before and after treatment in patients.

#### **Study Limitations**

This study presents a few limitations that warrant consideration. Firstly, the extended treatment duration, limited sample size, and relatively short follow-up period for patients with hypertensive cerebral hemorrhage may restrict the generalizability of our findings. To address these limitations and ensure the robustness of our conclusions, further research involving larger sample sizes and more extended, long-term clinical trials is essential. Such studies would provide more comprehensive insights into the effectiveness and safety of the therapeutic approaches assessed in this research, allowing for more robust and reliable recommendations for clinical practice.

#### CONCLUSION

In conclusion, our study demonstrates that the utilization of stereotactic puncture intracerebral hematoma removal, coupled with postoperative individualized exercise therapy, yields substantial benefits for patients afflicted with hypertensive cerebral hemorrhagic disease. This comprehensive treatment approach substantially enhances treatment outcomes, promotes neurological function recovery, and elevates patients' overall quality of life. The findings from this research not only offer a solid scientific foundation for the targeted management of hypertensive cerebral hemorrhage but also bear considerable practical significance. By highlighting the efficacy of this treatment strategy, our study provides valuable insights that can guide clinicians in delivering more effective care to patients with this challenging condition, ultimately improving their prognosis and well-being.

#### CONFLICT OF INTEREST

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

#### AUTHORS' CONTRIBUTIONS

 $QX \mbox{ and } LZ \mbox{ designed the study and performed the experiments, XZ collected the data, YD analyzed the data, and <math display="inline">QX \mbox{ and } LZ \mbox{ prepared the manuscript.}$  All authors read and approved the final manuscript.

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#### ETHICAL COMPLIANCE

This study was approved by the ethics committee of Hangzhou Ninth People's Hospital.

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