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Comparison of strategies based on DTI visualisation for stereotactic minimally invasive surgery in the treatment of moderate-volume thalamo-basal ganglia cerebral haemorrhage: a protocol for a multicenter prospective study

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Abstract

Introduction Hypertensive intracerebral hemorrhage (HICH) is a condition associated with significant morbidity, mortality, and disability, particularly among the elderly population. The management of moderate thalamic-basal ganglia cerebral hemorrhage primarily relies on conservative approaches. Nevertheless, the rate of long-term disability remains high. In recent years, there has been significant advancement in minimally invasive surgery and diffusion tensor imaging techniques. Consequently, the utilization of Diffusion Tensor Imaging (DTI) technology in patients with cerebral haemorrhage allows for the identification of the haematoma's location in relation to the Corticospinal Tract (CST). This enables the development of precise puncture pathways that can be visualized, thereby avoiding any potential damage to the CST.

Methods and analysis Diffusion Tensor Imaging (DTI) is a method used to assess the structural and physiological characteristics of biological tissue by examining the diffusion behavior of water molecules.In the central nervous system, limb paralysis will be inevitable if the corticospinal tract is damaged. By employing DTI imaging techniques on individuals, it becomes possible to visualize the spatial relationship between the hematoma and the CST. This approach allows avoidance of the CST during preoperative planning of the puncture path, thus reducing secondary injuries caused by the procedure. The primary objective of this study was to assess the ability of patients in the

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minimally invasive surgery group and the conservative group to perform activities of daily living after 6 months of treatment. In addition, secondary outcomes included assessment of hematoma resorption/clearance ratios, cytokine levels, complication rates, and therapeutic indexes at different treatment durations, as well as long-term safety and efficacy at 2–3 years of follow-up. Furthermore, subgroup analysis, and sensitivity analysis were conducted to further analyze the data. Logistic single-variate and multivariate regression analyses were applied to understand the adverse factors affecting prognosis.

Ethics and dissemination The clinical study was reviewed and approved by the Ethics Committee of the First People's Hospital of Yibin. The ethical number is: 2023 Review (64).

Registration number This protocol is registered in the Prospective Registry of Chinese Clinical Trial Registries (PROCCTR). The full date of first registration is 28/12/2023. The registration number for PROCCTR is ChiCTR2300079252.

Keywords Stereotactic technique, Diffusion ensor imaging(DTI), Moderate cerebral haemorrhage, Thalamus-basal ganglia, Randomised controlled trial, Prospective multicentre

Introduction

Hypertensive intracerebral hemorrhage (HICH) is a medical condition characterized by elevated rates of morbidity and mortality, as well as the manifestation of disability [1]. HICH constitutes approximately 20% of the nearly 20 million new stroke cases documented globally each year, with the majority of intracerebral hemorrhage occurrences concentrated in low- and middle-income countries [2]. Consequently, the effective management of cerebral hemorrhage remains a substantial challenge for the global population. A recent study conducted in 2021, utilizing global burden of disease data, revealed a significant decrease in age-standardized incidence rates (9.3%, 95% CI: 3.3-15.5%) and age-standardized mortality rates (39.8%, 95% CI: 28.6-50.7%) from 1990 to 2019. However, contrasting findings from other studies have suggested a plateau or even an upward trend in stroke incidence and mortality rates in China [3, 4]. Consequently, the management of cerebral hemorrhage remains a significant challenge for the global population.

The thalamo-basal ganglia region is frequently identified as the primary location for hypertensive cerebral hemorrhage. Notably, patients with hemorrhage in the thalamo-basal ganglia region exhibit a higher prevalence of severe neurologic deficits, even after receiving comprehensive treatment, in comparison to those with hemorrhage in other regions.This phenomenon has a substantial impact on the professional and personal lives of individuals affected by cerebral hemorrhage, presenting a contemporary challenge in the realm of cerebral hemorrhage treatment and research [4]. This is primarily attributed to the hematoma's location, which is surrounded by vital nerve nuclei and fiber tracts, rendering conventional surgery a potential source of secondary injury and lasting neurological impairments. Hence, when managing patients experiencing mild to moderate levels of hemorrhage, healthcare professionals, along with conscious patients and their families, may opt for conservative treatment as the primary approach [5, 6]. Although conservative drug therapy has been observed to partially aid in the absorption of hematoma, prolonged therapy and the hemotoxic consequences of liquefied hematoma could potentially exacerbate cerebral edema [7]. In severe instances, brain herniation or life-threatening complications may arise.

The International Surgical Trial in Intracerebral Hemorrhage (STICH) has established that early surgical intervention does not confer a substantial benefit compared to initial conservative management. Furthermore, the subsequent STICH II trial has demonstrated that early surgery does not yield a noteworthy reduction in mortality or disability rates at the 6-month post-treatment evaluation [8]. The management of patients presenting with moderate thalamic-basal ganglia cerebral haemorrhage(15-30 ml) primarily relies on conservative treatment. However, given the deep-seated nature of the haematoma and the severe neurological impairments experienced by these patients, significant residual neurological deficits persist even after treatment. Consequently, these patients continue to exhibit a high incidence of long-term disability, significantly compromising their daily functioning and occupational capacity [9, 10]. In recent years, there has been substantial progress in the field of minimally invasive surgery, with extensive literature confirming the safety and efficacy of stereotactic puncture surgery in neurosurgical interventions.Hence, the purpose of this study is to examine the impact of stereotactic minimally invasive puncture and drainage, aided by DTI, on perioperative indicators, haematoma clearance rate, CST damage, serological markers, as well as neurological impairments and daily functioning in individuals diagnosed with moderate-volume thalamus-basal ganglia cerebral haemorrhage. Additionally, a statistical analysis will be conducted comparing these outcomes with patients who received conservative treatment. It provides a basis for finding safer and more effective treatment options for further improvement of patients with moderate-volume thalamus-basal ganglia cerebral haemorrhage.

Objective

Currently, most reports on stereotactic localization techniques for the treatment of HICH have focused on efficacy studies, with few reports on their effects on serum-related factors. The aim of this study was to assign the recruited patients with moderate-volume thalamo-basal ganglia cerebral hemorrhage to either the traditional conservative treatment group or the DTI-assisted stereotactic puncture surgery group through randomized grouping. Various indicators, including hematoma clearance, CST injury, serologic markers, and neurologic impairment, as well as the ability to perform daily life activities, were assessed during the treatment and recovery periods. The rigorous statistical analysis provides a basis for finding treatment options that can more safely and effectively improve the long-term prognosis of patients with cerebral hemorrhage in the moderate-volume thalamic-basal ganglia region.

Methods and analysis

Design

This study will be conducted in accordance with the standards for multicenter clinical studies. The protocol of this study will be reported in accordance with the reporting guidelines for observational studies. The planned start date for this study is March 01, 2024, with an estimated completion date of December 30, 2025.

Registration information

This protocol is registered in the Prospective Registry of Chinese Clinical Trial Registries (PROCCTR). The registration number for PROCCTR is ChiCTR2300079252.

Patient and information source

The main recruits of this study will be hypertensive cerebral hemorrhage patients from West China Hospital of Sichuan University, Affiliated Cancer Hospital of Chongqing University and the First People's Hospital of Yibin City. All subjects will be screened strictly according to the enrollment criteria and will receive treatment with informed consent. Subsequently, the researchers will divide the patients into a surgical group (using DTI-assisted stereotactic minimally invasive puncture and drainage) and a conservative treatment group according to the treatment method they choose. The serum levels of nerve damage-related factors and inflammatory factors will have been assessed in all patients before and after treatment to determine their clinical utility. Subsequently, the study group will compare and analyze the clinical data of the two groups of patients. In addition, univariate and multivariate logistic regression analyses will be used to determine independent prognostic risk factors for patients within and outside the two groups. This comprehensive investigation will potentially provide a frame of reference for improving patient outcomes and prognosis.

Eligibility criteria

The inclusion criteria are as follows: (a) Age 50–80 years old; (b) complete clinical data; (c) meeting the diagnostic criteria in the Chinese Multidisciplinary Diagnostic and Treatment Guidelines for Hypertensive Cerebral Hemorrhage; (d) hematoma volume of 15–30 mL; (e) first-ever onset of disease; (f) all admitted to the hospital within 24 h of onset of disease; (g) Glasgow Coma Scale (GCS) score of 8–15; (h) and normal coagulation function.

Exclusion criteria: (a) combined with cerebral hernia and bilateral pupil dilatation at the time of admission; (b) cerebral hemorrhage caused by trauma, vascular malformation, intracranial aneurysm, tumor, stroke, etc.; (c) combined with a large number of intraventricular hemorrhage and hydrocephalus, which is not suitable for conservative or minimally invasive treatment; (d) combined with heart, liver, lung, and renal insufficiency, hematological system diseases and other serious underlying diseases; (e)Patients with coagulation dysfunction; (f) patients with previous history of brain surgery or trauma; (g) patients with brain death; (h) patients with respiratory failure, dilated pupils and ankylosis of the brain; (i) patients with contraindications to surgery during pregnancy or breastfeeding; (j) patients with expression disorders, poor adherence, or psychiatric disorders; (k) and patients who are transferred to other hospitals in the middle of the day or who have stopped the treatment.

Type of studies

Multi-center randomized controlled trial (The research content and technology flowchart are shown in Fig. 1).

Treatment regimens and controls

Group A conducted CT and DTI scans, saving the resulting data in DICOM format. Subsequently, the data were imported into stereotactic visualization and positioning software, which facilitated the creation of 3D models of the skull, hematoma, and CST after adjusting the image size. This enabled an understanding of the hematoma's boundary, size, and its alignment with the CST. The hematoma volume was calculated using the threshold method, allowing for the formation of the hemorrhage range. Subsequently, the central puncture target was identified at the highest magnitude of the hematoma, while adhering to visualization conditions, to determine the precise location for puncture. The selection of scalp and skull entry points was carefully planned to avoid the corticospinal tract under visualization, and the trajectory,

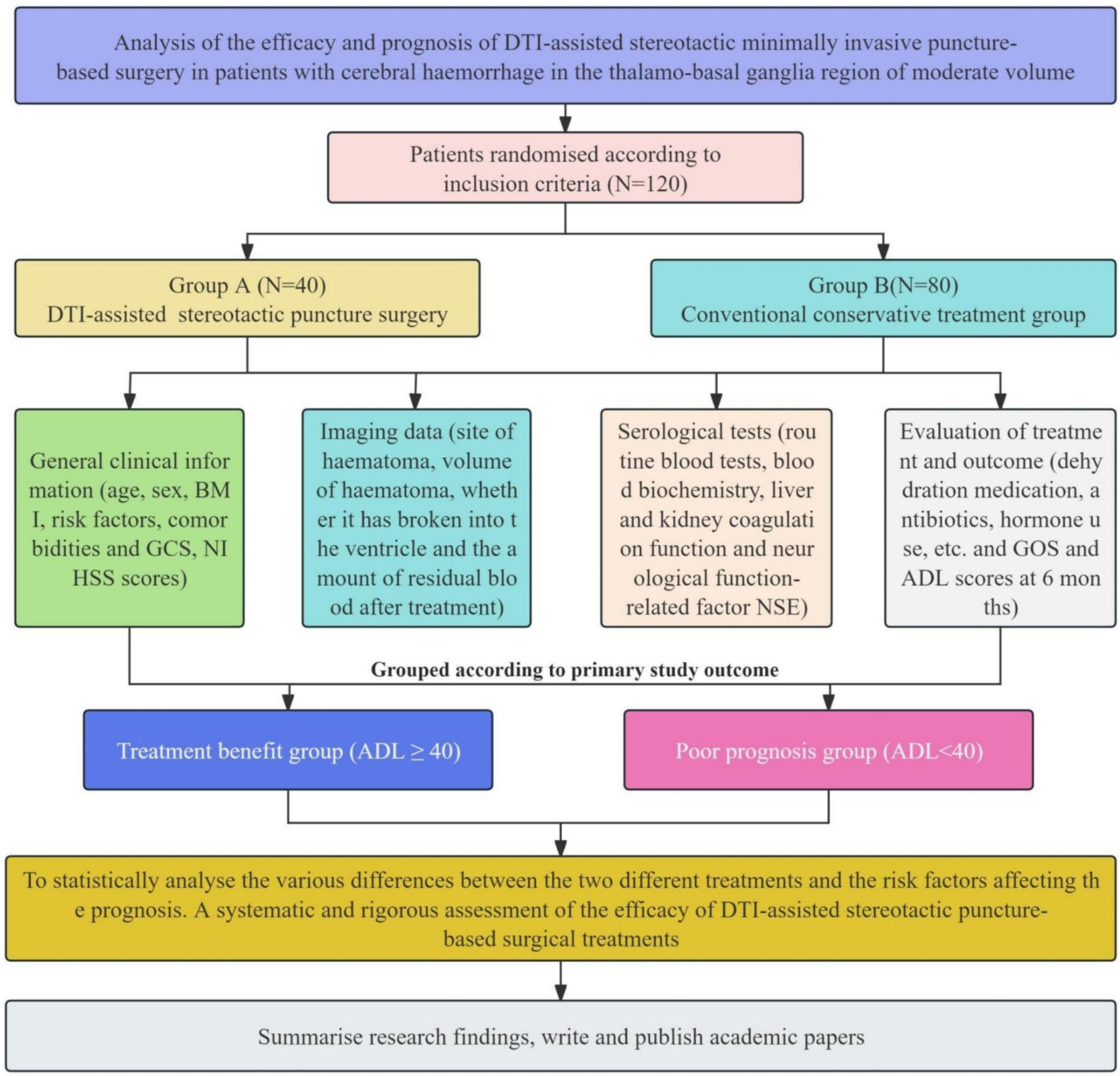

Fig. 1 Research Flowchart

angle, and depth of the puncture were precisely delineated. Once the necessary preparations were completed, the surgical procedure was carried out using stereotactic guidance to accurately identify the posterior scalp projection, followed by a straight incision (3 cm) to access the skull surface after dissecting and separating the scalp. A 5 mm diameter hole was created in the skull, allowing for puncturing of the dura. Subsequently, a brain-piercing needle was carefully inserted to a predetermined depth, ensuring controlled penetration. A drain was then inserted through the cerebral cortex channel, facilitating pulsatile fragmentation suction of the intracranial hematoma. The majority of the hematoma was aspirated based on preoperative calculations of its volume, followed by saline irrigation to address significant resistance. The drain was left in situ and connected to a closed drainage bag.Brain CT review was conducted at 12 h and 3 days postoperatively to determine whether urokinase should be administered to dissolve the remaining hematoma and remove the drainage tube. The decision was based on the software-calculated residual hematoma in the brain. In accordance with the technical protocol, data collection and relevant serological tests were performed, including assessments of neurological function-related factors such as NSE, S100β protein, Nogo-A, and inflammatory factor NF -kB p65. Subsequently, systematic rehabilitation was provided based on the patients' recovery progress after the operation (A schematic diagram of DTI-guided stereotactic puncture based on DTI is shown in Fig. 2).

Group B consisted of patients who received comprehensive treatment, which encompassed routine blood pressure management, dehydration to reduce cranial pressure, nutritional symptomatic support, maintenance of water-electrolyte balance, and administration of anti-infection measures to prevent complications. Subsequently, cranial CT scans were conducted at 3 days, 7 days, and 2 weeks following disease onset to assess the extent of intracranial hematoma and its subsequent absorption. The data collection and associated serological examinations, including the assessment of neurological function-related factors such as NSE, S100β protein, Nogo-A, and inflammatory factor NF-kB/p65, were conducted in a rigorous manner following the prescribed technical protocol. Additionally, comprehensive rehabilitation interventions were administered based on the

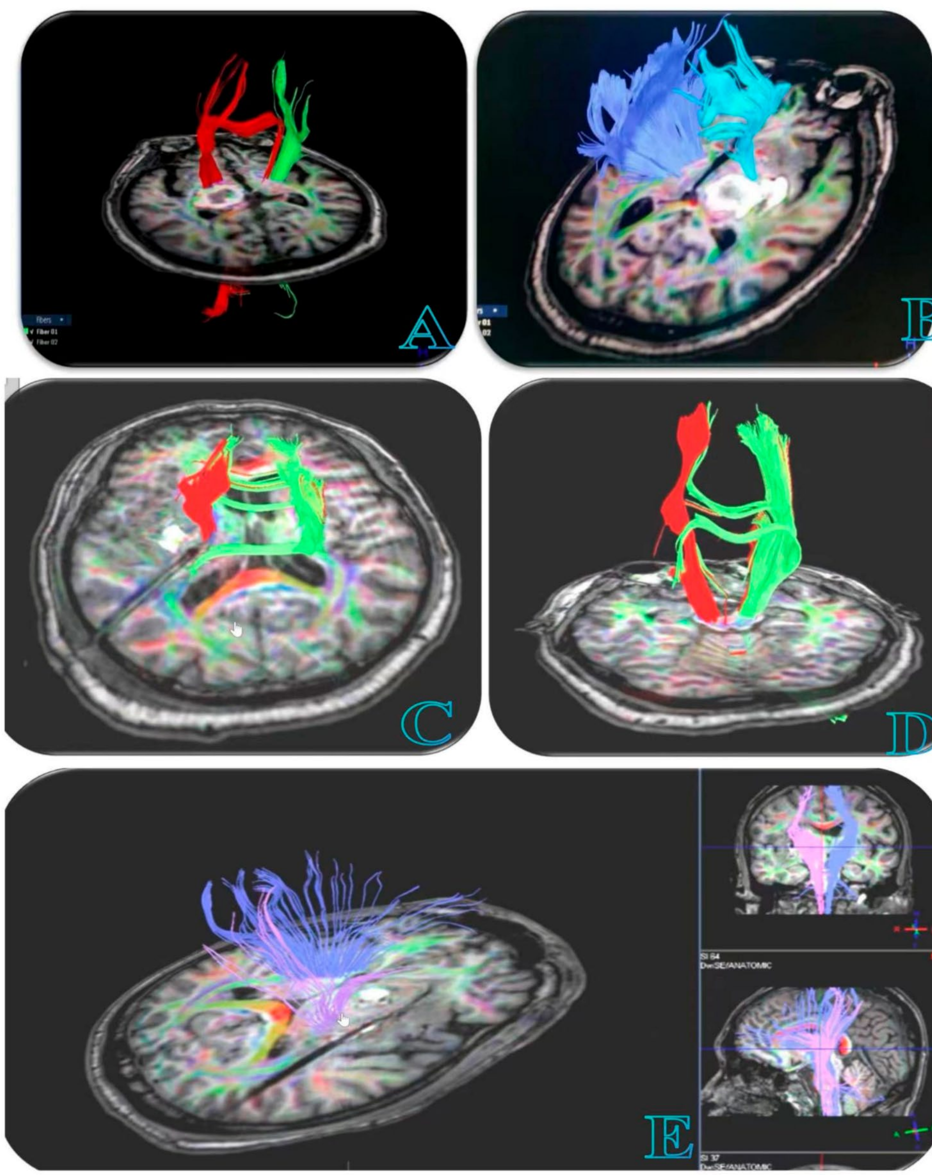

Fig. 2 Schematic image of DTI combined with cerebral haemorrhage. Schematic of brain haemorrhage based on DTI fusion. **A** suggests cerebral haemorrhage and corticospinal tract alignment in the right basal ganglia region; **B** suggests cerebral haemorrhage and corticospinal tract alignment in the left basal ganglia region; **C** and **D** suggest that the patient in Figure **A** was reviewed after trans-stereotactic paracentesis; **E** suggests that the patient in Figure B was reviewed after trans-stereotactic paracentesi

patient's postoperative recovery, and precise documentation of various scores was maintained.

Observation indicators

(a)The perioperative indicators in the surgical group encompass various factors, such as surgical time, intraoperative blood loss, rebleeding rate, postoperative wakefulness time, dermal incision, hospitalization time, hematoma clearance rate within 3 days, 7 days, and 2 weeks, as well as the average amount of mannitol administered per person per day during the postoperative period within 7 days. The hematoma clearance rate is calculated using the formula: (preoperative hematoma volume - postoperative hematoma volume)/preoperative hematoma volume × 100%. In addition, to ensure consistency of imaging data, the imaging technologist will use the DTI tractography software tool to establish uniform parameter settings. For example, the number and location of Region of Interest(ROIs)and Corticospinal Tract(CST), as well as the FA value, maximum angle and minimum length of fibers.

(b)Hematoma aspiration: observe the patient's intraoperative hematoma aspiration volume, the percentage of aspiration volume, the percentage of aspiration volume=intraoperative hematoma aspiration volume/preoperative hematoma volume×100%;

(c)The patients' consciousness state was evaluated at 3 days, 7 days, and 2 weeks post-surgery using the Glasgow Coma Scale (GCS) score. A GCS score of 15 indicated clear consciousness, while scores ranging from 12 to 14 indicated mild consciousness disorders. Moderate consciousness disorders were classified for scores ranging from 9 to 11, and a score of ≤8 indicated coma. It is important to note that lower scores on the GCS indicate more severe consciousness disorders in the patients;

(d)Neurologic function was evaluated using the National Institutes of Health Stroke Scale (NHISS) to measure the extent of neurologic deficits prior to surgery, as well as at 1 week and 2 weeks after surgery. The NHISS scores ranged from 0 to 42, with higher scores indicating more severe neurologic deficits in patients;

(e)The Activity of Daily Living (ADL) Scale is utilized to assess an individual's capacity to independently perform self-care tasks, encompassing dressing, eating, and grooming among others. This scale assigns a score out of 100, with a score above 95 indicating the patient's ability to fully care for themselves. Scores ranging from 70 to 95 suggest mild obstacles in daily living, while scores between 45 and 70 indicate moderate obstacles. A score falling within the range of 20 to 45 signifies severe obstacles, and a score below 20 indicates extremely severe obstacles in daily living.Patients were generally invited to the outpatient clinic for follow-up and scoring after 6 months of treatment;

(f)Cytokine levels were assessed in patients by collecting 3 mL of fasting venous blood before surgery, as well as 3 and 7 days post-surgery. The collected blood samples were then centrifuged at a speed of 3,000 r/min to separate the serum. Enzyme-linked immunoassay was utilized to measure the levels of S100β protein, NSE (a factor related to neurological function), Nogo-A (an axon growth inhibitory factor), and NF-kB p65 (an inflammatory factor).

(g)Additionally, complication rates encompassed various adverse events such as intracranial infections, gastrointestinal bleeding, pulmonary infections, and deep vein thrombosis;

(h)Short-term prognosis: patients' status after 6 months of treatment will be followed up, during which time patients' prognosis will be assessed using the Glasgow Outcome Score (GOS). In addition, patients' neurological function will be assessed using the Activity of Daily Living Scale (ADL).

(i)Extended follow-up: We will extend patient follow-up for at least 18–24 months to better understand patients' long-term recovery after surgery. This will include regular neurological function assessments and quality of life questionnaires for patients. Increased sample size: To ensure statistical validity of the data, we plan to increase the sample size so that there will be sufficient data to analyze the long-term effects of the surgery during long-term follow-up. Multiple time point analysis: We will analyze the data at different time points (e.g., 6 months, 12 months, 18 months) to observe trends in patient recovery and any possible late complications. Literature review: We will conduct a more extensive literature review to determine if long-term follow-up data on similar procedures are available from other studies so that we can compare them with our data.

Statistical analysis

Statistical analyses were performed using R 4.3.2 software and Free StatisticV18.1.1, with continuous variable information expressed as ($x \pm s$), comparisons between groups using the t-test, and comparisons between groups at different time points using repeated measures ANOVA. Categorical variable information was presented as n (%) and group comparisons were conducted using theχ [2] test. The selected factors were examined through one-way analysis of variance, and those factors that exhibited statistical significance ($P<0.05$) on Uni-variate analysis were subsequently subjected to Logistic regression analysis. The independent variables were screened using the backward elimination method to ensure statistical significance at $P<0.05$.

Type of outcomes

The primary objective of this study was to compare and analyse the ability to perform activities of daily living (ADL) scores of all patients in both groups after 6 months of treatment. According to previous literature, those with ADL scores greater than or equal to 40 were positioned as treatment gainers at follow-up. While those with scores less than 40 were considered to have a poor prognosis [11, 12]. Additionally, secondary outcomes include evaluating perioperative indexes in the surgical group and treatment indexes in the conservative group, hematoma aspiration, neurological function score, factors related to neurological function, and complication rate. To compare the effectiveness of DTI-based stereotactic puncture surgery with conventional conservative treatment, a comparative analysis of treatment efficacy and the analysis of near- and long-term prognosis will be conducted.

In addition, we will further analyse whether serological levels of S100β protein, the neurological function-related factor NSE, axon growth inhibitory factor A (Nogo-A) and the inflammatory factor nuclear factor-kB p65 (NF-kB p65), ADC values and FA values in DTI, are associated with a poor prognosis, and whether they are predictive.

Subgroup and sensitivity analyses

We will prepare subgroup analyses based on age, gender, ethnicity, time from onset to treatment, Glasgow Coma Scale score and haematoma site for statistical analysis. The effect of hyperbaric oxygen treatment status on outcome will be further analysed.

In addition, we designed several sensitivity analyses to test the stability of the results. For example, stereotactic puncture surgery in the non-DTI group was included in the control group to further explore the advantages of DTI reconstruction itself in the treatment of thalamo-basal ganglia hemorrhage.

Discussion

Hypertensive intracerebral hemorrhage (HICH) is a prevalent and recurrent ailment within the field of neurology. It represents a grave complication stemming from hypertension, displaying distinctive features of sudden onset and swift progression [13]. The morbidity rate for spontaneous cerebral hemorrhage ranges from 70 to 80%, while the mortality rate within 30 days ranges from 35 to 52%. Furthermore, HICH frequently results in severe disabilities, thereby imposing significant financial and psychological burdens upon both patients and their families [14]. The basal ganglia region is a frequently affected location for hemorrhage in hypertensive intracerebral hemorrhage (HICH), constituting approximately 50–60% of all HICH cases. The majority of these hemorrhages occur within the middle cranial fossa of the temporal lobe, which possesses a limited volume and proximity to the brainstem and other critical centers [15]. Consequently, this proximity contributes to the occurrence of severe secondary injuries and subsequent consequences. The prevalence of this disease is highest among the elderly population, and early-stage manifestations lack evident clinical signs.The patient's prognosis and survival rate can be significantly affected if treatment is not initiated promptly after the disease's onset [16]. In China, surgical intervention is advocated as the preferred method for managing basal ganglia hemorrhage cases with a bleeding volume exceeding 30 ml, as it offers a life-saving measure. By expeditiously eliminating the hematoma and enabling subsequent neurological rehabilitation, surgery presents a viable avenue for intervention [17].

Epidemiological studies have demonstrated that China exhibits the highest prevalence of hemorrhagic stroke globally, with an estimated incidence ranging from 114.8 to 159.8 cases per 100,000 individuals. In recent times, the aging phenomenon in China has intensified, leading to a notable surge in the number of individuals affected by hemorrhagic stroke, thereby posing a significant threat to the populace [13]. Notably, elderly patients often present with comorbidities and exhibit diminished surgical tolerance, alongside an elevated likelihood of experiencing postoperative complications. These factors contribute to the heightened intricacy and complexity associated with the treatment of this condition [18]. Despite the efficacy of traditional craniotomy in hematoma removal, it is associated with drawbacks such as prolonged operation duration, extensive trauma, susceptibility to tissue and blood vessel damage, and numerous postoperative complications. These factors can impede the patient's conscious state and neurological function recovery, particularly in individuals aged 65 and above [19]. The advancement of surgical techniques and equipment has led to the increasing utilization of minimally invasive procedures, such as endoscopic hematoma removal and minimally invasive puncture and drainage of hematoma, as the primary treatment approach for elderly patients with hypertensive intracerebral hemorrhage (HICH). However, it is important to note that the neuroendoscopic minimally invasive technique necessitates the creation of a working sheath measuring approximately 1.4 cm to reach the deepest part of the hematoma [20]. This action results in an increase in intracranial contents and subsequent alterations in intracranial pressure, which may potentially jeopardize patient safety.

Stereotactic localization technology is an advanced technique that integrates medical image informatics, image processing, and three-dimensional visualization. In contrast to alternative surgical approaches, stereotactic minimally invasive puncture and drainage offers several benefits, including a straightforward and expeditious procedure that enables prompt hematoma drainage. This technique also minimizes hematoma-induced brain tissue damage and lowers the likelihood of postoperative complications [21]. Furthermore, the previous literature has provided substantial evidence to support the efficacy and safety of this surgical procedure. Diffusion tensor imaging (DTI) is an important technique used in neurosurgery to guide and optimize surgical procedures. It provides information about the anisotropy of water molecules in different tissues by noninvasively measuring the translational motion of water molecules in the body, thus helping doctors understand the integrity of nerve fiber bundles in the white matter of the brain [22]. The applications of DTI technology in neurosurgery include, but are not limited to: (1) Precise localization: DTI helps doctors to accurately locate tumors, lesions, or brain areas of interest prior to surgery, as well as their relationship to the surrounding vital nerve fiber bundles, thus avoiding damage to these areas during surgery. (2) Surgical planning: With DTI imaging, doctors can perform detailed planning before surgery, including determining the best surgical path and approach to minimize damage to normal brain tissue. (3) Functional protection: During surgery, DTI can help identify and protect those neural pathways that are important for motor, sensory, speech and other functions. (4) Prognostic assessment: DTI can also be used to assess the recovery of neurological function after surgery, as well as to predict the long-term prognosis of patients [23]. However, despite the significant advantages of DTI technology in neurosurgery, there are a number of limitations and risks, including: (1) Accuracy variability: DTI imaging results may vary from patient to patient, which may be related to the patient's age, health status, and quality control of the imaging technology. (2) Technical limitations: DTI imaging may be affected by artifacts, image resolution limitations, and post-processing algorithms, all of which may affect the accuracy of image interpretation and surgical planning. (3) Surgical risk: although DTI can improve surgical accuracy, there are certain risks associated with any invasive procedure, including infection, bleeding, and nerve damage. (4) Patient factors: Variants in the patient's anatomy, changes in pathology, and unpredictable factors during surgery may affect the outcome [24]. To minimize these risks, the surgeon needs to carefully evaluate the patient's DTI images prior to surgery and combine them with other clinical information and imaging findings to develop an individualized surgical plan. In addition, physicians should fully communicate with patients to ensure that they understand the potential risks and expected outcomes of the procedure. In practice, DTI-guided stereotactic technology has shown its value in the treatment of a variety of neurosurgical conditions, such as Parkinson's disease, epilepsy, gliomas, and auditory neuromas. With this technique, surgeons are able to localize lesions more precisely and reduce damage to surrounding normal brain tissue, thereby improving the safety and effectiveness of surgery.

Neuron-specific enolase (NSE) is a sensitive indicator for evaluating the severity of craniocerebral injury and determining the prognosis of the disease, which is commonly used in clinical and experimental settings. Because of the high content of NSE in neural tissues, it has been used in clinical practice to monitor changes in the conditions of craniocerebral injuries caused by various reasons and to assess the overall prognosis of patients [25, 28]. Statistics in the literature show that the neurological function scores of patients with cerebral hemorrhage were positively correlated with the serum NSE levels and their bleeding volume.Inflammatory factor nuclear factor kappa-B (NF-kB) protein is a protein complex first discovered by David Baltimore. NF-kB plays a key role in regulating the immune response to infection. NF-KB/p65 positive cells around hematoma after cerebral hemorrhage began to increase at 6 h after surgery, and its expression continued to rise at 1d, reaching a peak at 3d, after which NF-KB/p65 expression began to decline and lasted until about 7d [26]. It was found that the concentration of S100β protein increased significantly within 6 h of brain injury, decreased significantly after 1 day, and a small peak appeared after 2–3 days, which may be related to secondary brain injury. The higher the concentration of S100β protein, the worse the prognosis [27]. The neurological injury of cerebral hemorrhage originates from the primary injury of hematoma, but more importantly from the secondary injury, which mainly includes cerebral edema, toxic injury of brain cells and secondary ischemia.To summarize, the blood markers NSE, S100β protein, Nogo-A, and nuclear factor ‐kB/p65 (NF ‐kB/p65) have demonstrated higher sensitivity in relation to neurological function after cerebral hemorrhage [28]. Our research group is prepared to gather specimens at various time intervals following cerebral hemorrhage as part of this clinical trial. Subsequently, a meticulous statistical analysis will be conducted to assess the correlation between each marker and prognosis.

In summary, this clinical trial centers on a distinct cohort of elderly individuals afflicted with thalamo-basal ganglia hemorrhage of moderate severity. These patients have small amount of cerebral hemorrhage, which is not life-threatening, but heavy neurological damage. Currently, the main clinical focus is on conventional conservative and comprehensive treatment. Nevertheless, owing to the significance of this neural nucleus, patients frequently endure substantial disability post-treatment, significantly impinging upon their personal and professional lives.In recent years, the significant advancements in minimally invasive surgery, particularly stereotactic surgery, have prompted our group to conduct a retrospective analysis of clinical data pertaining to this specific patient population within our hospital over the past decade. The findings revealed that patients who underwent stereotactic minimally invasive drainage surgery exhibited a notably superior ability to engage in activities of daily living six months post-treatment compared to those who received conventional conservative treatment.Hence, the primary focus of this study was the development of DTI-assisted stereotactic minimally invasive drainage surgery, which served as the reference group alongside conventional conservative treatment. Our analysis encompassed the evaluation of treatment efficacy throughout the duration of therapy, as well as the short-term and long-term prognosis. Additionally, we will investigat the potential correlation between factors such as S100β protein, NSE (a factor associated with neurological function), Nogo-A (an axon growth inhibitory factor), NF-kB p65 (an inflammatory factor), and the ADC and FA values obtained from DTI examinations, with regards to poor prognosis.These relevant research elements are significantly innovative in terms of the study population, surgical methods, and assessment indexes in similar studies.

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Author contributions
The authors of this work have satisfied the ICMJE criteria for authorship. The study was designed by H.X. and Y.S., while Y.S. authored the manuscript. Y.S.,L.Y., W.S., Q.X, P.H., and C.Z. were the principal investigators for the implementation of the project, in line with the enrolment screening of the cases and the collection of all clinical data. Y.A. and W.S. statistically analyzed clinical data. The report was thoroughly reviewed and edited by all authors, who subsequently granted their approval for the final draft.

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Data availability
The datasets generated and/or analyzed in this study are not publicly available due to the fact that the study is currently ongoing, but will be available from the corresponding author when our study is completed.

Declarations

Ethics approval and consent to participate
The clinical study was reviewed and approved by the Ethics Committee of the First People's Hospital of Yibin. The ethical number is: 2023 Review (64). All of our study participants conducted the clinical trial after fully understanding the instructions and obtaining their consent.

Consent for publication
All authors in our study group agreed to the order of authorship and publication. All study participants agreed to the scientific reporting of the study results. The manuscript for this protocol has no recognisable images and there are no details about the individual in the manuscript.

Competing interests
The authors declare no competing interests.

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