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Research article

Short-term outcomes of robot-assisted minimally invasive surgery for brainstem hemorrhage: A case-control study

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A R T I C L E I N F O

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Brainstem hemorrhage
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Outcome
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A B S T R A C T

Objective: This work focused on investigating if robot-assisted minimally invasive surgery improved middle term vital outcome for primary brainstem hemorrhage (PBSH).
Methods: This work obtained clinical data from patients with PBSH admitted from July 2019 to August 2021. All cases were classified as surgical or conservative treatment group. The general information, Glasgow coma scale (GCS) score, Glasgow outcome score (GOS), along with survival time in patients 60 days after robot-assisted surgery were recorded and analyzed.
Results: A prospective analysis was performed on 82 cases meeting eligibility criteria, including 36 from surgical group whereas 46 from the conservative group. Sixty days after onset, the death rate was found to be 19.44% and 50.00% of surgical and conservative groups, separately (cases versus controls, $P < 0.05$). Furthermore, postoperative GOS and GCS scores of surgical group were significantly higher, and hydrocephalus was lower compared with conservative group. Central fever incidence did not exhibit any significant difference between two groups.
Conclusion: Robot-assisted PBSH drainage may improve survivorship and reduce the occurrence of hydrocephalus.

1. Introduction

Stroke represents the major factor causing morbidity and mortality among the developed countries. Spontaneous intracerebral hemorrhage (ICH) takes up 19.6% of the entire stroke cases [1]. In addition, the incidence of cerebral hemorrhage tends to increase with age, with the highest incidence in the 40–60 year age group. About 6–10% of spontaneous brain haemorrhages are located within the brainstem [2,3]. Additionally, among the spontaneous ICHs, brainstem hemorrhage has the highest mortality rate of 47%–80% [4]. Brainstem hemorrhage stands for the suddenly occurring acute neurological disorder with major issues to overcome including the limited treatment options and poor prognosis.

In the past, PBSH was managed with conservative treatment. Recently, several studies have reported the efficacy of surgical treatment [5–7]. However, whether PBSH should be treated conservatively or surgically (e.g., craniotomy and drainage) remains

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controversial. With regard to primary posterior fossa hematoma, surgical resection is recommended by the American Heart Association/American Stroke Association (AHA/ASA) guidelines for cerebellar hemorrhage rather than for brainstem hemorrhage. As explicitly stated in the guideline, brainstem hematomas should not be surgically evacuated [8]. Neurosurgical treatments like hematoma debridement is still a source of controversy in ICH, as randomized clinical trials (RCTs) do not illustrate that surgical treatment is beneficial.

As surgical techniques and equipment develop, robot-assisted surgery has shown promising clinical application in the treatment of deep brain stimulation and basal ganglia ICH [9–11]. Currently, there are few reports on robotic surgery for the treatment of PBSH. To evaluate the efficacy of robot-assisted puncture aspiration surgery for PBSH, we prospectively analyzed 82 patients with PBSH treated at our center between July 2019 and August 2021. All cases were non-randomly classified as robot-assisted surgery or conservative treatment group. This study provides initial medical evidence for robot-assisted puncture aspiration to treat PBSH.

2. Material and methods

2.1. Patients

The surgical inclusion criterion was the diagnosis of PBSH. Patients conforming to following criteria were excluded, including those with brainstem hemorrhage after (1) traumatic brain injury or (2) brain tumor. Patients who met the surgical indications were screened. The indications for surgery were shown below, the volume of hematoma was >5 mL, the transverse diameter of hematoma was >2 cm, acute progressive symptoms, neurological dysfunction, hydrocephalus or distinct space-occupying effects. Two experienced neurosurgeons from our center explained the risks of surgery and possible outcomes to the patient's family in detail. We included patients who agreed to undergo surgery in the surgical group, and those who refused surgery for various reasons in the conservative group. In addition, we eliminated patients who died within 24 h after admission. The ethics committee of the hospital approved this study protocol. Family members provided informed consents preoperatively (Fig. 1). The clinical trial registration number is ChiCTR2100053458.

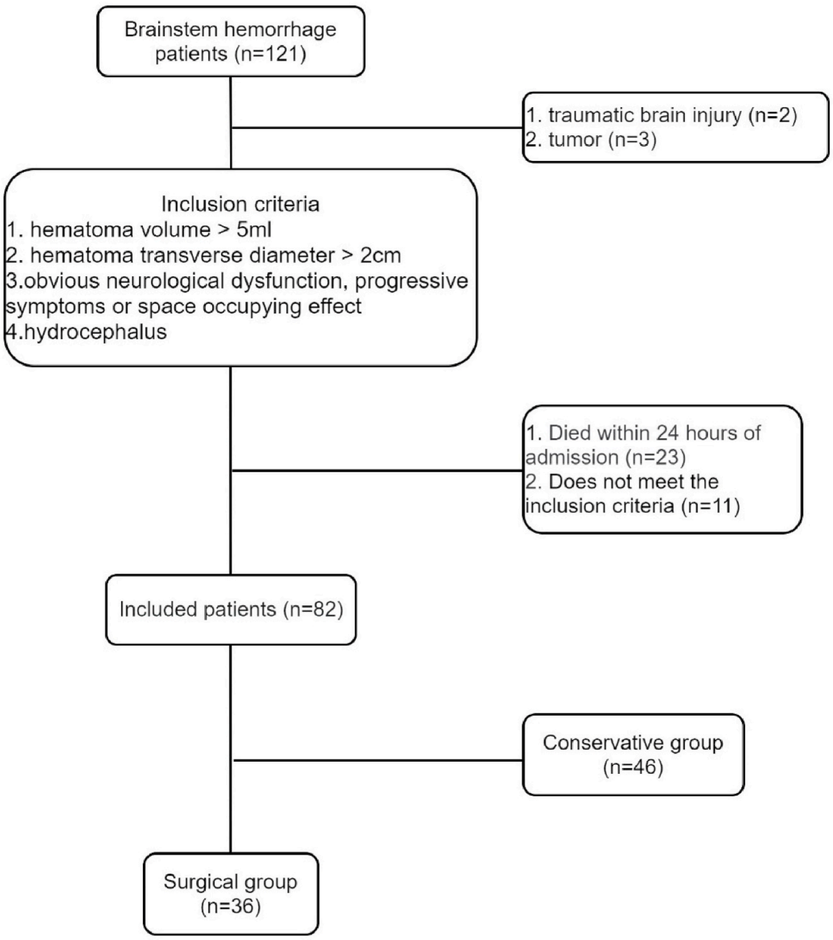

Fig. 1. Flow chart of study participant inclusion.

2.2. Treatment method

We performed a preoperative assessment and recorded neurological functional status for every qualified case with Glasgow coma scale (GCS). Additional examinations were performed to document pupillary changes and central high fever. The amount and site of bleeding according to the preoperative computed tomography (CT) were also used to measure bleeding (Fig. 2A). Every case received standard medications in line with AHA/ASA guidelines. The surgical team drained the brainstem hematoma using robotic assistance. This work performed CT angiography prior to the planning of surgery Preoperatively, we put five scalp markers onto the head of each case and later conducted CT scanning. CT angiography images together with CT image data of each case were transferred into computer workstation of the RM-100 system prior to surgery. Images were precisely fused and drainage tube was designed based on CT data. The planning procedure covered target locations within the hematoma/drainage tube paths to avoid the visible ventricles, blood vessels and dentate gyrus (Fig. 2B). In the procedure, each case was in the supine position, the Fisher head frame was applied to immobilize and securely attach the head onto surgical bed. Following registration, we made a surgical incision guided by a robotic arm, drilled a skull hole (10 mm in diameter), and resected dura mater (3 mm in diameter). In line with surgical planning, automatic movement of robotic to a specific location was conducted, followed by the placement of a puncture tube to aspirate hematoma. The drainage tube and the scalp were secured in succession. Drains were left in place for each case from surgical group. Postoperatively, we injected 30,000 U urokinase in hematoma cavity 2–3 times/day via the catheter. A head CT scan was made 24 h after surgery. Hematoma volumes were determined at baseline as well as on subsequent CT scans using the Analysis software (AnalyzeDirect, Overland Park, Kansas, USA). The patients in the conservative group received conventional symptomatic and supportive treatments (Fig. 2C). All the operations were performed by Dr. Bao.

2.3. Evaluation of outcomes

The GCS score and Glasgow Outcome Score (GOS) were adopted for assessing level of consciousness and regression of patients at postoperative follow-up, and CT scans were used to understand the changes in bleeding. Hydrocephalus and survival rates were recorded. The deaths of the patients were recorded accurately. To assess middle term vital outcome, we set the follow-up time at 60 days. Postoperative GCS score and GOS were assessed only in patients who survived 60 days postoperatively.

2.4. Statistical analysis

R (http://www.R-project.org) and Empower(R) (www.empowerstats.com; X&Y Solutions, Inc., Boston, MA, USA) were employed for statistical analysis. At first, variable normal distribution was analyzed by Kolmogorov–Smirnov test. Then, normally distributed variables were analyzed with one-way analysis of variance (ANOVA) or 2-tailed Student's t-test. Whitney test was conducted to compare non-parametric data across multiple groups. Log-rank test and Kaplan-Meier analysis were performed for plotting survival curves. $P < 0.05$ (two-tailed) stood for significant difference.

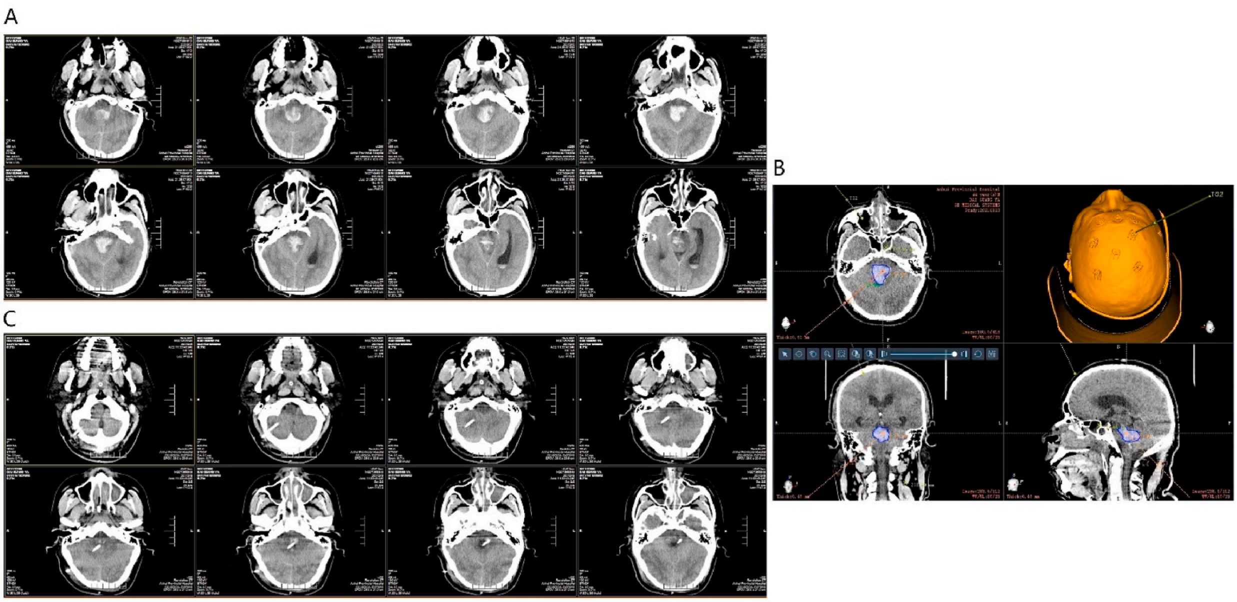

Fig. 2. Operative result. (A) Head computed tomography before operation. (B) Operative plan. (C) Head computed tomography after operation.

3. Results

Altogether 82 PBSH cases were enrolled into this work, including 36 undergoing robot-assisted hematoma puncture and aspiration surgery and were included in the surgical group, while 46 refusing surgery for various reasons and were included into conservative group. Sex, age, preoperative GCS score, and hematoma location were comparable between both groups. The number of hematomas of surgical group slightly increased compared with conservative group (Table 1).

Postoperative CT of patients in the surgical group showed that all drains were pushed to the designated preoperative target points. The duration between onset and surgical treatment was 6.7 ± 2.6 h (2.7–11.6 h), and the operative time was 33.4 ± 7.3 min. The average postoperative hematoma reduction was 3.7 ± 1.2 mL (2.1–7.1 mL). No serious surgery-related complications occurred in any case. One case experienced postoperative fever and received anti-infection treatment.

After 60 days of follow-up, 7 and 23 patients in the surgical and conservative groups died; the conservative group had a significantly increased mortality rate. Postoperative GCS score (Fig. 3A) and GOS (Fig. 3B) of surgical group markedly increased compared with conservative group (Table 2). Additionally, we analyzed the survival curves of patients in both groups within 60 days, as a result, surgical group showed a significantly higher survival rate compared with conservative group (Fig. 4).

4. Discussion

PBSH stands for the specific cerebral hemorrhage type that occupies approximately 10% of cerebral hemorrhages [12–14]. To date, although the conventional treatment for PBSH has been mainly conservative, the results have been unsatisfactory [15]. As reported by one Japanese article enrolling 212 cases receiving conservative treatment, the overall mortality was 57.5%, the moderate-to-severe disability was 25.4%, and satisfactory recovery was only 6.1% of patients [16]. Meanwhile, as discovered by Chen et al. in 52 patients, removing a brainstem hematoma through craniotomy is the efficient treatment for brainstem hemorrhage [6]. However, brainstem craniotomy is related to an increased complication risk. With regard to surgical treatment, blood clots should be removed as much as possible to minimize damage to the adjacent brain tissue for reducing systemic and local intracranial pressure while maintaining cerebrospinal fluid circulation. This modality can ensure direct removal of hematoma and efficient decompression, however, it can increase the incidence of surgery-related tissue injury. Giving rise to drawbacks of these therapeutic approaches, PBSH puncture drainage is the potential therapeutic approach. It is well known that the brainstem locates in a deep position within cranial cavity; as a result, puncture accuracy is the most important factor.

Conceptually, the purpose of hematoma removal is to reduce mass effect as well as intracranial pressure (ICP), and to remove hemorrhagic products inducing inflammation along with brain parenchymal degeneration. The brainstem shows particular sensitivity to cytotoxicity. Takahama et al. and Hara et al. from Japan put forward stereotactic suction, and discovered good functional outcomes of hematomas patients receiving surgical treatment relative to those receiving conservative treatment [17,18]. The early drainage of hematoma within brainstem may help decrease injury to adjacent tissues. The approach is useful to treat PBSH.

By analyzing clinical information from 82 PBSH cases, we found that patients with robot-assisted intracerebral hematoma drainage had superior neurological recovery and survival rates within the 60-day follow-up and a lower incidence of hydrocephalus than those with conventional conservative treatment. This indicates that the safety and effectiveness of robotic-assisted intracerebral hematoma drainage in treating PBSH.

Robot-assisted brainstem hematoma drainage promotes neurological recovery. The GCS score and GOS were higher in the surgical group, suggesting that robot-assisted minimally invasive hematoma resection is the possible major cause of the outcome. The robot-assisted surgery planning system allows for making surgery plans for individuals, avoiding injury to vital organs or large vessels. Hematoma removal relieves the local occupancy effects, improves local blood flow, reduces the release of hematoma breakdown products as well as vasoactive molecules following damage to brain tissues, and prevents cerebral edema [19–22]. The above functions offer beneficial conditions to recover neurological function. Drainage tube of surgical group was inserted precisely to target position (the center of the hematoma) in all patients. Immediately postoperatively, hematoma volume decreased by 3.7 mL on average. Additionally, drainage was also facilitated through urokinase injection in hematoma cavity, without increasing re-hemorrhage risk.

Table 1
Characteristics of patients.

Characteristics	Conservative Group (n=46)	Surgical Group (n=36)	*p*
Gender (male/female)	32/14	24/12	0.82
Age (years)	50.26 ± 10.68	48.98 ± 9.89	0.86
Preoperative GCS score			0.81
3	30 (65.22%)	25 (69.54%)	
4	13 (28.26%)	8 (22.22%)	
5	3 (6.52%)	3 (8.33%)	
Volume of hematoma (ml)	7.17 ± 1.78	10.79 ± 5.31	<0.01
Location of hematoma			
Pons	26 (56.52%)	17 (47.22%)	0.32
Midbrain	11 (23.91%)	9 (25.00%)	0.78
Medulla oblongata	4 (8.69%)	3 (8.33%)	0.83
Whole brainstem	5 (10.88%)	7 (19.44%)	0.34
Combined with ventricular hemorrhage	6 (13.04%)	5 (13.88%)	0.88

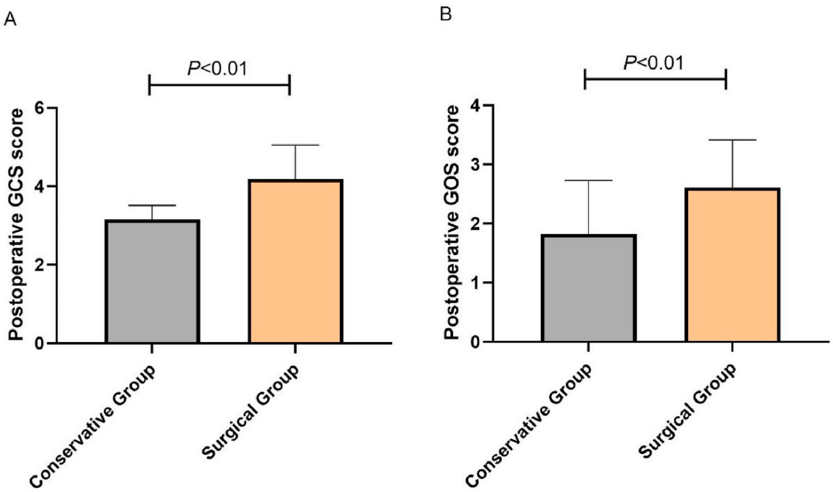

Fig. 3. Comparison of postoperative GCS (A) and GOS (B) scores between the 2 groups at 60 days after surgery.

Table 2
Comparison of curative outcome between conservative group and surgical group.

Characteristics	Conservative Group (n=46)	Surgical Group (n=36)	*p*
Postoperative GCS score			<0.01
3	16 (69.6%)	3 (10.3%)	
4	7 (30.4%)	9 (31.00%)	
5	0 (0.00%)	17 (58.6%)	
Postoperative GOS score			<0.01
2	8 (34.8%)	0 (0.00%)	
3	15 (65.2%)	29 (100.00%)	
Hydrocephalus			<0.01
Present	20 (43.48%)	28 (77.78%)	
Absent	26 (56.52%)	8 (22.22%)	
Central high fever	16 (34.78%)	11 (30.56%)	0.76
Death	23 (50.00%)	7 (19.44%)	<0.01

Postoperative GCS and GOS scores were assessed only for patients who survived 60 days after surgery.

The mean operation time was 33.4 min, suggesting the efficiency and safety of the procedure. That technique adopted in the present work was simple and operable by many primary care physicians. Previously, surgical treatment of PBSH was not thought to improve the prognosis [23,24]. However, our results and several other studies obtain different results [25]. In the present prospective work, the surgical group had a decreased mortality rate compared with conservative group. There were more patients showing favorable prognostic outcome in surgical group compared with conservative group. Relative to Takeuchi et al., this work reported a reduced death rate of the patients (19.4% vs. 57.5%). All survivors had a GOS greater than 2.

In our study, although the surgical group was superior to the conservative group in terms of survival and had some advantage in terms of scale scores. However, 69.9% of the conservative treatment group had a GCS score of 3 at 60 d postoperatively and 58.6% of the surgical treatment group had a GCS score of 5. The GOS score of 3 after 60 d in the conservative treatment group was 65.2%, whereas in the surgical group, all GOS scores were 3 (100%) after 60 d. GOS 3 implies that the patient has a severe disability and is completely unable to take care of himself in activities of daily living (ADLs). This remains a poorer outcome. Therefore, detailed communication of treatment expectations with the family is needed before performing surgery.

In this study, the use of a robotic arm allowed for minimally invasive suction drainage of all brain abscesses in a relatively short surgical time. In addition, the robotic arm provided a rigid and stable platform for cranial drilling, improving safety and precision. The use of frameless positioning devices, such as neuronavigation systems, could eventually be combined with portable robotic arms to perform rapid biopsies or punctures as well. In addition, frameless devices have been reported to have higher aiming errors compared to robotic devices, increasing surgical risk, especially when aiming at deep lesions. On the other hand, the robot demonstrated better accuracy and shorter operative time compared to "classical" frame-based stereotactic surgery, where accuracy is essential for clinical success. We have improved alignment accuracy by combining preoperative MRI and CT scans into the intraoperative Remebot 4.0 navigation system [26–28]. This improved accuracy allowed the initially planned trajectory to be used during the second surgical procedure without the need for new cranial drilling. In addition, the use of the Remebot 4.0 navigation system allowed control of the correlation between the planned trajectory and the true trajectory prior to the introduction of the puncture needle into the target. In case of deviations, the robot can micro-correct the surgical trajectory. This workflow is routinely used in DBS and complex stereotactic

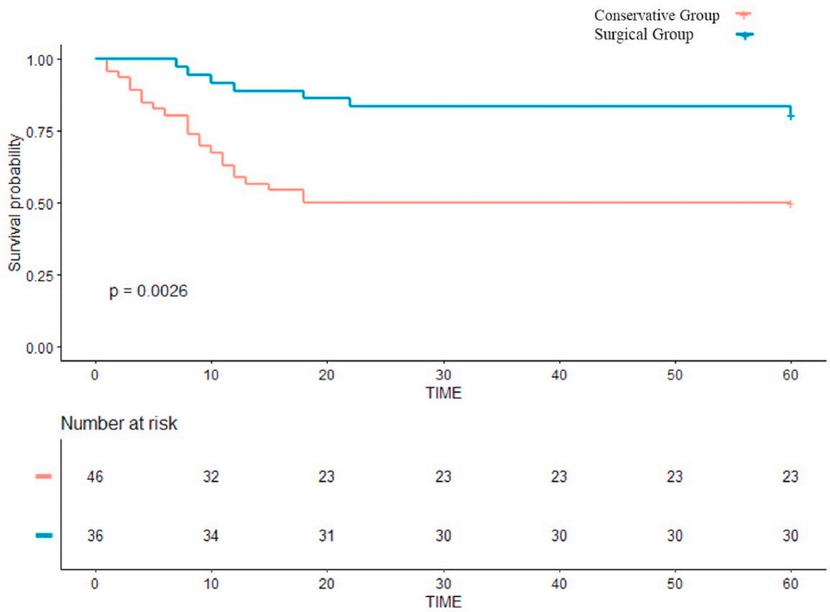

Fig. 4. The survival curves after conservative treatment and surgery.

biopsy procedures at our institution, improving accuracy and safety.

Conventional stereotactic surgery is mostly performed by mounting a head frame for positioning, which is performed under local anaesthesia, but the process is still painful and frightening for the patient, especially for non-compatible patients, is cumbersome and difficult to perform, and increases the possibility of additional medical injuries. In addition, the surgical operation is also greatly affected by the obstruction of the operating space and the surgical field by the frame. The robotic navigation and positioning system applied in this study consists of a six-degree-of-freedom robotic arm, a master computer and a binocular camera, which does not need to be installed with a traditional positioning frame, and allows the surgeon to complete the surgical planning and path design with the assistance of a real-time camera to expand the surgical workspace and avoid systematic human error, which saves the time of positioning and improves the positioning accuracy, and all operations are performed under general anaesthesia, which greatly reduces the patient's pain. All operations are performed under general anaesthesia, which greatly reduces patients' discomfort.

As a case-control study, bias was inevitable. Additionally, few cases were enrolled into the present work. It is still necessary to conduct large sample size cohort or case-control study involving hematoma volume, surgery timing, and surgical approach for obtaining high-level clinical evidence that can help guide PBSH treatment. In addition, considering the significantly lower incidence of hydrocephalus in the surgical group, further research into the mechanism of robot-assisted surgery for hydrocephalus, analysis of postoperative changes in cerebral pressure, and exploration of how to effectively drain the cerebrospinal fluid to reduce hydrocephalus will be necessary in the future.

5. Conclusion

We found robot-assisted PBSH puncture and drainage to be a safe, feasible, and effective treatment option. This technique resulted in better patient outcomes and survival rates than conservative treatments in patients with PBSH. However, high-quality prospective RCTs should be conducted for validating effectiveness of our results.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of University of Science and Technology of China (Anhui Provincial Hospital) (Number: 2020-SQ (H)-020).

Consent for publication

Not applicable.

Data availability statement

The authors do not have permission to share data. If data are required, E-mail the corresponding author.

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CRediT authorship contribution statement

Dejun Bao: Writing – original draft. **Shengyuan Ni:** Writing – original draft. **Bowen Chang:** Writing – original draft, Methodology, Data curation. **Wang Zhang:** Data curation. **Hong Zhang:** Data curation. **Chaoshi Niu:** Supervision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Dejun Bao reports financial support was provided by Health Commission of Anhui Province. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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List of abbreviations

AHA/ASAAmerican Heart Association/American Stroke Association.
CTComputed tomography.
GCSGlasgow coma scale.
GOSGlasgow outcome score.
ICHintracerebral hemorrhage.
ICPintracranial pressure.
PBSHprimary brainstem hemorrhage.

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