

# Development and initial experience of a novel classification system for patients with brain stem haemorrhage

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## Abstract

**Introduction:** There is no uniform classification standard for brain stem haemorrhage. On the basis of previous experience in the treatment of brainstem haemorrhage, this study explored and established a set of criteria for brainstem haemorrhage classification, risk-stratified such patients and guided the selection of treatment options so as to achieve accurate and standardized diagnosis and treatment.

**Material and methods:** Thirty patients with brainstem haemorrhage from April 2019 to May 2022 were included. According to the amount and location of the brain stem bleeding, it was divided into the following types: small haemorrhage type (type 1), medium haemorrhage type (lateral type 2a, dorsal type 2b, ventral type 2c), and large haemorrhage type (type 3), and the preoperative condition and postoperative outcome within 3 months were evaluated.

**Results:** The included 30 patients with brainstem haemorrhage were aged  $53.2 \pm 13.8$  years old, and 80% were men. Among them, 5 patients were type 1 (16.7%), 2 patients type 2a (6.7%), 7 patients type 2b (23.3%), 5 patients type 2c (16.7%) and 11 patients type 3 (36.7%). The prognosis among these subtypes was significantly different ( $p < 0.001$ ). All type 1 patients were cured, with the highest mortality rate in type 2c patients (100%). Compared with type 2b ( $5.5 \pm 3.5$  days) and type 2c ( $3.4 \pm 2.5$  days), type 3 patients tended to have fewer days to die ( $2.9 \pm 2.7$  days). The difference in NIHSS scores was significant among surviving patients ( $p < 0.001$ ). Type 1 is the lowest at  $1.8 \pm 2.2$  points; type 3 is the highest at  $35.0 \pm 3.5$  points.

**Conclusions:** Relying on the anatomical basis and treatment plan, we propose a different classification, which is conducive to quickly identifying the haemorrhage type and degree of disease, and putting forward an appropriate treatment plan, which is expected to improve the patient prognosis.

**Key words:** neurosurgery brain stem, brain stem haemorrhage, clinical classification.

## Introduction

Brain stem haemorrhage, one of the most severe types of cerebral haemorrhage, accounts for about 5-10% of cerebral haemorrhage, and the age of its onset is mostly 40-60 years. It mostly occurs in the pons, accounting for 77.2-94.5%, and the midbrain and medulla oblongata haemorrhage is rare [6]. Brain stem haemorrhage has a high fatality rate of about 47-80%. Without medical intervention, most of patients will die at 24-48 hours [3,7]. The traditional idea is that brainstem haemorrhage is a "taboo" for surgery. With

the development of neurosurgical microscopy technology and stereotactic technology, the neurosurgery department in many hospitals has gradually carried out the surgical treatment of brainstem haemorrhage, and has made some achievements. However, there is still a lack of standardized evidence-based medical research to systematically explain the diagnosis and treatment principles of brainstem haemorrhage [25].

At present, there is no unified classification standard for brainstem haemorrhage. Different types of classification are mainly based on the axial computed

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tomography (CT) characteristics of precise positioning and anatomical diffusion. Some classifications include the tegmental part (midbrain), while others only focus on pons haemorrhage [2,7,10,13]. Despite the differences in the anatomical classification systems, all previous studies have found that the hematoma size and radiological signs of acute hydrocephalus are associated with a poor prognosis [16,24,28]. Clinical typing can serve the treatment, and provide different treatment options to the families of patients [29]. On the one hand, the purpose of surgical treatment is to remove the hematoma, to reduce the primary injury and secondary injury caused by the hematoma to the brain stem, and on the other hand, to relieve the obstruction of the cerebrospinal fluid circulation system, and to reduce the excessive cranial pressure [20,27]. At present, the previous surgical schemes for brainstem haemorrhage include microscopic craniotomy and hematoma removal, stereotactic (ROSA robot) hematoma puncture and drainage, external ventricular drainage and other surgery [14].

Therefore, this study aimed to develop a novel classification system for evaluating patients with brainstem haemorrhage and preliminarily validate this system in our cohort. This study also aimed to refine the risk stratification of and guide their treatment strategy to achieve precision medicine for this subset of patients.

## Material and methods

### Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Shanghai Deji Hospital. Written informed consent was obtained from all participants.

## Study design and population

Thirty patients with brainstem haemorrhage in Shanghai Deji Hospital from April 2019 to May 2022 were retrospectively included. Inclusion criteria were as follows: 1) CT examination showed brain stem haemorrhage after admission; 2) no history of craniocerebral trauma; and 3) no history of anticoagulant medication. Exclusion criteria were as follows: 1) coagulation dysfunction and blood diseases; 2) patients with brain stem tumors or strokes; 3) brain stem vascular malformation; and 4) brain stem haemorrhage secondary to bleeding in other parts of the brain. The Glasgow Coma Scale (GCS) [12] and the National Institutes of Health Stroke Scale (NIHSS) [8] on the day of admission were collected to assess for dyspnoea on admission. After admission, conservative or surgical treatment was performed according to the patient condition, family opinion and physician judgment, and another follow-up was performed after three months to assess the NIHSS score. Based on the patient's symptoms and functional recovery, the prognosis was divided into cure, improvement and death. The study design protocol was approved by the ethics committee and the patient informed consent was waived as the study was a retrospective study.

## Classification standard

According to the amount and location of bleeding in the brain stem, we divided brainstem haemorrhage into the following types: small haemorrhage type (type 1), medium haemorrhage type (lateral type 2a, ventral type 2b, dorsal type 2c), and large haemorrhage type (type 3). The classification of patients was performed by two neuro-surgeons with at least ten years of experience.

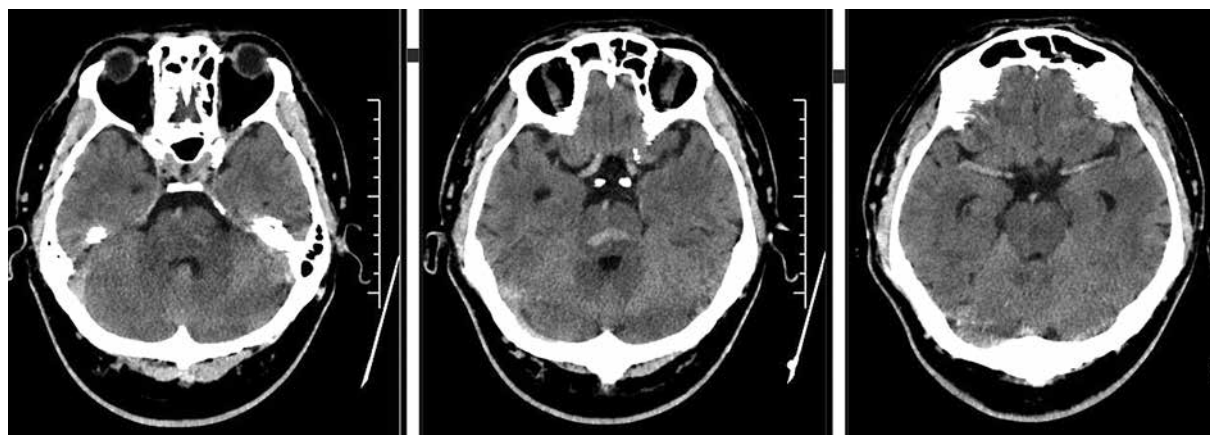


Fig. 1. CT of small haemorrhage (type 1)

rience and a senior clinician was involved in the final determination when there was any disagreement.

### Small haemorrhage type (type 1)

As shown in Figure 1, the bleeding volume was 3 ml or less, the clinical symptoms were not obvious or mild without disturbance of consciousness, and the bleeding side and patent nerve palsy and contralateral limb retardation hemiplegia can occur. Facial nerve and patent nerve palsy, and contralateral limb retardation and hemiplegia can occur on the bleeding side. This type of brain stem haemorrhage is not complicated with hydrocephalus, and surgery is not recommended. It is necessary to closely monitor the changes in vital signs, especially the respiratory rhythm, keep the blood pressure stable, maintain the airway unobstructed, and have invasive respiratory support therapy when necessary.

### Medium haemorrhage type (type 2)

Patients with bleeding volume of 3-8 ml developed severe neurological dysfunction and consciousness disorder with a poor prognosis. The choice of the treatment plan should comprehensively consider the hematoma site, the bleeding volume, the GCS score, the vital signs, and the wishes and expectations of the patient's family and so on. To facilitate the selection of treatment options, we divided brainstem haemorrhage into three subtypes according to the different locations of the hematoma. The left and right lateral 1/6 parts of the brainstem are of lateral type. The central 2/3 part of the brainstem, bounded by the middle, is divided into the dorsal type and the ventral type. See the subtyping diagram for details (Fig. 2).

Medium haemorrhage lateral type (type 2a): the main body of the hematoma is located on the side of the brainstem (Fig. 3), and can be treated non-surgically. The surgical plan can choose hematoma removal *via* retrosigmoid approach or ROSA robotic puncture and drainage. In the Figure 3, the patient underwent emergency microscopic hematoma removal *via* retrosigmoid

approach to remove the hematoma, and space-occupying effect, and reduce the brain stem damage.

Medium haemorrhage dorsal type (type 2b): the hematoma was located in the dorsal brainstem. Hematoma occupying effect or haemorrhage into the cerebral ventricular circulation system is often accompanied by secondary hydrocephalus caused by obstruction of the fourth ventricular and middle cerebral aqueducts. In the case of hydrocephalus, it is recommended to actively perform external ventricular drainage, which can relieve the obstruction of cerebrospinal fluid circulation, reduce high cranial pressure, and reduce brain tissue damage. This type can also be removed by the hematoma removal *via* infratentorial posterior median approach. Because the hematoma is located in the dorsal side of the brain stem, the craniotomy causes less iatrogenic damage to the brain stem (Fig. 4).

Medium haemorrhage ventral type (type 2c): the hematoma was located in the ventral brain stem. Stereotactic puncture or microscopic removal of craniotomy hematoma will bring great iatrogenic damage to the brain stem and have little benefit from surgery. For this type, surgical removal of the hematoma is not recom-

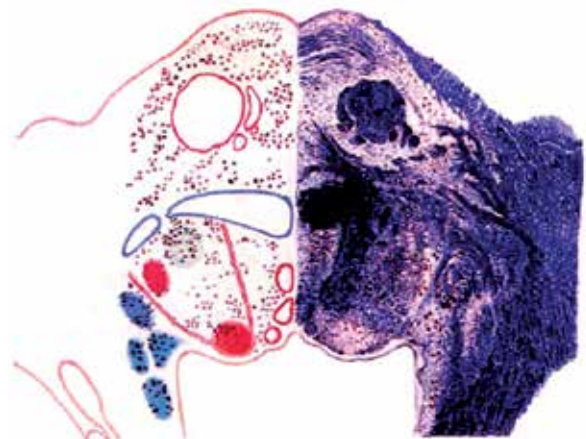


Fig. 2. Schematic diagram of the bleeding haemorrhage sites



Fig. 3. CT of medium haemorrhage lateral type (type 2a)

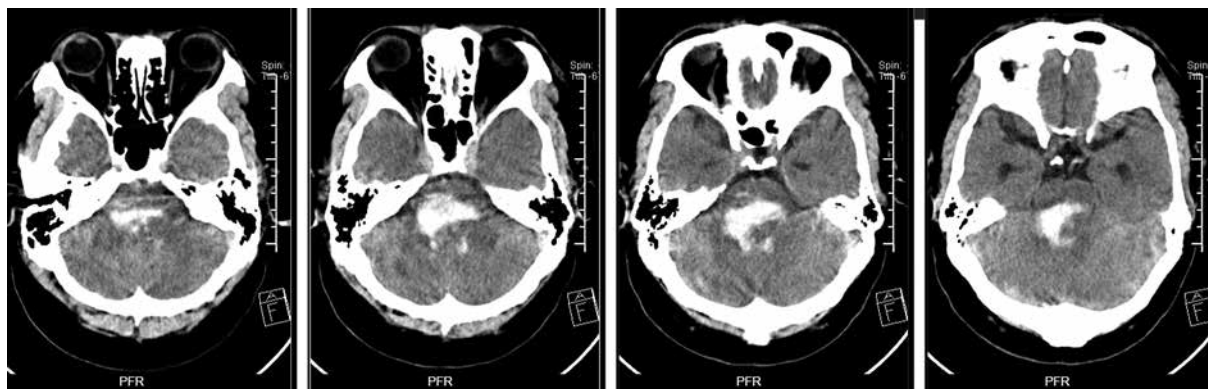


Fig. 4. Preoperative CT of medium haemorrhage dorsal type (type 2b)

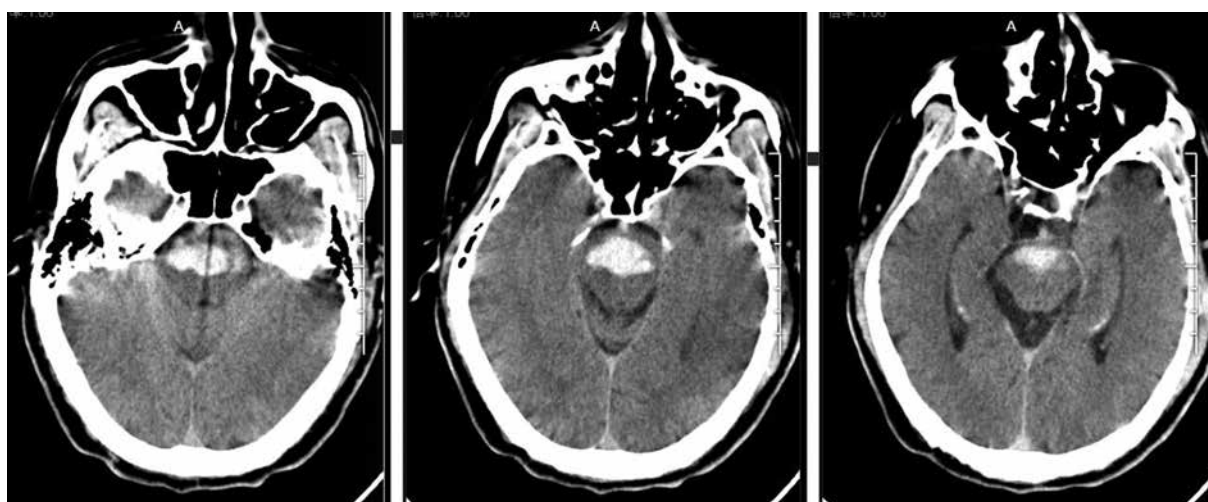


Fig. 5. CT of medium haemorrhage ventral type (type 2c)

mended. When combining ventricular hydrocephalus, it is recommended to perform external ventricular drainage (Fig. 5).

### Large haemorrhage type (type 3)

The amount of blood loss is greater than or equal to 8 ml. The patient has a large amount of bleeding, severe consciousness disorder, deep coma, or combined with respiratory failure, with an extremely poor prognosis and high mortality rate, and little surgical benefit. In clinical work, for young patients with large brain stem bleeding, although the patients' families are fully informed of the condition, prognosis and cost, many families still have a positive willingness to treat them and strongly require surgical treatment. As shown in Figure 6, the hematoma removal *via* infratentorial posterior median approach and external ventricular drainage showed an ideal hematoma removal effect, but a poor prognosis.

### Statistical analysis

All statistics were entered using the Excel forms, and all data analysis were performed using SPSS version 23.0 (IBM Corp., CA, USA). Quantitative data were expressed using the mean  $\pm$  standard deviation, and quantitative data from multiple groups were compared using one-way analysis of variance (ANOVA). Qualitative data are expressed by counts (percentage). Qualitative data for multiple groups were tested using chi-square or exact Fisher test. Differences were considered statistically significant at  $p < 0.05$ .

### Results

#### Patient baseline data

Among the 30 included patients with brainstem haemorrhage, the age was  $53.2 \pm 13.8$  years, and 80% were male. On the day of admission, the GCS score was  $5.87 \pm 4.45$ , the NIHSS score was  $29.43 \pm 12.48$ . Respi-

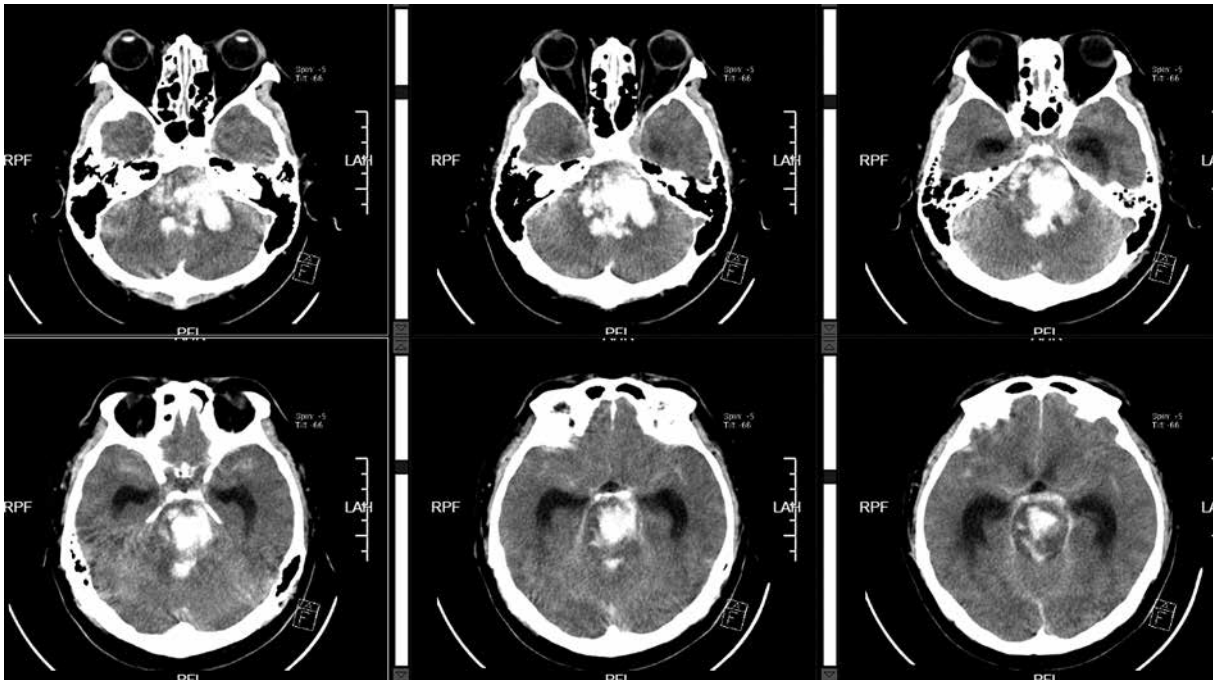


Fig. 6. CT of large haemorrhage type (type 3)

ratory disorder on admission was present in 63.3% of patients. Baseline patient data are shown in Table I.

**Classification and prognosis**

According to the amount and location of bleeding in the brain stem, brainstem haemorrhage was divided into the following types: small haemorrhage type (type 1), medium haemorrhage type (lateral type 2a, ventral type 2b, dorsal type 2c), and large haemorrhage type (type 3). Among them, 5 patients were type 1 (16.7%), 2 patients type 2a (6.7%), 7 patients type 2b (23.3%), 5 patients type 2c (16.7%) and 11 patients

**Table I.** Basic data of the study population

Parameter	Included patients (n = 30)
Age (years), mean ±SD	53.2 ±13.8
Gender	
Male, n (%)	24 (80.0)
Female, n (%)	6 (20.0)
The GCS score on the day of admission, mean ±SD	5.87 ±4.45
Respiratory disorder on the day of admission, n (%)	19 (63.3)
The NIHSS score on the day of admission, mean ±SD	29.43 ±12.48

**Table II.** Patient classification and prognosis

Parameter	Type 1 (n = 5)	Type 2a (n = 2)	Type 2b (n = 7)	Type 2c (n = 5)	Type 3 (n = 11)	P-value
Treatment regimen						0.166
Conservative treatment, n (%)	5 (100.0)	2 (100.0)	4 (57.1)	5 (100.0)	5 (45.5)	
External ventricular drainage, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (36.4)	
Craniotomy hematoma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	
ROSA robotic puncture and drainage, n (%)	0 (0.0)	0 (0.0)	3 (42.9)	0 (0.0)	1 (9.1)	
Patient prognosis						< 0.001
Cure, n (%)	5 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Improvement, n (%)	0 (0.0)	2 (100.0)	5 (71.4)	0 (0.0)	3 (27.3)	
Die, n (%)	0 (0.0)	0 (0.0)	2 (28.6)	5 (100.0)	8 (72.7)	
Death days	NA	NA	5.5 ±3.5	3.4 ±2.5	2.9 ±2.7	0.495
The NIHSS score after 3 months, mean ±SD	1.8 ±2.2	11.0 ±0.0	24.8 ±5.0	NA	35.0 ±3.5	< 0.001

type 3 (36.7%). The relationship between patient classification and prognosis is detailed in Table II. There is no statistical difference in the treatment options between the various subtypes ( $p = 0.166$ ), and all patients with type 1, 2a and 2c chose conservative treatment. However, the prognosis of patients was significantly different between groups ( $p < 0.001$ ). All of the type 1 patients were cured, and type 2c patients had the highest mortality rate, reaching 100%. Compared to type 2b ( $5.5 \pm 3.5$  days) and type 2c ( $3.4 \pm 2.5$  days), type 3 patients tended to have fewer days to die ( $2.9 \pm 2.7$  days). However, there was no statistically significant difference ( $p = 0.495$ ). There were significant statistical differences in the NIHSS scores after 3 months among the surviving patients ( $p < 0.001$ ). Type 1 was the lowest with  $1.8 \pm 2.2$ , and type 3 was the highest with  $35.0 \pm 3.5$ .

## Discussion

In this study, we developed and validated a novel classification system for risk stratification of patients with brainstem haemorrhage. The main findings can be summarized as follows: 1) despite comparable treatment strategies, the prognosis among different subtypes of patients was significantly different; 2) type 3 patients tended to have fewer days to die than types 2b and 2c but this needed further validation; 3) there was a significant difference in the NIHSS score among surviving patients – type 1 patients had the lowest score while type 3 patients had the highest score. This new classification system was a promising tool in grading the severity of brainstem haemorrhage and guiding clinical decision-making. However, external validation with a large sample size was warranted to refine this system.

Brainstem haemorrhage is an acute neurological disease with a very sudden onset. It is associated with early primary coma, motor dysfunction (e.g., tetraplegia, hemiplegia, or extensor posture), respiratory disorder, hypothermia, and pupil abnormalities (e.g., precision pupil, anisocoria) caused by basal or cover destruction [11]. In the era of CT and magnetic resonance imaging (MRI), even small bleeding can be identified, leading to a greater variety of symptoms. However, compared with pontine infarction, pontine haemorrhage is rare and develops sufficiently slow to present an initial symptom that reflects the presence of progressive damage to the cranial nerve and its cells [11,15]. Previous retrospective studies have highlighted that severe initial neurological dysfunction, especially early coma, required mechanical ventilation and hydrocephalus, and was associated with a poor prognosis [22,26], but that pupillary abnormalities were not significantly correlated with the outcome [7]. Patients with secondary bleeding in the brainstem due to a cavernous haeman-

gioma or arteriovenous malformations usually exhibit less severe initial symptoms and have a more favourable outcome [5,9]. These secondary bleeds have different dynamics from primary bleeding because they are more extended rather than destructive.

Current guidelines suggest that early intensive BP reduction to 140 mm Hg is safe for patients with GCS greater than 5 points and systolic blood pressure of 150-220 mm Hg. However, a 2017 meta-analysis included five studies and 4360 patients confirmed that intensive, acute antihypertensive was safe but found that it did not clinically benefit in mortality or functional outcomes [1,4,21]. The more common surgical procedure for brainstem hematoma is external ventricular drainage. It is required in patients with clinical and radiological signs of hydrocephalus, which is more likely when the bleeding extends into the ventricular system [18]. However, some studies have found no significant improvement in the results after hydrocephalus treatment with intraventricular drainage [17]. A retrospective, observational, single-centre study comparing the efficacy of bony flap decompression, medication, and external ventricular drainage placement in patients with posterior fossa haemorrhage found significant increases in hydrocephalus and intraventricular haemorrhage in patients treated with external ventricular drainage placement [23].

Previous studies have developed a different classification for brainstem haemorrhage. Some scholars have divided the brainstem hematoma into three types: central type, dorsolateral tegmental type and basal-tegmentum type, which mainly come from different pathophysiological mechanisms [13]. Large hematomas caused by hypertension usually occupy the central pons and cause a rapid, fatal clinical course due to the involvement of the reticulate system. Some pons hematoma, mainly due to the rupture of hidden vascular malformation, is limited to the lateral half of the pons, and the reticular system is not affected. These may be dorsolateral tegmentum or basal-tegmentum of pons. Subsequent studies were improved on this basis, and the proposed classification of brainstem haemorrhage included large, basal-tegmentum, transverse oval, and small unilateral ones. The mortality rate for transverse oval or small unilateral hematoma cases was 25%, whereas for large or basal-tegmentum hematoma cases it was 65% [19]. Based on the previous study, this study typed the brainstem hematoma according to the amount and site of brainstem haemorrhage. The obtained results fully combined bleeding volume and site information, undoubtedly enabling better risk stratification of patients. The results also proved that the prognosis of type 2c and type 3 patients was obviously poor, mainly because of the large amount of bleeding and the func-

tional importance of the damaged site. In addition, five subtypes are proposed, which are more detailed and more diverse than the previous systems, and can also provide more information for the treatment. However, this classification system needs more evidence-based studies with high-quality large samples before clinical application.

## Conclusions

Brain stem haemorrhage is critical, with a high mortality and disability rate, and its pathophysiological changes have time dependency. Elimination of the hematoma as soon as possible to reduce the space-occupying effect and secondary damage to the surrounding brain tissue is one of the keys to treatment. Relying on the anatomical basis and treatment plan, we put forward a different classification, which is conducive to the rapid identification of the bleeding type and degree of disease, and put forward the appropriate treatment plan, which can facilitate the promotion of primary hospitals and young doctors to master. With the development of neurosurgery, the treatment of brainstem haemorrhage is continuously improved, and more and more surgical schemes and monitoring methods are applied to the treatment of brainstem haemorrhage. It is believed that the prognosis of brainstem haemorrhage will be continuously improved.

## Disclosure

The authors report no conflict of interest.

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