Minimally invasive thalamic hematoma drainage can improve the six-month outcome of thalamic hemorrhage

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Abstract

Objective To explore predictors of the 6-month clinical outcome of thalamic hemorrhage, and evaluate if minimally invasive thalamic hematoma drainage (THD) could improve its prognosis. Methods A total of 54 patients with spontaneous thalamic hemorrhage were evaluated retrospectively. Clinical data, including demographics, stroke risk factors, neuroimaging variables, Glasgow Coma Score (GCS) on admission, surgical strategy, and outcome, were collected. Clinical outcome was assessed using a modified Rankin Scale, six months after onset. Univariate analysis and multivariate logistic regression analysis were performed to determine predictors of a poor outcome. Results Conservative treatment was performed for five patients (9.3%), external ventricular drainage (EVD) for 20 patients (37.0%), THD for four patients (7.4%), and EVD combined with THD for 25 patients (46.3%). At six months after onset, 21 (38.9%) patients achieved a favorable outcome, while 33 (61.1%) had a poor outcome. In the univariate analysis, predictors of poor 6-month outcome were lower GCS on admission ($P = 0.001$), larger hematoma volume ($P < 0.001$), midline shift ($P = 0.035$), acute hydrocephalus ($P = 0.039$), and no THD ($P = 0.037$). The independent predictors of poor outcome, according to the multivariate logistic regression analysis, were no THD and larger hematoma volume. Conclusions Minimally invasive THD, which removes most of the hematoma within a few days, with limited damage to perihematomal brain tissue, improved the 6-month outcome of thalamic hemorrhage. Thus, THD can be widely applied to treat patients with thalamic hemorrhage.

Keywords: Hematoma volume; Minimally invasive; Outcome; Predictor; Thalamic hematoma drainage; Thalamic hemorrhage

1 Introduction

Spontaneous intracerebral hemorrhage (ICH) is a frequent form of cerebrovascular diseases that accounts for 30% of all stroke cases in China, which is approximately double that in Western countries.[1,2] It is a devastating form of stroke with a higher mortality than that of ischemic stroke. The prevalence of thalamic hemorrhage ranges from 6% to 25% of intracerebral hemorrhage.[3-5] It usually ruptures into the ventricular system, damages the posterior limb of the internal capsule, and even compresses the midbrain and cerebral aqueduct, which can lead to obstructive hydrocephalus, paralysis, or even death. Further, perihematomal edema develops over time, resulting in secondary injury and neurological deterioration after the first day.[6-8]

Previous studies have shown that the prognosis of patients with thalamic hemorrhage is affected by a series of factors, such as age, hematoma volume, Glasgow coma scale (GCS) score on admission, stroke risk factors, underlying disease, neuroimaging, operation, complications, etc.[9-13] Currently, there are several treatment options for thalamic hemorrhage, such as conservative treatment, conventional craniotomy, and minimally invasive surgery, which also includes endoscopic evacuation, stereotactic aspiration, and CT-positioned hematoma puncture combined with liquefactive application. However, according to the current literature, it is still debatable as to which is the best therapeutic regimen for thalamic hemorrhage. Some studies showed that there was no significant benefit of surgical treatment over conservative medical treatment for thalamic hemorrhage[14-16] while others provide contrary evidence.[17-21] Therefore, future studies are required to explore the effec-
tiveness of these treatment options for thalamic hemorrhage.

In recent years, CT-positioned thalamic hematoma drainage (THD) combined with urokinase application was used in our hospital to treat thalamic hematoma, with satisfactory results. In the current study, we collected clinical data from 54 patients with thalamic hemorrhage, and analyzed the effect of minimally invasive THD on the prognosis and predictors of the 6-month clinical outcome.

2 Methods

2.1 Study population

All patients with spontaneous thalamic hemorrhage, who were admitted to the Emergency Neurosurgery Department of Shandong University Qilu Hospital from August 2011 to January 2015, were screened for this study. The inclusion criteria were the presence of primary thalamic hemorrhage and an intracerebral hematoma volume of 5–40 mL. The intracerebral hemorrhage volume was measured using the ABC/2 method with CT scanning.[22] The exclusion criteria were as follows: hematoma involving the basal ganglia region, non-first-time bleeding, secondary ICH (due to head trauma, aneurysm, vascular malformation, hemorrhagic infarction, cerebral vein and sinus thrombosis, tumor, anticoagulants, or coagulopathy-related hemorrhage), or a loss of follow-up. The study protocol was approved by the ethics committee of the hospital. The families of all the patients received a comprehensive description of the study and provided written informed consent for the patient’s participation in the study.

2.2 Surgery and postoperative treatment

Bilateral external ventricular drainage (EVD) was performed for patients with acute hydrocephalus or intraventricular hemorrhage (IVH). The necessity and risks of THD and conservative treatment were explained to the relatives of all patients, and surgery was performed for patients with informed consent from their relatives. The puncture position, depth (generally 7–8 cm), and direction were defined in accordance with the preoperative CT scan. A hole was bored in the temporal bone with a directional skull drill and the bone residue was removed with a special curette. Thereafter, a brain needle was punctured to the predetermined depth and direction, and the hematoma was drawn out gently by syringe to confirm the tube position. Finally, the passageway was formed using a 12F or 14F smooth rod, and the corresponding polyester tube with two side holes was punctured into the hematoma cavity. The position of the drainage tube and residual hematoma volume were immediately checked with a portable CT (NL3000, Neurologica CereTom, USA), and adjusted if necessary (Figure 1).

2.3 Postoperative treatment

To liquefy the hematoma, the liquefacient (i.e., a urokinase injection) was injected into the hematoma cavity (3 mL saline solution/30,000 U urokinase) and to the lateral ventricle with the hematoma (4–5 mL saline solution/20,000 U urokinase), twice a day. The risks such as re-bleeding, allergy, etc., were explained to the patients’ relatives, and their written informed consent was received before the injection. Urokinase injection was discontinued when the hematoma was eliminated or it could no longer be removed using the urokinase injection, according to the CT scan. The THD was then removed.

The timeline of EVD removal was as follows: The EVD was clipped when the hematoma in the lateral ventricle was mostly removed and that in the third and fourth ventricle disappeared. Two days later, the EVD was removed if the patient’s condition had not deteriorated and there was no hydrocephalus according to CT scan. Lumbar drainage was applied to eliminate residual hematoma in the ventricle and subarachnoid space.

If the EVD could not be removed, an endoscopic third ventriculostomy (ETV) was performed when the aqueduct of midbrain was pressed, or a ventriculoperitoneal shunt (VPS) was performed when the aqueduct of midbrain was not compressed or the ETV failed.

Other treatments (such as blood pressure control, sedation, antibiotics, water and electrolyte balance, dehydration drug use, pneumonia treatment, nutritional support, etc) were performed when necessary.

2.4 Clinical data collection

Clinical data of the patients were collected on admission or during hospitalization. The variables included demographics (age and sex), alcohol and tobacco abuse, a detailed history of stroke risk factors [hypertension, diabetes mellitus, coronary heart disease, and chronic obstructive pulmonary diseases (COPD)], neuroimaging variables at presentation (hematoma volume, intraventricular extension, midline shift, acute hydrocephalus, and brain edema), GCS on admission, surgery or conservative treatment, continuous hydrocephalus and treatment, and outcome. The midline shift was determined by the distance between the midline and third ventricle, according to the CT scan.

2.5 Functional outcome assessment

Clinical outcome was assessed using the modified Ran-
kin Scale (mRS), six months after onset. Follow-up was conducted with a telephone interview or face-to-face assessment. In the current study, since the status of the patients was relatively serious owing to the hematoma volume, a mRS score of three points was considered a good prognosis. Therefore, poor clinical outcome was defined as a mRS score of ≥ 4, when assessed at the 6-month follow-up.

2.6 Statistical analysis

Continuous variables that were normally distributed were expressed as mean ± SD, while those that were not normally distributed were reported as median [interquartile range (IQR)]. For the univariate analysis, normally distributed continuous variables were analyzed with a Student’s t-test, while those that were not normally distributed were analyzed with a Mann-Whitney U test. Categorical variables were analyzed with a chi-square test. Stepwise forward logistic regression was used to determine independent predictors for poor functional outcome at 6 months after ICH. All tests were two-tailed and statistical significance was determined at α-level of 0.05. Statistical analysis and charting were performed using SPSS19.0 and Excel 2010.

3 Results

3.1 Clinical data

The clinical data is listed in Table 1–3. Of the 89 patients...
with thalamic hemorrhage measuring 5–40 mL, who were treated in our department, a total of 54 patients met the inclusion criteria of this study. The patient cohort in this study had a mean age of 54.74 ± 10.85 years (IQR: 33–78 years), and comprised 34 men and 20 women. A total of 37 (82.2%) patients had one or more of the following underlying diseases: 33 (61.1%) patients had hypertension, 14 (25.9%) patients had diabetes mellitus, 6 (11.1%) patients had COPD, and 16 (29.6%) patients had coronary artery

| Characteristics       | Total (n = 54) | Good outcome (n = 21) | Poor outcome (n = 33) | OR (95% CI) | P value |
|-----------------------|---------------|-----------------------|-----------------------|-------------|---------|
| **Demographics**      |               |                       |                       |             |         |
| Male                  | 34 (63.0%)    | 11 (52.4%)            | 23 (69.7%)            | 2.091 (0.673–6.495) | 0.199   |
| Age, yrs              | 54.74 ± 10.85 | 51.95 ± 10.51         | 56.52 ± 10.85         |              |         |
| GCS score on admission| 9 (3)         | 10 (4)                | 8 (3)                 |              | 0.001   |
| **Risk factors**      |               |                       |                       |             |         |
| Smoking               | 18 (33.3%)    | 5 (23.8%)             | 13 (39.4%)            | 2.080 (0.612–7.067) | 0.236   |
| Alcohol abuse         | 13 (24.1%)    | 5 (23.8%)             | 8 (24.2%)             | 1.024 (0.284–3.688) | 0.971   |
| Hypertension          | 33 (61.1%)    | 13 (61.9%)            | 20 (60.6%)            | 0.947 (0.308–2.913) | 0.924   |
| Diabetes mellitus     | 14 (25.9%)    | 5 (23.8%)             | 9 (27.3%)             | 1.200 (0.339–4.243) | 0.777   |
| Coronary heart disease| 16 (29.6%)    | 4 (19.0%)             | 12 (36.4%)            | 2.429 (0.662–8.909) | 0.174   |
| COPD                  | 6 (11.1%)     | 1 (4.8%)              | 5 (15.2%)             | 3.571 (0.387–32.962) | 0.236   |
| **Radiologic variables** |             |                       |                       |             |         |
| Hematoma volume, mL   | 22.04 ± 8.55  | 16.19 ± 6.10          | 25.76 ± 7.82          |              | 0.000   |
| Intraventricular extension | 43 (79.6%) | 17 (81.0%)            | 26 (78.8%)            | 0.874 (0.222–3.447) | 0.847   |
| Acute hydrocephalus   | 30 (55.6%)    | 8 (38.1%)             | 22 (66.7%)            | 3.250 (1.039–10.162) | 0.039   |
| Midline shift ≥ 1 cm  | 35 (64.8%)    | 10 (47.6%)            | 25 (75.8%)            | 3.438 (1.068–11.068) | 0.035   |
| **Operation**         |               |                       |                       |             |         |
| THD                   | 29 (53.7%)    | 15 (71.4%)            | 14 (42.4%)            | 0.295 (0.091–0.951) | 0.037   |
| EVD                   | 45 (83.3%)    | 17 (81.0%)            | 28 (84.8%)            | 1.318 (0.310–5.597) | 0.708   |
| Continuous hydrocephalus | 11 (20.4%) | 2 (9.5%)              | 9 (27.3%)             | 3.563 (0.687–18.479) | 0.114   |

Data were presented as n (%), mean ± SD or median (interquartile range). COPD: chronic obstructive pulmonary diseases; EVD: external ventricular drainage; GCS: Glasgow Coma Score; THD: thalamic hematoma drainage.
There were 18 (33.3%) patients who were smokers and 13 (24.1%) patients who drank alcohol regularly. The GCS score on admission was $8.56 \pm 2.52$ (4–14).

CT was performed for all 54 patients. The average intracerebral hematoma volume was $22.04 \pm 8.55$ mL (7–38 mL); 43 (79.6%) patients had intraventricular extension, 30 (55.6%) patients had acute hydrocephalus, and 35 (64.8%) patients had a midline shift $\geq 1$ cm.

Conservative treatment was performed on five (9.3%) patients, EVD on 20 (37.0%) patients, THD on four (7.4%) patients, and EVD combined with THD on 25 (46.3%) patients. All of the operations were performed 3–36 h after onset. On average, urokinase injection with EVD was performed on 33 patients for $2.36 \pm 0.45$ days (1–5 days) and the EVD was removed $6.21 \pm 0.71$ days (4–9 days) after surgery. In contrast, urokinase injection with THD was performed on all 29 patients with THD for an average of $2.59 \pm 0.39$ days (2–5 days), and the THD was removed $3.62 \pm 0.47$ days (2–7 days) after surgery. At least 80% of the thalamic hematoma was removed in the 29 patients with THD (Table 2).

Nine patients suffered from continuous hydrocephalus. ETV was performed for four of these patients, while VPS was performed for the remaining five patients and for an additional patient after the failure of ETV.

Mechanical ventilation was required for 19 (35.2%) patients and pneumonia was diagnosed in 34 (67.0%) patients. The body temperature was controlled between 36.0ºC and 37.0ºC with the help of drugs or physical cooling. Osmotherapy (mannitol or hypertonic saline) was used pre- or post-operation. Mannitol was used in accordance with the clinical manifestations and imaging.

Seven patients died during hospitalization owing to critical condition, and one patient died owing to atrial fibrillation and circulatory failure. At 6-month follow-up, 0, 4 (7.4%), 8 (14.8%), 9 (16.7%), 11 (20.4%), 14 (25.9%), and 8 (14.8%) patients had a mRS score of 0–6, respectively. Thus, 21 (38.9%) patients achieved a favorable functional outcome (i.e., a mRS score $\leq 3$), while 33 (61.1%) patients had a poor functional outcome (i.e., a mRS score of 4–6) (Table 1).

### 3.2 Predictors of poor outcome six months after thalamic hemorrhage

According to the univariate analysis, the predictors of poor 6-month outcome were a low GCS score on admission ($P = 0.001$), larger hematoma volume ($P < 0.001$), midline shift ($P = 0.035$), acute hydrocephalus on admission ($P = 0.039$), and no THD ($P = 0.037$). There were no significant differences in terms of sex, age, the rest of the evaluated risk factors, intraventricular extension, EVD, or continuous hydrocephalus (Table 3). The prognostic accuracy for 6-month outcome was assessed using receiver operating characteristic curve analysis. The area under the curve for no THD was 0.645 (95% CI: 0.494–0.796), while that for a low GCS score on admission, hematoma volume, acute hydrocephalus on admission, and midline shift were $0.626–0.904$), $0.816$ (95% CI: 0.704–0.928), $0.643$ (95% CI: 0.490–0.796), and $0.641$ (95% CI: 0.485–0.796), respectively (Figure 2).

Figure 2. The ROC curve of predictors to predict the poor 6-month outcome. The AUC of no THD, GCS score on admission, hematoma volume, acute hydrocephalus on admission and midline shift were 0.645 (95% CI: 0.494–0.796), 0.765 (95% CI: 0.626–0.904), 0.816 (95% CI: 0.704–0.928), 0.643 (95% CI: 0.490–0.796), and 0.641 (95% CI: 0.485–0.796), respectively (Figure 2).

In the multivariate analysis, the entrance cutoff of the variables was set to 0.10, according to the results of univariate analysis. Therefore, GCS score on admission, acute hydrocephalus, hematoma volume, midline shift, and THD were selected for multivariate analysis using logistic regression. According to the stepwise logistic regression, no THD and a larger hematoma volume were independent predictors for a poor 6-month outcome.

### 4 Discussion

The current study examined the relationship among clinical data on admission, surgery, and the 6-month outcome, following thalamic hemorrhage. A low GCS score on
admission, larger hematoma volume, acute hydrocephalus on admission, no THD, and midline shift were predictors of a poor 6-month functional outcome. Further, no THD and larger hematoma volume were independent predictors of a poor 6-month outcome.

4.1 Hematoma volume and outcome

Hematoma volume is the most powerful predictor of mortality and prognosis, and a larger hematoma is widely believed to be an indication for surgical treatment[9–12,23] since it can lead to more serious damage to the thalamus, internal capsule, brain stem, and a higher incidence of acute hydrocephalus and secondary damage. In the current study, the volume of thalamic hematomas was closely associated with the 6-month outcome, according to the univariate and multivariate analysis, which was consistent with previous studies. A midline shift ≥ 1 cm, which was positively correlated with hematoma volume, was also a risk factor of poor outcome, according to the univariate analysis.

4.2 Glasgow coma scale score on admission and outcome

In this study, the GCS score on admission was closely associated with 6-month outcome, according to the univariate analysis. It is a comprehensive reflection of the damage to thalamus, internal capsule, and brain stem that is caused by thalamic and intraventricular hematoma. A lower GCS score on admission, which indicates more serious primary injury, is also an important reference in determining whether conservative or surgical treatment should be performed for thalamic hemorrhage.[10,11,13]

4.3 Hydrocephalus and outcome

It is interesting to note that acute hydrocephalus, but not continuous hydrocephalus, was closely associated with the 6-month outcome. The reason for this might be that acute hydrocephalus was caused by the sudden, primary damage of the thalamic and intraventricular hematoma, while continuous hydrocephalus was caused by chronic damage of midbrain aqueduct obstruction or communicating hydrocephalus. Continuous hydrocephalus could be cured by ETV or VPS, which can be performed when the midbrain aqueduct is still obstructed after the hematoma is removed, when communicating hydrocephalus occurs, or when ETV fails.

4.4 Controversies of thalamic hemorrhage treatment

According to the current literature, there is considerable controversy regarding the value of surgical therapy over conservative therapy for spontaneous thalamic hemorrhage.[15,18] The “surgical treatment for intracerebral hemorrhage” (i.e., STICH) trial failed to demonstrate that evacuation of hematoma within 72 h after onset resulted in a better outcome, compared with medical management alone.[14] This finding is also supported by other studies, which had similar conclusions.[15,16,24] Since the effect of the mass can lead to brain damage, such as intracranial hypertension and cerebral hernia, the toxic substances released from the hematoma are important factors in the pathological mechanism of thalamic hemorrhage. The purpose of surgery is to reduce the clot burden, relieve the pressure on perihematomal brain tissue, decrease the incidence of hydrocephalus, and reduce secondary brain injury (via the reduction of cytotoxic edema and additional neuronal injury).[10,21,24,26]

Thalamic hematoma is usually deeper and smaller than basal ganglia hemorrhage. The hematoma can be completely removed using conventional craniotomy, thus, reducing intracranial pressure. However, this approach has some shortcomings, including a long operation duration, severe damage to normal brain tissue on the passageway, pulling of the brain during the operation, and damage to perihematomal brain tissue due to electrocoagulation, which is used to stanch bleeding. Therefore, conventional craniotomy is rarely used to treat deep-seated thalamic hemorrhage.[16,27]

4.5 The advantages of minimally invasive thalamic hematoma drainage

Minimally invasive procedures, such as THD, endoscopic evacuation, and stereotactic aspiration, are current trends in the neurosurgical treatment of ICH.[17,20,21,27–30] In the current study, minimally invasive THD, in combination with subsequent thrombolysis, was closely associated with a good outcome. Compared with conventional craniotomy, with THD, the majority of the hematoma was removed within a few days, with very limited damage to normal brain tissue. Further, the duration of the operation was short, typically lasting approximately 10–20 min. Damage to brain tissue was equal to the diameter of the drainage tube, which was approximately 5 mm. Since the blood vessels around the passageway were pushed aside by the smooth rod before puncturing the drainage tube into the hematoma cavity, the risk of rebleeding during the operation was also significantly reduced. Thus, THD can be performed safely in a relatively uniform manner, and be widely applied to treating patients with thalamic hemorrhage.

4.6 Limitations of this study

There are still several limitations in the current study that should be addressed. The volume of the smallest hematoma on which THD was performed was 8 mL and the highest
GCS score on admission was 13. However, it is still not clear if THD can be recommended for all patients with thalamic hemorrhage, since the indications of performing THD are still unknown. Further, according to this study, it is unclear if the time interval between surgery and onset affected the prognosis and mortality rate. Since these limitations can be attributed to the relatively small number of cases that were studied, a prospective study with a larger cohort will be required to clarify these issues and lead to a more convincing result.

4.7 Conclusions

We concluded that a lower GCS score on admission, larger hematoma volume, midline shift, acute hydrocephalus on admission, and no THD were risk factors affecting the 6-month outcome of thalamic hemorrhage, of which no THD and a larger hematoma volume were independent predictors of outcome according to the multivariate logistic regression analysis. Minimally invasive THD was adept at removing the majority of the hematoma within a few days, with limited damage to the perihematomal brain tissue and short operation duration. Thus, it is a good option for patients with thalamic hemorrhage. However, further prospective studies are required to explore the indications and ideal timing of THD.

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