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Surgery for Patients With Spontaneous Deep Supratentorial Intracerebral Hemorrhage

A Retrospective Case-Control Study using Propensity Score Matching

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Abstract: Spontaneous intracerebral hemorrhage (sICH) is one of the most dangerous cerebrovascular diseases, especially when in deep brain. The treatment of spontaneous deep supratentorial intracerebral hemorrhage is still controversial. We conducted a retrospective case-control study using propensity score matching to compare the efficacy of surgery and conservative treatment for patients with deep surpatentorial hemorrhage.

We observed the outcomes of consecutive patients with spontaneous deep supratentorial hemorrhage retrospectively from December 2008 to July 2013. Clinical outcomes of surgery and conservative treatments were compared in patients with deep sICH using propensity score matching method. The primary outcome was neurological function status at 6 months post ictus. The second outcomes included mortality at 30 days and 6 months, and the incidence of complications. Subgroup analyses of 6-month outcome were conducted.

Sixty-three (22.66%) of the 278 patients who received surgery had a favorable neurological function status at 6 months, whereas in the conservative group, 66 of 278 (23.74%) had the same result ($P = 0.763$). The 30-day mortality in the surgical group was 19.06%, whereas 30.58% in the conservative group ($P = 0.002$). There was significant difference in the mortality at 6 months after ictus as well (23.38% vs 36.33%, $P = 0.001$). The subgroup analyses showed significantly better outcomes for the surgical group when hematoma was >40 mL (13.33% vs 0%, $P = 0.005$) or complicated with intraventricular hemorrhage (16.67% vs 7.27%, $P = 0.034$). For complications, the risk of pulmonary infection, gastrointestinal hemorrhage, urinary infection, pulmonary embolus, and need for tracheostomy/long term ventilation in the surgical group was higher than the conservative group (31.29% vs 15.47%, $P < 0.001$; 6.83% vs 3.96%, $P = 0.133$; 2.88% vs 1.80%, $P = 0.400$; 1.80% vs 1.08%, $P = 0.476$; 32.73% vs 23.38%, $P = 0.014$).

Surgery could reduce the short-term mortality as well as long-term mortality in patients with spontaneous deep supratentorial hemorrhage. Moreover, surgery might improve the functional outcome in patients with large hematoma or with IVH compared with conservative treatment. Surgery might be a beneficial choice for part of the patients with spontaneous deep supratentorial hemorrhage, but further detailed research is still needed.

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Abbreviations: AHA/ASA = American Heart Association/American Stroke Association, BMEC = Biological and Medical Ethics Committee, CT = Computed Tomography, DC = Decompressive Craniotomy, GCS = Glasgow Coma Scale, ICP = Intracranial Pressure, IVH = Intraventricular Hemorrhage, mRS = Modified Rankin Scale, MS = Midline Shift, SD = Standard Deviations, sICH = Spontaneous Intracerebral Hemorrhage, STICH = International Surgical Trial in Intracerebral Hemorrhage.

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INTRODUCTION

It is reported that over 1 million people suffer from spontaneous intracerebral hemorrhage (sICH) every year worldwide.[1,2] The 30-day mortality is about 30% to 55%. The majority of the survivors live with serious neurological sequelae that require long-term medical and social care.[2–4] Only 12% to 39% of the survivors have favorable neurological functions recovered.[4,5] Most sICHs happen in the deep area of brain such as basal ganglia and thalamus.[6] Some studies showed that prognosis of sICH was related to the depth of the hematoma. Patients with deep sICH showed poor outcome compared to those with superficial lobar hemorrhage.[7,8]

The treatment of sICH is still debatable among the surgeons up to now. The focus of the controversy is whether evacuation of hematoma will be able to improve the prognosis. Some clinical and experimental evidence showed that the removal of hematoma might reduce nervous tissue damage, possibly by relieving local ischemia and removing noxious chemicals.[9–11] Nevertheless, deep hematoma is inaccessible and the surgical approach paths might interfere with the cerebral functional areas. Therefore, most neurologists are more likely to adopt conservative treatment rather than surgically removing the deep hematoma. Nonetheless, for patients with large hematoma and rapid neurological deterioration, surgery might be a better choice.[12]

Several studies aiming to explore the efficacy of surgery for patients with sICH have been carried out. However, the results were inconclusive. The first prospective randomized controlled trial was reported by Mckissock et al[13] in 1961, which came to the conclusion that the patients received surgery had a worse outcome than the patients receiving conservative treatment. Another influential prospective study is the STICH trail, which was reported by Mendelow et al[7] in 2005. Subgroup analysis of the study showed that the patients with deep sICH did not benefit from early surgery when compared with initial conservative treatment. In 2006, Pantazis et al[14] reported the opposite result in a trail of 108 patients with subcortical and putaminal hematoma. Furthermore, some minimally invasive techniques such as neuroendoscope and stereotactic aspiration have been applied to the surgery of sICH. Two initial trials and a meta-analysis showed that minimally invasive surgery was significantly better than conservative treatment in some subgroup analysis.[15–17] However, no consensus was reached concerning the patients with deep sICH. Until now, there is no further study investigating the effect of surgery for patients with deep sICH exclusively. To provide evidence for clinical practice, here we present a retrospective case-control study using propensity score matching to explore the effect of surgery for patients with deep sICH.

METHOD

Study Design

This retrospective case–control study compared the clinical outcomes of surgery and conservative treatment in patients with deep sICH using the propensity score matching method. A one-to-one matching analysis was performed between patients who underwent surgery or conservative treatment on the basis of the estimated propensity scores of each patient.

Patient Population

The present study was approved by the Biological and Medical Ethics Committee (BMEC) of West China Hospital. We retrospectively reviewed the medical records of the patients with spontaneous intracerebral hemorrhage from December 2008 to July 2013. Patients were included if: CT scan showed the hematoma was located in basal ganglia or thalamus; hematoma was $\geq$1 cm in depth from the cortex surface of the brain; the volume of hematoma was $\geq$ 20 mL. Patients were excluded if: hematoma was caused by secondary factors (intracranial tumor, arteriovenous malformation or aneurysm); contraindications of surgery existed; hematoma affected the brain stem; known advanced dementia or disability existed before ICH happened. In the present study, the contraindications of surgery were listed as followed: with coagulation disorders or history of anticoagulant medications; with severe hepatic and renal dysfunction; with terminal brain hernia (bilateral pupils dilated and central respiratory failure). Patients with uncompleted data were also excluded. Hematoma volume was calculated from CT scans using the formula $A \times B \times C/2$, where A is the greatest diameter on the largest hemorrhage slice, B is the maximal diameter perpendicular to A, and C is the vertical hematoma depth.[18] The patients were all followed up for over 6 months.

Treatment

All patients were managed in the stroke unit with standard medical treatment and care. CT scans, blood routine, biochemical examinations (eg, hepatic and renal function, electrolytes), and routine coagulation studies were performed immediately when the patients were admitted to the emergency department. The medical history and neurologic physical examination were also recorded immediately after hospitalized into the stroke unit. All patients had their vital signs monitored and were given supportive treatment at the same time.

Surgery

All the surgeries were conducted by a special sICH treatment team, which was consisted by well-trained neurosurgeons. All the patients received hematoma evacuation. The techniques used were craniotomy or neuroendoscopy. Decompressive craniotomy was conducted if necessary. In some conditions, an extraventricular drainage was conducted before or after the operation. The surgical method was decided by the surgeons preoperatively. All the craniotomy hematoma evacuation was assisted by operative microscope and followed the principle of minimally invasiveness.

Medical Treatments

All the patients received standard medical treatments of sICH. The medical treatments included decreasing intracranial pressure, blood pressure control, prevention of complications, and other treatments individually. The mannitol or glycerin fructose was administered with appropriate dose based on the clinical conditions of patients. All the medical managements followed the recommendations of AHA/ASA guidelines and clinical experience.[19,20]

Outcomes and Data Collection

Patients were followed up for at least 6 months. The primary outcomes assessed were neurological functional status of survivors at 6 months post ictus. The secondary outcomes included: mortality at 30 days, mortality at 6 months post ictus, and complications. The neurological functional status was evaluated by using the Modified Rankin Scale (mRS). Complications including pulmonary infection, gastrointestinal bleeding, urinary tract infection, pulmonary embolus, and need for tracheostomy/long-term mechanical ventilation were also collected.

Statistical Analysis

Given the selection bias inherent to retrospective observational studies, a one-to-one matching analysis was performed between the surgical group and conservative group on the basis of the estimated propensity scores of each patient in the present study.[21] To estimate the propensity score, a function was built by logistic regression model for the receipt of surgery on the basis of patients' clinical factors. The clinical factors included age, admission Glasgow coma scale (GCS), location of hematoma, midline shift (MS), volume of hematoma, depth of hematoma, and medical histories. Cases in the 2 groups were matched according to the similarity of their propensity score noreplacemently by the method of nearest-neighbor matching.

The 6-month mRS was dichotomized as poor outcome (mRS 3–6) and favorable outcome (mRS 0–2). Primary analysis was to compare 6-month neurological functional outcomes post ictus between the surgical group and conservative group. A further subgroup analysis of 6-month outcome was stratified by age, Glasgow coma scale (GCS), location of hematoma, hematoma volume, midline shift (MS), and with/without intraventricular hemorrhage (IVH). Other analysis included 30-day mortality, 6-month mortality, and complications.

Statistically significance was assumed with a probability value of <0.05. Chi-square test was used for analyzing the categorical value. Continuous variable data were expressed as the means $\pm$ standard deviations (SD) and analyzed by t test.

RESULT

From December 2008 to July 2013, a total of 856 patients meet the inclusion criteria. In the 824 patients, 79 patients were

TABLE 1. Baseline of the Patients Before and After Propensity Score Matching

	Before PSMatching			After PSMatching		
	Surgical Group (n = 278)	Conservative Group (n = 441)	*P*	Surgical Group (n = 278)	Conservative Group (n = 278)	*P*
Male	184	316	0.121	184	190	0.588
Age, y	54.23 ± 11.62	58.49 ± 13.28	0.000	54.23 ± 11.62	54.85 ± 12.41	0.537
Time ictus, h	11.78 ± 13.51	11.05 ± 12.07	0.447	11.78 ± 13.51	11.94 ± 12.84	0.887
GCS			0.111			0.978
3–8	113	197		113	111	
9–12	93	159		93	93	
13–15	72	85		72	74	
Paralyzed	230	364	0.947	230	239	0.293
Dysphasic or aphasic	135	231	0.318	135	129	0.610
History						
Hypertension	150	229	0.596	150	152	0.865
Diabetes mellitus	15	16	0.256	15	12	0.554
Previous stroke	7	14	0.611	7	7	1.000
Smoker	74	97	0.102	74	78	0.703
Alcohol	75	81	0.006	75	67	0.437
Location of hematoma			0.019			0.702
Basal ganglia	231	330		231	236	
Thalamus	32	85		32	26	
Both	15	26		15	16	
Volume of hematoma, mL	35.25 ± 15.59	35.42 ± 21.10	0.910	35.25 ± 15.59	34.74 ± 20.44	0.738
Depth of hematoma, cm	1.59 ± 0.32	1.66 ± 0.32	0.002	1.59 ± 0.32	1.61 ± 0.29	0.442
MS, mm	6.86 ± 3.45	6.71 ± 4.81	0.659	6.86 ± 3.45	7.00 ± 4.78	0.692
With IVH	102	187	0.128	102	110	0.485

GCS = Glasgow coma scale, IVH = intraventricular hemorrhage, MS = midline shift.
*Data are mean ± SD or number of patients.

lost to follow-up and 26 patients have uncompleted data. A total of 719 patients were included in the present study, of whom 278 patients underwent surgery. Patients' baseline characteristics at the time of hospitalization are listed in Table 1. There are significant differences between the 2 groups in age, history of smoke, alcohol consumption, location of hematoma, and depth of hematoma. After propensity score matching, the baselines were well matched. In the matched cases, the range of age was between 22 and 90 years (mean 54.55 ± 12.01 years). A total of 512 (92.09%) patients were hospitalized in 24 h after ictus and the rest of the patients 72 h. Two hundred twenty-four (40.29%) patients were in coma (GCS ≤8) and only 146 (26.26%) patients had a GCS of ≥13. Positions of hematoma included basal ganglia (467, 83.99%), thalamus (58, 10.43 %), and both (31, 5.58%). The volume of hematoma varied from 20.1 to 130.49 mL (mean 34.99 ± 18.16 mL), 424 (76.26%) of which were between 20 and 40 mL. The minimum depth from edge of hematoma to the cortical surface varied from 1 to 3.25 cm (mean 1.60 ± 0.30 cm). The patients with MS of 0 to 5 mm, 6 to 10 mm, >10 mm were 194 (34.89%), 250 (44.96%) and 112 (20.14%), respectively. Two hundred twelve (38.13%) patients had concurrent intraventricular hemorrhage.

Outcomes were listed in Table 2. Of the 556 patients, 138 (24.82%) died within 30 days post ictus, and 166 (29.86%) within 6 months. The 30-day mortality in surgical group was 19.06%, whereas the 30-day mortality was 30.58% in conservative group. Significant differences were observed between the 2 groups in 30-day mortality ($P = 0.002$) as well as 6-month mortality (23.38% vs 36.33%, $P = 0.001$) after ictus. At 6 months after ictus, conservative group were more likely to develop a fatal central respiratory-circulatory failure (65.35% vs 52.31%, $P = 0.094$). In contrast, patients who received surgery were more likely to die of complications (38.46% vs 26.73%, $P = 0.112$). As for complications, the risk of pulmonary infection and need for tracheostomy/long-term mechanical ventilation in the surgical group was higher than that in the conservative group (31.29% vs 15.47%, $P < 0.001$; 32.73% vs 23.38%, $P = 0.014$). The incidences of gastrointestinal hemorrhage, urinary tract infection, and pulmonary embolus in the surgical group were higher compared with conservative group as well, without statistical difference (6.83% vs 3.96%, $P = 0.133$; 2.88% vs 1.80%, $P = 0.400$; 1.80% vs 1.08%, $P = 0.476$).

At 6 months, a total of 129 (23.20%) patients had a favorable functional outcome. Sixty-three patients (22.66%) in the surgical group and 66 patients (23.74%) in the conservative group had favorable outcomes. There was no significant difference between the 2 groups on 6-month neurological functional outcomes ($P = 0.763$). Subgroup analyses of 6-month functional outcome were listed in Table 3. Of all the subgroup analyses, 2 showed heterogeneity. Patients with hematoma >40 mL were more likely to have a favorable outcome in surgical group than in the conservative group (13.33% vs 0%, $P = 0.005$). Another factor was IVH. Patients with IVH showed better outcome from surgery than conservative treatment (16.67% vs 7.27%, $P = 0.034$).

TABLE 2. Outcomes

	Surgical Group* (n = 278)	Conservative Treatment Group* (n = 278)	*P*
Neurological functional status			0.763
Favorable	63	66	
Unfavorable	215	212	
Mortality			
30 Days			0.002
Dead	53	85	
Alive	225	193	
6 Months			0.001
Dead	65	101	
Alive	213	177	
Complications			
Pulmonary infection	87	43	<0.001
Gastrointestinal bleeding	19	11	0.133
Urinary infection	8	5	0.400
Pulmonary embolus	5	3	0.476
Need for tracheostomy/long-term ventilation	91	65	0.014
ICU LOS (days)	5.38 ± 8.512	1.72 ± 6.603	<0.001
LOS (days)	14.41 ± 11.064	7.34 ± 9.836	<0.001

ICU LOS = Intensive care unit length of stay, LOS = overall length of stay.
* Data are number of patients or means ± SD.

DISCUSSION

From the present study, we found that surgery could reduce the short-term and long-term mortality in patients with spontaneous deep supratentorial hemorrhage. The long-term functional outcomes were similar between the 2 groups. However, patients who received surgery might have a better outcome in certain conditions: volume of hematoma >40 mL, and patients with concurrent IVH.

So far, a total of 13 randomized clinical trials comparing surgery and conservative treatment for patients with sICH have been published, 8 of which provided data of deep brain hemorrhage (Table 4).[7,14–16,22–29] Among these trials, the largest one is the STICH trial.[7] The STICH is an international multicenter prospective randomized clinical trial, which included 1033 patients from 27 countries from 1998 to 2003, among whom 442 patients diagnosed with deep supratentorial hemorrhage were analyzed in the subgroup analysis. In these 442 patients, 208 patients underwent early surgical treatment, and the rest 234 patients received initial conservative treatment. Favorable outcomes at 6 months did not significantly differ between the 2 groups. Another 4 previously published studies got a similar outcome that patients with hematoma located in the basal ganglia or thalamus did not benefit from hematoma evacuation by craniotomy.[22,24–26] However, a study published by Pantazis et al[14] in 2006 had a different result. A total of 108 patients with sICH were enrolled in this study from 1998 to 2003. Among them, 57 patients with hematoma in putamen were analyzed in the subgroup. The result showed that patients who underwent craniotomy had a better functional outcome than those received conservative treatment. Like most previous studies, result of the present study showed a poor outcome in patients with deep supratentorial hemorrhage. Besides, surgery did not improve the long-term outcome compared with conservative treatment. Most neurosurgeons attributed such result to the additional surgical traumatization. To reduce surgical traumatization, some minimal invasive techniques were adopted in hematoma evacuation. Though the long-term follow-up of some prospective randomized controlled trials showed that patients with deep hematoma might benefit from minimally invasive surgery, these kind of procedures still had some limitations including higher risk of rehemorrhage and intracranial infection.[31]

In the present study, we found that patients with volume of hematoma >40 mL were more likely to have a favorable outcome from surgery. In patients with sICH, volume of hematoma is one of the most important parameter to evaluate the severity of the condition. Patients with larger hematoma always have a higher intracranial pressure (ICP) and severer neurological functional damage. Early evacuation of hematoma might protect brain tissue from the ischemia caused by the elevated ICP and reduce the noxious chemicals generated from hematoma. Our result differs from most previous studies in which patients enrolled were complicated with lobar hematoma. The different patient populations might cause the difference between our results and the previous ones.

Previous study showed that the sICH patients with IVH were more likely to have a poor outcome in previous studies.[32] Mainstream views attribute this to 4 pathophysiological mechanisms: the mass effect of the hematoma, toxicity of blood-breaking products, acute obstructive hydrocephalus, and chronic hydrocephalus.[33] In the present study, patients with deep supratentorial hemorrhage with IVH had a poor prognosis likewise. However, patients with IVH who received surgery were more likely to get a favorable outcome. By contrast, the STICH II study showed that surgery could have survival advantage for patients with superficial hematoma without IVH.[8] Such difference might be caused by different locations of the primary hemorrhage. Generally, for patients with deep hematoma and IVH, we evacuated part of the hematoma in the ventricle with the aid of operative microscope, and placed the drainage tube in the fistula of ventricle. In some cases of

TABLE 3. Subgroup Analysis of 6-month Functional Outcome

	Surgical Group* (n/N)	Conservative Group* (n/N)	*P*
Age, y			
≤65	55/230	57/228	0.787
>65	8/48	9/50	0.862
GCS			
3–8	15/113	8/111	0.135
9–12	28/93	35/93	0.278
13–15	20/72	23/74	0.662
Location of hematoma			
Basal ganglia	60/231	62/236	0.942
Thalamus	3/32	4/26	0.769
Both	0/15	0/16	/
Volume of hematoma, mL			
≤40	53/203	66/221	0.390
>40	10/75	0/57	0.005
MS			
MS ≤5 mm	26/87	46/107	0.060
5 mm < MS≤10 mm	31/140	14/110	0.054
MS >10 mm	6/51	6/61	0.742
IVH			
With IVH	17/102	8/110	0.034
Without IVH	46/176	58/168	0.090

GCS = Glasgow coma scale, IVH = inraventricular hemorrhage, MS = midline shift.
* n = number of patients with favorable outcomes; N = number in the group.

TABLE 4. Summary of Previous Randomized Controlled Trials Enrolled Patients With Deep Supratentorial Hemorrhage During the CT Era

			Subgroup Analyse*		
Author (Publish Time)	Surgery Methods	Study Population*	Surgery†	Conservative Treatment†	Odds Ratio (95% CI)‡
Auer et al[22]	Edoscopy	40 putaminal 15 thalamic	23/26	29/29	0.11 (0.01, 2.31)
Juvela et al[23]	Craniotomy	30 basal ganglia 5 thalamic		Not mentioned	
Batjer et al[24]	Craniotomy ICP monitoring	21 putaminal	10/12	7/9	1.43 (0.16, 12.7)
Chen et al[25]	Craniotomy Sterotaxy	70 putaminal/or basal ganglia 14 thalamic 27 putaminal and thalamic	37/55	27/56	2.21 (1.02, 4.77)
Morgenstern et al[26]	Craniotomy	31 Putaminal	9/15	11/16	0.68 (0.16, 2.99)
Zuccarello et al[27]	Craniotomy Stereotaxy	7 Putaminal/or basal ganglia 3 Thalamic		Not mentioned	
Chen et al[28]	Craniotomy Stereotaxy Endoscopy	74 external capsule or putaminal 358 internal capsule or thalamic		Not mentioned	
Zhou et al[29]	Stereotaxay Endoscopy	186 basal ganglia 22 thalamus		Not mentioned	
Teernstra et al[30]	Stereotaxy	33 deep-seated		Not mentioned	
Hattori et al[15]	Stereotaxy	242 putaminal	60/121	82/121	0.47 (0.28, 0.79)
Mendelow et al[7]	Cranotomy Endoscopy Sterotaxy	442 deep-seated	174/208	184/234	1.39 (0.86, 2.25)
Pantazis et al[14]	Cranotomy	57 putaminal	22/29	28/28	0.05 (0.00, 0.97)
Wang et al[16]	Sterotaxy	377 basal ganglia	174/297	178/286	0.70 (0.50, 0.99)

CI = confidence interval, CT = computed tomography.
* Data were only from the patients with hematoma located in the deep area of brain.
† Data are number of unfavorable outcome/number of patents randomized to the group.
‡ The OR are calculated to compare the outcomes of surgery and conservative treatment.

thalamus hemorrhage with IVH, an external ventricular drainage was placed before or after craniotomy hematoma evacuation. These measures could not only reduce the mass effect of hematoma, but also lower the risk of acute hydrocephalus. This might be the reason that sICH patients with IVH had a better outcome in surgical group.

The mortality is a hot subject of debate in the present study. Increased ICP will lead to hernia, which is the main cause of death in patients with sICH. Patients with serious deep intracerebral hemorrhage usually die from central respiratory-circulatory failure caused by herniation in the acute phase. Early hematoma evacuation could reduce ICP and help patients with sICH go through the acute phase. In our opinion, ICP is one of the most important parameters to evaluate in the surgical decision making process. A recent study showed that decompressive craniotomy (DC) might be useful to decrease the ICP and improve the prognosis in patients with large basal ganglia hemorrhage.[34] Our finding is similar to the guideline. The last edition of AHA/ASA guideline hold the opinion that DC with or without hematoma evacuation might reduce mortality for patients with supratentorial ICH who are in a coma, have large hematomas with significant midline shift, or have elevated ICP refractory to medical management.[12]

We must admit that the present study had some limitations. First, the present study was a single-center retrospective case-controlled study using propensity score matching. Potential selective bias still existed though greatly reduced. The sample size of the present study was not large enough to provide robust evidence for clinical practice. Second, even though most of the patients received surgery within 8 hours post ictus in the present study, some of the patients underwent surgery after 24 hours post ictus, which might affect the efficacy of surgery. The reason why we did not discuss the time of surgery was that there was a large span of time from onset to surgery in the present study. Third, we only used a radiographic index, the MS, to evaluate the preoperational ICP. There are some other radiographic indexes such as changes of ventricle to evaluate the ICP. Using a CT score calculating from both the MS and changes of ventricle to evaluate preoperational ICP might be preferable. To further investigate this topic, some high quality, rigorous, randomized controlled trials are needed.

CONCLUSION

The treatment of patients with spontaneous deep supratentorial hemorrhage had puzzled the neurosurgeons for quite a long time. Though many studies had been carried out, there is still no sufficient evidence to justify whether a patient with spontaneous deep supratentorial hematoma should be treated surgically. The present study showed that surgery could reduce the short-term and long-term mortality in patients with spontaneous deep supratentorial hemorrhage. Moreover, surgery might improve the functional outcome in patients with large hematoma or with IVH compared with conservative treatment. The result of the present study might help the surgical decision making for patients with spontaneous deep supratentorial hemorrhage in the future. Surgery might be a beneficial choice for part of the patients with spontaneous deep supratentorial hemorrhage, but further detailed research is still needed.

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