

## Original Article

# New approach of minimally invasive evacuation for spontaneous supratentorial intracerebral hemorrhage

Qiang Cai<sup>1\*</sup>, Wenju Wang<sup>1\*</sup>, Zhiyang Li<sup>1\*</sup>, Ping Song<sup>1</sup>, Long Zhou<sup>1</sup>, Li Cheng<sup>2</sup>, Hangyu Wei<sup>1</sup>, Pan Lei<sup>1</sup>, Qianxue Chen<sup>1</sup>, Zhaohui Yang<sup>3</sup>

Departments of <sup>1</sup>Neurosurgery, <sup>2</sup>Critical Care Medicine, Eastern Campus, <sup>3</sup>Radiology, Renmin Hospital of Wuhan University, Hubei Province, China. \*Equal contributors.

Received October 24, 2021; Accepted March 3, 2022; Epub March 15, 2022; Published March 30, 2022

**Abstract:** Objective: We developed a new clinical surgery approach termed the “two-in-one technique” that combines neuroendoscopy with stereotactic aspiration for spontaneous supratentorial intracerebral hemorrhage (SSICH). This study was designed to explore its feasibility, safety, and effectiveness. Methods: Starting in December 2018, 40 patients (Group A) were prospectively studied after undergoing this new technique. The time to access the hematoma, average hematoma evacuation rate, and Glasgow Coma Scale (GCS) improvement at discharge were analyzed. Two patients had increased intracranial pressure (ICP) caused by the transparent plastic sheath and two other patients experienced ICP decreases following the two-in-one technique. The control groups included 42 patients treated by stereotactic aspiration (Group B) and 40 cases treated by neuroendoscopy (Group C). Results: All procedures were successfully completed. The average access time to hematoma was 4.675 minutes in Group A, which was much less than in Group C (10.20 minutes). The average hematoma evacuation rate was 91.91% which was much higher than Group B (44.2%), and the average GCS improvement at discharge was 3.82. The ICP increased sharply when the transparent plastic sheath was inserted, while ICP decreased significantly when using the new technique. Conclusions: The two-in-one technique can decrease ICP quickly and avoid transient ICP increases caused by transparent sheath insertion. This approach can also avoid the shortcomings of stereotactic aspiration and offers the advantages of neuroendoscopy. More importantly, it was effective and safe, making it a promising method for the surgical treatment of SSICH.

**Keywords:** Spontaneous supratentorial intracerebral hemorrhage, transcranial neuroendoscopic approach, minimally invasive surgery

## Introduction

Spontaneous supratentorial intracerebral hemorrhage (SSICH) is the most deadly subtype of stroke, with a 30-day mortality rate of approximately 40% [1]. More than 5 million brain hemorrhages occur annually [2]. The prognosis of SSICH remains dismal, with up to 75% of patients suffering significant disability [3]; only 12-39% of the long-term survivors have favorable neurological function recovery [1, 4].

Minimally invasive surgery (MIS) including stereotactic aspiration and neuroendoscopic surgery is an important and promising option for SSICH treatment, showing markedly better outcomes than a classical craniotomy [5-9]. Although, stereotactic aspiration offers the

shortest access time to the hematoma, it is associated with a lack of effective hemostasis and lower evacuated rate. Neuroendoscopic techniques are able to evacuate a hematoma with high efficiency and stop the bleeding under direct vision; however, they are more time-consuming than stereotactic aspiration to the hematoma, and the transparent plastic sheath might further increase intracranial pressure (ICP). Since both types of MIS have important limitations, the development of a safer and more effective method is warranted.

Since December 2018, we have used a new approach termed the “two-in-one technique” that combines the endoscopic techniques with stereotactic aspiration to treat 40 cases of SSICH. Four patients were evaluated for ICP

changes caused by the transparent plastic sheath or from undergoing the new approach. The results were excellent, indicating that this approach might be a safe and reliable alternative for the treatment of SSICH.

## Materials and methods

### *Surgical indications and patient selection*

Forty patients with SSICH who were treated using this new approach (Group A) in our department were prospectively studied from December 2018 to October 2020. The time access to the hematoma, average hematoma evacuation rate, and Glasgow Coma Scale (GCS) improvement at discharge were analyzed. All patients underwent computed tomography (CT) scans before surgery and within 24 h postoperatively. The hematoma volumes were analyzed by 3D Slicer software, and the hematoma evacuation rate was calculated as:  $[(\text{preoperative volume} - \text{postoperative volume}) / \text{preoperative volume}] \times 100\%$ . Patients were sent to the intensive care unit, where blood pressure and excessive fluid consumption were controlled. Two patients were evaluated for ICP increases caused by the transparent plastic sheath, while two others were assessed for ICP decreases after undergoing surgery with the new approach. The control groups were made up of 42 patients treated by stereotactic aspiration (Group B) and 40 cases treated by neuroendoscopy (Group C).

The inclusion criteria were as follows: diagnosis of acute SSICH, hematoma volume  $\geq 20$  ml, and GCS score  $\geq 5$ . Patients with GCS  $< 5$ , serious clotting disorders, or caused by secondary factors were excluded.

### *“Two-in-one technique”*

This study was approved by the ethics committee of Renmin Hospital of Wuhan University (WDRY2022-KS002, Wuhan, China). All patients or their family members provided written informed consent, and all procedures were conducted in accordance with the tenets of the Declaration of Helsinki.

The operation included two parts: 1) Insert a soft catheter into the hematoma and partially aspirate the clot to rapidly decrease ICP. 2) Use a neuroendoscope to remove the residual

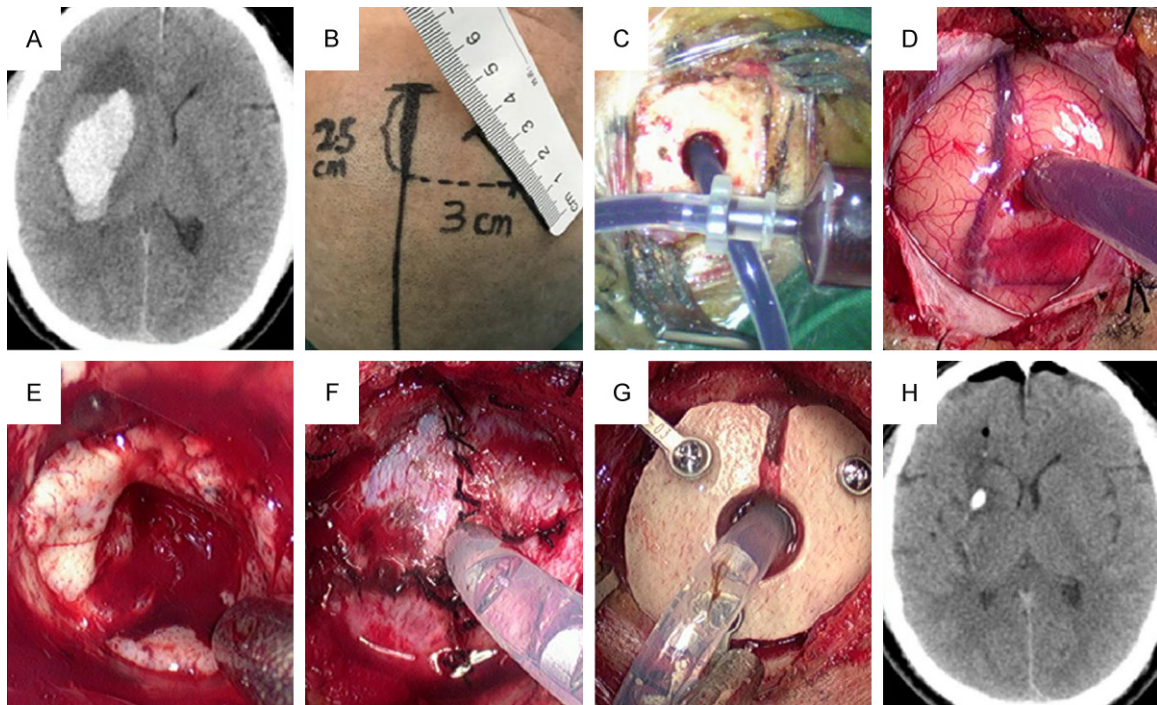
hematoma and stop the bleeding. First, a linear scalp incision (4-5 cm) was performed according to the hematoma location. The burr hole was made, the dura matter was cut, and a soft catheter was inserted into the hematoma cavity. Then, approximately one-third of the clot was aspirated through the catheter using a syringe. Next, a small bone flap (~2.5 cm) was created and the dura matter opened, a 1.5-cm cortical incision was performed, and a transparent plastic sheath was inserted into the hematoma cavity. A 0° rigid endoscope (Karl Storz, Germany) was introduced into the hematoma cavity, and suction was used to remove the residual hematoma. Obvious intraoperative bleeding was stopped using a bipolar coagulator. After removing the hematoma, a soft catheter was placed inside the cavity, the bone flap was recovered, and the skin incision was sutured (**Figures 1A-H, 2A-H**).

### *Statistical analysis*

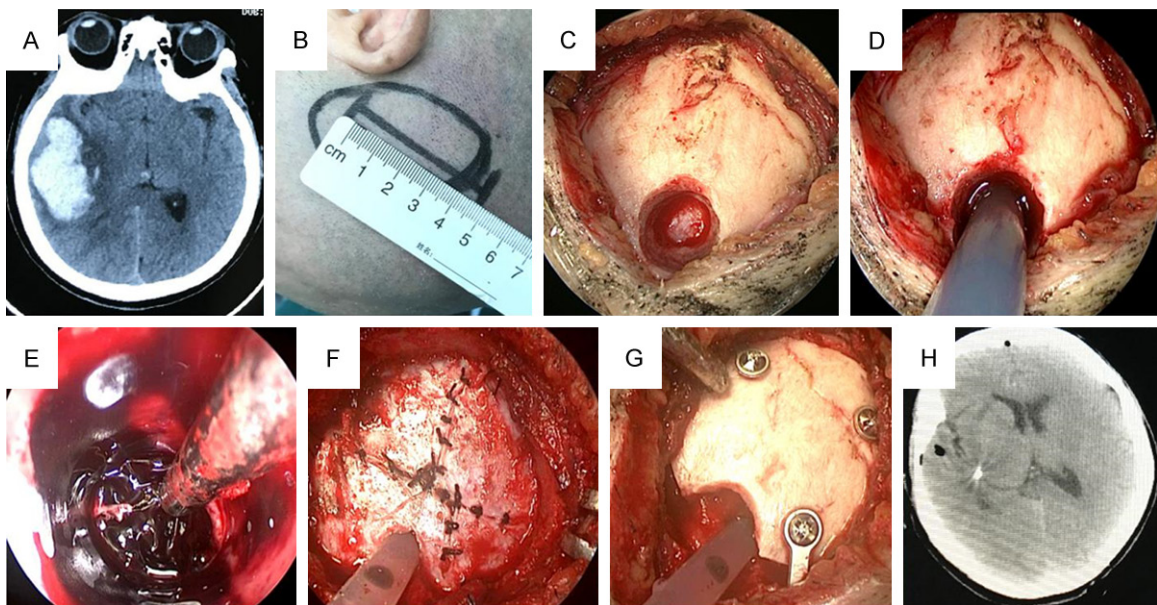
Descriptive analysis (mean, standard deviation, and median) was used for continuous variables and percentages for categorical variables. Chi-square test was used for dichotomous variables and Analysis of variance (ANOVA) used for continuous variables. GCS score data that did not comply with the normal distribution were analyzed by applying the Kruskal-Wallis test. Statistical analyses were conducted using SPSS 21.0 software (IBM, Armonk, NY, USA).  $P < 0.05$  was considered statistically significant.

## Results

A total of 40 patients were successfully treated with the new approach (Group A), including 31 men and 9 women (median age: 55.15 years; range: 31-77 years). The average time access to the hematoma with the two-in-one approach was 4.675 minutes, which was similar to the stereotactic aspiration group but significantly shorter than neuroendoscopy group (**Figure 3**). The mean preoperative hematoma volume was 45.07 ml, and the average hematoma evacuation rate was 91.91%, with the highest hematoma evacuation rate reaching 100% (**Figures 3-5**). The average preoperative and postoperative GCS scores were 9.55 and 13.35, respectively, which was much higher than in the stereotactic aspiration group (**Table 1; Figure 6**).



**Figure 1.** The two-in-one surgical approach for basal ganglia hemorrhage. A. CT scan showing a hematoma located in right basal ganglia, and the midline structure was shifted. B. A 4-cm linear scalp incision was performed; the central point was 2.5 cm behind the hairline and 3 cm from the sagittal line. C. A burr hole was made, a soft catheter was inserted into the hematoma cavity and approximately one-third of the hematoma was aspirated through the catheter using a syringe. D. A small bone flap (~2.5 cm) was created, the dura was tented and opened in a cruciate fashion. E. The residual hematoma was evacuated under direct neuroendoscopic view. F. After evacuation of the hematoma, the soft catheter was laid inside the hematoma cavity, and the dura was closed. G. The small bone flap was recovered and fixed. H. Postoperative CT scan showing the hematoma was removed satisfactory.

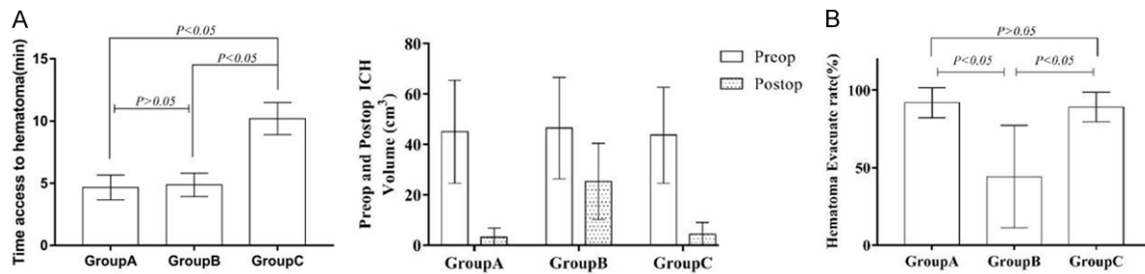


**Figure 2.** The two-in-one surgical approach for subcortical hemorrhage. A. Preoperative CT scan showing a hematoma in the right temporal lobe. B. A 5-cm linear scalp incision was performed near the hematoma. C. The burr hole was made at the back of the hematoma. D. A soft catheter was inserted into the hematoma cavity, and approximately one-third of the hematoma was aspirated through the catheter using a syringe. E. The residual hematoma



## Evacuation intracerebral hemorrhage by a new approach

was evacuated under direct neuroendoscopic view. F. Following evacuation, a soft catheter was laid inside the hematoma cavity, and the dura was closed. G. The small bone flap was recovered and fixed. H. Postoperative CT scan showing satisfactory hematoma removal.



**Figure 3.** Time to access hematoma (A) and hematoma evacuation rates (B) by group. (A) There were no significant differences between Groups A and B, which were both significantly shorter than the time to access for Group C. (B) Preoperative hematoma volumes were similar, but there were significant differences in postoperative hematoma volumes and hematoma evacuation rates among the three groups.

### Evaluation of ICP changes caused by transparent plastic sheath insertion

The average volume of the transparent plastic sheath was 10-15 ml, which will increase ICP when it is inserted into the brain. We use a ventricular catheter with a sutured glove that is ballooned with water and developed a water sac model to simulate this process. ICP monitoring was performed and recorded when the volume of the balloon was increased from 0 to 15 ml (Figure 7).

ICP monitoring was performed in four patients to evaluate fluctuations and demonstrate the benefits of this new approach. Evaluation of the increase in ICP in two patients caused by the transparent plastic sheath revealed that ICP sharply increased when 0-15 ml of water was injected into the brain. In two other patients, we found that ICP was significantly decreased when we aspirated part of the hematoma (Figures 8, 9).

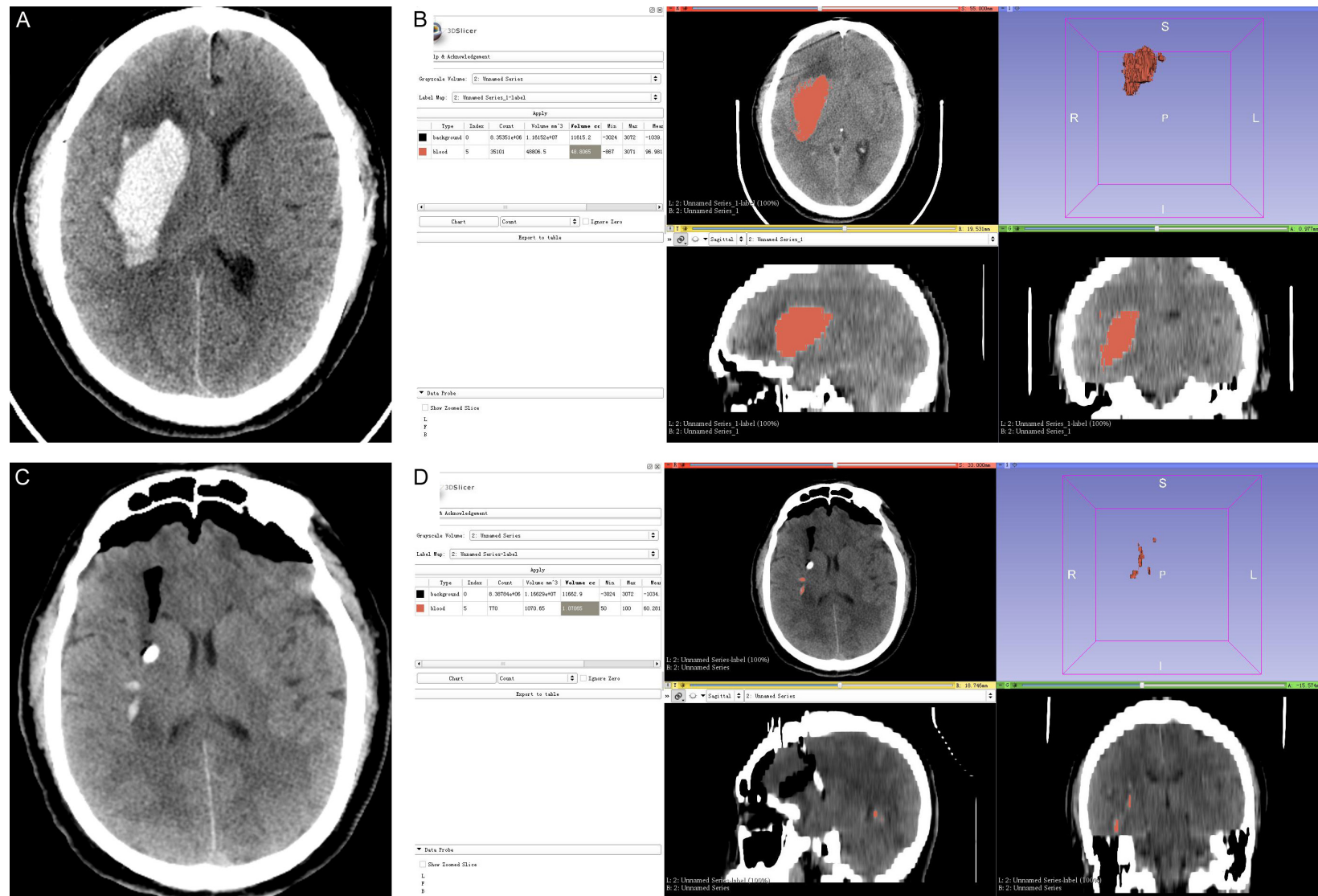
### Discussion

Surgical treatment is an important option for patients with medium-to-large ICHs. This method can be used to evacuate hematomas, decrease ICP, reduce perihematomal edema, limit toxic effects of the hematoma, and reduce mechanical compression on normal brain tissue. These effects limit brain injury, lower mortality, and improve survival rates [10-12]. Craniotomy, stereotactic aspiration, and neuroendoscopic surgery are the three main surgical

methods applied in this setting; however, each method has specific advantages and shortcomings [7]. Conventional craniotomy can be used to evacuate hematoma and simultaneously remove the bone flap, offering an extraordinary decompression effect. However, this invasive procedure fails to protect functional brain tissue surrounding the hematoma and is associated with excessive damage. These observations were reported in large pragmatic trials, which did not show improvements in functional outcome or mortality [13, 14]. Stereotactic aspiration is another common and effective surgical approach for SSICH. While it is the most minimally invasive and has the shortest duration, it is limited by its partial clearance rate and high rebleeding rate [7]. Neuroendoscopy is minimally invasive, enables direct visualization, and has an effective hematoma evacuation rate [7, 15]; however, it is more time-consuming than stereotactic aspiration [16].

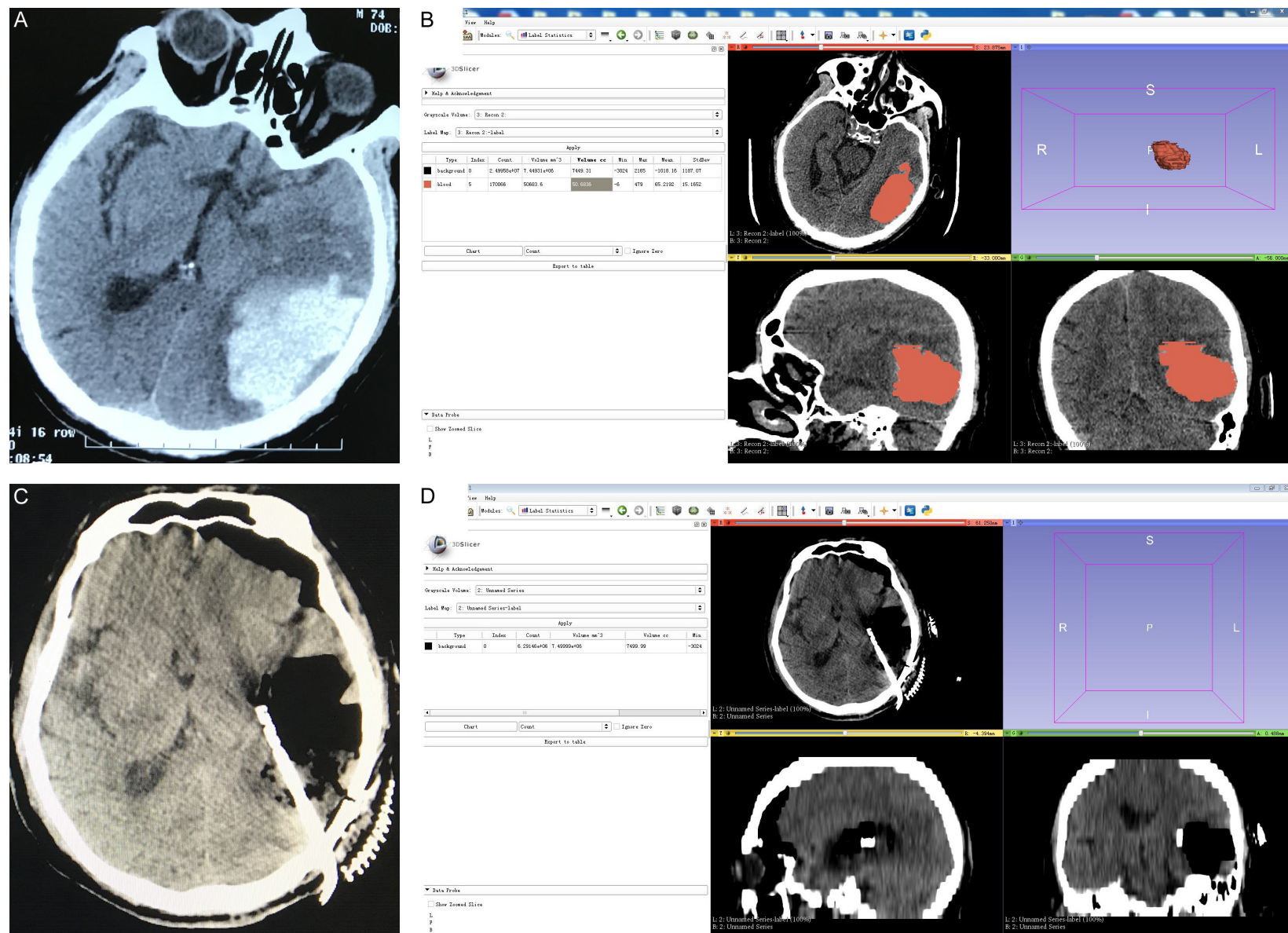
The best therapeutic option for medium-to-large SSICH remains controversial [6], but MIS approaches including neuroendoscopic surgery and stereotactic aspiration are accepted as effective, safe, and promising alternative methods to craniotomy [5, 17, 18]. The key advantages of MIS are drastically reduced manipulation of viable brain tissue and significantly faster access to the hematoma. These variables may have significant impacts on the rates of mortality and morbidity, especially in patients with impending cerebral herniation.

## Evacuation intracerebral hemorrhage by a new approach



**Figure 4.** The intracerebral hematoma volume and hematoma evacuation rate of a right basal ganglia was analyzed and calculated with 3D Slicer software. A. Preoperative CT scan showing a hematoma in the right basal ganglia. B. The preoperative hematoma volume was 48.8 ml. C. Postoperative CT confirmed successful hematoma removal. D. The postoperative hematoma volume was 1.07 ml, corresponding to a hematoma evacuation rate of 97.8%.

## Evacuation intracerebral hemorrhage by a new approach



**Figure 5.** The intracerebral hematoma volume and hematoma evacuation rate of a left temporal lobe hematoma were analyzed and calculated by the 3D Slicer software. A. Preoperative CT scan showing a hematoma in the left temporal lobe. B. The preoperative hematoma volume was 50.68 ml. C. Postoperative CT scan confirming hematoma removal. D. The postoperative hematoma volume was 0 ml, and the hematoma evacuation rate was 100%.

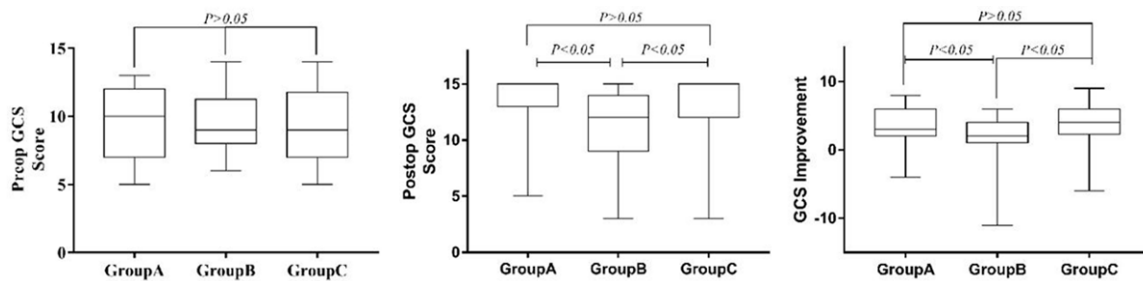


# Evacuation intracerebral hemorrhage by a new approach

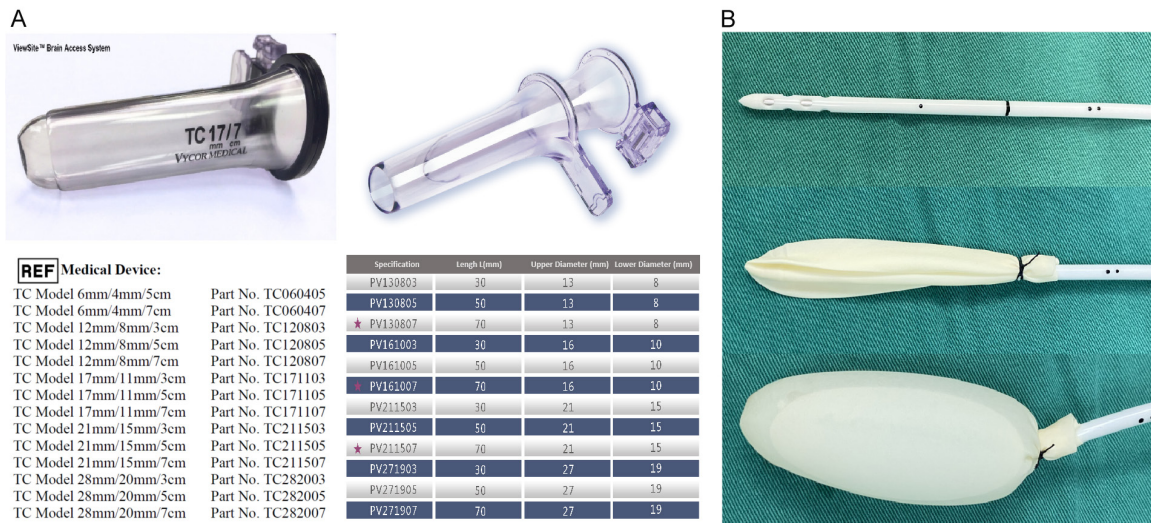
**Table 1.** General information and results of 122 SICH patients treated by different methods

Information		Group A	Group B	Group C	K/F/ $\chi^2$	P
Sex	M	31	33	24	4.37 <sup>a</sup>	0.113
	F	9	9	16		
Age (yrs)		55.15 ± 10.40	54.93 ± 10.53	57.7 ± 10.11	0.873 <sup>b</sup>	0.42
Preop GCS score		9.55 ± 2.42	9.45 ± 2.27	9.10 ± 2.51	0.69 <sup>c</sup>	0.71
Postop GCS score		13.35 ± 2.64	11.36 ± 2.64	12.93 ± 3.26	16.67 <sup>c</sup>	<0.01
GCS improvement		3.8 ± 2.44	1.9 ± 2.61	3.83 ± 3.29	18.12 <sup>c</sup>	<0.01
Preop ICH volume (cm <sup>3</sup> )		45.07 ± 20.43	46.47 ± 20.13	43.67 ± 19.06	0.197 <sup>b</sup>	0.82
Postop ICH volume (cm <sup>3</sup> )		3.19 ± 3.62	25.37 ± 15.14	4.46 ± 4.59	69.40 <sup>b</sup>	<0.01
Hematoma evacuation rate (%)		91.91 ± 9.72	44.2 ± 33.10	89.20 ± 9.55	66.08 <sup>b</sup>	<0.01
Time to access hematoma (min)		4.675 ± 0.985	4.88 ± 0.93	10.20 ± 1.29	332.22 <sup>b</sup>	<0.01

<sup>a</sup> $\chi^2$  test, <sup>b</sup>F (analysis of variance), <sup>c</sup>K (Kruskal-Wallis test). Group A, two-in-one group; Group B, stereotactic aspiration group; Group C, neuroendoscopic group. F, female; ICH, intracerebral hemorrhage; GCS, Glasgow Coma Scale. M, male.



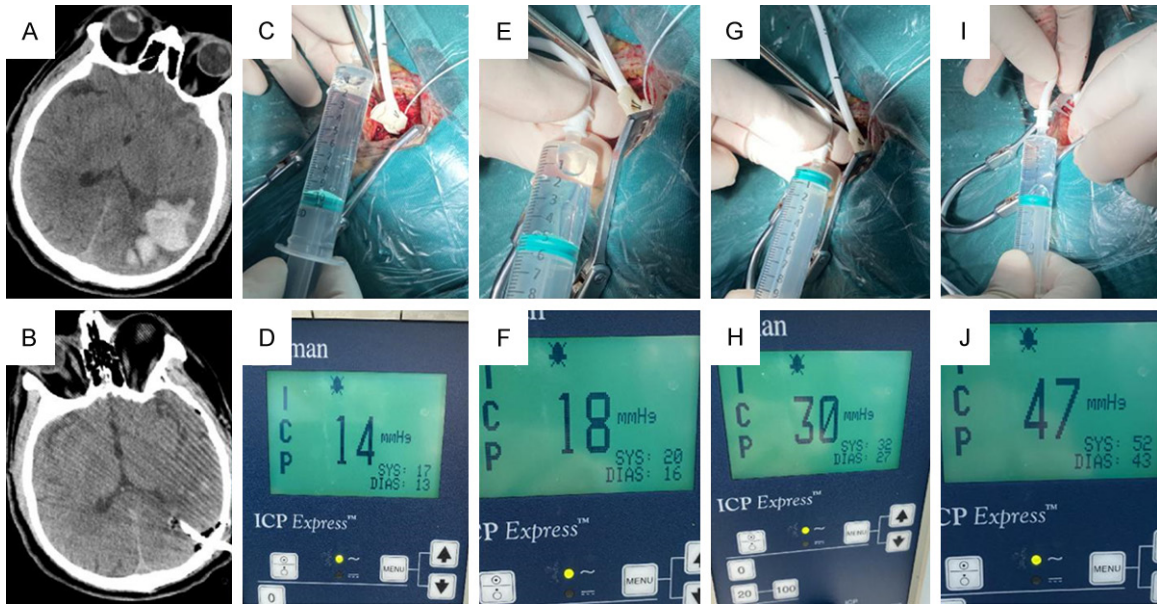
**Figure 6.** GCS improvements by group. Preoperative GCS scores were similar among all three groups, but there were significant differences in postoperative GCS and GCS improvement.



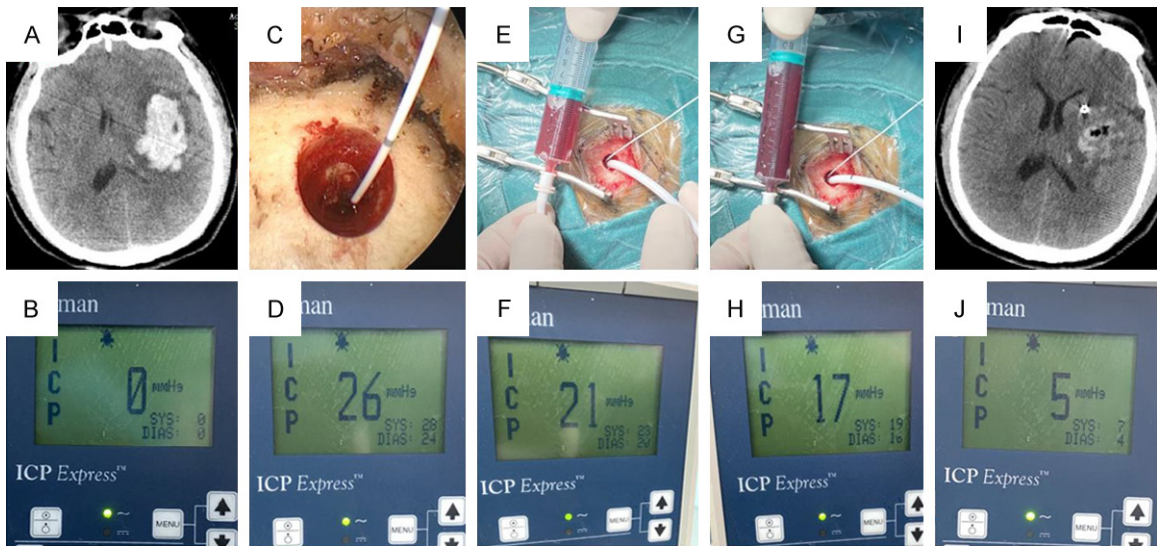
**Figure 7.** Transparent plastic sheaths and water sac model. A. Different types of transparent plastic sheaths with an average volume of ~15 ml. B. Water sac model to simulate transparent plastic sheath insertion.

Stereotactic aspiration offers the fastest access to the hematoma, but it also associated with a higher rebleeding rate ranging from 5-18.2% [7, 19]. Furthermore, this approach is

not suitable for ultra-early surgery patients, as hematoma expansion often occurs within 20 h from hemorrhage onset. In general, neurosurgeons must wait for the hematoma to stabilize



**Figure 8.** ICP was monitoring with the water sac model to simulate the process of transparent plastic sheath insertion. A, B. Pre- and postoperative CT scan of a patient with a 32.7-ml hematoma. C, D. The ICP was 14 mmHg before hematoma evacuation and water injection. E, F. The ICP was up to 18 mmHg when 5 ml water injected. G, H. The ICP increased to 30 mmHg when 10 ml water was injected. I, J. ICP reached 47 mmHg when 15 ml water was injected.



**Figure 9.** ICP monitoring during the two-in-one surgical procedure. A. Preoperative CT scan of a patient with a 35.5-ml hematoma. B. Zero setting of intracranial pressure monitor before operation. C, D. The preoperative ICP was 26 mmHg. E, F. ICP decreased to 21 mmHg when 5 ml of the hematoma was aspirated. G, H. ICP reached 17 mmHg after 10 ml of the hematoma was aspirated. I, J. The ICP was down to 5 mmHg following hematoma evacuation.

prior to performing clot evacuation, and this may contribute to a poor prognosis [16]. Additionally, according to the latest study conducted by Hanley and colleagues, this treatment is not recommended for large SSICH [20]. In the MISTIE III trial, aspiration and thrombolytic irrigation of large SSICHs with alteplase via

an image-guided catheter did not improve functional outcomes compared with standard medical care [20].

Neuroendoscopic surgery is another useful minimally invasive approach for SSICH. Accumulating evidence indicates that this treat-



ment may provide the best outcomes in terms of clot removal and maximum patient safety [5, 6, 21]. It offers the advantages of immediate clot evacuation, shorter surgical duration, and less surgery-related morbidity [21]. Moreover, it allows longer trajectories and can be applied to deep hemorrhages, with fewer disadvantages and drastically reduced brain manipulation compared to craniotomy. It also provides better hemostatic control since the surgeon can stop bleeding under direct vision [7, 21], so this approach carries a minimal rebleeding rate compared with stereotactic aspiration [6].

Space-occupying hematomas may contribute to increased ICP, and it has been reported that ultra-early clot removal may limit the toxic effects of a hematoma, reduce mechanical compression of normal brain tissue, prevent vasogenic edema evolution, and substantially reduce perihematoma edema. Thus, the time to access hematoma and rapid ICP reduction are important factors contributing to the prognosis of patients with SSICH, especially those with cerebral herniation. Although stereotactic aspiration offers the shortest access time, it has inherent shortcomings that can be addressed by combining it with other techniques. In this case series, we developed a new approach combining neuroendoscopy and stereotactic aspiration. In the first part of this procedure, we directly inserted a catheter into the clot in several minutes and partly removed the hematoma to quickly decrease ICP, while also avoiding the transient ICP increase caused by the transparent sheath. In the second part, we used neuroendoscopy to evacuate the residual clot and manage active bleeding. In our study, all 40 patients achieved excellent postoperative evacuation rates, proving that this new approach is a fast, effective, and safe treatment for SSICH.

## Conclusion

Our two-in-one technique quickly decreased ICP and avoided the transient increase caused by transparent sheath insertion. It overcame stereotactic aspiration's shortcomings of poor hematoma removal efficiency and high rebleeding rate by exploiting neuroendoscopic advantages of efficient hematoma removal and reliable hemostasis. Hemorrhage evacuation using this new approach was effective and

safe, suggesting it could be a promising method for the surgical treatment of SSICH.

## Acknowledgements

This work was supported by National Natural Science Foundation of China (81971158; 81671306), Wuhan Science and Technology plan project (2019020701011470) and the foundation of China Scholarship Council.

## Disclosure of conflict of interest

None.

## Abbreviations

GCS, Glasgow Coma Scale; ICP, intracranial pressure; MIS, minimally invasive surgery; SSICH, spontaneous supratentorial intracerebral hemorrhage.

**Address correspondence to:** Dr. Qiang Cai, Department of Neurosurgery, Renmin Hospital of Wuhan University, No. 238, Jiefang Road, Wuchang District, Wuhan 430060, Hubei Province, China. Tel: +86-15072358160; E-mail: cqno@sina.com; Dr. Zhaohui Yang, Department of Radiology, Renmin Hospital of Wuhan University, No. 238, Jiefang Road, Wuchang District, Wuhan 430060, Hubei Province, China. Tel: +86-13871062269; E-mail: zhaohui.yang@whu.edu.cn

## References

- [1] van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A and Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol* 2010; 9: 167-176.
- [2] Krishnamurthi RV, Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, Moran AE, Sacco RL, Anderson LM, Truelsen T, O'Donnell M, Venketasubramanian N, Barker-Collo S, Lawes CM, Wang W, Shinohara Y, Witt E, Ezzati M, Naghavi M and Murray C. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. *Lancet Glob Health* 2013; 1: e259-281.
- [3] Anderson CS, Huang Y, Wang JG, Arima H, Neal B, Peng B, Heeley E, Skulina C, Parsons MW, Kim JS, Tao QL, Li YC, Jiang JD, Tai LW, Zhang JL, Xu E, Cheng Y, Heritier S, Morgenstern LB and Chalmers J. Intensive blood pressure re-

# Evacuation intracerebral hemorrhage by a new approach

- duction in acute cerebral haemorrhage trial (INTERACT): a randomised pilot trial. *Lancet Neurol* 2008; 7: 391-399.
- [4] Mayer SA and Rincon F. Treatment of intracerebral haemorrhage. *Lancet Neurol* 2005; 4: 662-672.
- [5] Beynon C, Schiebel P, Bösel J, Unterberg AW and Orakcioglu B. Minimally invasive endoscopic surgery for treatment of spontaneous intracerebral haematomas. *Neurosurg Rev* 2015; 38: 421-428.
- [6] Cai Q, Guo Q, Li Z, Wang W, Zhang W, Ji B, Chen Z and Liu J. Minimally invasive evacuation of spontaneous supratentorial intracerebral hemorrhage by transcranial neuroendoscopic approach. *Neuropsychiatr Dis Treat* 2019; 15: 919-925.
- [7] Cai Q, Zhang H, Zhao D, Yang Z, Hu K, Wang L, Zhang W, Chen Z and Chen Q. Analysis of three surgical treatments for spontaneous supratentorial intracerebral hemorrhage. *Medicine (Baltimore)* 2017; 96: e8435.
- [8] Scaggiante J, Zhang X, Mocco J and Kellner CP. Minimally invasive surgery for intracerebral hemorrhage. *Stroke* 2018; 49: 2612-2620.
- [9] Xia Z, Wu X, Li J, Liu Z, Chen F, Zhang L, Zhang H, Wan X and Cheng Q. Minimally invasive surgery is superior to conventional craniotomy in patients with spontaneous supratentorial intracerebral hemorrhage: a systematic review and meta-analysis. *World Neurosurg* 2018; 115: 266-273.
- [10] Gregson BA, Broderick JP, Auer LM, Batjer H, Chen XC, Juvela S, Morgenstern LB, Pantazis GC, Teernstra OP, Wang WZ, Zuccarello M and Mendelow AD. Individual patient data subgroup meta-analysis of surgery for spontaneous supratentorial intracerebral hemorrhage. *Stroke* 2012; 43: 1496-1504.
- [11] Prasad K, Mendelow AD and Gregson B. Surgery for primary supratentorial intracerebral haemorrhage. *Cochrane Database Syst Rev* 2008; CD000200.
- [12] Zhou X, Chen J, Li Q, Ren G, Yao G, Liu M, Dong Q, Guo J, Li L, Guo J and Xie P. Minimally invasive surgery for spontaneous supratentorial intracerebral hemorrhage: a meta-analysis of randomized controlled trials. *Stroke* 2012; 43: 2923-2930.
- [13] Mendelow AD, Gregson BA, Fernandes HM, Murray GD, Teasdale GM, Hope DT, Karimi A, Shaw MD and Barer DH. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial. *Lancet* 2005; 365: 387-397.
- [14] Mendelow AD, Gregson BA, Rowan EN, Murray GD, Gholkar A and Mitchell PM. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomised trial. *Lancet* 2013; 382: 397-408.
- [15] Wang WH, Hung YC, Hsu SP, Lin CF, Chen HH, Shih YH and Lee CC. Endoscopic hematoma evacuation in patients with spontaneous supratentorial intracerebral hemorrhage. *J Chin Med Assoc* 2015; 78: 101-107.
- [16] Wang WM, Jiang C and Bai HM. New insights in minimally invasive surgery for intracerebral hemorrhage. *Front Neurol Neurosci* 2015; 37: 155-165.
- [17] Barnes B, Hanley DF and Carhuapoma JR. Minimally invasive surgery for intracerebral haemorrhage. *Curr Opin Crit Care* 2014; 20: 148-152.
- [18] Rennert RC, Signorelli JW, Abraham P, Pannell JS and Khalessi AA. Minimally invasive treatment of intracerebral hemorrhage. *Expert Rev Neurother* 2015; 15: 919-933.
- [19] Gebel JM and Broderick JP. Intracerebral hemorrhage. *Neurol Clin* 2000; 18: 419-438.
- [20] Hanley DF, Thompson RE, Rosenblum M, Yenokyan G, Lane K, McBee N, Mayo SW, Bistran-Hall AJ, Gandhi D, Mould WA, Ullman N, Ali H, Carhuapoma JR, Kase CS, Lees KR, Dawson J, Wilson A, Betz JF, Sugar EA, Hao Y, Avadhani R, Caron JL, Harrigan MR, Carlson AP, Bulters D, LeDoux D, Huang J, Cobb C, Gupta G, Kitagawa R, Chicoine MR, Patel H, Dodd R, Camarata PJ, Wolfe S, Stadnik A, Money PL, Mitchell P, Sarabia R, Harnof S, Barzo P, Unterberg A, Teitelbaum JS, Wang W, Anderson CS, Mendelow AD, Gregson B, Janis S, Vespa P, Ziai W, Zuccarello M and Awad IA. Efficacy and safety of minimally invasive surgery with thrombolysis in intracerebral haemorrhage evacuation (MISTIE III): a randomised, controlled, open-label, blinded endpoint phase 3 trial. *Lancet* 2019; 393: 1021-1032.
- [21] Alberio N, Cicero S, Iacopino DG, Giammalva GR, Visocchi M, Olivi A, Francaviglia N, Battaglia R, Spitaleri A, Lipani R, Ruggeri L, Alessandrello R, Cinquemani A and Maugeri R. Minimally invasive management of spontaneous supratentorial intracerebral lobar hemorrhages by a "homemade" endoscopic strategy: the evangelical doctrine of "venite ad me" allied to the legacy of King Leonida. *World Neurosurg* 2019; 122: 638-647.