ABSTRACT

AIM: Keyhole endoscopy is a promising therapeutic option for spontaneous intracerebral hemorrhage (ICH). We sought to compare the clinical outcomes between keyhole endoscopy surgery and craniotomy for basal ganglia ICH.

MATERIAL and METHODS: The authors performed a retrospective analysis of the clinical and radiographic data obtained in 28 keyhole endoscopic procedures and 30 craniotomy procedures. Hematoma evacuation rate, infection rate, rebleeding and mean operation time were recorded as primary end points. Outcome Scale (GOS) values were recorded at the 3-month postoperative follow-up. The operation time from symptom onset is also studied between <8 hours group and 8-24 hours group.

RESULTS: The evacuation rate was significantly higher in the endoscopy group compared with the craniotomy group (P<0.05), and infectious rate was lower in the endoscopy group compared with the craniotomy group( P<0.05). Mortality rates between the 2 groups did not show statistically significant differences. The patients operated within 8h had better outcome (GOS 4 and 5) than that operated between 8-24h (p <0.05).

CONCLUSION: The data indicate that in patients with ICH, keyhole endoscopic surgery is safe and feasible, while operation within 8h can promote recovery of patients. These preliminary results warrant further study in a large, prospective, randomized trial in the near future.

KEYWORDS: Keyhole endoscopy, Intracerebral hemorrhage, Operation timing, Minimally invasive surgery

INTRODUCTION

Surgical management of ICH is still a matter of controversy with regard to indications, timing, and method. Minimally invasive hematoma evacuation using a neuroendoscope and the rapid development of neuroendoscope technology for the surgical treatment of ICH provides a useful option (4,16,20). According to the AHA/ASA guidelines for the management of spontaneous intracerebral hemorrhage (3), the effectiveness of minimally invasive ICH evacuation utilizing the endoscopic method is still uncertain and needs to be further tested in clinical trials. Supporting evidence from controlled trials is lacking. Therefore, we present our series of cases involving patients with basal ganglia ICH who underwent keyhole endoscopic and traditional craniectomy hematoma evacuation and discuss the safety and effectiveness of neuroendoscopic surgery, The operation time from symptom onset is also studied.

MATERIAL and METHODS

To qualify for inclusion in this study, patients had to have the following features: 1) Aged 35-70 years; 2) CT-confirmed basal ganglia hemorrhage; 3) Hematoma volume >30ml;...
4) Surgery to be instituted within 24 hours of the onset of clinical symptoms. Cases of deep coma with Glasgow Coma Scale (GCS) score of 3 and 4 were excluded. We also excluded patients with posttraumatic intracerebral hematomas, tumor bleeding, aneurysmal or arteriovenous hemorrhage, and bleeding tendencies caused by uremia, liver cirrhosis, or anticoagulation therapy.

The study group (keyhole endoscopy group) consisted of 28 consecutive adult patients between July 2008 and November 2010. The keyhole endoscopy group was matched to a historical control group (traditional craniotomy group), a series of 30 consecutive patients treated by craniotomy at our department between January 2007 and November 2010. Clinical characteristics of the patients for hematoma volume and age showed a significant difference between the groups (p < 0.05), as detailed in Table I.

**Traditional craniotomy**

Under general anesthesia, our surgical team drew a question mark on the temporal scalp of each patient. After opening the dura, we entered the hematoma cavity via a transcortical corridor through the inferior temporal gyrus or middle temporal gyrus approach. After removing the hematoma, the dura was closed and the bone flap was put back to its position.

**Keyhole endoscopic surgery**

For all basal ganglia hemorrhage, we used the transtemporal approach. A 5-cm vertical incision was made over the temporalis muscle and extended superiorly slightly. The temporalis muscle was split and a burr hole was made. The bone flap was made into a craniectomy about 2.5 cm in diameter. A cruciate dural opening was made. The authors confirmed the location of the hematoma using a stylet. A cortical incision was then made over a relatively silent area of the cortex and as near to the hematoma as possible. The transparent plastic sheath (10 mm in inside diameter) was inserted along with the stylet. The 4-mm endoscope was introduced into the transparent sheath to provide visualization during hematoma removal. Depending on the surgeon’s preference, the surgeon may hold the suction in his right hand and the endoscope in his left hand, and the assistant may hold the sheath. The hematoma was then evacuated using mild suction. High-pressure suction was usually avoided as it may cause further damage to the walls of the hematoma cavity. Clots that are adherent to the walls of the cavity especially anteriorly and medially are left alone, as evacuation of these may stir up further bleeding or may cause extensive damage to the internal capsule and thalamus. The ventricle can be opened if hemorrhage is associated with rupture into ventricle. When a bleeding vessel was encountered, the surgical field was kept clear with continuous irrigation and suction. Hemostasis was achieved by continuous saline irrigation and pressure packing. The identified bleeding artery was electrically coagulated with a suction cannula. When all procedures were completed, an external ventricular drain was left in the ventricle for several days if the ventricle was opened.

**Assessments and End Points**

Outcome variables included hematoma evacuation rate, infection rate, rebleeding rate, and mean operation time. The outcome was also measured three months later. The 3-month Glasgow Outcome Scale (GOS) was the major end point. Hematoma volume was estimated by the following equation: \( V = \text{length} \times \text{width} \times \text{thickness}/2 \). The hematoma evacuation rate (%) was defined as (preoperative volume-postoperative volume)/preoperative volume)\times 100\% . Re-bleeding was identified when the postoperative CT volume was either greater than the preoperative volume or there was a 5ml difference in the pre- and postoperative CT blood volume measurements. We also discuss the operation timing from symptom onset. The categories for the timing of surgery were as follows: Ultra-early (<8 hours), and early (8-24 hours). We compared mortality, good outcome and postoperative rebleeding between the 2 groups after 3 months.

**Statistic analysis**

Statistical analysis was carried out using T-analysis and Fisher’s exact or \( \chi^2 \) test. A P value <0.05 was considered statistically significant.

**Illustrative case**

A 60-year-old woman was admitted to our hospital because of an altered level of consciousness and right hemiparesis. On initial consultation, his level of consciousness was E1V2M4 on the GCS. Head CT revealed left ICH in the basal ganglia with

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**Table I: The Clinical Features Between the Keyhole Endoscopy Group and the Control Group of Traditional Craniotomy**

<table>
<thead>
<tr>
<th></th>
<th>Endoscopy group</th>
<th>Craniotomy group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>28</td>
<td>30</td>
<td>/</td>
</tr>
<tr>
<td>Male:Female</td>
<td>17:11</td>
<td>15:15</td>
<td>0.441</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>60.6±7.2’</td>
<td>64.6±5.0</td>
<td>0.017</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>21 (75%)</td>
<td>21 (70%)</td>
<td>0.670</td>
</tr>
<tr>
<td>Hematoma volume (ml)</td>
<td>53.7±15.8’</td>
<td>63.9±17.0</td>
<td>0.021</td>
</tr>
<tr>
<td>GCS</td>
<td>8±2</td>
<td>7±2</td>
<td>0.136</td>
</tr>
<tr>
<td>IVH, n (%)</td>
<td>14 (50.0%)</td>
<td>22 (73.3%)</td>
<td>0.067</td>
</tr>
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</table>

\( P <0.05 \)
an estimated volume of 60 ml. The patient was intubated and underwent endoscopic surgery as previously described to evacuate the hematoma. Postoperative CT scanning revealed almost complete removal of the thalamic hematoma (Figure 1). A drain was kept in place for 2 days after the operation. No intraventricular injection of an anticoagulant, such as urokinase, was needed for this patient. She regained consciousness 4 day later and displayed a right-sided hemiparesis and motor aphasia.

RESULT
Twenty-eight cases of endoscopic surgery (keyhole endoscopy group) and 30 historical controls (craniotomy group) were evaluated. All patients had altered level of consciousness with or without focal neurologic deficit. Baseline characteristics are summarized in Table I. More than half of the group was male, and the mean patient age was 62.6 years. The median time from ictus to surgery was 8 hours in the endoscopy group and 6 hours in the craniotomy group. The hematoma volume was 31-88 ml (median, 60.6 ml) in the endoscopy group and 40-115 ml (median, 64.6 ml) in the craniotomy group. The between-group difference in hematoma volume and age were statistically significant (P<0.05).

The evacuation rate in the endoscopy group was from 88% to 100%, while the evacuation rate of the craniotomy group was from 50% to 100%. The evacuation rate was significantly higher in the endoscopy group than in the craniotomy group (92.1% vs 86.5%; P<0.01). There was 1 rebleeding case in the endoscopy group and 3 cases in the craniotomy group, and there was no significant difference between the two groups (P>0.05). Infectious complication involved pneumonia and wound infection. There were 12 cases of pneumonia and 3 cases of wound infection in the craniotomy group; and 5 cases of pneumonia and 1 case of wound infection in the endoscopy group with a significant difference between the two groups (21.4% vs. 50.0%, P<0.05). Median operative time was longer in the craniotomy group than the endoscopic group (232 min vs. 138 min, P<0.001, Table II).

There were 7 cases of death among the 58 patients. Two patients in the endoscopy group died from respiratory failure due to pneumonia. Three deaths in the craniotomy group were due to pneumonia, and 2 deaths resulted from rebleeding. Mortality rates were 7.1% for the endoscopy group, and 16.7% for the craniotomy group, but mortality rates between the 2 groups did not show a statistically significant difference (P>0.05). There was no difference in the GOS score between the 2 groups 3 months later (P>0.05, Table III and Figure 2), although the endoscopy group had a better outcome trend (GOS4 and GOS5) than the craniotomy group.

Traditional craniotomy group timing from surgery to onset was 3-20 hours. In the minimally invasive surgical operation group, the shortest duration was 4 hours and the longest 18 hours from the onset, with an average of 8 hours. There

<table>
<thead>
<tr>
<th></th>
<th>Endoscopy group</th>
<th>Craniotomy group</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Median evacuation rate (%)</td>
<td>92.1±3.9*</td>
<td>86.5±9.1</td>
<td>0.004</td>
</tr>
<tr>
<td>Rebleeding, n (%)</td>
<td>1(3.6%)</td>
<td>3(10.0%)</td>
<td>0.612</td>
</tr>
<tr>
<td>Infection, n (%)</td>
<td>6(21.4%)*</td>
<td>15(50.0%)</td>
<td>0.024</td>
</tr>
<tr>
<td>Median operative time (min)</td>
<td>138±15*</td>
<td>232±16</td>
<td>&lt;0.001</td>
</tr>
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*P<0.05

Figure 1: A) Axial CT scan showing a large left sided basal ganglia hemorrhage with an estimated volume of 60 ml. B) Postoperative CT scan demonstrating only a little left of the hematoma.
Zhu H. et al: Keyhole Endoscopic Hematoma Evacuation

frequent and the proportion was higher than hemorrhagic stroke in Chinese populations, which is close to the subtype composition in the Western society (9). It should be noted that with today’s China becoming an aging society, the number of high-risk people older than 55 years will gradually increase and the annual ICH incidence may be on the rise (1).

Surgical treatment in ICH

The role of surgery in treating ICH is not fully established. Results from the STICH trial have greatly influenced the clinical management of ICH (10,13). However, there were some limitations to STICH trial, which as a worldwide multicenter trial involved diverse patient inclusion and surgical procedures. Surgical treatment is recommended when supratentorial ICH volume is at least 30 ml for life-saving purposes, which has been recognized by many surgeons (6). The purpose of surgery is to reduce the mass effect of hematoma, and thus decrease ICP, and restrict the cerebral edema by the blood components. Traditional craniotomy degrades the operative effect because of its long operation time, big wound and more postoperative complications. It is plausible that early and complete removal of ICH via a minimally invasive method can reduce the secondary injury associated with ICH (5).

Table III: Clinical Outcomes

<table>
<thead>
<tr>
<th>GOS 1, n (%)</th>
<th>Endoscopy group</th>
<th>Craniotomy group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (7.1%)</td>
<td>5 (16.7%)</td>
<td>0.425</td>
<td></td>
</tr>
<tr>
<td>2 (7.1%)</td>
<td>3 (10.0%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>17 (60.7%)</td>
<td>19 (63.3%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>5 (17.9%)</td>
<td>3 (10.0%)</td>
<td>0.464</td>
<td></td>
</tr>
<tr>
<td>2 (7.1%)</td>
<td>0</td>
<td>0.229</td>
<td></td>
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</table>

Table IV: The Surgical Result and Complications Between the <8h group and 8-24h Group

<table>
<thead>
<tr>
<th>Mortality, n (%)</th>
<th>&lt;8h</th>
<th>8-24h</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (14.7%)</td>
<td>2 (8.3%)</td>
<td>0.688</td>
<td></td>
</tr>
<tr>
<td>Good outcome, n (%)</td>
<td>9 (26.5%)*</td>
<td>1 (4.2%)</td>
<td>0.035</td>
</tr>
<tr>
<td>Rebleeding, n (%)</td>
<td>2 (5.9%)</td>
<td>2 (8.3%)</td>
<td>0.719</td>
</tr>
</tbody>
</table>

*P <0.05

Figure 2: Clinical outcomes.

were 34 cases operated within 8 hours and 24 cases operated within 8-24 hours. The ultra-early group had better outcomes (GOS 4 and 5) than the early group (26.5% vs. 4.2%; P <0.05, Table IV and Figure 3).

DISCUSSION

ICH in China mainland

There are no comprehensive statistics about the incidence of stroke in China mainland currently. The data of 2000, from Beijing, Shanghai, Changsha, three major cities of the information, reveal that the incidence of stroke is from 76.1 to 150.0/10 million, and ICH accounted for 18.9-47.6% of all stroke cases (8). Another study including more information from more cities showed that ICH accounted for 17.1-39.4% in subtypes of stroke (21). In Western populations, ICH accounted for a rate of 6.5% to 19.6% and the annual incidence rate is 20.9-28.0/10 million. The average mortality rate after 1 month of ICH is 40.4%, of which Japan has 16 .7%, the lowest in the world, and China 49.4%, higher than the world average (1,21). Chinese populations are rapidly adopting Western dietary habits, including increased energy intake, fat intake, and alcohol consumption, and decreased physical activity and cigarette smoking in recent years, together with China’s economic development. Ischemic stroke was more frequent and the proportion was higher than hemorrhagic stroke in Chinese populations, which is close to the subtype composition in the Western society (9). It should be noted that with today’s China becoming an aging society, the number of high-risk people older than 55 years will gradually increase and the annual ICH incidence may be on the rise (1).

Figure 3: Surgical result and rebleeding.

Surgical treatment in ICH

The role of surgery in treating ICH is not fully established. Results from the STICH trial have greatly influenced the clinical management of ICH (10,13). However, there were some limitations to STICH trial, which as a worldwide multicenter trial involved diverse patient inclusion and surgical procedures. Surgical treatment is recommended when supratentorial ICH volume is at least 30 ml for life-saving purposes, which has been recognized by many surgeons (6). The purpose of surgery is to reduce the mass effect of hematoma, and thus decrease ICP, and restrict the cerebral edema by the blood components. Traditional craniotomy degrades the operative effect because of its long operation time, big wound and more postoperative complications. It is plausible that early and complete removal of ICH via a minimally invasive method can reduce the secondary injury associated with ICH (5).
Endoscopic surgery
Evacuation of ICH by the endoscope was first reported by Auer in 1985 (2). The last decade has brought significant advances in endoscopic surgical instruments and techniques that have improved patient outcomes (12,16,20). Recent reports on the rate of hematoma evacuation through endoscopic surgery have reached rates of 99% (15,17), and comparative studies about minimally invasive surgery and craniotomy are still rare. We believe that as long as the positioning is accurate, keyhole endoscopic surgery can achieve the effect of large craniotomy surgery. Direct identification of the bleeding point and coagulation of responsible vessels under endoscopic visual control facilitate hematoma evacuation, without overstretching the brain tissue. The hematoma evacuation rate in the endoscopic keyhole hematoma group was significantly higher than the traditional craniotomy group (P <0.05), and the incidence of infection in the keyhole surgery group was significantly lower than the craniotomy group (P <0.05), because of the mild brain injury, shorter operation time and quicker recovery. When we began to use endoscopic techniques in the treatment in ICH, we preferred to choose open craniotomy when the hematoma volume was large. However, we did not have much experience and worried about the lower evacuation rate with endoscopy in large hematomas. We later found that endoscopic hematoma removal could provide a good evacuation rate even if the hematoma volume was bigger. This may be the reason hematoma volume was larger in the craniotomy group than that in endoscopy group (p<0.05).

Clinical Outcomes
Differences in patient selection, surgical indication, operation timing, technique, and perioperative care made direct comparison difficult. The published research results by Nagasaka with a combination irrigation-coagulation suction cannula or multifunctional suction cannula showed the rate of good outcome (good recovery and moderate disability) at discharge as 17.3% (4/23), and 0 (0/20) for the craniotomy group (17). Recently Kuo reviewed 68 cases of endoscopic treatment in cerebral hemorrhage with a mortality rate of 5.9%, and surgery-related morbidity of 4.4% (12). In our group, systemic complications, and especially pulmonary infection in addition to the brain-related factors were an important cause leading to death. Four cases died because of respiratory failure following pneumonia among the 8 deaths. The incidence of infection was significantly lower in the keyhole endoscopic group than the craniotomy group, so if we control post-operative complications the lower incidence of lung infection can improve the prognosis of patients. Some authors believe that later (6-month) survival was correlated with age (7). We chose patients aged from 30 to 70 years old as they would have relative good tolerance to the operation and we could compare the clinical result. The age in the craniotomy group was older than that in the endoscopy group (P<0.05), and it did not reach a significant difference in clinical outcome between the 2 groups. A larger, more balanced study would be needed to further confirm the clinical result of endoscopy.

When to operate and Rebleeding
It has been demonstrated that serum proteins originating from the intracerebral hematoma can result in early and prolonged (8 hours) edema after experimental ICH in a pig model (18). Clot removal at 3 hours has been proven to markedly reduce mass effect and edema at 24 hours in the same pig model of ICH (19). If very early surgery can remove most of the hemorrhage with minimal additional brain tissue damage, physicians may be able to reduce edema development and mass effect, prevent white matter damage, and improve clinical outcome in some patients. The problem linked with ultra-early surgery is rebleeding. A trial of 11 patients randomized within 4 hours of hemorrhage onset found that rebleeding occurred in 40% of the patients treated within 4 hours compared with 12% of the patients treated within 12 hours using the craniotomy method (14). There was a relationship between rebleeding and mortality in the 4-hour surgery group. According to Guidelines for the management of spontaneous intracerebral hemorrhage in adults, 2007 update, the preponderance of evidence supports operative removal within 12 hours, particularly through less-invasive methods (3). Our study showed that operation within 8h could lead to improved outcomes. In a nonrandomized report of putamenal clot evacuation in 100 patients within 7 hours of symptom onset, Kaneko point out the critical need to identify the bleeding lenticulostriate branch and coagulate it to prevent rebleeding postoperatively (9). We think that the bleeding point is better left untouched in cases that have achieved hemostasis. Meanwhile, continuous oozing from ruptured vessels should be exposed and be coagulated. This group of patients did not show that ultra-early surgery group compared with group operation in 8-24h was much more likely to rebleed. We believe that intraoperative blood pressure rising to normal levels after coagulation to test whether the effect is exactly, and postoperative control of blood pressure in a relatively stable state is an important measure to prevent further bleeding.

STUDY LIMITATION
Our study has several potential limitations. This was a retrospective nonrandomized study involving a relatively small group. The patients in this study were highly selected patients with a GCS score of 3 and 4, and coagulopathy was excluded. These patients usually have a poor prognosis compared with the patients included in this study, and there was a significant difference in hematoma volume and age in our group. Therefore, the good surgical outcomes and functional results may be due to patient selection.

CONCLUSION
Keyhole endoscopic surgery significantly improved the hematoma evacuation rate in our cohort. Our findings indicate that keyhole endoscopic surgery is safe and feasible. We support the idea that keyhole endoscopic surgery can
play a crucial role in the treatment of spontaneous ICH and that operation within 8h could lead to improved outcomes in selected patients. However, these preliminary results warrant further study in a large, prospective, randomized trial in the near future.

REFERENCES