Neuroendoscopic Surgery versus Stereotactic Aspiration in the treatment of supratentorial intracerebral hemorrhage: a meta-analysis

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Abstract

Background
No consensus has been reached on the superiority between Neuroendoscopic Surgery (NS) versus Stereotactic Aspiration (SA) in the treatment of supratentorial intracerebral hemorrhage (ICH). Therefore, this study conducted in-depth analysis and aimed to evaluate the efficacy and safety of NS versus SA for supratentorial ICH.

Methods
We searched for the all-relevant studies systematically from English databases including PubMed, Embase, Web of Science and the Cochrane Library. Two independent researchers identified and selected these literatures that met the inclusion criteria. Then we evaluated the quality of these studies according to the Cochrane Collaboration's risk of bias tool and the Newcastle-Ottawa Scale. RevMan 5.4 statistical software was used to conduct this meta-analysis.

Results
Fifteen studies, including 2600 supratentorial ICH patients, were included in our meta-analysis. The pooled results showed that NS could effectively reduce the postoperative mortality \((P<0.00001)\) and increase the hematoma evacuation rate \((P<0.00001)\). However, no significant difference was found between NS and SA in improving the functional prognosis \((P=0.15)\). In the aspect of hospital stays \((P<0.00001)\), no enough evidence could support that SA could shorten the hospital stays better than NS. However, SA had more advantages in shortening operation time \((P<0.00001)\) and reducing intraoperative blood loss \((P<0.00001)\). In the aspect of complications, NS could have a positive effect on preventing intracranial infection \((P=0.004)\). In the subgroup analysis, we found that Initial GCS might be a risk factor affecting prognosis and hematoma volume might be an important factor affecting mortality.

Conclusion
NS might have more advantages than SA in the treatment of supratentorial ICH. However, SA was also an effective alternative for middle-aged and elderly patients. More high-quality studies were needed to verify our conclusions in the future.

Introduction
Intracerebral hemorrhage (ICH) has always been a major disease threatening human health, with high morbidity and mortality.\(^1\) It was reported that the median 30-day fatality was up to 40%.\(^2\) Arterial
hypertension and cerebral amyloid angiopathy are the main risk factors.\textsuperscript{3,4} The bleeding site is more common in the supratentorial area, including the basal ganglia, thalamus, cerebral lobes, etc. The primary injury caused by the hematoma itself and the secondary injury caused by neurotoxic chemicals\textsuperscript{5} produced during the decomposition of the hematoma are the main reasons lead to the deterioration of neurological function or even death.\textsuperscript{6,7} Hematomas in different parts of the brain can cause different symptoms. Supratentorial ICH is more likely to cause nerve compression symptoms such as hemiplegia, aphasia, poor consciousness or death in severe cases. Therefore, early surgical intervention to remove the hematoma is the key to treating patients with supratentorial ICH and improving their prognosis.

The traditional surgical approach to treat supratentorial ICH is hematoma evacuation by craniotomy. However, with the advancement of medical equipment and therapeutic ideas, minimally invasive surgery (MIS) has played an important role in treating supratentorial ICH, especially deep hematoma.\textsuperscript{1,8–10} Most scholars believed that MIS could reduce the surgery-related injuries and achieve a better prognosis, when compared with craniotomy.\textsuperscript{11–13} Neuroendoscopic surgery (NS) and stereotactic aspiration (SA), as the major representatives of MIS, have been widely applied. However, no consensus has been reached on the superiority between NS versus SA in the treatment of supratentorial ICH. Some scholars hold that SA has less damage to the surrounding brain tissue and is a safer and more convenient surgical method.\textsuperscript{14,15} Some studies have found that SA had lower mortality and rebleeding rate than NS.\textsuperscript{16,17} However, the opposing argument has also been made that NS is more advantageous than SA in improving prognosis and reducing mortality.\textsuperscript{18} Actually, there have been two related meta-analyses comparing the two surgical methods before, but with certain shortcomings.\textsuperscript{19,20} Firstly, the included literature was incomplete. In addition, some risk factors, such as different sites of hematoma (e.g., supratentorial and infratentorial hematomas) and different hematoma volumes, may lead to different symptoms, functional prognosis and mortality. They ignored the effect of these factors on outcome measures, which might increase the bias and reduce the validity of the results.

Therefore, we carried out this meta-analysis and hoped to evaluate the efficacy and safety of NS and SA in the treatment of supratentorial ICH from a more comprehensive and deep perspective.

**Materials And Methods**

**Literature search**

All the relevant studies were searched from English databases including PubMed (November 1981 to May 2022), Embase (October 1990 to May 2022), web of science (March 1986 to May 2022) and the Cochrane Library (March 1996 to March 2021) by three independent researchers (SW. S, X. H and XB. F). The search terms included “intracerebral hemorrhage”, “cerebral hemorrhage”, “ICH” “endoscopy”, “endoscopic”, “neuroendoscopy”, “aspiration”, “minimally invasive”, “stereotactic aspiration”, “puncture”. We conducted this search by combining MeSH terms with free words. The literatures included in this study were limited to English, but there was no restriction for publication time. Three
researchers (SW. S, X. H and XB. F) determined the search strategy and assessed the study based on the titles and abstracts. Full versions of all included articles were obtained and viewed. In addition, we checked the references of included articles to find out potential studies that met the inclusion criteria.

Study selection

The inclusion criteria were as follows: (1) studies reporting primary or secondary outcomes of comparing NS with SA; (2) randomized controlled trials (RCTs) or observational studies (OSs), whether blind or not; (3) spontaneous supratentorial ICH confirmed by image diagnosis; (4) hematoma volume more than 20 ml. Literatures would be excluded if any of the following conditions existed: (1) participants with multiple organ dysfunction; (2) cerebella or brainstem hemorrhage; (3) hemorrhage caused by a coagulation disorder, aneurysm, vascular malformation or tumor.

Outcome measures

The primary outcomes were as follows: (1) good functional outcome (GFO), defined as a patient who could take care of himself (better than moderate disability), corresponding to a Glasgow Outcome Scale (GOS) score of 4 or 5, a modified Rankin Scale score of 0, 1, or 2 or an Activities of Daily Living (ADL) score of 1, 2, or 3; (2) hematoma evacuation rate; (3) mortality.

Secondary outcomes included the following: (1) operation time and blood loss; (2) hospital stays and ICU stays; (3) rebleeding, intracranial infection, pneumonia, digestive tract ulcer and epilepsy.

Data extraction and qualitative assessment

Through reading the full texts of included studies, we extracted the following information: reference, publication year, design, group (cases, gender [M/F]), age, hematoma volume, GCS score, hematoma location, thrombolysis, time to surgery, follow-up, data regarding primary and secondary outcomes. The methodological quality of RCTs and OSs was assessed according to the Cochrane Collaboration’s risk of bias tool
 and the Newcastle-Ottawa Scale (NOS) separately. All of these works were accomplished by three independent researchers.

Statistical analysis

RevMan 5.4 statistical software was used to conduct this meta-analysis. The odds ratio (OR) and the weighted mean difference (WMD) were applied as the effect indicators for the dichotomous variable and the continuous variable respectively. Each pooled result was expressed in a 95% confidence interval (95% CI). We evaluated the heterogeneity of the included studies by the I^2 test. If the heterogeneity test showed I^2 < 50% (indicating a low heterogeneity), we selected the fixed-effect model to calculate the pooled statistics. Otherwise, the randomized-effect model was chosen. In addition, we conducted the subgroup analysis to explore the impact of year of publication, Glasgow Coma Scale (GCS) score, age, hematoma volume, hematoma location, and follow-up on the outcome measures. The funnel plots were used to evaluate the publication bias. A probability value P < 0.05 was considered statistically significant.
Results

Study inclusion

Through systematic searching, a total of 1473 potentially relevant articles (including 867 duplicate studies) were identified. After removing the duplicates, we browsed the titles and abstracts of the remaining 606 articles and excluded 528 studies subsequently for these reasons: (1) cases, reports, reviews, comments, and editorials; or (2) irrelevant researches. Next, we conducted a full-text search of the remaining 78 literatures and read their contents carefully. After repeated confirmation by three researchers (SW. S, X. H and XB. F), most of them (n=63) were removed further due to these reasons: (1) had no controls; (2) contained subtentorial hemorrhage, inappropriate outcome indicators; (3) did not provide the full text. Finally, only 15 studies, including 2600 supratentorial ICH patients, met the inclusion criteria and were accepted in this meta-analysis. These studies included one RCT and fourteen OSs and the publication time ranged from 1998 to 2021. The characteristics of the included studies are listed in Table 1. The literature selection is presented in Figure 1, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

In the study of Fu et al., they divided the subjects (patients with thalamic hemorrhage breaking into the ventricle) into Anteromedial group and Posterolateral group based on the location of hemorrhage. Therefore, we designed them into group A (Anteromedial group) and group B (Posterolateral group) for comparison in the same way. Besides, the SA group was divided into two groups according to the volume of the hematoma (C1: 50-80 mL; C2: 20-49 mL) in the study of Chi et al., so we designed it into two groups A and B in this study (Group A: NE vs SA with C1; Group B: NE vs SA with C2). In the study of Nishihara et al., they mentioned some patients with cerebellar hemorrhage. Since these patients did not belong to the research object of this study, we removed the data of patients with cerebellar hemorrhage and re-extracted the effective data.

Table 1. Basic characteristics of included studies.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Design</th>
<th>Case, Gender(M/F)</th>
<th>Age(y)</th>
<th>HV(ml)</th>
<th>GCS score</th>
<th>Hematoma location</th>
<th>thrombolysis</th>
<th>Time to surgery(h), Follow-up (month)</th>
<th>Quality evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cai et al., 2017</td>
<td>OS</td>
<td>20/11</td>
<td>22/13/9</td>
<td>59.6±10.1</td>
<td>58.7±12.4</td>
<td>≥ 20</td>
<td>7.6/8.3</td>
<td>supratentorial</td>
<td>UK</td>
</tr>
<tr>
<td>Chi et al., 2014</td>
<td>Group A</td>
<td>144/119</td>
<td>306/227</td>
<td>62.8±9.2</td>
<td>57.3±10.1</td>
<td>≥ 20</td>
<td>≥ 5</td>
<td>supratentorial</td>
<td>NG</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>144/119</td>
<td>169/101</td>
<td>62.8±9.2</td>
<td>63.3±8.63</td>
<td>≥ 20</td>
<td>≥ 5</td>
<td>supratentorial</td>
<td>NG</td>
</tr>
<tr>
<td>Cho et al., 2006</td>
<td>RCT</td>
<td>30/19</td>
<td>30/20</td>
<td>56.67±8.66</td>
<td>56.56±8.98</td>
<td>≥ 20</td>
<td>7.6/8.3</td>
<td>basal ganglion</td>
<td>UK</td>
</tr>
<tr>
<td>Dong et al., 2019</td>
<td>Group A</td>
<td>144/119</td>
<td>81/63</td>
<td>62.8±9.2</td>
<td>57.3±10.1</td>
<td>≥ 20</td>
<td>≥ 5</td>
<td>supratentorial</td>
<td>NG</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>144/119</td>
<td>81/63</td>
<td>62.8±9.2</td>
<td>63.3±8.63</td>
<td>≥ 20</td>
<td>≥ 5</td>
<td>supratentorial</td>
<td>NG</td>
</tr>
<tr>
<td>Fu et al., 2018</td>
<td>Group A</td>
<td>33/17</td>
<td>17/16</td>
<td>57</td>
<td>62</td>
<td>10-30</td>
<td>7</td>
<td>thalamus + ventricle</td>
<td>UK</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>35/18</td>
<td>36/17</td>
<td>60</td>
<td>63</td>
<td>10-30</td>
<td>8</td>
<td>thalamus + ventricle</td>
<td>UK</td>
</tr>
<tr>
<td>Guo et al., 2020</td>
<td>OS</td>
<td>105/64</td>
<td>64/41</td>
<td>&lt; 60</td>
<td>&lt; 60</td>
<td>≥ 60</td>
<td>(56.7%)</td>
<td>basal ganglion</td>
<td>UK</td>
</tr>
<tr>
<td>Li et al., 2017</td>
<td>OS</td>
<td>32/18</td>
<td>17/16</td>
<td>60.7±8.8</td>
<td>61.3±8.4</td>
<td>&gt; 30</td>
<td>8.6/8.6</td>
<td>Supratentorial</td>
<td>Lobar</td>
</tr>
<tr>
<td>Li et al., 2017</td>
<td>OS</td>
<td>58/32</td>
<td>54/35</td>
<td>61.8±9.9</td>
<td>59.7±7.5</td>
<td>&gt; 30</td>
<td>8.6/8.4</td>
<td>basal ganglion</td>
<td>UK</td>
</tr>
<tr>
<td>Liu et al., 2020</td>
<td>OS</td>
<td>60/39</td>
<td>99/57</td>
<td>18.80</td>
<td>18.80</td>
<td>≥ 40</td>
<td>≤ 8</td>
<td>basal ganglion</td>
<td>UK</td>
</tr>
<tr>
<td>Mao et al., 2020</td>
<td>OS</td>
<td>63/35</td>
<td>54/47</td>
<td>56.48±9.70</td>
<td>60.19±11.92</td>
<td>&gt; 30</td>
<td>9/10</td>
<td>basal ganglion</td>
<td>UK</td>
</tr>
<tr>
<td>Nishihara et al., 2007</td>
<td>OS</td>
<td>24/17</td>
<td>17/18</td>
<td>69.2</td>
<td>65.3</td>
<td>6.9-130</td>
<td>6.15</td>
<td>Putamen, thalamus, subcortical</td>
<td>UK</td>
</tr>
<tr>
<td>Zhang et al., 2019</td>
<td>OS</td>
<td>53, NG</td>
<td>45, NG</td>
<td>40.75</td>
<td>40.75</td>
<td>≥ 25</td>
<td>8.9/8.3</td>
<td>supratentorial</td>
<td>UK</td>
</tr>
</tbody>
</table>

NS: neuroendoscoptic surgery; SA: stereotactic aspiration; RCT: Randomized Controlled Trial; OS: Observational Study; GCS: Glasgow Coma Scale; NG: not given; UK: urokinase; HV: Hematoma volume

**Primary outcome**

**GFO**

We could find that there were seven studies reporting the data about GFO, as shown in Figure 2. Significant heterogeneity was observed ($I^2 = 71\%$) and we used the randomized effect model to calculate the statistic result. The proportion of patients with GFO was 60.61% in the NS group, compared with 55.61% in the SA group. The pooled OR of GFO was 1.40 (95% CI: 0.88–2.24; $P = 0.15$), implying that there was no significant difference between NS and SA in improving the functional prognosis of patients with supratentorial ICH.

**Hematoma evacuation rate**
In Figure 3, seven studies contained the date about hematoma evacuation rate. Obvious heterogeneity was found between these studies ($I^2 = 98\%$), so the random-effects model was applied. The 95% CIs of these studies were on the right side of the baseline. The difference of the hematoma evacuation rate between the two groups was obvious (WMD: 34.51; 95% CI: 22.14–46.89; $P < 0.00001$), suggesting that NS was superior in clearing the hematoma.

*Mortality*

Seventeen studies mentioned the mortality, as shown in Figure 4. Due to a low heterogeneity in each study ($I^2 = 40\%$), we used the fixed-effects model to calculate. The mortality was 10.79% in the NS group, compared to 24.83% in the SA group. The pooled OR was 0.40 (95% CI: 0.32–0.51; $P < 0.00001$), implying that the difference of mortality between NS and SA was significant. NS could effectively reduce the postoperative mortality.

**Secondary outcome**

*Operation time and blood loss*

In terms of operation time, 8 studies were included to analyze (Figure 5A). Obvious heterogeneity was indicated from the result ($I^2 = 95\%$). Therefore, we used the random-effects model. The pooled results showed that the difference of operation time was significant (WMD: 39.76; 95% CI: 29.57–49.94; $P < 0.00001$), suggesting that SA could shorten the operation time obviously.

Four studies mentioned the blood loss volume, as shown in Figure 5B. The random-effects model was accepted because of the high heterogeneity in each study ($I^2 = 99\%$). The pooled WMD of blood loss volume was 68.37 (95% CI: 34.58–102.16; $P < 0.0001$), suggesting that SA could reduce blood loss better than NS during the operation.

*Hospital stays and ICU stays*

Four studies reported the hospital stays (n = 180 in the NS group and 219 in the SA group), as shown in Figure 6A. The test of heterogeneity showed little heterogeneity between studies ($I^2 = 0\%$). The fixed-effects model was applied. The pooled WMD was 1.29 (95% CI: 0.99–1.58; $P < 0.00001$). Meanwhile, we conducted the sensitivity analysis to evaluate the stability of this result. Finally, it was found that the $P$ value would change to 0.11 (WMD: 0.77; 95% CI: -0.17 to 1.72; $P = 0.11$) if the study of Liu et al was removed. This result was different from the original one, which indicated that the pooled result was unstable. So, there was not enough evidence to support that SA could shorten the hospital stays better than NS.

In Figure 6B, only three studies mentioned the intensive care unit (ICU) stays (n = 86 in the NS group and 83 in the SA group). Obvious heterogeneity was observed between studies ($I^2 = 70\%$). The random-effects model was applied. The pooled WMD was $-2.02$ (95% CI: $-5.29$ to $1.25$; $P = 0.23$), suggesting
that there was no significant difference in ICU stays between NS and SA. Sensitivity analysis showed that this result was stable.

**Complications**

As shown in Figure 7, 11 studies mentioned rebleeding. Likewise, 4 studies mentioned digestive tract ulcer, 3 studies referred to epilepsy, 10 studies referred to intracranial infection, 7 studies referred to pneumonia. No significant heterogeneity ($I^2 < 50\%$) was apparent between these studies. The fixed-effects model was adopted for this analysis. We could find that there was no statistically significant difference between NS and SA in terms of postoperative rebleeding (OR: 0.57; 95% CI: 0.33–0.99; $P = 0.05$), digestive tract ulcer (OR: 1.37; 95% CI: 0.77–2.45; $P = 0.29$), epilepsy (OR: 1.17; 95% CI: 0.43–3.16; $P = 0.76$), pneumonia (OR: 0.93; 95% CI: 0.46–1.88; $P = 0.85$). However, obvious statistical differences could be discovered in terms of postoperative intracranial infection (OR: 0.42; 95% CI: 0.23–0.76; $P = 0.004$). It suggested that NS could have a positive effect on preventing intracranial infection.

Qualitative assessment and publication bias

The quality evaluation of the included studies appears in Table 1. One RCT conformed to five scores, based on the Cochrane Collaboration’s risk of bias tool. The funnel plots were slightly asymmetric for the primary outcomes by visual inspection. Therefore, we found that the publication bias was low regarding GFO (Figure 8), mortality (Figure 10), and moderate regarding hematoma evacuation rate (Figure 9).

Subgroup analysis

Considering several variables, including year of publication, Glasgow Coma Scale (GCS) score, age, hematoma volume, hematoma location, and follow-up, might affect the primary outcomes, therefore we performed the subgroup analysis. As shown in Table 2, our results showed that year of publication, age, hematoma volume, hematoma location, and follow-up did not affect the hematoma evacuation rate significantly. However, no studies mentioned the hematoma evacuation rate in the subgroup of Initial GCS score $\leq$ 8. As for the outcome indicator of GFO, the difference between NS and SA was statistically significant in the subgroup of Initial GCS $\leq$ 8 (OR: 1.52; 95% CI: 1.11–2.07; $P = 0.008$), suggesting that NS might be more advantageous in improving functional prognosis for patients with more severe condition at admission (GCS $\leq$ 8). Similarly, the significant difference in GFO was found in the subgroup of hematoma location (basal ganglion 100%) (OR: 1.43; 95% CI: 1.07–1.90; $P = 0.01$). It implied that NS was more effective in improving the prognosis for basal ganglia cerebral hemorrhage alone. However, as for hematoma elsewhere, the advantages between NS and SA needed to be carefully treated and further studied. In addition, there was no significant difference in the pooled data about GFO in the subgroups of publication time, mean age, hematoma volume and follow-up, suggesting that these factors had no significant effect on the postoperative prognosis. In the subgroups related to mortality, these factors including Year of publication, age, Hematoma volume and follow-up all had significant effects on mortality. In the subgroup of Year of publication before 2010, the combined data suggested that there
was no significant difference in mortality between NS and SA (OR: 0.35; 95% CI: 0.07–1.63; P = 0.18). Similarly, no significant difference about mortality (OR: 0.70; 95% CI: 0.44–1.11; P = 0.13) was found in the subgroup of mean age > 60-year. Through further research, we were surprised to find that the mortality in the subgroup of mean age > 60-year was significantly lower than that in the subgroup of mean age ≤ 60-year (15.96% vs. 29.85%), however little change in NS group (11.60% vs. 10.74%). This outcome suggested that age might be an important factor influencing postoperative mortality in SA. Besides, the result showed no significant difference in mortality between NS and SA in the subgroup of Hematoma volume more than 50ml (OR: 0.68; 95% CI: 0.35–1.34; P = 0.27). However, both surgical groups had significantly higher mortality rates in the subgroup of Hematoma volume greater than 50ml than in the subgroup of Hematoma volume less than 50ml (NS: 15.47% vs. 2.69%; SA: 24.09% vs. 7.61%). It replied that Hematoma volume might be also an important factor affecting mortality. Finally, in the subgroup of Follow-up > 6-month, the data indicated that the variable of follow-up time also had an impact on mortality (OR: 1.04; 95%CI: 0.45–2.38; P = 0.93). However, due to the limited number of studies eligible for subgroup inclusion requirements (only two studies), the validity of the results suffered a bit of influence and further verification was needed.

### Table 2. Subgroup analysis for primary outcomes

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Good Functional Outcome</th>
<th>Hematoma Evacuation Rate</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>OR (95%CI)</td>
<td>P</td>
</tr>
<tr>
<td>Year of publication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>before 2010</td>
<td>2</td>
<td>1.12 (0.40–3.18)</td>
<td>0.83</td>
</tr>
<tr>
<td>after 2010</td>
<td>5</td>
<td>1.45 (0.85-2.49)</td>
<td>0.17</td>
</tr>
<tr>
<td>Initial GCS score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 8</td>
<td>2</td>
<td>1.52 (1.11-2.07)</td>
<td>0.008</td>
</tr>
<tr>
<td>&gt; 8</td>
<td>3</td>
<td>1.30 (0.46-3.70)</td>
<td>0.62</td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 60</td>
<td>3</td>
<td>1.32 (0.97-1.81)</td>
<td>0.08</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>2</td>
<td>2.23 (0.85-5.83)</td>
<td>0.10</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>basal ganglion</td>
<td>4</td>
<td>1.43 (1.07-1.90)</td>
<td>0.01</td>
</tr>
<tr>
<td>supratentorial</td>
<td>3</td>
<td>1.37 (0.44-4.30)</td>
<td>0.59</td>
</tr>
<tr>
<td>Hematoma volume (ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 50</td>
<td>3</td>
<td>1.03 (0.54-1.97)</td>
<td>0.93</td>
</tr>
<tr>
<td>&gt; 50</td>
<td>2</td>
<td>1.00 (0.50-2.02)</td>
<td>0.99</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 6-month</td>
<td>6</td>
<td>1.42 (0.87-2.32)</td>
<td>0.16</td>
</tr>
<tr>
<td>&gt; 6-month</td>
<td>1</td>
<td>1.11 (0.16-7.51)</td>
<td>0.91</td>
</tr>
</tbody>
</table>

CI: confidence interval; OR: odd ratio; WMD: Weighted Mean Difference; GCS: Glasgow Coma Scale

### Discussion

The treatment of ICH has been the research focus of Neurosurgery all over the world, because of its high incidence and serious sequelae. A goal is pursued constantly by surgeons during the process of surgical treatment of ICH: how to improve the neurological function prognosis on the basis of ensuring the survival rate of patients. Therefore, the application of MIS to treat ICH has gradually been concerned and researched. Nowadays, the methods of MIS treatment mainly include NS, SA, and microscopically assisted craniotomy with keyhole approach, etc. It was reported that patients
with supratentorial ICH could benefit from MIS more than conventional treatment (including medical treatment and conventional craniotomy). This study mainly focused on patients with supratentorial ICH as the research object and compared the safety and efficacy of NS and SA. The advantage of our study was more systematic, comprehensive and persuasive. Additionally, our findings were somewhat different from previous studies, especially in terms of functional prognosis and mortality.

It is well known that neuroendoscopy has the characteristics of deep illumination, amplification effect and Fish-eye effect. So, it has an outstanding advantage in clearing hematoma, which is consistent with the result of our study. For SA, although the clearance rate of hematoma may be less in the short term, the hematoma will be slowly drawn out with the passage of drainage time. It was reported that no significant difference in the hematoma clearance rate would be found between NS and SA approximately third day after surgery. In terms of functional prognosis, no significant difference was found between the two groups in our study, which was different from the previous study. The prognosis of patients is closely related to primary brain injury and secondary brain injury (caused by hematoma and its degradation products), with the latter having higher impact. NS had a higher hematoma evacuation rate and could significantly reduce secondary brain injury. However, SA could lighten the injury to brain tissue during the operation with shorter operation time and less intraoperative bleeding. Therefore, we should take this result from a comprehensive perspective. In addition, our study confirmed that NS did have an obvious advantage in reducing mortality, which was different from the conclusion of Yao et al’s study ($P = 0.35$). In terms of postoperative complications, some people believed that the incidence of rebleeding after SA might be higher, especially after injection of thrombolytic (or UK) into the hematoma cavity. However, the result of our meta-analysis showed that SA + UK did not increase the rebleeding incidence compared with NS group significantly, which suggested that the use of UK after operation might be also safe and effective. Even so, the selection of SA for ICH was usually based on the premise that the hematoma was relatively stable. In some cases, such as ultra-early surgery (time to surgery < 6h) or the existence of active bleeding, SA might be not applicable. Actually, Li et al had conducted a retrospective study including 59 supratentorial ICH with negative CTA spot sign, and found that ultra-early SA could reduce brain edema and improve neurological function to a certain extent, without increasing the rebleeding rate and mortality. However, it might be not need to pay too much attention to these situations for NS, because endoscopic surgery could completely stop bleeding under direct vision. Although there was no significant difference in the incidence of postoperative digestive tract ulcer, epilepsy, pneumonia, etc., the disadvantage of SA still existed in the aspect of intracranial infection. This might be related to the longer time of postoperative catheter drainage. In addition, intracranial infection might be also one of the factors leading to high mortality of SA. Pulmonary infection was the most common complication in the treatment of ICH. Commonly, long periods in bed, consciousness disturbance and prolonged tracheal intubation can trigger or aggravate pulmonary infection. There was no difference in the incidence of postoperative pulmonary infection between the two groups, suggesting that both of two surgical methods were effective in improving patient’s condition.
and helping consciousness recovery. On the respect of economic cost, our study did not make a specific combined comparison.

In subgroup analysis, we further explored the impact of various factors on the primary outcomes. First of all, although there was no significant difference in the GFO between NS and SA, NS still had an obvious advantage in improving the prognosis of patients with severe conditions at admission (GCS ≤ 8). It was also consistent with some findings of the Li YQ’s study (GOS score in NS higher than that in SA for patients with poor consciousness). In addition, we found that the influence of hematoma volume on GFO was not obvious. Thus, we could not just rely on the volume of hematoma, but more on the severity of illness at admission (or GCS score), when we evaluated whether NS had an advantage over SA in improving outcomes. Although the volume of hematoma had no significant effect on GFO, it could significantly affect the mortality. The mortality in the subgroup with large hematoma volume (> 50ml) was higher than the other one, which indicated that the advantage of NS in reducing mortality was weakened as the volume of hematoma increased. In terms of age, it is generally believed that advanced age was a risk factor affecting the prognosis of surgery. The higher the age, the greater the risk and the worse the prognosis. However, it was surprised that we found that the postoperative mortality of middle-aged and elderly patients (age > 60 year) was lower than that of young and middle-aged patients in the SA group. And SA was similar to NS in the aspects of mortality and GFO. This result indicated that SA might be also safe and effective for middle-aged and elderly patients. Reviewing the above results, we considered that SA was also a substitutable and effective choice for middle-aged and elderly patients with a large volume of ICH, especially for those with serious background diseases who were not suitable for long-term anesthesia or surgery. In the aspect of location of supratentorial ICH, it is most common in basal ganglia, followed by thalamus, lobar, subcortical and so on. In the subgroup analysis, it was found that NS had more obvious advantages in the treatment of basal ganglia hemorrhage. But for the patients in the whole supratentorial hemorrhage group, the difference on GFO between the two groups was not significant. Therefore, whether SA was advantageous to the prognosis of patients with supratentorial ICH in other sites (except for basal ganglia), which was worth to further research and discuss in the future. In fact, several studies had been published and supported the use of NS for thalamic hemorrhage. Fu et al analyzed the treatment of 211 patients with thalamic hemorrhage breaking into ventricles and found that endoscopy was more effective and safer in the treatment of thalamic hemorrhage, especially in the anteromedial group.

Some limitations still existed in our study. Firstly, most of included studies were retrospective studies (only one RCT study). In addition, due to limited data, it was a pity that we could not further explore the influence of different hematoma sites in the supratentorial area and time to surgery on the various outcome indicators between NS and SA. Although a previous study held that the optimal operation time was 6-12h after ICH, more works needed to be continued to verify. Moreover, the data about some patients with cerebral hernia included in our study could not be extracted. Therefore, we could not assess whether cerebral hernia had an impact on the outcome indicators. Finally, the sample size of
some studies was limited, which might increase the bias of the results. However, the validity of our findings would not be weakened, even if the above defects existed.

Conclusions

In general, NS might have more advantages than SA in the treatment of supratentorial ICH. However, SA was also an effective alternative for middle-aged and elderly patients, especially for those with serious background diseases who were not suitable for long-term anesthesia or surgery. Due to the existence of some limitations, more high-quality studies were still needed to verify our conclusions in the future.

References


Declarations

Acknowledgments and Funding

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Figures
Figure 1

PRISMA flow diagram of the meta-analysis.
Figure 2

The OR estimate for GFO between NS and SA. *(OR: odds ratio; GFO: good functional outcome; NS: Neuroendoscopic Surgery; SA: Stereotactic Aspiration)*

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>NS Events</th>
<th>Total</th>
<th>SA Events</th>
<th>Total</th>
<th>Weight</th>
<th>M-H. Random 95% CI</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chi (A) 2014</td>
<td>111</td>
<td>144</td>
<td>254</td>
<td>306</td>
<td>16.5%</td>
<td>0.69 [0.42, 1.12]</td>
<td></td>
</tr>
<tr>
<td>Chi (B) 2014</td>
<td>111</td>
<td>144</td>
<td>87</td>
<td>169</td>
<td>16.5%</td>
<td>3.17 [1.94, 5.19]</td>
<td></td>
</tr>
<tr>
<td>Du 2021</td>
<td>118</td>
<td>221</td>
<td>162</td>
<td>343</td>
<td>20.7%</td>
<td>1.40 [0.99, 1.98]</td>
<td></td>
</tr>
<tr>
<td>Kim 1998</td>
<td>5</td>
<td>6</td>
<td>6</td>
<td>10</td>
<td>4.7%</td>
<td>1.11 [0.16, 7.51]</td>
<td></td>
</tr>
<tr>
<td>Liu 2020</td>
<td>24</td>
<td>60</td>
<td>24</td>
<td>99</td>
<td>15.4%</td>
<td>2.08 [1.04, 4.16]</td>
<td></td>
</tr>
<tr>
<td>Mao 2020</td>
<td>16</td>
<td>63</td>
<td>14</td>
<td>54</td>
<td>13.4%</td>
<td>0.97 [0.42, 2.24]</td>
<td></td>
</tr>
<tr>
<td>Nishihara 2007</td>
<td>12</td>
<td>24</td>
<td>8</td>
<td>17</td>
<td>8.8%</td>
<td>1.13 [0.32, 3.90]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>397</td>
<td>555</td>
<td>998</td>
<td>106.0%</td>
<td>1.40</td>
<td>[0.88, 2.24]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 397

Heterogeneity: Tau² = 0.24; Chi² = 20.30, df = 6 (P = 0.002); I² = 71%

Test for overall effect: Z = 1.43 (P = 0.15)

Figure 3

The WMD estimate for hematoma evacuation rate between NS and SA. *(WMD: weighted mean difference; NS: Neuroendoscopic Surgery; SA: Stereotactic Aspiration)*

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>NS Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference IV. Random 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho 2006</td>
<td>87</td>
<td>8</td>
<td>30</td>
<td>75</td>
<td>13</td>
<td>30</td>
<td>14.4%</td>
<td>12.00 [6.54, 17.46]</td>
</tr>
<tr>
<td>Fu 2018</td>
<td>89.8</td>
<td>7.9</td>
<td>61</td>
<td>35.2</td>
<td>9.4</td>
<td>56</td>
<td>14.7%</td>
<td>55.60 [52.44, 58.76]</td>
</tr>
<tr>
<td>Li YQ 2017</td>
<td>91.3</td>
<td>3.8</td>
<td>32</td>
<td>41.5</td>
<td>9.9</td>
<td>36</td>
<td>14.7%</td>
<td>49.80 [46.31, 53.29]</td>
</tr>
<tr>
<td>Li ZH 2017</td>
<td>82.7</td>
<td>23.7</td>
<td>58</td>
<td>41.2</td>
<td>20</td>
<td>54</td>
<td>14.0%</td>
<td>41.50 [33.40, 49.60]</td>
</tr>
<tr>
<td>Mao 2020</td>
<td>84.5</td>
<td>14.4</td>
<td>63</td>
<td>68.6</td>
<td>19.4</td>
<td>54</td>
<td>14.3%</td>
<td>15.90 [9.62, 22.18]</td>
</tr>
<tr>
<td>Nishihara 2007</td>
<td>94.7</td>
<td>4.47</td>
<td>24</td>
<td>61.59</td>
<td>23.23</td>
<td>17</td>
<td>13.2%</td>
<td>33.11 [21.92, 44.30]</td>
</tr>
<tr>
<td>Zhang 2019</td>
<td>84</td>
<td>7.1</td>
<td>53</td>
<td>51</td>
<td>8.4</td>
<td>45</td>
<td>14.7%</td>
<td>33.00 [26.89, 39.11]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>321</td>
<td>292</td>
<td>321</td>
<td>100.0%</td>
<td>34.51</td>
<td>[22.14, 46.89]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 286.51; Chi² = 302.38, df = 6 (P < 0.00001); I² = 98%

Test for overall effect: Z = 5.47 (P < 0.00001)
Figure 4

The OR estimate for mortality between NS and SA. *(OR: odds ratio; NS: Neuroendoscopic Surgery; SA: Stereotactic Aspiration)*

Figure 5

The WMD estimate for operation time (A) and blood loss volume (B) between NS and SA. *(WMD: weighted mean difference; NS: Neuroendoscopic Surgery; SA: Stereotactic Aspiration)*
Figure 6

The WMD estimate for hospital stays (A) and ICU stays (B) between NS and SA.  (*WMD: weighted mean difference; ICU: Intensive Care Unit; NS: Neuroendoscopic Surgery; SA: Stereotactic Aspiration*)
Figure 7

The OR estimate for postoperative complications (including rebleeding, digestive tract ulcer, epilepsy, intracranial infection, pneumonia) between NS and SA. (OR: odds ratio; NS: Neuroendoscopic Surgery; SA: Stereotactic Aspiration)
Figure 8

The funnel plot of GFO analysis. *(GFO: good functional outcome)*

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Figure 9
The funnel plot of hematoma evacuation rate analysis.

Figure 10

The funnel plot of mortality analysis.