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Minimally Invasive Surgery for Spontaneous Supratentorial Intracerebral Hemorrhage

A Meta-Analysis of Randomized Controlled Trials

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Background and Purpose—There has been a nonstandard surgical procedure and extensive international controversy in minimally invasive surgery (MIS) for the management of spontaneous supratentorial intracerebral hemorrhage. This meta-analysis assessed the effectiveness of MIS as compared with other treatment options, including conservative medical treatment and conventional craniotomy, in patients with supratentorial intracerebral hemorrhage.

Methods—PubMed, Embase, Cochrane Controlled Trials Register (CCTR), Web of Science, European Association for Grey Literature Exploitation (EAGLE), National Technical Information Service (NTIS), Current Controlled Trials, Clinical Trials, International Clinical Trials Registry, Internet Stroke Center, Chinese Biomedical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI) (last searched December 2011) were searched. Randomized controlled trials on MIS in patients with computed tomography-confirmed supratentorial intracerebral hemorrhage were included. We excluded low-quality randomized controlled trials. The death or dependence at the end of follow-up was defined as the primary outcome, and the death at the end of follow-up was defined as the secondary outcome.

Results—The 313 randomized controlled trials met the included criteria. We only analyzed 12 high-quality randomized controlled trials involving 1955 patients. The quality of the included trials was consistently high. OR of the primary outcome and secondary outcome of MIS both showed significant reductions (OR, 0.54, $P<0.00001$; OR, 0.53, $P<0.00001$).

Conclusions—Patients with supratentorial intracerebral hemorrhage may benefit more from MIS than other treatment options. The most likely candidates to benefit from MIS are both sexes, age of 30 to 80 years with superficial hematoma, Glasgow Coma Scale score of ≥9, hematoma volume between 25 and 40 mL, and within 72 hours after onset of symptoms. Our study could help select appropriate patients for MIS and guide clinicians to optimize treatment strategies in supratentorial intracerebral hemorrhage. **(*Stroke*. 2012;43:2923-2930.)**

Key Words: acute stroke ■ cerebrovascular accident ■ intracerebral hemorrhage ■ meta-analysis ■ minimally invasive surgical procedures

Spontaneous intracerebral hemorrhage is a common subtype of stroke with high incidence rates and mortality worldwide of which over two thirds of deaths are in developing countries, where are >100 000 deaths and approximately 300 000 disabilities annually in China.[1–3] Supratentorial spontaneous intracerebral hemorrhage (SICH), which accounts for 78% to 88% of intracerebral hemorrhages, is primarily caused by spontaneous rupture of small vessels in individuals with arterial hypertension.[4] Since the first successful surgery of SICH in 1908, many scholars have done research on the management of SICH.[5,6] The choice between surgery and conservative treatment has still been the focus of international controversy.[7,8] A previous systematic review, published in 2007, reported that surgery could possibly benefit more in patients with SICH compared with conservative medical treatment.[9] However, its evidence was not very robust and some recent randomized controlled trials (RCTs) appeared to provide novel views on this issue.[10–12]

In the last 20 years, minimally invasive surgery (MIS) techniques, including endoscopic surgery and stereotactic aspiration, have been widely used in the treatment of patients with SICH.[13] In China, there are >150 000 patients with

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Drs Zhou, Chen, Li, and Ren contributed equally to this meta-analysis.

The sponsor had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

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SICH for MIS treatment every year. Advantages of MIS for treatment of SICH are not only suitable for minimal surgical trauma, but also associated with a shorter operative time and the potential to use local anesthesia.[14] A high-quality trial reported significantly improved functional outcomes in patients with SICH treated with minimally invasive craniopuncture, a modified procedure of stereotactic aspiration form China, compared with conservative medical treatment.[15] However, some scholars believed that MIS could not completely remove hematomas compared with conventional craniotomy because of reducing surgical exposure. There is a potential risk for rebleeding related to the use of fibrinolytics and an increased risk of infection related to prolonged use of indwelling catheters.[16] The results of 2 studies demonstrated that the outcome of endoscopic evacuation and stereotactic aspiration were not better than those of conservative medical treatment.[17,18] This controversy challenges clinicians and scholars to engage in innovative thinking of selecting the appropriate treatment strategies for SICH.

In our previous studies, we have investigated the epidemiology, prevention, and management strategies for stroke in China.[1,19,20] In addition, we also participated in a prospective randomized controlled study, which compared the effectiveness of minimally invasive stereotactic puncture therapy versus conventional craniotomy in SICH.[10] Recently, several large RCTs on the management of SICH have been published,[21,22] and there is an urgent need for additional systematic review to assist clinicians in establishing an optimal treatment strategy.

Methods

Search Strategy and Selection Criteria

We searched relevant international databases (PubMed, Embase, Cochrane Controlled Trials Register [CCTR], and Web of Science), 2 gray databases (European Association for Grey Literature Exploitation [EAGLE] and National Technical Information Service [NTIS]), 2 Chinese databases (Chinese Biomedical Literature Database-disc and Chinese National Knowledge Infrastructure [CNKI]), and relevant web sites (Current Controlled Trials, Clinical Trials, International Clinical Trials Registry, and Internet Stroke Center) up to December 2011 with different combinations of the following key words: "intracerebral" or "intracranial" or "cerebral" or "brain" or "putaminal" or "intraparenchymal" or "basal ganglia hemorrhage" or "thalamic" or "h(a)emorrhagic stroke" and "h(a)emorrhage" or "h(a)ematoma" and "minimally invasive" or "minimal surgical procedures" or "endoscopy(ic)" or "stereotaxy(ic)" or "aspiration" or "keyhole" or "craniopuncture." We obtained additional relevant articles by scanning conference summaries and reference lists of articles identified in the initial searches and contacted authors to obtain additional information for relevant trials.

Inclusion criteria were as follows: (1) CT-confirmed diagnosis of SICH; and (2) RCTs comparing MIS (endoscopic evacuation or stereotactic aspiration) with other treatment options, including routine medical treatment or craniotomy. Exclusion criteria were as follows: (1) hemorrhage caused by brain injury, brain tumor bleeding, coagulopathy, intracranial aneurysm, cerebral arteriovenous malformation, subdural hemorrhage, epidural hemorrhage, subarachnoid hemorrhage, or pituitary apoplexy; (2) infratentorial intracerebral hemorrhage, including cerebellar hemorrhage or brain stem hemorrhage; and (3) a total study quality assessment score of <2. Patients with infratentorial hematomas were not included because treatment seems to be associated with an unpredictable and high-risk outcome and there has been a consensus among experts.[23]

The study quality assessment referred to the Cochrane criteria: (1) random sequence generation ("yes"=2, "unclear"=1, and "no"=0); (2) allocation concealment ("yes"=2, "unclear"=1, and "no"=0); (3) blinding of outcome assessment ("yes"=2, "unclear"=1, and "no"=0); and (4) incomplete outcome data reported ("yes"=1 and "no"=0). We viewed studies with a total score of <2 as low-quality literature.

Data Extraction

Two review authors (J.J.C., X.Y.Z.) independently identified the articles by inclusion and exclusion criteria, assessed the quality of the articles, and completed a standardized data extraction form. Any disagreements were resolved by discussion.

We used the composite outcome of death or dependence in activities of daily living at the end of follow-up as the primary outcome. Death at the end of follow-up was considered as the secondary outcome. These were chosen because clinicians not only want information on patient survival, but also pay more attention to survivors whether they are functionally dependent or independent.[24] In this review, patients' dependence or independence was classified by certain activities of daily living scales. The cutoff points of dependence in the activities of daily living scales were a Barthel Index (score of ≤60, modified Rankin Scale score of >2, and a Glasgow Outcome Scale score of ≤3.[25,26] However, in the Auer 1989 study, dependence was considered to be Grade 5 according to its own scale.[17] If there was more than one scale to evaluate the patients' functional outcome within one article, we first selected the Barthel Index as the assessment scale, then the modified Rankin Scale and Glasgow Outcome Scale.[27]

Statistical Analysis

The summary OR was used as the effect parameter for the meta-analysis, and the 95% CI was used to interpret the results. We assessed heterogeneity using the χ^2 test and I^2. A probability value of ≤0.10 was taken as statistically significant, and an I^2 of 25%, 50%, and 75% represented low, moderate, and high heterogeneity, respectively.[28] With low heterogeneity for outcome data, we used a fixed-effect model to analyze it. On the other hand, we used a random-effect model to analyze the pooled data with moderate or high heterogeneity. Considering the possibility that effectiveness may differ according to the surgical technique used, we conducted 2 subgroup analyses according to the type of MIS techniques and the type of other treatment options. We also conducted subgroup analysis regarding age, Glasgow Coma Scale (GCS) score, hematoma volume, and the timing of surgery. Inverted funnel plots and a regression test were used to assess the potential presence of publication bias. The protocol of the systemic review followed the recommendations for conducting a meta-analysis. We used Statistical Analysis System (Version 9.0; SAS Institute, Cary, NC) and RevMan5 software (Cochrane Information Management System) for all statistical analyses. All tests were 2-sided, and statistical significance was defined as a probability value of <0.05 if not specially stated otherwise.

Results

We initially retrieved 5602 potentially relevant studies. Of these, 3788 articles were excluded because the titles did not meet the inclusion criteria. One thousand one hundred fifty-six trials were removed by reviewing the abstracts. A total of 345 studies were excluded after 2 reviewers independently read the full texts (J.J.C., X.Y.Z.). Then 313 RCTs of included criteria were assessed the total score of study quality. Finally, a total score of <2 was the cutoff for study quality, which resulted in the exclusion of 301 studies. Thus, 12 trials of 1955 patients were considered to be eligible for inclusion in the meta-analysis (Figure 1).

In our study, there were 2 primary outcome data and one secondary outcome data available to incomplete data. In the Hosseini study,[29] the authors did not evaluate the patients' independence or dependence by any activities of daily living scales. Moreover, despite our best efforts such as by searching other related references, e-mail, and fax to all authors, we could not acquire the complete data of the Cho study and the Mendelow study.[30,31]

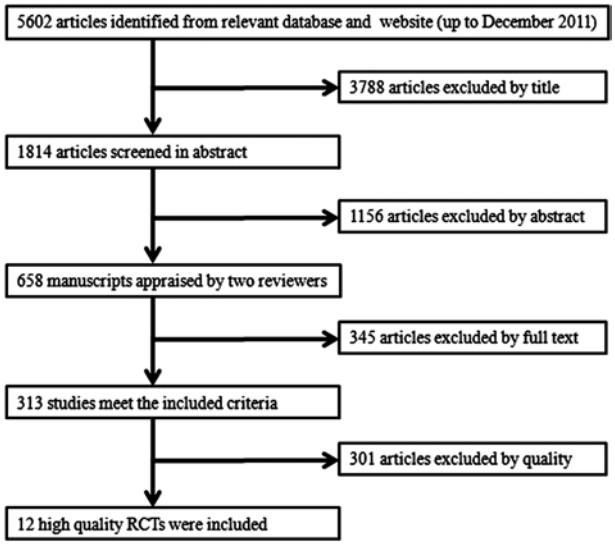

Figure 1. Literature search.

In the MIS group, 8 trials involved stereotactic aspiration, 2 involved endoscopic surgery, and 2 involved both stereotactic aspiration and endoscopic surgery. In the other treatment group, 9 trials involved conservative medical treatment and 3 involved conventional craniotomy (Table 1). In additional, the main baseline characteristics, including age, hematoma location, hematoma volume, GCS score and timing of surgery, and the score of quality assessment of all trials, are shown in Table 2.

Data on death or dependence at final follow-up were available for 10 studies (Figure 2A). MIS was associated with a significant reduction in death or dependence at the end of follow-up. The value of OR was 0.54 (95% CI, 0.39–0.76). Statistically significant moderate heterogeneity was among the studies (P=0.01, I^2=59%). However, after excluding the Mendelow study, there was statistically nonsignificant low heterogeneity (P=0.12, I^2=38%), and the value of OR was 0.48 (95% CI, 0.36–0.63).

Data on death at final follow-up were available for 11 studies (Figure 2B). We found that MIS was associated with a statistically significant reduction in the OR of death at the end of follow-up. The value of OR was 0.53 (95% CI, 0.40–0.71). Heterogeneity among the studies was statistically nonsignificant low (P=0.30, I^2=15%).

We conducted subgroup analyses based on the type of MIS: stereotactic aspiration or endoscopic surgery (Figure 3A), and the type of other treatment options: conservative medical treatment or conventional craniotomy (Figure 3B). Besides, we performed subgroup analysis regarding some main baseline characteristics, including age, GCS score, hematoma volume, and the timing of surgery (Figure 4).

In this review, 8 studies (66.7%) were allocation concealment, and all studies reported incomplete outcome data or did intention-to-treat analysis. As far as we know, blinding is difficult in a surgical trial, but 5 studies (41.7%) blinded the outcome assessment. Thus, all included studies in this review were consistently high quality. Moreover, we visually inspected the inverted funnel plots of these studies, which appeared to be approximately symmetrical. Because the total number of studies was too small to show clear asymmetry, we performed the Egger test and the results showed the primary outcome (t=0.95, P=0.377) and secondary outcome (t=–0.26, P=0.805) were not influenced by publication bias.

Table 1. Design Characteristics of the Included Trials

	Treatments		Outcomes	
Trials	MG	OG	Primary (MG:OG)	Secondary (MG:OG)
Zhou 2011[10]	Minimally invasive craniopuncture	Conventional craniotomy with large bone flap	12 mo BI (24/90:38/78)	12 mo death (17/90:19/78)
Sun 2010[22]	Minimally invasive craniopuncture	Conventional craniotomy with small bone flap	30 mo BI (90/159:93/145)	3 mo death (23/159:36/145)
Wang 2009[15]	Minimally invasive craniopuncture	Conservative medical treatment	3 mo BI (56/195:82/182)	3 mo death (13/195:16/182)
Kim 2009[11]	Stereotactic aspiration	Conservative medical treatment	6 mo mRS (67/204:109/183)	6 mo death (11/204:7/183)
Miller 2008[21]	Endoscopic surgery	Conservative medical treatment	3 mo mRS (6/6:4/4)	3 mo death (1/6:2/4)
Cho 2006[30]	Endoscopic surgery plus Stereotactic aspiration	Conventional craniotomy	N	6 mo death (2/60:4/30)
Mendelow 2005[31]	Endoscopic surgery plus Stereotactic aspiration	Conservative medical treatment	6 mo BI (51/69:58/86)	N
Hattori 2004[42]	Stereotactic aspiration	Conservative medical treatment	12 mo mRS (60/121:82/121)	12 mo death (9/121:20/121)
Hosseini 2003[29]	Stereotactic aspiration	Conservative medical treatment	N	12 mo death (3/20:9/17)
Teernstra 2003[43]	Stereotactic aspiration	Conservative medical treatment	6 mo mRS (33/36:29/34)	6 mo death (20/36:20/34)
Zuccarello 1999[44]	Stereotactic aspiration	Conservative medical treatment	3 mo BI (0/4:7/11)	3 mo death (0/4:3/11)
Auer 1989[17]	Endoscopic surgery	Conservative medical treatment	6 mo outcome (28/50:37/50)	6 mo death (21/50:35/50)

MG indicates minimally invasive surgery; OG, other treatment options group; mo, months of follow-up; BI, Barthel Index (score of ≤60 was viewed as dependent); mRS, modified Rankin Scale (score of >2 was viewed as dependent); N, not available; m, months of follow-up.

Table 2. Characteristics of Patients and Quality Assessments of the Included Trials

	Baseline Characteristics					Literature Quality				
Trials	Age, y/Year	ICHL (MG/OG)	GCS Score (MG/OG)	ICHV/mL (MG/OG)	Timing of Surgery/h	Randomized Generation	Outcome Blinding	Incomplete Data	Allocation Concealment	Total Score
Zhou 2011[10]	40–75	Basal ganglia; brain lobe	≥4 (8.1/8.4)	30–100 (—)	<24	2	0	1	0	3
Sun 2010[22]	40–75	Basal ganglia	N	30–80 (52.3/21.7)	<72	1	2	1	2	6
Wang 2009[15]	40–75	Basal ganglia	≥9 (11.7/12.3)	25–40 (33.8/31.3)	<72	2	2	1	2	7
Kim 2009[11]	30–80	Basal ganglia; thalamus	≥13 (14.2/14.3)	<30 (24.3/21.0)	<120	1	0	1	2	4
Miller 2008[21]	≥18	Supratentorial	≥4 (12/11)	>15 (56.4/35.5)*	<24	1	0	1	0	2
Cho 2006[30]	N	Basal ganglia	9 to 13 (9.68/9.32)	≥25 (43.8/42.1)	<24	1	0	1	0	2
Mendelow 2005[31]	19–93	Supratentorial	≥5	Diameter >2 cm	<24	2	2	1	2	7
Hattori 2004[42]	35–85	Putaminal	N	– (48/40)	<24	2	2	1	2	7
Hosseini 2003[29]	30–73	Supratentorial	N	40–120 (–)	<24	1	1	1	1	4
Teernstra 2003[43]	>45	Supratentorial	≥4 (9.5/10)	>10 (66/52)	<72	2	0	1	2	5
Zuccarello 1999[44]	>18	Brain lobe; putaminal; thalamus; basal ganglia	≥4 (14.5/10.1)*	>10 (29/38)	<24	2	0	1	2	5
Auer 1989[17]	30–80	Subcortical; putaminal; thalamus	N	>10 (—)	<48	1	0	1	0	2

ICHL indicates intracerebral hematoma location; MG, minimally invasive surgery group; OG, other treatment options group; GCS, Glasgow Coma Scale; ICHV, intracerebral hematoma volume; N, not mentioned; —, no significant difference.

*Significant difference.

Discussion

This review first reported that death and dependence of MIS were significantly lower than those of other treatment options in patients with SICH. Moreover, we showed the characteristics of the most likely candidates to benefit from MIS, including sex, age, hematoma location, GCS score, hematoma volume, and the timing of surgery. Although a previous systematic review reported that the effectiveness of surgery was better than routine medical treatment, its evidence was not very robust and did not emphasize the role of MIS in the management of SICH.[9]

We have included almost all relevant RCTs in this review. However, some studies published in journals that were not indexed by international databases might have been missed. Fortunately, these studies are likely to be of low quality and would not significantly affect the results of this review.[32] Moreover, we excluded the low-quality RCTs with total quality assessment score of <2. These excluded studies, mostly from China, always lacked truly randomization and analysis of complete data, resulting in a potential risk of gross imbalance. On the other hand, these numerous RCTs studies reflected the severe challenges of Chinese clinicians and the important role of MIS in the management of SICH.[33]

In our study, the missing data of 2 articles would not significantly affect the results of this review. Although dependence data were lacked in the Cho study,[30] the Barthel Index was significantly better in the endoscopic group (50.45±28.59) than in the craniotomy group (16.39±20.93; P=0.006), and mortality rates were significantly lower in the endoscopic group (3.3%) than in the craniotomy group (13.3%). Therefore, we have reason to speculate that the primary outcome in the Cho study was statistically lower in the endoscopic group than in the craniotomy group, which is consistent with the conclusion of this review. In addition, the incomplete data in the Mendelow study was only a secondary outcome, which would not significantly affect the result of this review.[31]

There was statistical heterogeneity for the primary outcome, whereas there was low heterogeneity for the secondary outcome. After a sensitivity analyses by excluding the Mendelow study,[31] however, the primary outcome did not show significant heterogeneity (P=0.12, I^2=38%) and there was no difference in the overall effect. A possible reason is that the inconsistency of the main baseline in this trial, resulting from a considerable number of patients in the MIS group, was deteriorating patients from the medical arm. Because this study was an international multicenter trial, the difference in surgical approach and conservative treatment in many countries with different medical levels may have led to potential heterogeneity.

In this review, MIS was associated with a 46% relative reduction in the OR of death or dependence and a 47% relative reduction in the OR of death. Although the control event rate is high, these relative risk reductions are still considerable. Furthermore, the relative risk reductions, which may better reflect the efficacy, were 21% for death or dependence and 36% for death. Both of them demonstrated that MIS has a significant benefit compared with other treatment options. In addition, we demonstrated that stereotactic aspiration was more effective in preventing death or dependence compared with endoscopic surgery, and conservative medical was more effective than conventional craniotomy in the death or dependence by subgroup analyses.

It is possible that the benefit is greater than that indicated because the 2 most important prognostic factors, hematoma volume and GCS score on admission,[34] differed between the MIS group and the other treatment options group. The baseline in 6 trials showed that the hematoma volume of the MIS group was larger than that of the conservative medical group. The GCS of the MIS group in 4 trials was less than that in the conservative medical group. Although most of these imbalances were not significant in individual trials, the cumulative effect might have been significant. So it is possible that an underestimation

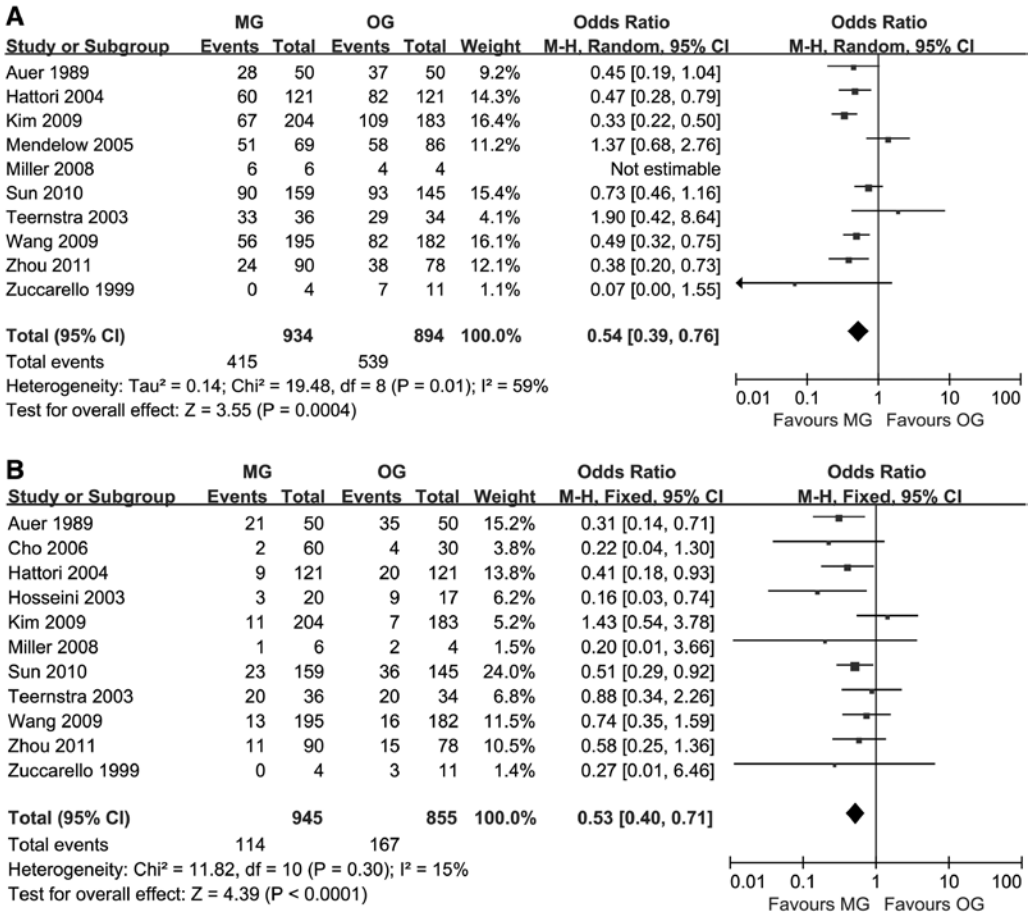

Figure 2. Primary outcome and secondary outcome: OR of death or dependence. **A**, Comparison of minimally invasive surgery versus other treatment options for primary outcome: death or dependence at end of follow-up. **B**, Comparison of minimally invasive surgery versus other treatment options for secondary outcome: death at end of follow-up. MG indicates minimally invasive surgery group; OG, other treatment options group.

of the benefit of MIS occurred. In addition, the management of routine medical treatment may play a role in the benefit of MIS. As we know, differences in this management exist in individual trials depending on doctors' experience and the quality of medical service.[35,36] Strictly speaking, excellent routine medical treatment will improve the outcome of SICH treatment.

The most likely candidates to benefit from MIS are both sexes, age of 30 to 80 years with superficial hematoma, GCS score of ≥9, hematoma volume between 25 and 40 mL, and within 72 hours after onset of symptoms. We should emphasize that these clinical characteristics of patients would not become the limitation for MIS treatment in patients with SICH. Under some circumstances, clinicians could be appropriate to expand the indications according to the patient's condition.

In our subgroup analysis, the patients who were aged ≥18 years had no statistical difference between MIS and other treatment options, but the patients undergoing MIS aged ≥30 years had a significantly beneficial outcome. We consider that the patients aged 18 to 30 years would recommend having conservative medical treatment although there was a lack of relative studies. Because most of included trials limited the age to ≤80 years, we suggest that the appropriate age is 30 to 80 years. In this review, we ignore the issue of MIS applying to the patients aged <18 years.

Patients with superficial hematoma are likely to benefit more from endoscopic surgical removal. An early study demonstrated that patients with subcortical hematomas benefited from endoscopic surgical removal by subgroup analysis, whereas those with putaminal or thalamic hemorrhage did not.[17] Another trial showed that hematomas at a ≤1 cm depth from the cortical surface were more suitable for surgical treatment.[31] Because of a lack of enough evidence from subgroup analysis of hematoma location, this potential benefit of hematoma location for SICH needs more related studies for confirmation.

The impact of the GCS score on the benefit of MIS may be closely related to the volume of SICH. With a GCS score of ≥4, the treatment choice in patients with SICH is largely controversial.[7,21] Cho et al reported that, with a GCS score of 4 to 12, the mortality rate of MIS was lower than that of conservative treatment with the hematoma volume >30 mL. However, when the intracerebral hemorrhage volume was ≤30 mL, the mortality rates were the opposite.[37] This study supported our subgroup analysis result, which in the MIS group would not be better than other treatment options with a GCS score of ≥4. Interestingly, with a GCS score of ≥9, the MIS group showed it to be significantly beneficial. In additional, 2 studies have shown no difference in good outcomes between conservative medical treatment and MIS

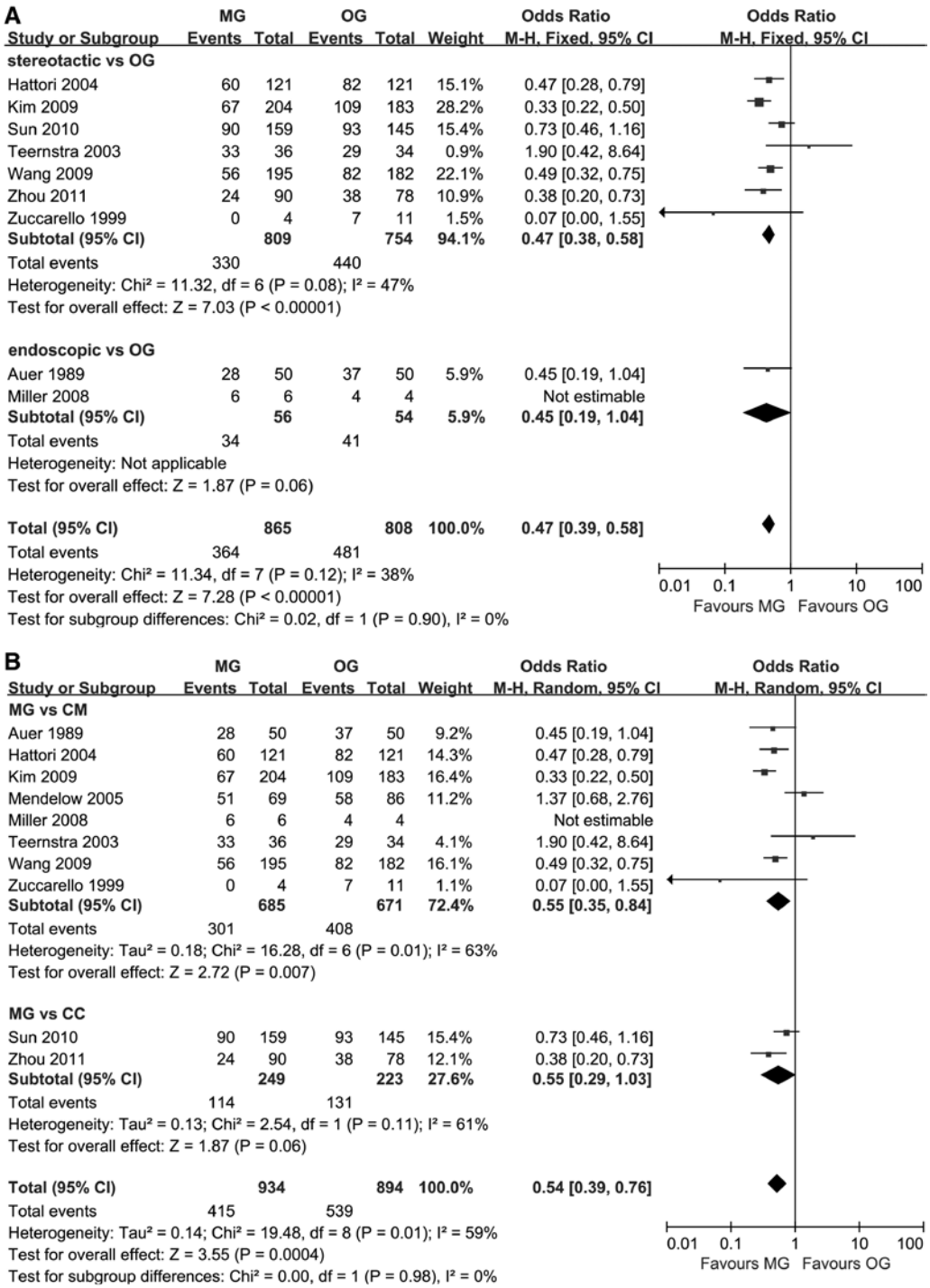

Figure 3. Subgroup analyses: type of minimally invasive surgery (MIS) and other treatment options. Subgroup analyses according to: (**A**) type of MIS: endoscopic or stereotactic. **B**, Type of other treatment options: conservative medical or conventional craniotomy. MG indicates minimally invasive surgery group; OG, other treatment options group; CM, conservative medical; CC, conventional craniotomy.

in patients with a GCS score of 13 to 15.[11,34] None of the studies included patients with GCS score of <4; therefore, whether surgery will benefit individuals who undergo surgery with a GCS score of <4 is still unknown.

Wide international variation exists in terms of what hematoma volume is suitable for MIS. The majority of scholars believed that surgical treatments, including MIS and craniotomy, are suitable for patients with SICH with a hematoma volume of ≥30 mL.[10,15,22] In this subgroup analysis, MIS of hematoma volume ≥25 and ≤40 mL were both significantly better as far as primary outcome than other treatment options. Thus, we think the patients with hematoma volume between 25 and 40 mL would benefit most from MIS; however, because only few studies used this limit, the validity of this analysis is limited. Because there were wide controversies on this issue and its benefit would be influenced by other baseline characteristics,[17,37]

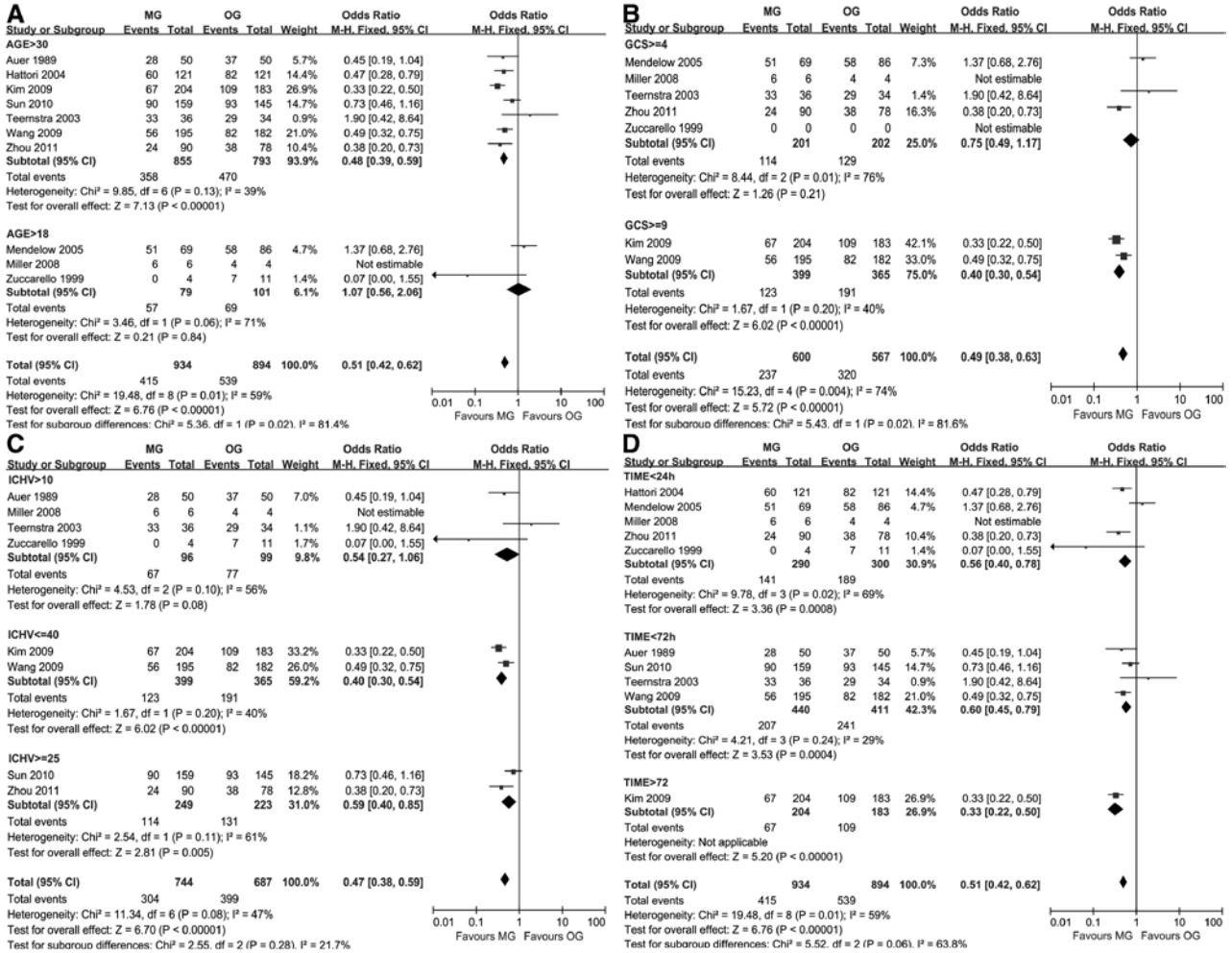

Figure 4. Subgroup analyses: main baseline characteristics. Subgroup analyses according to: (**A**) age; (**B**) GCS score; (**C**) ICHV; (**D**) timing of surgery. MG indicates minimally invasive surgery group; OG, other treatment options group; GCS, Glasgow Outcome Scale; ICHV, intracerebral hemorrhage volume.

the hematoma volume could not become only one standard to triage patients for MIS or other treatment options.[38]

Some clinical studies have reported a classification of the surgery timing, that is from the onset of symptoms to the time of operation, ranging from within 24 hours (ultraearly stage), within 24 to 72 hours (early stage), and up to 72 hours (deferred stage).[39,40] In our study, ultraearly surgery might be more beneficial for patients with SICH. However, this seems not to be better in earlier surgery. A small, single-center randomized study showed that the rebleeding rate of craniotomy within 4 hours of symptom onset was higher than that within 12 hours.[41] In this review, the patients undergoing MIS within 72 hours would significantly improve the primary outcome compared with other treatment options.[42–44] Because only one small study was involved in deferred staged surgery, we could not demonstrate whether patients will benefit from MIS beyond 72 hours of onset.

Summary

This meta-analysis first provides powerful evidence from high-quality RCTs that the effectiveness of MIS was significant better than those of other treatment options, including craniotomy and conservative treatment. Furthermore, we described the characteristics of the most likely candidates to benefit from MIS. Above all, this review would guide clinicians to judge treatment options and appropriate patients for minimally invasive surgery in SICH. Promisingly, some recruiting studies (Surgical Trial in Lobar Intracerebral Hemorrhage [STICH] II, Minimally Invasive [stereotactic] Surgery Plus rtPA for ICH Evaluation [MISTIE]) have been in progress and these results may strengthen our conclusion.[45]

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Disclosures

None.

References

1. Liu M, Wu B, Wang WZ, Lee LM, Zhang SH, Kong LZ. Stroke in China: epidemiology, prevention, and management strategies. *Lancet Neurol*. 2007;6:456–464.
2. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol*. 2009;8:355–369.
3. Wang CJ, Wang CX, Zhang L, Wang YL, Wang YJ. Advances in stroke care and research in 2010. *Clin Exp Pharmacol Physiol*. 2011;38:562–569.
4. Kocaeli H, Zuccarello M. Management of spontaneous intracerebral hematomas. *Neurosurg Quarterly*. 2008;18:207–215.
5. Greenblatt SH, Dagi TF, Epstein MH. *A History of Neurosurgery: in Its Scientific and Professional Contexts*. New York, NY: The American Association of Neurological Sugeons; 1997:625.
6. Li Q, Lv F, Li Y, Luo T, Li K, Xie P. Evaluation of 64-section CT angiography for detection and treatment planning of intracranial aneurysms by using DSA and surgical findings. *Radiology*. 2009;252:808–815.
7. Gurdjian ES, Webster JE. Surgical management with particular reference to massive intracranial hemorrhage. *AMA Arch Surg*. 1951;62:724–736.
8. Qureshi AI. Intracerebral haemorrhage. *Lancet*. 2009;373:1632–1644.
9. Prasad K, Mendelow AD, Gregson B. Surgery for primary supratentorial intracerebral haemorrhage. *Cochrane Database Syst Rev*. 2008;8:CD000200.
10. Zhou H, Zhang Y, Liu L, Han X, Tao Y, Tang Y, et al. A prospective controlled study: minimally invasive stereotactic puncture therapy versus conventional craniotomy in the treatment of acute intracerebral hemorrhage. *BMC Neurol*. 2011;11:76.
11. Kim YZ, Kim KH. Even in patients with a small hemorrhagic volume, stereotactic- guided evacuation of spontaneous intracerebral hemorrhage improves functional outcome. *J Korean Neurosurg Soc*. 2009;46:109–115.
12. Morgan T, Zuccarello M, Narayan R, Keyl P, Lane K, Hanley D. Preliminary findings of the minimally-invasive surgery plus rtPA for intracerebral hemorrhage evacuation (MISTIE) clinical trial. *Acta Neurochir Suppl*. 2008;105:147–151.
13. Blacker DJ, Musuka T. Management of intracerebral hemorrhage in 2020. *Future Neurol*. 2011;6:745–756.
14. Rincon F, Mayer SA. Intracerebral hemorrhage: getting ready for effective treatments. *Curr Opin Neurol*. 2010;23:59–64.
15. Wang WZ, Jiang B, Liu HM, Li D, Lu CZ, Zhao YD, et al. Minimally invasive craniopuncture therapy vs. conservative treatment for spontaneous intracerebral hemorrhage: results from a randomized clinical trial in China. *Int J Stroke*. 2009;4:11–16.
16. Broderick J, Connolly S, Feldmann E, Hanley D, Kase C, Krieger D, et al. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: a guideline from the American Heart Association/ American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group. *Circulation*. 2007;116:e391–e413.
17. Auer LM, Deinsberger W, Niederkorn K, Gell G, Kleinert R, Schneider G, et al. Endoscopic surgery versus medical treatment for spontaneous intracerebral hematoma: a randomized study. *J Neurosurg*. 1989;70:530–535.
18. Deinsberger W, Lang C, Hornig C, Boeker DK. Stereotactic aspiration and fibrinolysis of spontaneous supratentorial intracerebral hematomas versus conservative treatment: a matched-pair study. *Zentralbl Neurochir*. 2003;64:145–150.
19. Yang J, Liu M, Zhou J, Zhang S, Lin S, Zhao H. Edaravone for acute intracerebral haemorrhage. *Cochrane Database Syst Rev*. 2011;16:CD007755.
20. Fang J, Zhuo-Ga C, Zhao Y, Kong F, Si Y, Liu M, et al. Characteristics of stroke in Tibet autonomous region in China: a hospital-based study of acute stroke. *Eur Neurol*. 2011;66:151–158.
21. Miller CM, Vespa P, Saver JL, Kidwell CS, Carmichael ST, Alger J, et al. Image-guided endoscopic evacuation of spontaneous intracerebral hemorrhage. *Surg Neurol*. 2008;69:441–446.
22. Sun H, Liu H, Li D, Liu L, Yang J, Wang W. An effective treatment for cerebral hemorrhage: minimally invasive craniopuncture combined with urokinase infusion therapy. *Neurol Res*. 2010;32:371–377.
23. Pérez-Núñez A, Alday R, Rivas JJ, Lagares A, Gómez PA, Alén JF, et al. Surgical treatment for spontaneous intracerebral haemorrhage. Part II: infratentorial haematomas. *Neurocirugia (Astur)*. 2008;19:101–112.
24. Steer CB, Marx GM, Galani E, Harper PG, Khayat D. Quality of life: it's never too late. *J Clin Oncol*. 2002;20:2915–2917.
25. Balu S. Differences in psychometric properties, cut-off scores, and outcomes between the Barthel Index and modified Rankin Scale in pharmacotherapy-based stroke trials: systematic literature review. *Curr Med Res Opin*. 2009;25:1329–1341.
26. Shih MM, Rogers JC, Skidmore ER, Irrgang JJ, Holm MB. Measuring stroke survivors' functional status independence: five perspectives. *Am J Occup Ther*. 2009;63:600–608.
27. Uyttenboogaart M, Luijckx GJ, Vroomen PC, Stewart RE, De Keyser J. Measuring disability in stroke: relationship between the modified Rankin Scale and the Barthel Index. *J Neurol*. 2007;254:1113–1117.
28. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557–560.
29. Hosseini H, Leguerinel C, Hariz M, Melon E, Palifi S, Deck P, et al. Stereotactic aspiration of deep intracerebral hematomas under computed tomographic control: a multicentric prospective randomised trial. *Cerebrovasc Dis*. 2003;16:57.
30. Cho DY, Chen CC, Chang CS, Lee WY, Tso M. Endoscopic surgery for spontaneous basal ganglia hemorrhage: comparing endoscopic surgery, stereotactic aspiration, and craniotomy in noncomatose patients. *Surg Neurol*. 2006;65:547–555.
31. Mendelow AD, Gregson BA, Fernandes HM, Murray GD, Teasdale GM, Hope DT, et al. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomized trial. *Lancet*. 2005;365:387–397.
32. Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman DG, eds. *Systematic Reviews in Health Care: Meta-Analysis in Context*. II ed. London, UK: BMJ Publication Group; 2001.
33. Liu M. Stroke: encouragement and disappointment in clinical trials. *Lancet Neurol*. 2008;7:5–7.
34. Sarnvivad P, Chumnanvej S. Outcome predictor of spontaneous intracerebral hemorrhage management: ten-year neurosurgical experience at Ramathibodi Hospital. *J Med Assoc Thai*. 2011;94:1471–1475.
35. Steiner T, Bösel J. Options to restrict hematoma expansion after spontaneous intracerebral hemorrhage. *Stroke*. 2010;41:402–409.
36. Mirsen T. Acute treatment of hypertensive intracerebral hemorrhage. *Curr Treat Options Neurol*. 2010;12:504–517.
37. Cho DY, Chen CC, Lee HC, Lee WY, Lin HL. Glasgow Coma Scale and hematoma volume as criteria for treatment of putaminal and thalamic intracerebral hemorrhage. *Surg Neurol*. 2008;70:628–633.
38. Yilmaz C, Kabatas S, Gulsen S, Cansever T, Gurkanlar D, Caner H, et al. Spontaneous supratentorial intracerebral hemorrhage: does surgery benefit comatose patients? *Ann Indian Acad Neurol*. 2010;13:184–187.
39. van de Beek D, Farrar JJ, de Gans J, Mai NT, Molyneux EM, Peltola H, et al. Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data. *Lancet Neurol*. 2010;9:254–263.
40. Rohde V, Uzma N, Rohde I, St Clair E, Samadani U. Fibrinolytic therapy versus craniotomy for anticoagulant-associated intracerebral hemorrhage. *Clin Neurol Neurosurg*. 2009;111:518–522.
41. Morgenstern LB, Demchuk AM, Kim DH, Frankowski RF, Grotta JC. Rebleeding leads to poor outcome in ultra-early craniotomy for intracerebral hemorrhage. *Neurology*. 2001;56:1294–1299.
42. Hattori N, Katayama Y, Maya Y, Gatherer A. Impact of stereotactic hematoma evacuation on activities of daily living during the chronic period following spontaneous putaminal hemorrhage: a randomized study. *J Neurosurg*. 2004;101:417–420.
43. Teernstra OP, Evers SM, Lodder J, Leffers P, Franke CL, Blaauw G. Stereotactic treatment of intracerebral hematoma by means of a plasminogen activator: a multicenter randomized controlled trial (SICHPA). *Stroke*. 2003;34:968–974.
44. Zuccarello M, Brott T, Derex L, Kothari R, Sauerbeck L, Tew J, et al. Early surgical treatment for supratentorial intracerebral hemorrhage: a randomized feasibility study. *Stroke*. 1999;30:1833–1839.
45. Mendelow AD, Gregson BA, Mitchell PM, Murray GD, Rowan EN, Gholkar AR; STICH II Investigators. Surgical Trial in Lobar Intracerebral Haemorrhage (STICH II) protocol. *Trials*. 2011,12;124.