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Craniotomy versus endoscopic approach in basal ganglia haemorrhage: A systematic review and meta-analysis

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Abstract

Objectives: Basal ganglia haemorrhage (BGH) is the most common type of intracerebral bleed with high morbidity and mortality rate. Despite advancements in minimally invasive techniques in recent years, the efficacy between craniotomy and endoscopic approach for BGH is still debatable. The aim of this systematic review and meta-analysis was to evaluate the outcomes of craniotomy and endoscopic approach for BGH. *Methods:* Databases of Pubmed, EMBASE, MEDLINE and CENTRAL were systematically searched from its inception until December 2020. All randomized clinical trials and observational studies comparing craniotomy versus endoscopic approach in BGH were included. *Results:* Twelve studies enrolling 1,297 patients (craniotomy:675, endoscopy:632) were included for qualitative and quantitative analysis. Endoscopic approach was associated with significantly lower postoperative mortality (OR:0.35, P<0.001), higher haematoma evacuation rate (MD:4.95, P<0.001), shorter operative time (MD:-117.03, P<0.001), lower intraoperative blood loss (MD:-328.47, P<0.001), higher postoperative Glasgow Coma Scale (GCS) (MD:1.14, P=0.01), higher postoperative Glasgow Outcome Scale (GOS) (MD:0.44, P=0.05), shorter length of hospital stay (MD:-2.90, P<0.001), lower complication rate (OR:0.30, P=0.001), lower infection rate (OR:0.29, P<0.001) and lower modified Rankin Scale (mRS) (MD:-0.57, P=0.004) compared to craniotomy. No significant difference was detected in re-operation, and re-bleeding.
Conclusion: The best available evidence suggest that endoscopic approach has better outcomes in mortality rate, operative time, haematoma evacuation rate, intraoperative blood loss, length of hospital stay, mRS, postoperative GCS and GOS compared with craniotomy in the management of BGH. However, there is a need for high quality randomised controlled trials with large sample size for definitive conclusions.

Keywords: Endoscopy, craniotomy, basal ganglia haemorrhage, meta-analysis

INTRODUCTION

Spontaneous intracerebral haemorrhage (sICH) contributes approximately 15% of strokes and affects more than 5 million people per year.[1,2] They commonly occur within the basal ganglia and can lead to life-threatening situations as a result of brain stem compression, haematoma expansion and raised intracranial pressure. Furthermore, due to the blood degradation products, secondary brain injury arises, leading to inflammation, neurotoxicity and development of perihematomal oedema, eventually resulting in increase of mass effect.[3-6] The benefit of surgical evacuation of sICH over conservative management remains controversial and is widely debated in the literature.

Surgical evacuation of ICH has long been the preferred choice. However, a meta-analysis of randomised controlled trials comparing surgical treatment and minimally invasive approach in spontaneous ICH did not produce robust results.[7] Mendelow *et al*. (2005) reported neutral conclusions overall between surgery and conservative management for all types of sICH in the landmark STICH trial (Surgical Trials in

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Intracerebral haematoma).[8] The findings led to a second trial showing a small but clinically relevant survival advantage for those patients who underwent surgery for superficial lobar haemorrhages.[9] The MISTIE (Minimally Invasive Surgery Plus Rt-PA for ICH Evacuation) II trial reported better functional outcome when patients were treated with minimally invasive surgery and thrombolysis.[10]

Although minimally invasive surgery may provide better recovery and potentially lower morbidity and mortality, craniotomy still plays an important role in this critical condition for example, in cases where there is large haematoma volume or cerebral oedema. When comparing treatment strategies in management of basal ganglia haemorrhage (BGH), the efficacy between craniotomy and neuroendscopy is still debatable due to the limited evidence.[11-14] While there are a handful of meta-analyses investigating the outcomes between craniotomy and neuroendoscopy for sICH, there is a paucity of information available for the management in BGH alone. Hence, a systematic review and meta-analysis is warranted to comparatively assess the use of neuroendoscopy and craniotomy in BGH.

The primary aim of this systematic review and meta-analysis was to compare the mortality rate and haematoma evacuation rate in neuroendoscopy and craniotomy. Secondary aims were to examine the outcomes on operative time, intraoperative blood loss, postoperative Glasgow Coma Scale (GCS), postoperative Glasgow Outcome Scale (GOS), shorter length of hospital stay, complication rate, infection rate, modified Rankin Scale (mRS), reoperation rate, intracranial infection and re-bleeding rate.

METHODS

This systematic review was conducted based on an agreed predefined protocol and is presented as per Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards.[15] The protocol was published online on PROSPERO (CRD42020206525).

Criteria for considering studies for this review

Types of studies: We included all comparative studies (randomised controlled trials [RCTs] and observational studies) comparing the outcomes of neuroendoscopy and craniotomy for the evacuation of basal ganglia haemorrhage.

Inclusion criteria were: 1) Age > 18 years old; 2) Spontaneous basal ganglia haemorrhage; 3) Haematoma volume more than 25 ml; 4) GCS: 4 to 14; 5) Studies that compared craniotomy and endoscopy approach in basal ganglia haemorrhage

Exclusion criteria were: 1) Patients with secondary basal ganglia haemorrhage caused by vascular malformation, aneurysm, trauma, coagulopathy, intracranial tumour or moyamoya disease; 2) Multiple intracranial haemorrhage; 3) Patients with massive intraventricular haemorrhage who required external ventricular drainage; 4) Patients with systemic illness; 4) Haematoma in the brainstem or posterior fossa; 5) Comatose patients (identified as GCS 3); 5) Haemorrhage with an epicentre beyond the basal ganglia; 6) Case report/series or review articles

Types of interventions: Neuroendoscopic surgery was considered as intervention of interest and craniotomy was considered as the comparison of interest.

Types of outcome measures

Primary outcome: Postoperative mortality and haematoma evacuation rate (percentage of haematoma volume evacuated) were considered as primary outcome measures.

Secondary outcome: The secondary outcome measures included intraoperative blood loss, operative time, postoperative Glasgow Coma Scale (GCS), postoperative Glasgow Outcome Scale (GOS), modified Rankin Score (mRS) intracranial infection, re-bleeding, need for reoperation, total postoperative infection, postoperative complication and length of hospital stay. Re-bleeding was defined as the incidence of intracranial bleed post-operatively.

Search methods, study selection and data extraction

Two authors independently performed the search of electronic databases, selection of eligible studies and data extraction. A third reviewer was consulted if no agreement could be reached. The search was conducted on PUBMED, MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL). The search strategy is outlined in eTable 1 and 2. The last search was performed on inspection until December 2020 which included no restriction in languages. After running the search strategy, both the titles and abstracts of the identified studies were screened

against the eligible criteria for inclusion (Figure 1). After selection of the eligible studies, a data extraction spread sheet was created and pilot-tested in randomly selected articles and was adjusted to match our study. The extracted data included study-related data (first author, year of publication, country of the corresponding author, journal, study design, and sample size), baseline demographic and clinical data (age, gender, type of procedure, background of hypertension, diabetes, preoperative GCS, preoperative haematoma volume, time to operation, intraoperative blood loss) and the outcome data. When the values were presented as median, range or interquartile range, a calculation formula was utilised to convert the values into mean ± standard deviation.[16]

Risk of bias assessment

Two authors independently assessed the methodological quality and risk of bias of the included articles using the Cochrane tool and the ROBINS-I for assessing the risk of bias of randomized trials and observational studies, respectively.[17,18] The Cochrane tool assesses domains including selection bias, performance bias, detection bias, attrition bias, reporting bias and other sources of bias and, for each individual domain, classifies studies into low, unclear, and high risk of bias. Disagreements were resolved by discussion between the reviewers. If no agreement could be reached, a third author acted as an adjudicator.

Data analysis

We used the Review Manager 5.3 software for data synthesis. The odds ratio (OR) and mean difference (MD) were calculated as summary measures for dichotomous and continuous

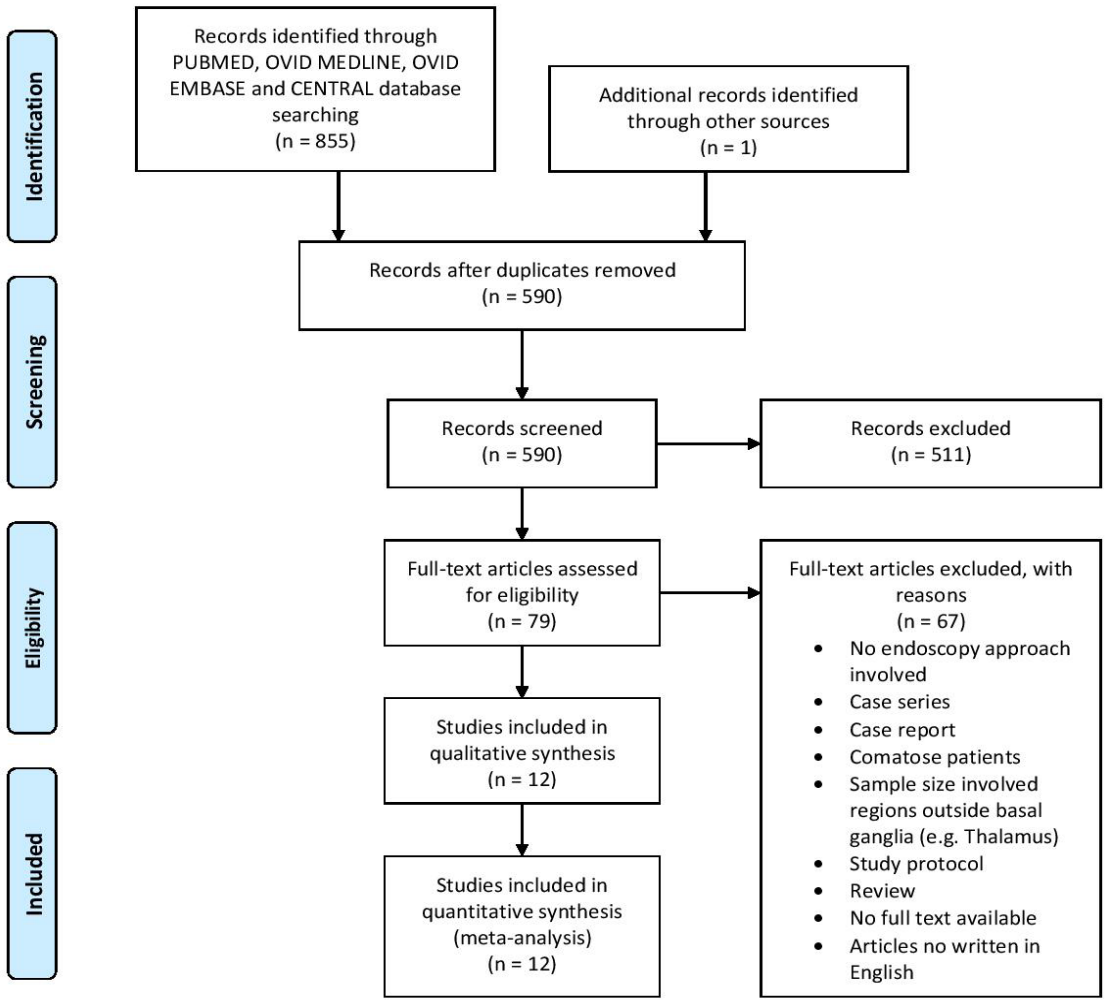


Figure 1. PRISMA flow diagram

outcome variables, respectively. An individual patient was considered as the unit of analysis. The analyses were based on intention to- treat data from the individual clinical studies. Random modelling was applied for analyses. The Cochran Q test ($\chi 2$) was used to evaluate heterogeneity and I^2 was reported to quantify it.[17] In terms of interpretation of I^2, we considered I^2 of less than 40% as low heterogeneity, 40-60% as moderate heterogeneity and more than 60% as substantial degree heterogeneity. Fixed-effect modelling was used for all the data analysis, if the heterogeneity was reported to be substantial, random-effect modelling was adopted. Funnel plots was constructed to evaluate their symmetry to visually assess publication bias for outcomes reported by at least 10 studies where possible. A subgroup analysis was conducted based on the age, preoperative GCS, time to operation and preoperative haematoma volume.

Sensitivity analyses

We perform sensitivity analyses for the outcomes that were reported by at least four comparative studies in order to determine the robustness of the analyses. First, the risk ratio (RR) and risk difference (RD) were calculated instead of OR for dichotomous variables. In order to determine the influence of each study on the overall effect size and heterogeneity, each study was eliminated at a time and the analysis was repeated.

RESULTS

Results of the search

The search of the 4 database (PUBMED, OVID MEDLINE, OVID EMBASE and CENTRAL) and external sources identified 855 articles. After removing the duplicates, 590 articles remained. Applying the inclusion and exclusion criteria, 79 articles were included for full text screening. Among the 79 articles, 12 articles were recruited for qualitative and quantitative analysis.[19-30] Figure 1 demonstrates the study flow chart

Study characteristics

The publication dates of all the included studies ranged from 2006 to 2020. Two RCTs were recruited and the remaining 10 studies are observational studies. The included studies enrolled a total of 1,297 patients, 622 patients were assigned to endoscopy group and 675 patients were assigned to craniotomy group. The baseline characteristics of the included studies and included population are demonstrated in Table 1a and Table 1b, respectively.

Risk of bias in included studies

The summary of methodological quality assessment of the 12 studies is demonstrated in Table 2a and Table 2b. The overall risk of bias assessment of the included studies ranged from low risk to high risk with majority of them being in the high-risk category. The two RCTs included in our study were reported to have high risk of bias due to high risk in allocation concealment and blinding in participants and personal.[21,22] Moderate risk in bias due to confounding was reported in four studies and high risk in three studies. High risk of bias in selection of participants into the study was detected in two studies and moderate in three studies, the rest were reported to be in low risk category. Only two studies were reported to have high risk in bias due to deviation from intended intervention.

Outcome synthesis

Primary outcomes

Eleven studies with the total sample size of 1085 patients studied the outcome of postoperative mortality rate. Our meta-analysis revealed that endoscopic approach had significantly lower postoperative mortality rate compare to craniotomy (OR: 0.35, [95% CI, 0.23 to 0.54], $\varrho<0.001$). The heterogeneity of this analysis was reported to be low ($I^2=0\%$).

In comparison to haematoma evacuation rate, the endoscopy group is associated with greater evacuation rate compared to craniotomy group (studies=10, patients=926, MD: 4.95 [95% CI, 2.38 to 7.52], $\varrho<0.001$). The statistical heterogeneity was reported to be substantial ($I^2=95\%$).

Secondary outcomes

In terms of intraoperative blood loss, craniotomy was associated with higher volume of blood loss (studies=5, patients=559, MD: -328.47 [95% CI, -445.56 to -211.38], $\varrho<0.001$; $I^2=97\%$). Similar trend was reported in operative time (studies=8, patients=684, MD: -117.03 [95% CI, -154.26 to -79.80], $\varrho<0.001$; $I^2=98\%$), mRS (studies=3, patients=336, MD: -0.57 [95% CI, -0.96 to -0.18], $\varrho=0.004$; $I^2=29\%$), length of hospital stay (studies=4, patients=368, MD: -2.90 [95% CI, -3.23 to -2.58], $\varrho<0.001$; $I^2=22\%$), postoperative infection (studies=6, patients=113,

Table 1a: Baseline characteristics of all the included studies

First Author	Year	Country	Journal	Type of study design	Total sample size	No in endoscopic group	No in Craniotomy group
Cho[26]	2006	China	Surgical Neurology	Randomized Controlled Trial	60	30	30
Zhu[30]	2012	China	Turkish Neurosurgery	Retrospective Cohort Study	58	28	30
Zhang[29]	2014	China	BioMed Research International	Prospective Case Controlled Study	51	21	30
Wang[26]	2015	Taiwan	Jornal of Chinese Medical Association	Retrospective Cohort Study	45	21	24
Feng[22]	2016	China	Turkish Neurosurgery	Randomized Controlled Trial	184	93	91
Xu[28]	2018	China	Journal of Neurosurgery	Retrospective Cohort Study	151	82	69
Fu[23]	2018	China	World Neurosurgery	Retrospective Cohort Study	121	61	60
Guo[27]	2018	China	Journal Of Neurological Surgery Part A. Central European Neurosurgery	Retrospective Cohort Study	64	27	37
Xiong[19]	2019	China	World Neurosurgery	Retrospective Cohort Study	58	28	30
Guo[20]	2019	China	Journal Of Neuro-interventional Surgery	Retrospective Cohort Study	212	105	107
Katsuki[24]	2020	Japan	Scientific Reports	Retrospective Cohort Study	134	66	68
Liu[25]	2020	China	Frontiers in Neurology	Retrospective Cohort Study	159	60	99

OR: 0.29 [95% CI, 0.18 to 0.46], ϱ<0.001; I^2=0%) and postoperative complication (studies=9, patients=868, OR: 0.30 [95% CI, 0.16 to 0.55], ϱ<0.001; I^2=64%).

In contrast, the endoscopic approach had statistically better outcomes in postoperative GCS (studies=6, patients=505, MD: 1.14 [95% CI, 0.22 to 2.06], ϱ=0.01; I^2=76%) and GOS (studies=3, patients=217, MD: 0.44 [95% CI, 0.00 to 0.88], ϱ=0.05; I^2=62%). However, no significant difference was detected in rebleeding rate, reoperation rate and intracranial infection rate.

Subgroup analysis

Subgroup analysis was conducted with the aim to evaluate the effect of age, preoperative GCS, time to operation (hr) and preoperative haematoma volume (ml) on postoperative mortality rate, haematoma evacuation rate (%), postoperative complication rate and postoperative GCS (Table 3).

Table 1b: Baseline characteristics of all the included studies (con't)

First Author	Year	Age	Male gender	Hypertension	Diabetes	Preoperative GCS	Preoperative haematoma volume (ml)	Time to operation (hr)
Cho[26]	2006	Endoscopy: 56.67 ± 8.66 Craniotomy: 54.22 ± 10.47	Endoscopy: 19/30 VS Craniotomy: 21/30	Endoscopy: 21/30 VS Craniotomy: 24/30	NR	Endoscopy: 9.26 ± 1.22 VS Craniotomy: 9.32 ± 1.03	Endoscopy: 55.48 ± 23.25 VS Craniotomy: 42.11 ± 18.43	Endoscopy: 112 ± 0.77VS Craniotomy: 1.11 ± 0.74
Zhu[30]	2012	Endoscopy: 60.6 ± 7.2 Craniotomy: 64.6 ± 5.0	Endoscopy: 17/28 VS Craniotomy: 15/30	Endoscopy: 21/28 VS Craniotomy: 21/30	NR	Endoscopy: 8 ± 2 VS Craniotomy: 7 ± 2	Endoscopy: 53.7 ± 15.8 VS Craniotomy: 63.9 ± 17.0	Endoscopy: 8 (median) VS Craniotomy: 6 (median)
Zhang[29]	2014	Endoscopy: 59.90 ± 12.85 Craniotomy: 61.45 ± 9.25	Endoscopy: 16/21 VS Craniotomy: 22/30	Endoscopy: 15/21 VS Craniotomy: 23/30	NR	Endoscopy: 9.19 ± 3.76 VS Craniotomy: 8.37 ± 2.39	Endoscopy: 58.28 ± 18.84 VS Craniotomy: 62.16 ± 15.62	Endoscopy: 9/21 within 12 hr VS Craniotomy: 10/30 within 12 hour
Wang[26]	2015	Endoscopy: 58.9 ± 12.97 Craniotomy: 52.9 ± 15.92	Endoscopy: 15/21 VS Craniotomy: 19/24	Endoscopy: 20/21 VS Craniotomy: 21/24	Endoscopy: 12/21 VS Craniotomy: 14/24	Endoscopy: 8.5 ± 2.65 VS Craniotomy: 8 ± 2.57	Endoscopy: 73.1 ± 29.11 VS Craniotomy: 59.05 ± 20.03	Endoscopy: within 6hr: 19/21 VS Craniotomy: 20/24
Feng[22]	2016	Endoscopy: 66.35±12.23 Craniotomy: 69.10±10.26	Endoscopy: 56/93 VS Craniotomy: 58/91	NR	Endoscopy: 16/93 VS Craniotomy: 11/91	NR	NR	NR
Xu[28]	2018	Endoscopy: 52.9 ± 12.3 Craniotomy: 53.8 ± 13.5	Endoscopy: 58/82 VS Craniotomy: 46/69	NR	NR	Endoscopy: 7.9 ± 2.2 VS Craniotomy: 7.8 ± 3.1	Endoscopy: 55.2 ± 28.4 VS Craniotomy: 55.9 ± 27.6	Endoscopy: 15.6 ± 14.9 VS Craniotomy: 13.7 ± 11.6
Fu[23]	2018	Endoscopy: 61.6 ± 9.2 Craniotomy: 63.2 ± 9.4	Endoscopy: 30/61 VS Craniotomy: 28/60	Endoscopy: 48/61 VS Craniotomy: 46/60	Endoscopy: 14/61 VS Craniotomy: 12/60	Endoscopy: 8.0 ± 2.9 VS Craniotomy: 7.9 ± 2.8	Endoscopy: 49.8 ± 11.3 VS Craniotomy: 50.8 ± 12.4	Endoscopy: 9.1 ± 3.1 VS Craniotomy: 9.5 ± 3.2

Guo[27]	2018	Endoscopy: 59.8 ± 12.9 Craniotomy: 56.9 ± 13.1	Endoscopy: 14/27 VS Craniotomy: 21/37	Endoscopy: 22/27 VS Craniotomy: 30/37	NR	Endoscopy: 8.2 ± 3.4 VS Craniotomy: 7.5 ± 2.9	Endoscopy: 50.4 ± 20.5 VS Craniotomy: 56.5 ± 22.9	Endoscopy: 5.2 ± 6.4 VS Craniotomy: 5.4 ± 4.9
Xiong[19]	2019	Endoscopy: 61.89 ± 10.32 Craniotomy: 60.37 ± 11.42	Endoscopy: 16/28 VS Craniotomy: 16/30	NR	NR	Endoscopy: 8.39 ± 2.38 VS Craniotomy: 7.93 ± 2.18	Endoscopy: 52.36 ± 11.58 VS Craniotomy: 57.98 ± 15.25	NR
Guo[20]	2019	Endoscopy: 70/105 less than 60 year old Craniotomy: 65/107 less than 60 year old	Endoscopy: 64/105 VS Craniotomy: 71/107	Endoscopy: 88/105 VS Craniotomy: 81/107	Endoscopy: 7/105 VS Craniotomy: 4/107	NR	Endoscopy: ≥40–<80: 69/105 VS Craniotomy: 50/107	Endoscopy: 17/105 less than 8hr VS Craniotomy: 35/107 less than 8 hour
Katsuki[24]	2020	Endoscopy: 74.25 ± 3.62 Craniotomy: 73.25 ± 4.45	Endoscopy: 36/66 VS Craniotomy: 42/68	Endoscopy: 58/66 VS Craniotomy: 54/68	Endoscopy: 16/66 VS Craniotomy: 6/68	Endoscopy: 10.33 ± 3.79 VS Craniotomy: 9.67 ± 4.54	Endoscopy: 102.33 ± 55.33 VS Craniotomy: 128 ± 74.23	NR
Liu[25]	2020	Endoscopy: ≥60 :21/60 Craniotomy: ≥60: 42/99	Endoscopy: 39/60 VS Craniotomy: 61/99	Endoscopy: 51/60 VS Craniotomy: 79/99	Endoscopy: 5/60 VS Craniotomy: 5/99	Endoscopy: GCS: 6-8: 47/90 VS Craniotomy: GCS:6-8: 31/99	Endoscopy: ≥80: 20/60 VS Craniotomy: 56/99	Endoscopy: >8(hr): 48/60 VS Craniotomy: 57/99

NR: Not Reported

Table 2a: ROBINS-I Risk of Bias summary of all the included observationall studies

Study		Pre-Intervention		At Intervention	Post-Intervention				Overall risk of bias
First Author	Year	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of intervention	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	
Zhu[30]	2012	Low Risk	High Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	High Risk
Zhang[29]	2014	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Unclear	Low Risk	Low Risk
Wang[26]	2015	Moderate Risk	Moderate Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk
Xu[28]	2018	Low Risk	Moderate Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk
Fu[23]	2018	High Risk	High Risk	Low Risk	High Risk	Low Risk	Low Risk	Low Risk	High Risk
Guo[27]	2018	Moderate Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk
Xiong[19]	2019	Moderate Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk
Guo[20]	2019	Moderate Risk	Moderate Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk
Katsuki[24]	2020	High Risk	Low Risk	Low Risk	High Risk	Low Risk	Low Risk	Low Risk	High Risk
Liu[25]	2020	High Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	High Risk

Table 2b: The Cochrane Risk of Bias summary of all the included randomised clinical trials

Study	Cochrane Risk of Bias Tool							Overall
	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other sources of bias	
Cho 2006[26]	Low	High Risk	High Risk	Unclear Risk	Low Risk	Low Risk	Low Risk	High Risk
Feng 2016[22]	Low	High Risk	High Risk	Unclear Risk	Low Risk	Low Risk	Low Risk	High Risk

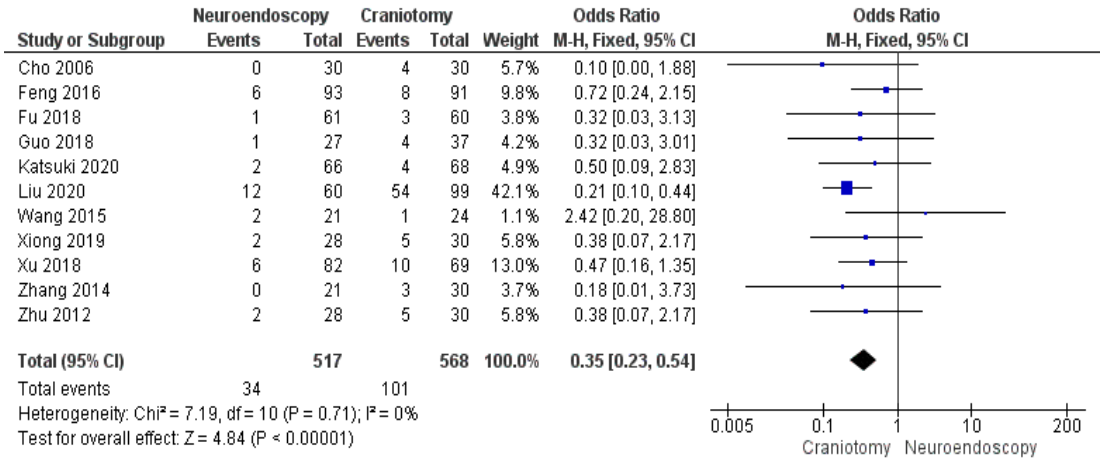
Table 3: Subgroup analysis

	Mortality				Haematoma Evacuation Rate				Complication				Postoperative GCS			
Subgroup	**ME**	**N**	**OR (95% CI)**	**P**	**ME**	**N**	**MD (95% CI)**	**P**	**ME**	**N**	**OR (95% CI)**	**P**	**ME**	**N**	**MD (95% CI)**	**P**
Age																
≤60	FME	4	0.44 (0.20, 0.99)	0.05	RME	4	7.14 (2.70, 11.58)	0.002	RME	3	0.63 (0.29, 1.37)	0.24	RME	4	1.20 (-0.20, 2.59)	0.09
>60	FME	7	0.32 (0.20, 0.53)	<0.00001	RME	6	3.33 (0.99, 5.68)	0.005	RME	5	0.23 (0.10, 0.52)	0.0004	RME	2	1.12 (0.30, 1.94)	0.007
Preoperative GCS																
≤8	FME	5	0.28 (0.17, 0.49)	<0.00001	RME	5	6.29 (2.24, 10.34)	0.002	FME	3	0.31 (0.18, 0.56)	<0.0001	RME	2	1.77 (-1.08, 4.61)	0.22
>8	FME	6	0.40 (0.16, 0.99)	0.05	RME	5	3.53 (0.73, 6.33)	0.01	FME	4	0.52 (0.30, 0.87)	0.01	RME	4	0.71 (0.21, 1.22)	0.006
Time To Operation (hr)																
≤8	FME	3	0.41 (0.12, 1.43)	0.16	RME	3	8.72 (4.17, 13.27)	0.0002	FME	3	0.59 (0.28, 1.27)	0.18	RME	3	0.43 (-0.14, 1.00)	0.14
>8	FME	5	0.28 (0.16, 0.48)	<0.00001	RME	5	6.00 (2.16, 9.84)	0.002	FME	3	0.24 (0.13, 0.44)	<0.00001	RME	2	2.00 (-0.47, 4.46)	0.11
Preoperative Haematoma Volume (ml)																
≤60	FME	5	0.35 (0.17, 0.74)	0.006	RME	5	4.50 (-0.94, 9.94)	0.11	FME	4	0.30 (0.17, 0.52)	<0.0001	RME	3	1.26 (-0.58, 3.11)	0.18
>60	FME	5	0.29 (0.16, 0.52)	<0.0001	RME	4	5.21 (-2.11, 12.53)	0.16	FME	3	0.56 (0.33, 0.97)	0.04	RME	3	1.09 (0.38, 1.79)	0.002

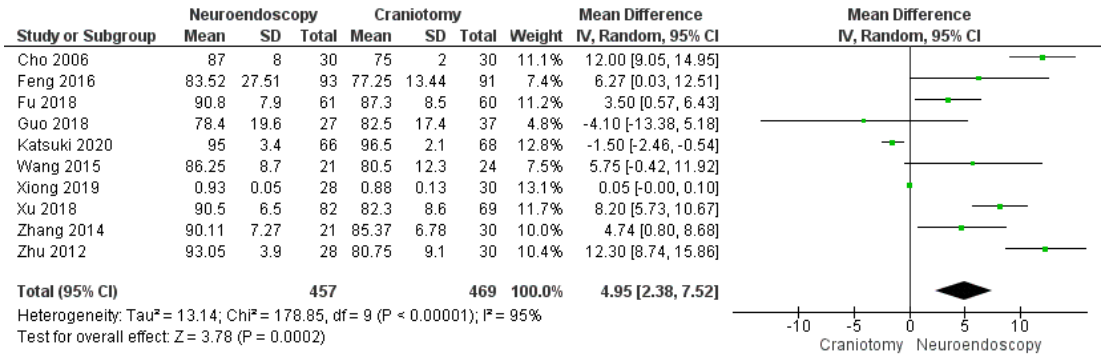
FME: Fixed Modelling Effect
RME: Random Modelling Effect

Figure 2: Summary of findings for primary and secondary outcomes:

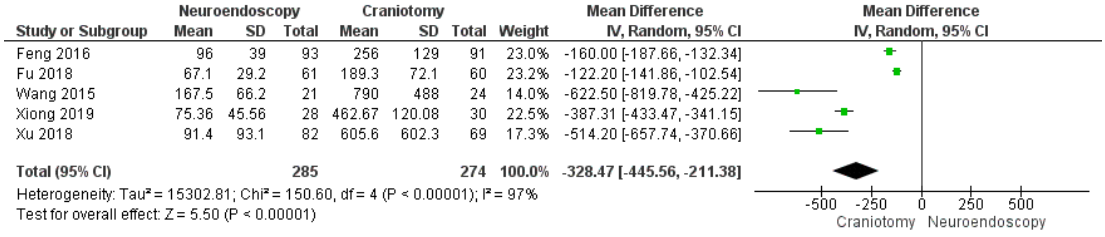
(a) Mortality



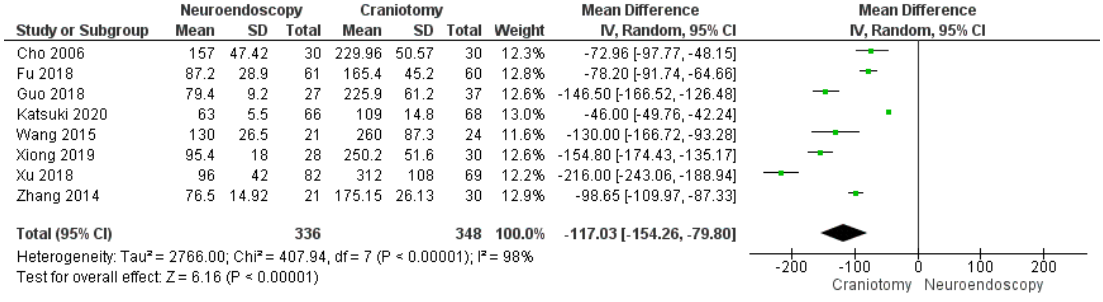
(b) Haematoma evacuation rate (%)



(c) Intraoperative blood loss (ml)



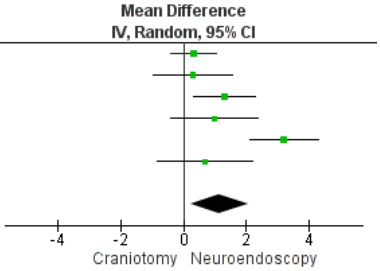
(d) Operative time (minutes)



(e) Postoperative GCS

Study or Subgroup	Neuroendoscopy Mean	SD	Total	Craniotomy Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cho 2006	14.47	0.96	30	14.15	1.78	30	19.9%	0.32 [-0.40, 1.04]
Guo 2018	9	2.46	27	8.7	2.6	37	16.0%	0.30 [-0.95, 1.55]
Katsuki 2020	13	1.5	66	11.7	3.8	68	18.1%	1.30 [0.33, 2.27]
Wang 2015	11.3	1.9	21	10.3	2.8	24	15.0%	1.00 [-0.38, 2.38]
Xu 2018	11.5	2.9	82	8.3	3.8	69	17.2%	3.20 [2.11, 4.29]
Zhang 2014	9.71	2.64	21	9.03	2.85	30	14.0%	0.68 [-0.84, 2.20]
Total (95% CI)			**247**			**258**	**100.0%**	**1.14 [0.22, 2.06]**

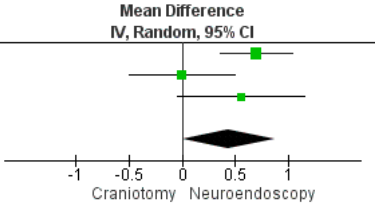
Heterogeneity: Tau² = 0.96; Chi² = 20.60, df = 5 (P = 0.0010); I² = 76%
Test for overall effect: Z = 2.44 (P = 0.01)



(f) Postoperative GOS

Study or Subgroup	Neuroendoscopy Mean	SD	Total	Craniotomy Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Fu 2018	4.1	0.9	61	3.4	1	60	41.1%	0.70 [0.36, 1.04]
Wang 2015	2.8	0.9	21	2.8	0.8	24	31.9%	0.00 [-0.50, 0.50]
Zhang 2014	3.61	0.92	21	3.05	1.26	30	27.1%	0.56 [-0.04, 1.16]
Total (95% CI)			**103**			**114**	**100.0%**	**0.44 [0.00, 0.88]**

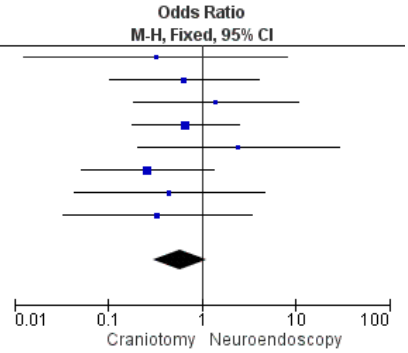
Heterogeneity: Tau² = 0.09; Chi² = 5.20, df = 2 (P = 0.07); I² = 62%
Test for overall effect: Z = 1.96 (P = 0.05)



(g) Rebleeding

Study or Subgroup	Neuroendoscopy Events	Total	Craniotomy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Cho 2006	0	30	1	30	6.2%	0.32 [0.01, 8.24]
Fu 2018	2	61	3	60	12.3%	0.64 [0.10, 4.00]
Guo 2018	2	27	2	37	6.5%	1.40 [0.18, 10.62]
Katsuki 2020	4	66	6	68	23.3%	0.67 [0.18, 2.48]
Wang 2015	2	21	1	24	3.5%	2.42 [0.20, 28.80]
Xu 2018	2	82	6	69	26.6%	0.26 [0.05, 1.35]
Zhang 2014	1	21	3	30	9.9%	0.45 [0.04, 4.65]
Zhu 2012	1	28	3	30	11.7%	0.33 [0.03, 3.41]
Total (95% CI)		**336**		**348**	**100.0%**	**0.58 [0.30, 1.13]**
Total events	14		25			

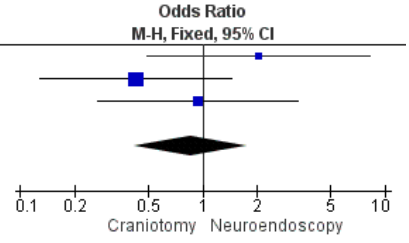
Heterogeneity: Chi² = 3.35, df = 7 (P = 0.85); I² = 0%
Test for overall effect: Z = 1.59 (P = 0.11)



(h) Reoperation rate

Study or Subgroup	Neuroendoscopy Events	Total	Craniotomy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Feng 2016	6	93	3	91	17.4%	2.02 [0.49, 8.35]
Guo 2019	4	105	9	107	52.5%	0.43 [0.13, 1.45]
Liu 2020	4	60	7	99	30.2%	0.94 [0.26, 3.35]
Total (95% CI)		**258**		**297**	**100.0%**	**0.86 [0.42, 1.76]**
Total events	14		19			

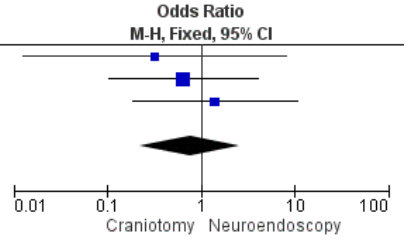
Heterogeneity: Chi² = 2.67, df = 2 (P = 0.26); I² = 25%
Test for overall effect: Z = 0.41 (P = 0.68)



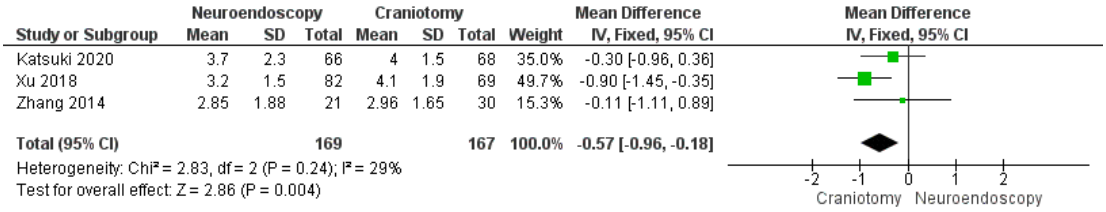
(i) Intracranial infection

Study or Subgroup	Neuroendoscopy Events	Total	Craniotomy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Cho 2006	0	30	1	30	24.7%	0.32 [0.01, 8.24]
Fu 2018	2	61	3	60	49.1%	0.64 [0.10, 4.00]
Guo 2018	2	27	2	37	26.2%	1.40 [0.18, 10.62]
Total (95% CI)		**118**		**127**	**100.0%**	**0.76 [0.22, 2.59]**
Total events	4		6			

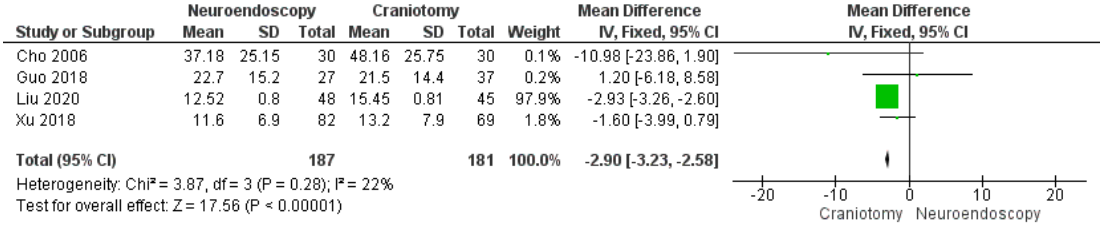
Heterogeneity: Chi² = 0.65, df = 2 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.43 (P = 0.66)



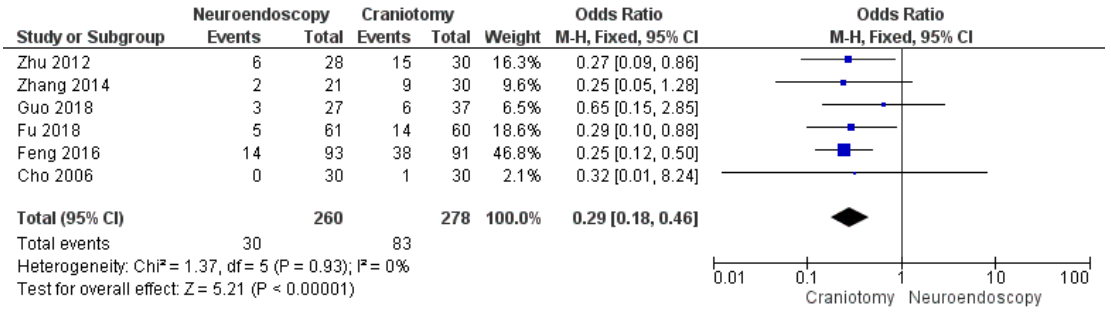
(j) mRS



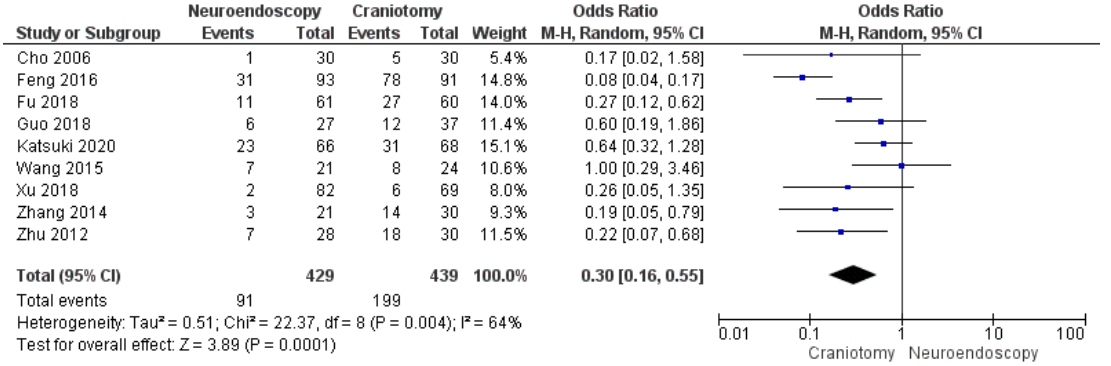
(k) Length of hospital stay (days)



(l) Postoperative infection



(m) Postoperative complication



The analysis demonstrated that age, preoperative GCS and preoperative haematoma volume did not have significant effect on the postoperative mortality rate. Similar trend was noted in haematoma evacuation rate when the variable of age, preoperative GCS, preoperative haematoma and time to operation were considered. As for postoperative complication, the preoperative GCS and preoperative haematoma volume did not affect much on this outcome. In terms of postoperative GCS, time to operation demonstrated no significant effect on it.

In the outcome of postoperative mortality rate, our analysis showed that the endoscopic approach is significantly associated with better mortality rate compared to craniotomy. Our pooled analysis demonstrated age and time to operation had significant impact on the outcome of postoperative complication. It is reported that endoscopic approach had significantly lower complication rate when the patients age were more than 60 years old and were operated after 8 hours since the onset. As for postoperative GCS, the patients in the craniotomy group had statistically significant lower score if the preoperative GCS was more than 8 and the haematoma volume was more than 60 ml.

Publication bias

Assessment of publication bias was conducted on postoperative mortality rate and haematoma evacuation rate (Figure 3). The funnel plot analysis showed that symmetrical distribution was achieved on postoperative mortality rate, indicating low publication bias. However, asymmetrical distribution was reported in haematoma evacuation, indicating high risk of publication bias.

Sensitivity analyses

The first set of analysis showed that the overall effect remained the same when risk ratios, odd ratios and risk difference were calculated independently. Eliminating one study at a time did not have significant effect except postoperative GCS (MD: 1.10; 95% CI -0.05 to 2.26; p=0.06) and length of hospital stay (MD: -1.63; 95% CI -3.86 to 0.61; p=0.15) where the overall effect became insignificant when Katsuki 2020 and Liu 2020 were removed respectively.[24,25]

DISCUSSION

We performed a systemic review and meta-analysis to compare the outcomes of neuroendoscopy versus craniotomy in the management of basal ganglia haemorrhage. Analysis of the results from twelve studies, enrolling 566 patients, showed that craniotomy was associated with higher risk of postoperative mortality, longer operative time, higher intraoperative blood loss, reduced postoperative GCS, reduced postoperative GOS, higher mRS, longer length of hospital stay, higher postoperative infection rate and higher postoperative complication rate compared with endoscopic approach. There was no difference between the two techniques in terms of intracranial infection, re-bleeding and need for reoperation.

Haematoma volume

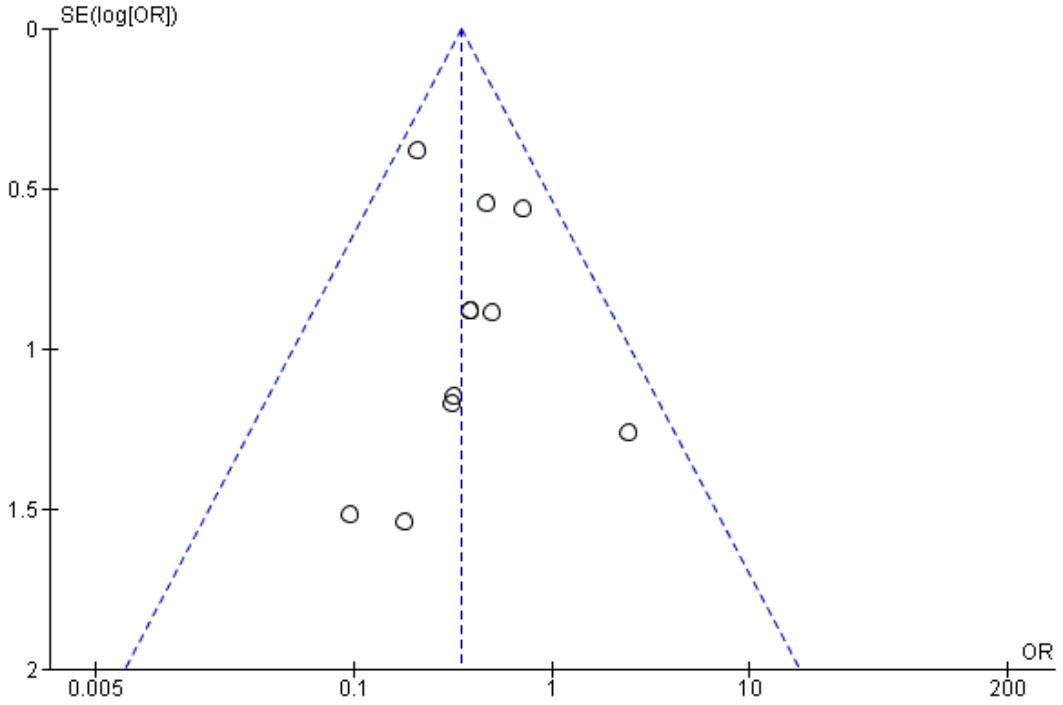
A systematic review by Zhou *et al*. suggested neuroendoscopy was preferable in managing haematomas with a volume ranging from 25 to 40ml.[32] Among the studies recruited for our analysis, the preoperative mean haematoma volume ranged between 42ml and 128ml. Although the majority of studies recruited had a haematoma volume of more than 40ml, our results revealed that neuroendoscopy achieved a more favourable mortality rate than craniotomy. Fu *et al*. showed no significant difference in mortality rate in patients aged over 70 years presenting with basal ganglia haemorrhage, indicating that mortality rate is higher in older patients.[23] Some studies showed no significant relationship between old age and mortality but this finding has been seen in intracerebral bleeding but not specifically in basal ganglia haemorrhage.[34-36] Furthermore, neuroendoscopic procedures can be performed under local anaesthesia which increases the safety and feasibility for patients with major comorbidity.[26] Zhang *et al*. revealed that it is easier to determine the bleeding point and achieve haemostasis with the endoscopic approach.[29]

Evaluation rate

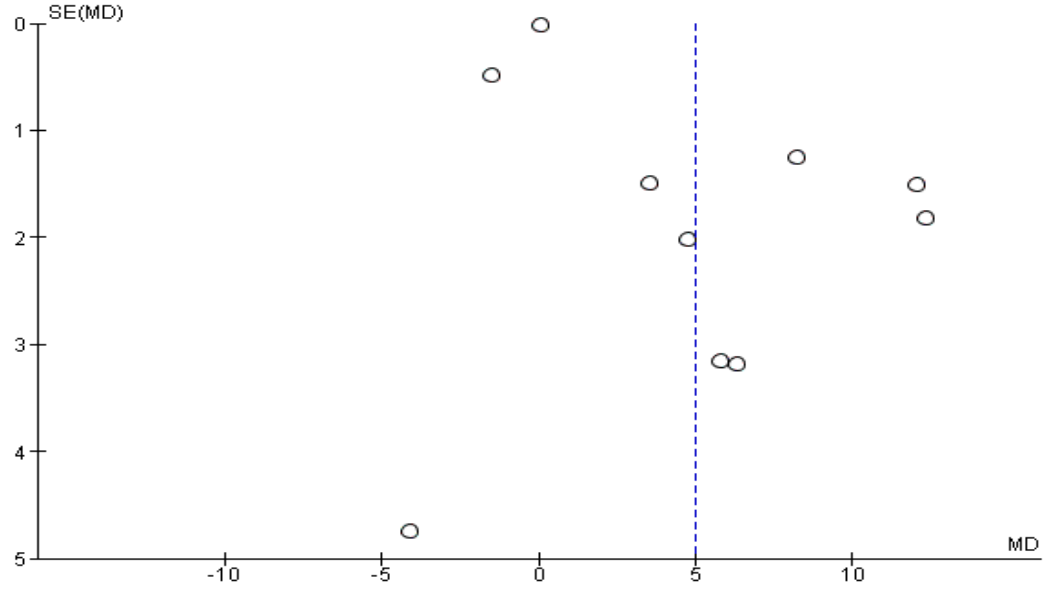
Intracerebral haemorrhage results in a rapid rise of intracranial pressure and this effect could result in cerebral ischaemia.[37] Previous studies reported higher evacuation rates of haematoma using neuroendoscopy and our analysis supported their findings. Neuroendoscopic approach generally causes less trauma to the brain tissue and offers a clear and direct vision of the haematoma, enabling the surgeon to directly evacuate the haematoma in a much shorter time without increasing the amount of haemorrhage.[38] The effect of raised intracranial

Figure 3. Funnel plot

(a) Postoperative Mortality



(b) Haematoma evacuation rate



pressure caused by the haematoma shifts the surrounding brain tissue, but the endoscopic channel provides negative pressure compared with the brain tissue and haematoma.[39] Hence, the shifted brain tissue causes the haematoma to move into the visible channel. As the result of the "pulling effect" without the usage of spatula to manipulate the brain tissue, it minimised the unnecessary damage to the brain tissue without compromising the clearance rate.

Intraoperative time and blood loss

The analysis results from our review demonstrated positive impacts of neuroendoscopy in achieving shorter intraoperative time and blood loss. Our results are consistent with the available evidence.[31,38,40] This could be due to the advantage of the endoscopic procedure which by its very nature of minimal invasion of the brain tissue, causes less damage and shortens the operative time.[38] Another benefit of neuroendoscopic technique is that it has high manipulation proficiency with high definition view which enables the surgeon to quickly reduce the mass effect from the basal ganglia haemorrhage.[38] On the other hand, craniotomy has been demonstrated to be effective in removing large haematomas and relieving acutely raised intracranial pressure.[41]

On the contrary, the haematoma pressure gradient is difficult to establish in craniotomy due to formation of cortical fistula. This causes the evacuation of haematoma to become more difficult and required the spatula to pull the brain tissue, which increases the operating time, lower haematoma evacuation rate and damaging more brain tissue. Traditional haematoma evacuation in endoscopic approach was conducted with the guidance of a syringe or trocar.[42] To date, many advanced cannula systems are available with the aim to reduce damage and improve the access to the haematoma.[43-45] This technique is helpful in distributing the intracranial pressure evenly, thus reducing stretching and the incidence of brain edema. Moreover, after evacuating the haematoma, the fistula and stoma will retract to a diameter of less than 1 cm, causing less damage to the brain tissue.[38] Due to the minimal invasive approach and multi-angle observation technique, which offers a good protection to brain tissue, and the advanced cannula system adapted in the endoscopic technique, it significantly reduces the postoperative infection and complication which is consistent.[22] Furthermore, the level of consciousness at presentation and anaesthetic duration are major contributing factors.[22,29]

Rebleed

However, the postoperative rebleeding rate was reported to be insignificant in our study, this finding is similar with the meta-analysis conducted by Sun and colleagues.[31] It was proposed that the aetiology of rebleeding is mainly due to the uncontrolled hypertension.[26]

Neurological outcome

Cho *et al*. demonstrated better neurological function outcomes and less tissue damage.[21]
The mRS measures the global disability and is commonly used in evaluating stroke recovery.[46,47] Its reliability was assessed by Jamie et al and was reported to have strong test-re-test reliability (κ=0.81 to 0.95).[48] Our study analysed the outcome of mRS in 3 studies and revealed that endoscopy group had statistically significant lower mRS score. This finding was consistent with the current available evidence.[28] Furthermore, similar trend in postoperative GCS and GOS, indicating that patients in the endoscopy group achieved better recovery rate compared to the patients in the craniotomy group. These findings may be attributed to the nature of minimally invasiveness in the endoscopic approach and the low complication rate achieved.[28]

In the subgroup analysis, it was demonstrated that neuroendoscopic approach is a better choice in achieving low postoperative mortality rate regardless of age, preoperative GCS and preoperative haematoma volume. Indicating that, age, preoperative GCS and preoperative haematoma volume are not the influencing factors affecting the surgical approach.

Time to surgery

Endoscopy appeared to have better outcome than craniotomy for patients who were presented to theatre later than 8 hours. Similar findings were reported in haematoma evacuation rate, showing that age, preoperative GCS, time to operation and preoperative haematoma volume have no obvious correlation with the surgical approach. One of the explanations may be that haematoma evacuation is easier within 24 hours as the haematoma is still partially liquified.[49] However, the subgroup analysis suggests that neuroendoscopy is a better choice regardless of the preoperative haematoma volume as reported by previous literature.[50] In terms of postoperative complication, our subgroup analysis revealed that the endoscopy is better for patients who are more than 60 years old or

presented to theatre later than 8 hours. Lastly, postoperative GCS is not dependent on the time to operation.

Based on the best available evidence presented in this study neuroendoscopy has a better outcome profile compared to craniotomy. In this study, we used a systematic approach to provide summary of best available comparative evidence and to assess the risk of bias of relevant studies. However, the outcomes of this study possessed some limitations. Firstly, the timeline of the postoperative measures were not consistent in all the 12 studies. Most of the included studies had non-randomised design which are subject to selection and confounding bias. Moreover, some of the included studies had retrospective design that increases the likelihood of indication bias. The between study heterogeneity was low for all the outcomes except intraoperative blood loss, operative time, haematoma evacuation rate, postoperative GCS, postoperative GOS and postoperative complication where the heterogeneity was substantial. The quality of the available evidence was low due to the high risk of bias of the included studies.

As for the inclusion criteria in this study, it was reported that medical treatment is effective in managing haematoma less than 25 ml and GCS of more than or equal to 14. Furthermore, previous review of RCTs suggested endoscopic technique to be indicated for haematoma volume between 25 ml to 40 ml.[32] Hence, we proposed our study to include patients with brain haematoma of more than 25 ml and GCS in the range of 4 to 14.[51-53]

In conclusion, the best available evidence suggest that endoscopic approach may be associated with lower risk of postoperative mortality, better haematoma evacuation rate, lesser intraoperative blood loss, shorter operative time, higher postoperative GCS and GOS, lower mRS, lower postoperative infection and complication compared with craniotomy in management of BGH. The available evidence is derived from observational studies and is subject to bias by indication. There is a need for high quality randomised controlled trials for definite conclusions.

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DISCLOSURE

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Conflict of interest: None

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Supplemental

eTable 1: PICO table

Population	Intervention	Control	Outcome
Adult patients (>18 years old) with basal ganglia hemorrhage	Neuroendoscopy	Craniotomy	Postoperative mortality Haematoma evacuation rate Intraoperative blood loss Operative time Postoperative Glasgow Coma Scale Postoperative Glasgow Outcome Scale Intracranial infection Rebleeding Reoperation Postoperative infection Postoperative complication Length of hospital stay Modified Rankin Score

eTable 2: Search Strategy

PUBMED DATABASE

Steps	Search String
1.	MeSH Terms: [Craniotomy]
2.	All Text: (Craniotomy)
3.	All Text: (open surgery)
4.	#1 OR #2 OR #3
5.	MeSH Terms: [neuroendoscopy]
6.	All Text: (neuroendoscopy)
7.	All Text: (endoscopy)
8.	All Text: (neuroendoscopic)
9.	All Text: (endoscopic)
10.	All Text: (minimal invasive)
11.	All Text (minimally invasive)
12.	#6 OR #7 OR #8 OR #9 OR #10 OR #11
13.	MeSH Terms: [basal ganglia hemorrhage]
14.	All Text: (basal ganglia hemorrhage)
15.	All Text: (basal ganglia bleed)
16.	All Text: (basal ganglia)
17.	All Text: (intracranial hemorrhage)
18.	All Text: (intracranial bleed)
19.	All Text: (intracerebral bleed)
20.	All Text: (intracerebral hemorrhage)
21.	All Text: (hypertensive cerebral hemorrhage)
22.	All Text: (cerebral hemorrhage)
23.	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
24.	#4 AND #12 and #23

CENTRAL Database

Steps	Search String
1.	MeSH descriptor: [Basal Ganglia Hemorrhage] explode all trees
2.	(Basal Ganglia Hemorrhage)
3.	MeSH descriptor: [Basal Ganglia] explode all trees
4.	(Basal Ganglia)
5.	MeSH descriptor: [Intracranial Hemorrhage] explode all trees
6.	(intracranial haemorrhage)
7.	MeSH descriptor: [Cerebral Hemorrhage] explode all trees
8.	(intracerebral haemorrhage)
9.	(cerebral haemorrhage)
10.	("intracerebral haemorrhage-induced brain injury")
11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
12.	MeSH descriptor: [Endoscopy] exploded all trees
13.	(Endoscopy)
14.	("endoscopic")
15.	MeSH descriptor: [Neuroendoscopy] exploded all trees
16.	(neuroendoscopy)
17.	MeSH descriptor: [Minimally Invasive Surgical procedure] exploded all trees
18.	(Minimally Invasive Surgical procedure)
19.	#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
20.	MeSH descriptr: [Craniotomy] exploded all trees
21.	(Craniotomy)
22.	(open surgical approach)
23.	#20 OR #21 OR #22
24.	#11 AND #19 AND #23

OVID MEDLINE and OVID EMBASE DATABASE

Steps	Search String
1.	basal ganglia hemorrhage.mp. or Cerebral Hemorrhage/ or Basal Ganglia Hemorrhage/ or Basal Ganglia/
2.	basal ganglia hemorrhage*.m.p. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
3.	Exp "Intracerebral Hemorrhage, Hypertensive/ or exp "Cerebral Hemorrhage/
4.	Intracerebral hemorrhage.mp. or exp* Cerebral Hemorrhage/
5.	1 or 2 or 3 or 4
6.	Endoscopy.mp. or exp "Endoscopy/
7.	Endoscopy*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
8.	Neuroendoscopy.mp. or exp *Neuroendoscopy/ or exp *Endoscopes/
9.	Neuroendoscopy*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

10.	Minimal invasive.mp. or exp “Minimally Invasive Surgical Procedures/
11.	exp “Minimally Invasive Surgical Procedures/ or minimally invasive. mp.
12.	6 or 7 or 8 or 9 or 10 or 11
13.	craniotomy*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
14.	Craniotomy.mp. or exp *Craniotomy/
15.	Open surgery.mp.
16.	13 or 14 or 15
17.	5 and 12 and 16

eTable 3: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2,3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5, 6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5, 6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6, 7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6, 7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7, 8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7, 8

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9, 10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10, 11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10, 11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9, 10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13, 14, 15, 16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17, 18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1