Correlation of the long-term neurological outcomes with completeness of surgical evacuation in spontaneous supratentorial intracerebral haemorrhage: a retrospective study

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ABSTRACT

Introduction: The treatment of primary spontaneous supratentorial intracerebral haemorrhage (ICH) by evacuation is not supported by randomised controlled trials. We investigate the effectiveness of the completeness of surgical evacuation of spontaneous supratentorial ICH with respect to the functional neurological outcome and mortality.

Methods: A retrospective review of patients who underwent supratentorial ICH evacuations in the Neurosurgical Unit of the National University Hospital, Singapore, between January 2002 and December 2005 was conducted. Preoperative and postoperative computed tomography images were compared, and the patients or their family members completed follow-up questionnaires two years post surgery, in order to assess the neurological outcome.

Results: The patients were subdivided into two groups based on the Glasgow Outcome Scale and haematoma volume. Patients with small pre-evacuation haematoma had a median percentage change in volume and a midline shift of 97.63 percent and 63 percent, respectively. Patients with a large haematoma volume had a median percentage change in volume and midline shift of 99.54 percent and 100 percent, respectively (the p-values for percentage change in volume and midline shift are 0.764 and 0.742, respectively). The median percentage change in volume for the poor outcome subgroup was 97.63 percent, compared to 100 percent for the good outcome subgroup (p-value is 0.288). The median change in midline shift in the poor and good outcome subgroups was 63 percent and 100 percent, respectively (p-value is 0.576).

Conclusion: Although not statistically significant with regard to the completeness of haematoma evacuation, a trend toward better outcome with more complete evacuation is observed with ICH.

Keywords: Glasgow Outcome Scale, spontaneous intracerebral haemorrhage, surgical evacuation

Singapore Med J 2010;51(4):320-325

INTRODUCTION

Currently, the two major types of stroke, ischaemic and haemorrhagic, result in significant patient mortality and morbidity. Although ischaemic stroke still affects the vast majority of patients, as shown in both Asian and Western data, up to 20% of new strokes in the United States of America and United Kingdom are haemorrhagic. In addition, almost 20%–30% of new strokes in Japan and China are haemorrhagic in nature. In Singapore, the statistics are similar, and there is a 1.8 per 1,000 person-years incidence of strokes, 24% of which are haemorrhagic. This constitutes an incidence of 4.32 per 10,000 person-years.[1]

It has been widely established that intracerebral haemorrhage (ICH) has a high early case-fatality rate. In fact, it has a mortality rate of 44% after 30 days.[2-5] Significantly, this mortality is much higher than that for ischaemic stroke and for patients with spontaneous subarachnoid haemorrhage. Of all ICHs, basal ganglia (BG) haematomas are by far the most common in location, comprising 42% of all ICHs.[2,6,7] The commonest aetiology for such bleeds is small vessel vasculopathy secondary to chronic long-term hypertension.

ICH in the acute hazardous phase is potentially amenable to surgical treatment. There have been many recent advances in surgical techniques with the application

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of endoscopy, minimally invasive stereotactically guided evacuation techniques and the instillation of fibrinolytic agents. However, there is still a wide variation in practice among neurosurgeons throughout the world with regard to the best management of ICH.[2,8-10] This controversy is largely attributed to the lack of reliable evidence regarding the safety and effectiveness of even surgical evacuation. In fact, there is currently no conclusive Level 1 evidence that supports the surgical management of ICH. The most recent trial was the landmark International Surgical Trial in Intracerebral Haemorrhage (STICH), which concluded that patients with spontaneous supratentorial ICH in neurosurgical units showed no overall benefit from early surgery when compared with initial conservative treatment.[11]

Due to the lack of benefits observed in the STICH trial, many neurosurgeons have concluded that emergency surgical evacuation should be reserved for patients with large lobar haemorrhage causing a mass effect and patients with a rapidly deteriorating clinical condition. It is believed that the mechanism of injury in large haemorrhages with a haematoma of increased size is associated with the mass effect and midline shift leading to higher mortality and morbidity.[12] Other postulated mechanisms of injury include those of decreased cerebral blood flow due to raised intracranial pressure, disruption of the blood-brain barrier, and toxicity and inflammation secondary to the breakdown products of the haematoma, such as iron and haemoglobin.[13] Currently, there is no literature that studies how residual haematoma post evacuation influences the outcome. Hence, our study is unique, as we set out to correlate the completeness of surgical evacuation of the haematoma in patients who have had operative intervention with long-term functional neurological outcome and mortality.

METHODS

A retrospective study was conducted of patients with spontaneous intracerebral BG haemorrhage who were surgically evacuated in a single tertiary institution. All these patients had undergone craniectomy with surgical evacuation of their haematoma in our neurosurgical unit. Inclusion criteria for the study included the following: (1) Patients who presented with computed tomography (CT) evidence of spontaneous BG haemorrhage without extension into the thalamus, midbrain or ventricles within 24 hours of symptom onset; (2) Patients whose emergency surgical evacuation was performed within 48 hours of CT imaging; (3) Patients whose post surgery CT imaging was done within five days; and (4) Patients or family members who were contactable by telephone-administered survey to allow for assessment of the outcome after the operation. The survey was done at least two years from the time of surgery, as the consensus among neurosurgeons is that maximal functional recovery will have occurred within two years, and plateaus thereafter. All the patients admitted during the period January 2002 to December 2005 were retrospectively reviewed. Based on the inclusion criteria, 26 patients were included in the study, 24 of which were contactable by a single interviewer via telephone survey.[14]

Each patient who was included in the study underwent a large craniectomy and transcortical evacuation of the haematoma through the non-eloquent brain cortex. The completeness of surgical evacuation of the haematoma was based on the preoperative CT image of the head on presentation, compared with the first available CT image of the head performed postoperatively. The parameters that were measured pre- and postoperatively included the maximal midline shift, measured as the distance of shift from the midline (cm) and the volume of the haematoma (ml) calculated using Broderick's formula:[15] Volume (ml) = (A × B × C)/2, where A is the largest diameter (cm) of the haematoma, B is the diameter (cm) of the haematoma perpendicular to A, and C is the height (cm) of the haematoma calculated by multiplying the number of slices involved with the slice in thickness. The percentage change in the volume and midline shift after the operation was then calculated.[15] The average measurements of three separate readings by a single neurosurgeon blinded to the final outcome were made, and the same method was applied to both the pre- and postoperative images in order to reduce error. Preoperative haematoma volumes were classified into large (> 80 ml) and small haematomas (20–80 ml). Haematomas with volumes < 20 ml were not included in the study, as haematomas of this small a size are generally treated conservatively.[16-18]

Data on long-term outcome measures was collected via a telephone-administered survey based on the Modified Barthel Index and Glasgow Outcome Scale (GOS).[19] The Modified Barthel Index includes a standard battery of questions on activities of daily living (ADL), including continence (bladder and bowel), grooming, toilet use, feeding, transfer, mobility on flat surfaces, dressing, stair climbing and bathing. The GOS (Table I) consists of a spectrum, with GOS 1 showing good recovery and GOS 5 showing a highly undesirable outcome, from severe disability to death.

In this study, taking into account each individual patient's baseline prognosis, the patients were classified into good or poor outcome groups based on the GOS, with good outcome patients having a score of GOS 1 or

Table I. Glasgow Outcome Scale (GOS).

Score	Functional outcome	Functional assessment
1	Good recovery	Resumption of normal activities even though there may be minor neurological or psychological deficits.
2	Moderate disability	Independent as far as daily life is concerned; disabilities include varying degrees of dysphasia, hemiparesis or ataxia, intellectual and memory deficits, personality changes.
3	Severe disability	Conscious but disabled; dependent on others for daily support due to mental or physical disability, or both.
4	Persistent vegetative state	Exhibits no obvious cortical function.
5	Death	Death

Table II. Pre-evacuation haematoma volume cross-tabulated with Glasgow Outcome Scale (GOS).

Pre-evaluation volume no.	GOS Group		Total
	Poor outcome (3–5)	Good outcome (1–2)	
Small			
Count	11	6	17
Within pre-evacuation volume no. (%)	64.7	35.3	100.0
Within GOS group (%)	64.7	85.7	70.8
Total (%)	45.8	25.0	70.8
Large			
Count	6	1	7
Within pre-evacuation volume no. (%)	85.7	14.3	100.0
Within GOS group (%)	35.3	14.3	29.2
Total (%)	25.0	4.2	29.2
Total			
Count	17	7	24
Within pre-evacuation volume no. (%)	70.8	29.2	100.0
Within GOS group (%)	100.0	100.0	100.0
Total (%)	70.8	29.2	100.0

2 and poor outcome patients having a score of GOS 3, 4 or 5. This is a broad and reliable outcome measure, as a score of GOS by two different raters with 50 patients each had an agreement of 92%, which indicated high inter-observer reliability. In fact, it has been reported that collapsing the scale to a binary outcome of favourable vs. unfavourable is a conventional approach to an analysis of Phase III trials in head injury or stroke, and clinicians are generally familiar with this approach.[20,21]

RESULTS

The analysis of the number of patients with complete vs. incomplete evacuation showed a comparable number of ten complete and 14 incomplete evacuations. There was also a comparable number of complete and incomplete changes in midline shift, with 11 and 13 patients, respectively.

The median age of our study population was 52.5 years and the mean age was 53 years. The median and mean age of patients with complete evacuation was 52 and 53.7 years, respectively. The median and mean age of patients with incomplete evacuation was 53 and 52.5 years, respectively. 17 patients were Chinese, nine of whom had complete evacuation and eight had incomplete evacuation. Seven were non-Chinese, six of whom had incomplete evacuation, while only one had complete evacuation. The demographics also showed that there were more male (18, with nine having complete evacuation and the other nine incomplete evacuation) than female patients (six, with one having complete evacuation and five incomplete evacuation). Of these patients, 19 had right-sided haemorrhages, of which six were complete and 13 incomplete. Five had left-sided haemorrhages, of which four were complete and one incomplete.

Of the 24 patients, 17 had a small pre-evacuation haematoma (20–80 ml). Of these patients, six (35.3%) had a good outcome (GOS 1–2) while 11 had a poor outcome (GOS 3–5). Out of the seven patients with large pre-evacuation haematoma, only one (14.3%) had a good outcome (Table II). The median percentage change in volume of a small haematoma is 97.63%, and 99.54% in a large haematoma. The mean change in a small haematoma is 75.02%, and 84.46% in a large haematoma (p-value = 0.764).

The percentage change in midline shift showed a difference in the median but not the mean change, when comparing between small and large haematomas; the median change in midline shift in small haematomas was

Table III. Pre-evacuation haematoma volume cross-tabulated with the change in haematoma volume and midline shift post evacuation.

Pre-evacuation volume	Median	Min	Max	Mean	SD	Valid no.
Small						
Change in volume (%)	97.63	−84.18	100.00	75.02	48.33	17
Change in midline shift (%)	63	−10	100	63	38	17
Large						
Change in volume (%)	99.54	47.78	100.00	84.46	25.10	7
Change in midline shift (%)	100	−32	100	64	52	7

Min: minimum; Max: maximum; SD: standard deviation

63%, and 100% in large haematomas. The mean change in midline shift in small haematomas, 63%, and in large haematomas, 64% (p-value = 0.742). The median change in midline shift resulting in a subsequent poor outcome (GOS 3–5) was 63%, as compared to 100% resulting in a good outcome (GOS 1–2). The mean change in midline shift resulting in a poor outcome (GOS 3–5) was 59%, as compared to 75% resulting in a good outcome (GOS 1–2), at a p-value of 0.576. Although this comparison was not statistically significant, a trend was observed in our study in terms of the outcome in relation to the percentage change in midline shift, which suggested that the greater the midline change, the better the outcome.

The median change in volume resulting in a poor outcome (GOS 3–5) was 97.63% as compared to 100% resulting in a good outcome (GOS 1–2). The mean change in volume resulting in a poor outcome (GOS 3–5) was 71.21%, as compared to 93.72% resulting in a good outcome (GOS 1–2), at a p-value of 0.288. Again, this was suggestive of a trend that a greater change in volume number was associated with a better outcome.

All 24 patients in the study were ADL-independent prior to the incidence of intracranial bleeding. Of these 24 patients, 22 had hypertension, five had diabetes mellitus, six had ischaemic heart disease and eight had hyperlipidaemia. Four (16.7%) patients experienced re-bleeding after surgical evacuation, with incomplete evacuation (28.6%). Of these four patients, three had a good outcome and one had a poor outcome.

DISCUSSION

In the pre-CT era, McKissock et al conducted the first landmark trial on the management of intracerebral haemorrhage and reported that there was no difference between medical and surgical therapy. This prospective, randomised, controlled trial on the surgical evacuation of ICHs was published by McKissock and his co-workers in 1961 in the Lancet. In fact, they found that not only was surgical intervention non beneficial, it was also associated with worse clinical outcomes and an increased mortality rate when compared with medical treatment.[22] However, with the current widespread availability of CT scanners, many have been critical of the study as it was completed in an era before CT imaging was available. Consequently, many factors, such as unascertained haematoma volume and delayed treatment, may have significantly influenced the study results.

Since the study of Mckissock et al was published, other authors have reported similar results during the previous half century. However, almost three decades later, in 1989, Juvela et al published a randomised study of 52 patients, which compared craniotomy evacuation within 48 hours of the onset of symptoms to medical treatment, and found increased mortality in the surgical group.[23] This was obviously conducted in the post CT-era.

On the contrary, there was only one randomised trial that demonstrated improved neurological and overall functional outcomes as well as reduced mortality rate with stereotactic surgery, and this was reported during the same time period as Juvela et al's paper. Auer et al evaluated ultrasonic-guided endoscopic haematoma evacuation and compared it with medical therapy alone. 100 patients were randomised and a mortality rate of 42% was reported in the surgical group and 70% in the medical group. This was a statistically significant difference in mortality. However, patients in the surgical group were younger, and the subgroup analysis suggested that only younger patients appeared to have benefitted from surgery.[24]

The most recent trial that has been published is the landmark paper, International Surgical Trial in Intracerebral Haemorrhage (STICH). It involved a large study population of 1,033 patients from 83 centres in 27 countries.[11] This international multicentre trial compared the early evacuation of intracerebral haematomas to initial medical management. It utilised the GOS obtained by questionnaires that were posted to patients at the six months follow-up as the primary outcome measure. The patients were dichotomised into either the good or poor prognosis group based on their clinical status at randomisation. For the group with a good prognosis, a favourable outcome was defined as good recovery or

Table IV. Glasgow Outcome Scale (GOS) cross-tabulated with the change in haematoma volume and midline shift post evacuation.

GOS group	Median	Min	Max	Mean	SD	Valid no.
Poor outcome (3–5)						
Change in volume no. (%)	97.63	−84.18	100.00	71.21	48.77	17
Change in midline shift (%)	63	−32	100	59	44	17
Good outcome (1–2)						
Change in volume no. (%)	100.00	64.59	100.00	93.72	13.00	7
Change in midline shift (%)	100	23	100	75	33	7

Min: minimum; Max: maximum; SD: standard deviation

moderated disability on the GOS. However, for the poor prognosis group, a favourable outcome also included the upper level of severe disability. At six months, the authors reported no significant difference in mortality between the two groups. A favourable outcome was demonstrated in 26% of the surgical group compared to 24% in the medical group. The investigators therefore concluded that there was no overall benefit from early surgery when compared with initial medical therapy.[11] However, a subsequent subgroup analysis found a trend toward benefits for patients with haematoma evacuation with lobar bleeds within 1 cm from the outer surface of the brain cortex. As a result of this finding, STICH II is currently recruiting patients in order to evaluate this further.

On the other hand, we were interested to determine whether the completeness of surgical evacuation of the haematoma in patients who have had an operative intervention has any effect on long-term functional neurological outcome and mortality. Our patient population profile showed more male patients with intracranial bleeds, which is comparable to the worldwide figures. The median and mean age was also comparable, at 52.5 and 53 years, respectively. We found that those patients with large pre-evacuation haematoma volumes had a poorer outcome. This is consistent with many studies which have found the volume of the intracerebral haemorrhage to be a strong predictor of mortality and morbidity.[15]

From our study, the median change in volume of moderate and large haematomas is comparable at 97.63% and 99.54%, respectively. The mean change of 84.46% in large haematomas is, in fact, greater than that of 75.02% in small haematomas. Similarly, the median and mean changes in midline shift of 63% and 63%, respectively, in moderate haematomas and 100% and 64%, respectively, in large haematomas were not significantly different (Table III). Hence, this reflects that the size of the pre-evacuation haematoma and midline shift did not affect the completeness of surgical evacuation.

The median of change in volume resulting in a good outcome was 100% compared to 97.6% resulting in a poor outcome. A similar trend was observed in the median change of 100% in midline shift resulting in a good outcome compared to only 63% resulting in a poor outcome (Table IV). This shows that long-term functional outcome may be improved by the completeness of surgical evacuation. However, the median percentages in volume number (p-value 0.288) and midline shift (p-value 0.576) for patients with good functional outcomes were not significantly higher than those for patients with poor functional outcomes. Although this finding did not reach statistical significance, it reflects a trend toward a better outcome.

Lastly, our patient population had a variety of background medical conditions. Although nine patients had hypertension, one had diabetes mellitus, two had ischaemic heart disease and three had hyperlipidaemia, all 24 patients were ADL-independent prior to the event of intracerebral haemorrhage.

Based on our data analysis, there is a trend toward a better outcome with a more complete haematoma evacuation as well as correction of the midline shift. However, as this was a retrospective review, there were several limitations in our study. Firstly, selection bias and missing data may potentially compromise the review. We minimised this by adhering to the inclusion criteria that was set from the outset of the study. We also sought to reduce bias by blinding the neurosurgeon who was measuring the haematoma volume and midline shifts to the eventual patient outcome. Secondly, the study population of only 24 patients is relatively small. Hence, the conclusions should be interpreted with this consideration in mind. Ideally, a larger study population would be required to detect any significant differences. However, despite the results of the benefit not reaching statistical significance, the trend in improvement that was observed warrants further evaluation. The authors intend to conduct a larger prospective study in the future, so that some of these issues can be addressed.

In conclusion, although statistically insignificant due to the small sample size, this study does demonstrate a trend that long-term functional outcome may be

improved by the completeness of surgical evacuation and the restoration of midline shift. Conducting a larger prospective study might serve to confirm these trends in improvement.

ACKNOWLEDGEMENTS

We would like to thank Dr Chan Yiong Huak from the Clinical Trials and Epidemiology Research Unit for his kind assistance in providing statistical support during the analysis of the study data.

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