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Original research article

Age as a prognostic factor in relation to surgical evacuation of spontaneous supratentorial intracerebral haemorrhage

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ABSTRACT

Aim and clinical rationale for the study: Spontaneous intracerebral haemorrhage (sICH) is an acute life-threatening injury and constitutes 10–15% of first-ever stroke cases. The Surgical Trials in Intracerebral Haematoma studies (STICH and STICH II) represent the two foremost studies in the field, however, with arguable shortcomings. To find more accurate criteria, we aimed to correlate the preoperative neurological and neuroimaging findings with the clinical outcome of operated patients.

Materials and methods: In this retrospective study, sICH patients were recruited from the Central Denmark Region from 2010 to 2016. We evaluated the patients' medical records regarding preoperative Glasgow Coma Scale (GCS) 6 months and one year after surgery, focal neurological defects, thrombolytic treatment, pupil status, and haemorrhage localization visualized by neuroimaging. The patients' clinical outcome was assessed using the Glasgow Outcome Scale (GOS).

Results: Based on logistic multiple linear analysis, age, basal ganglia haemorrhage and mass effect had significant effect on the mortality rate. Besides, age, basal ganglia haemorrhage, intra ventricular haemorrhage and pupil difference had significant correlation with good outcome (GOS > 3).

Conclusions and clinical implications: Neurosurgical treatment of the sICH patients is indicated only if age and potentially improved morbidity is carefully evaluated considering the STICH and this study; otherwise, we will just increase the health care burden with a number of extremely care-dependent patients.

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1. Introduction

Spontaneous supratentorial intracerebral haemorrhage (sICH) is an acute life-threatening event with high mortality and morbidity rates. The incidence rate is 12–20 cases per 100,000, and despite a high level of treatment, the six-month mortality rate is 24%. Out of all treated patients, 50% survived to dependency and nursery home. Only 26% of patients survive to a favourable clinical outcome [1,2]. The decision between conservative or surgical treatment is still controversial. Some studies have reported a borderline lower 30-day mortality of operated vs non-operated patients, but the overall morbidity and mortality for the two groups does not differ significantly [3]. The Surgical Trials in Intracerebral Haematoma studies (STICH and STICH II) [1,3] represent the two foremost studies in the field. STICH was unable to show an overall benefit of early surgery compared to conservative treatment [4,5]. The impact of the STICH studies on the policy of patient admission in neurosurgery is also controversial, as some studies indicate that the number of patient admissions and neurosurgical evacuation have decreased [6]. However, other studies of neurosurgical departments having implemented STICH as principle guideline show that the rate of surgery is stable and in-hospital ICH mortality decrease. Nevertheless, it is not clear whether this is associated with longer-term mortality or improved functional outcomes [7]. Therefore, further studies and optimization of clinical criteria for surgical treatment of sICH is still in high demand. Proper decisive classification of patients based on symptoms and para-clinical findings would support decision-making.

Although it is the policy of our department to base sICH treatment on the recent STICH I and II studies, the decision to operate a patient with sICH is ultimately made by the consultant on-call and is expert level III evidence at best. As we had no local data to support our decisions, we set out to analyze our surgical results, considering morbidity, mortality and to identify subgroups. The aim of this study was to correlate pre-operative neurological status and neuroimaging findings with the clinical outcome of operated patients with sICH in order to help determine more accurate criteria for surgical intervention.

2. Materials and methods

In a retrospective manner, we evaluated all the medical records of all sICH patients in the Central Denmark Region who had been primarily operated after sICH from 2010 to 2016. The patient data was collected under a permission issued by the Danish Ministry of Health. All patients were assigned to the same neurosurgical department, and after treatment, all were referred to the neuro rehabilitation centre in the same region. All patient medical records in the region, as well as the rest of Denmark, are available in the national register system (E-journal) which makes the informative follow-up possible. Patient medical characteristics concerning pre-morbidity and preoperative status such as gender, age, performance status (based on WHO's classification), thrombolytic treatment, initial GCS, pupil status, and focal neurological deficits were registered.

Own home or nursing home accommodation of patients after discharge from the rehabilitation centre was used as evidence of functional adequacy and registered. The outcome of the surgery followed by rehabilitation was also enumerated either as the 6-month mortality rate or as the functional state, based on Glasgow Outcome Scale (GOS) after a year [8]. A good clinical outcome, equivalent to living self-reliantly, was considered as GOS ≥ 4 [8]. Intracerebral haematoma characteristics such as depth, volume, the involvement of basal ganglia, the openness of basal cisterns, the existence of intraventricular haemorrhage, and mass effect were also investigated and evaluated by a CT-scan. All patients with posterior fossa haemorrhage and secondary cause of bleeding such as an aneurysm, vascular malformation, neoplasm, and coagulopathy were excluded in line with the STICH studies. Outcome is given in percentages, group differences were analyzed by multiple linear regression tests, and p-values ≤0.05 was considered significant.

3. Results

Medical records from 153 patients were evaluated and 71 were included for further analysis after assessing inclusion criteria for spontaneous ICH.

The six-month mortality rate for all the patients was 18.3%. Results in comparison to the surgical results of the STICH 2 study are shown in Table 1. The median age of STICH subjects was 63 years and in our study the median age was also 63 (std. dev. 13.5 yrs. range 23–85 yrs.). Only 6.1% of the treated patients above 65 years survived to an independent life, against 42.1% of patients below 65 years with a good outcome after surgery (GOS 4–5). Table 2 illustrates GOS and mortality in the different data sets.

Of all the patients who received surgical treatment, 74.6% survived with GOS ≤ 3, while only 25.3% had shown improvement and recovery with GOS ≥ 4, which indicates the ability to live independently. About 40% of all treated patients were admitted to a nursing home after treatment.

To sum up, two logistic multiple linear regression models have been used on the data. One model focusing on the relationship between the mortality rate and some variables (called predictors), and another model focusing on the relationship between the good outcome probability (GOS > 3) and some predictors.

Table 1 – Comparison between the outcome of sICH-operations in Central Denmark Region and the STICH study.

	NK	STICH 1
Mortality (6 mths)	18.3%	36%
GOS 1–3	74.65%	38%
GOS 4–5	25.35%	26% (Rankin 0–3)
Average hospitalization day	10.4	NS[a]
Additional procedure (EVD, shunt)	18%	16%
Nursing home (among GOS 1–3)	56.34%	NS[a]

[a] NS, not stated.

Table 2 – Mortality and GOS of subjects based on different predictors.

		Death (proportion)		GOS more than 3 (proportion)		Death (number)		GOS more than 3 (number)	
		No	Yes	No	Yes	No	Yes	No	Yes
Gender	F	76.5	23.5	73.5	26.5	26	8	25	9
	M	86.5	13.5	75.7	24.3	32	5	28	9
Older than 65	No	94.7	5.3	57.9	42.1	36	2	22	16
	Yes	66.7	33.3	93.9	6.1	22	11	31	2
Antithrombotic treatment	No	85.7	14.3	67.4	32.7	42	7	33	16
	Yes	72.7	27.3	90.9	9.1	16	6	20	2
GCS less than 8	No	80.0	20.0	71.1	28.9	36	9	32	13
	Yes	84.6	15.4	80.8	19.2	22	4	21	5
Paresis	No	78.6	21.4	50.0	50.0	11	3	7	7
	Yes	82.5	17.5	80.7	19.3	47	10	46	11
Aphasia	No	80.0	20.0	77.1	22.9	28	7	27	8
	Yes	83.3	16.7	72.2	27.8	30	6	26	10
Pupil difference	No	82.5	17.5	67.5	32.5	33	7	27	13
	Yes	80.7	19.4	83.9	16.1	25	6	26	5
IVH	No	90.9	9.1	60.6	39.4	30	3	20	13
	Yes	73.7	26.3	86.8	13.2	28	10	33	5
Basal ganglia haemorrhage	No	87.0	13.0	66.7	33.3	47	7	36	18
	Yes	64.7	35.3	100.0	0.0	11	6	17	0
Mass effect	No	94.1	5.9	82.4	17.7	16	1	14	3
	Yes	77.8	22.2	72.2	27.8	42	12	39	15

To find a subset of the available predictive variables resulting in the best performing model, we used the stepwise regression method.

The result of this method showed that mortality rate depends on the age of the patient, and on whether the patient has mass effect and/or basal ganglia haemorrhage (model-I). Besides, the probability of a patient having a good outcome ($GOS > 3$) depends on the age of the patient, and on whether the patient has basal ganglia haemorrhage, IVH and/or pupil difference (model-II).

The p-value from testing whether a model including mortality rate versus all available predictive variables (called full model) differs from a model including mortality rate versus age, mass effect and basal ganglia haemorrhage equals 0.5417. This value suggests that none of the other variables such as gender, antithrombotic treatment, GCS, size of haematoma, paresis, aphasia, pupil difference, IVH and depth of bleeding were statistically significant. On the other hand, removing any of the following three variables would be significant; age (p-value = 0.00002), mass effect (p-value = 0.038), and basal ganglia haemorrhage (p-value = 0.040). Likewise, the p-value from testing whether a model including probability of good outcome ($GOS > 3$) versus all available predictive variables differs from a model including probability of good outcome versus age, basal ganglia haemorrhage, IVH, and pupil difference equals 0.302. Therefore, none of the other variables were statistically significant. However, removing any of the following four variables would be significant; age (p-value = 0.00019), basal ganglia haemorrhage (p-value = 0.006), IVH (p-value = 0.037), and pupil difference (p-value = 0.099).

Age has the lowest p-value in both models, which suggests a strong association of age with the probability of surviving or having a good outcome. Basal ganglia haemorrhage has also a very significant association with good outcome. As an example considering the effect of basal ganglia haemorrhage on GOS, the chance of surviving to an independent life for a 30 yrs. old subject with basal ganglia haemorrhage and without IVH and pupil difference is estimated to 2.46×10^{-7}, whereas the chance for a 30 yrs. old subject without basal ganglia haemorrhage and IVH and pupil difference is estimated to 0.961.

The estimated coefficients for age (0.1695), mass effect (2.1791) and basal ganglia haemorrhage (1.64) in model-I are positive. This point is illustrated in Fig. 1. The black line in this figure shows the estimated probability of mortality for patients who have mass effect and basal ganglia haemorrhage at different ages. The light green, dark green and blue lines respectively show these estimations for the patients who do not have basal ganglia haemorrhage but mass effect, do not have mass effect but basal ganglia haemorrhage and finally have neither. Clearly, the estimations for patients with both basal ganglia haemorrhage and mass effect is higher. Furthermore, the estimated probability of mortality for patients increases with the age. On the other hand, the estimated coefficients for age (−0.096), basal ganglia haemorrhage (−18.44), IVH (−1.53) and having pupil difference (−1.19) in model II are negative. The negative coefficients suggest that if all other variables are equal, the older people who have basal ganglia haemorrhage, IVH and pupil difference are less likely to have an independent life, i.e. the estimated probability of having good outcome decreases with the age of patients. This point is illustrated in Fig. 2.

4. Discussion

In order to facilitate decision-making and evaluate our regional treatment efficacy in sICH, we performed a retrospective study of morbidity and mortality in our surgically treated patients. Our results after logistic multiple linear regression

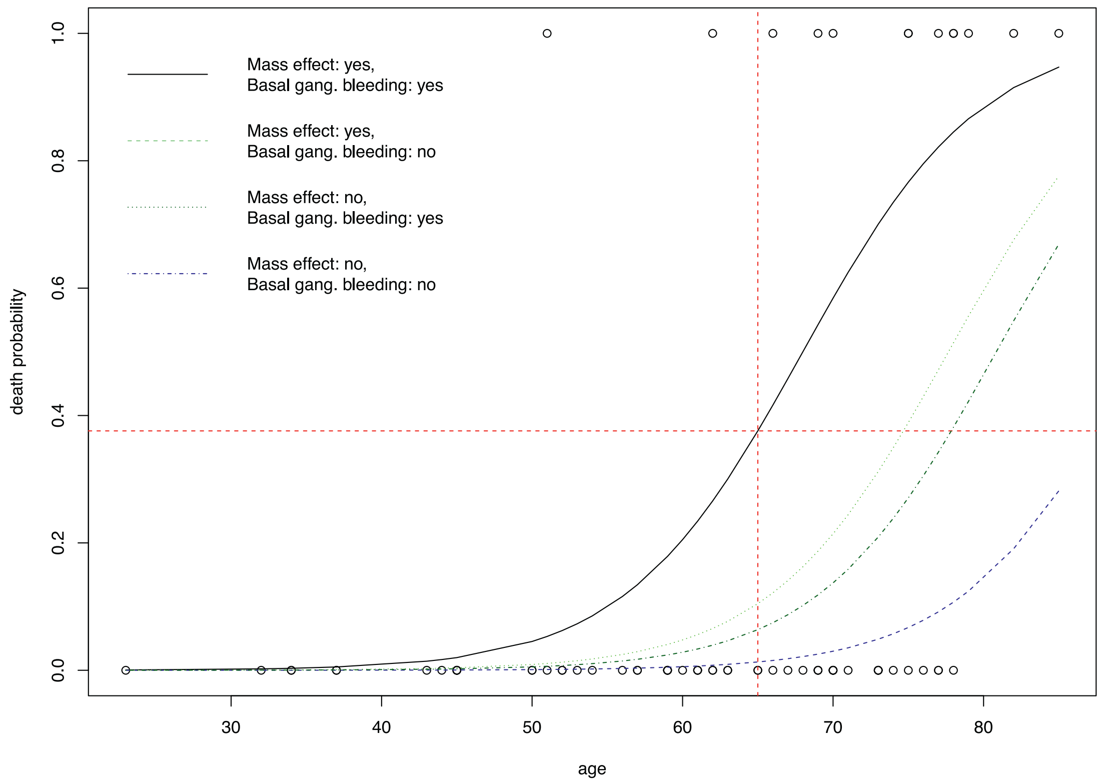

Fig. 1 – The estimated mortality rate vs. age considering mass effect and basal ganglia haemorrhage.

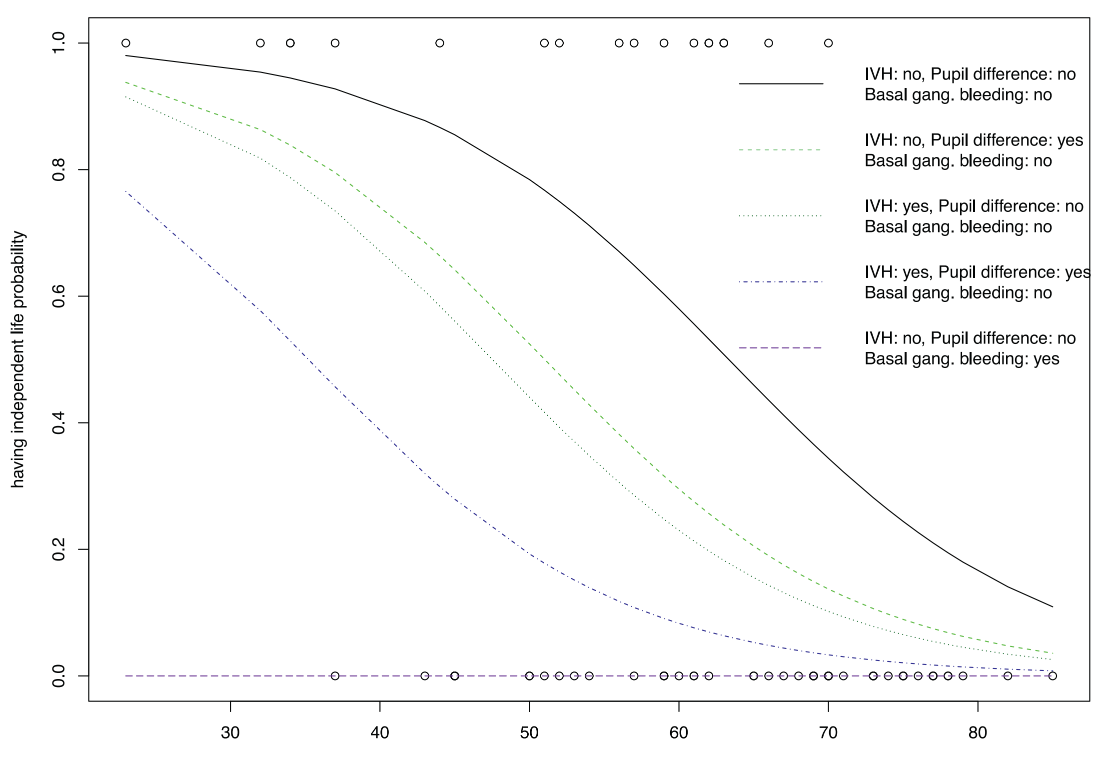

Fig. 2 – The estimated probability of good outcome (GOS > 3) vs. age considering basal ganglia haemorrhage, IVH, and pupil difference.

analysis were comparable to international studies and showed that despite surgical treatment, sICH is still a very serious event, with a mortality rate of 18.3% and only 25.3% survival chance for an independent life (GOS > 3). These numbers are worryingly close to previous data and indicate that surgery may improve the patients' chance of surviving sICH, but only by increasing the number of patients who are care-dependent, particularly considering patients over 65-years old. This is not a surprising outcome but this study actually is the first study to document that age is a factor to be considered in the decision-making, when treating intracerebral hematomas in a neurosurgical unit.

Considering mortality rate, only age, basal ganglia haemorrhage and mass effect are significant as variables. Age has the lowest *p*-value suggesting a very strong association of age with the probability of surviving. The positive coefficient for age, basal ganglia haemorrhage and mass effect suggests that all other variables being equal, the older people, who have mass effect and basal ganglia haemorrhage are less likely to survive.

This study shows that older people who have basal ganglia haemorrhage, IVH and pupil difference are less likely to have an independent life after surgery. As shown in Fig. 2, considering negative coefficient between good outcome and having IVH or pupil difference, especially when patients are older or has basal ganglia haemorrhage, performing surgery may be worthless or at least cannot provide a better prognosis.

According to the results, age and basal ganglia haemorrhage have strong effect both on mortality and on good outcome, which means that performing surgery on older patients with basal ganglia haemorrhage is almost without survival chance (Figs. 1 and 2). Interestingly, bleeding in the basal ganglia region is a strong predictor of having poor outcome even in younger subjects without other variables.

As the study subjects had already been selected for operation, Bias is conceivable in our study; however, the study can be considered as an evaluation of the effect of the current surgical inclusion criteria in our region, which is in line with the STICH studies. Furthermore, in the STICH studies, initially randomized patients for conservative management, could also undergo surgery depending on the clinically judgement of the attendant physician [9], which is almost like the policy of our department.

In brief, the STICH study concluded that there was no general advantage of surgery, but that a slight benefit from surgery was probable if the haematoma was less than 1 cm from the cerebral surface on conscious patients. STICH II went on to look more closely at this subgroup of patients, only including conscious patients with smaller haematomas less than 1 cm from cerebral surface. Considering inclusion criteria, STICH II showed that the number of patients eligible for recruitment is low, indicating that an aggressive recruitment approach for surgery may be beneficial [10]. Results were once again sparse, but the authors ended up concluding that this subgroup (of the subgroup) would benefit from surgical treatment. The conclusions of these two major studies are still debated. Similarly, there are some shortcomings in the STICH studies such as the surgical approach, which was mostly (77%) craniotomy. For this reason, conclusions cannot be made on the effect of other surgical approaches. Furthermore, the median time from onset to surgery was relatively long (about 30 h), so the benefits of surgery e.g. within 12 h remain unresolved [9]. Some studies have shown that there is no difference between patients receiving an early haematoma evacuation (8 h between onset and surgery) and conservative treatment, however the number of subjects in the study was very low [11].

Moreover, the survival advantage in STICH studies appears to be greatest when the prognosis is poorer (Glasgow Coma Score 9–12), and when patients are randomly assigned to surgery within 21 h [5], which means the effect of GCS on the result of surgery is probably affected by the judgement of the surgeons. Although our study does not show a strong correlation between GCS and good clinical outcome, it is maybe more careful to describe a potential trend towards a correlation.

Our retrospective study did not let us to choose the time of surgery or surgical technique, which was mostly craniotomy, like STICH studies, but it seems relevant to design some studies in the future with other methods, and definitely with a shorter period between bleeding onset and surgery.

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Clinical implications

Based on our results, it is our opinion that the surgery of sICH should be reserved for conscious patients with a favourable prognosis, who deteriorate after a period of observation, and that surgery only has a role in treating sICH if patients are carefully selected, by taking haematoma characteristics and patient age into consideration in order to improve outcome.

Conflict of interest

None declared.

Ethics

Ethical approval was not necessary for the preparation of this article.

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