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Variation in medical management and neurosurgical treatment of patients with supratentorial spontaneous intracerebral haemorrhage

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Abstract

Introduction: The role of surgery in spontaneous intracerebral haemorrhage (sICH) remains controversial. This leads to variation in the percentage of patients who are treated with surgery between countries.

Patients and methods: We sent an online survey to all neurosurgeons (n = 140) and to a sample of neurologists (n = 378) in Dutch hospitals, with questions on management in supratentorial sICH in general, and on treatment in six patients, to explore current variation in medical and neurosurgical management. We assessed patient and haemorrhage characteristics influencing treatment decisions.

Results: Twenty-nine (21%) neurosurgeons and 92 (24%) neurologists responded. Prior to surgery, neurosurgeons would more frequently administer platelet-transfusion in patients on clopidogrel (64% versus 13%; p = 0.000) or acetylsalicylic acid (61% versus 11%; p = 0.000) than neurologists. In the cases, neurosurgeons and neurologists were similar in their choice for surgery as initial treatment (24% and 31%; p = 0.12), however variation existed amongst physicians in specific cases. Neurosurgeons preferred craniotomy with haematoma evacuation (74%) above minimally-invasive techniques (5%). Age, Glasgow Coma Scale score and ICH location were important factors influencing decisions on treatment for neurosurgeons and neurologists. 69% of neurosurgeons and 80% of neurologists would randomise patients in a trial evaluating the effect of minimally-invasive surgery on functional outcome.

Discussion: Our results reflect the lack of evidence about the right treatment strategy in patients with sICH.

Conclusion: New high quality evidence is needed to guide treatment decisions for patients with ICH. The willingness to randomise patients into a clinical trial on minimally-invasive surgery, contributes to the feasibility of such studies in the future.

Keywords
Intracerebral haemorrhage, treatment variation, neurosurgery

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Introduction

Spontaneous intracerebral haemorrhage (sICH) is the deadliest stroke subtype with a 30-day case fatality up to 40%.[1,2] Of those who survive, only 12–42% of patients regain independence within 6–12 months after sICH.[1,2] To date there is no treatment of proven benefit,[3] apart from organised stroke unit care[4] and possibly early control of elevated blood pressure.[5–7] In particular the role of surgery in supratentorial sICH remains controversial. This controversy leads to

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large variation in the percentage of patients who are treated with surgery between countries,[8] with a relatively larger proportion of patients in some Asian countries than in other parts of the world.[9] The guidelines of the American Stroke Association and of the European Stroke Organisation state that the usefulness of surgery in patients with supratentorial ICH is not well established, but might be considered as a life-saving measure.[10,11] In a systematic review and meta-analysis of 21 randomised controlled trials, including the neutral results of the MISTIE III trial, we recently showed that surgical treatment might be beneficial (RR 1.40, 95% CI 1.22–1.60 for surgery compared to medical management), in particular with minimally invasive procedures (RR 1.47, 95% CI 1.26–1.72) and when performed early after symptom onset.[12] However, when the analyses were restricted to the four high quality studies, the effect of surgical treatment was no longer statistically significant.[12] Platelet transfusion seems inferior to standard care for patients taking antiplatelet therapy before presenting with sICH and in whom no surgical evacuation is planned.[13] However, it is unclear whether patients undergoing surgical evacuation should be treated with platelet transfusion and platelet transfusions are still commonly used in the acute setting prior to surgery.[14] Administration of glucocorticoids (such as dexamethasone)[15] and osmolar therapy[16] have not been shown to improve outcome after sICH. Nevertheless, in recent randomised clinical trials of medical management of ICH, 62-84% of patients were treated with osmolar therapy.[5,7] Current guidelines recommend hyperosmotic therapy if a patient has acute elevated intracranial pressure with signs of herniation, but advice against the use of glucocorticoids.[10,11,17,18]

Prediction scores used in the acute phase have limited accuracy for the prediction of 30-day mortality and functional outcome,[19–23] and appear especially unreliable for the higher scores that predict poor outcome.[24] Furthermore, these prediction scores do not facilitate physicians in their choice for a certain treatment strategy. The decision to perform surgery for supratentorial sICH often depends on assumptions based on personal experiences.[25]

Active treatment, including rapid anticoagulant reversal, intensive blood pressure lowering and better access to neurosurgery, has been shown to reduce case fatality at 30 days by a third.[26]

The Dutch Intracerebral Haemorrhage Surgery Trial (DIST) pilot study [www.dutch-ich.nl] is currently assessing the safety and feasibility of minimally-invasive, endoscopy-guided surgery for supratentorial sICH within eight hours after symptom onset in the Netherlands. To inform the design of a planned randomised phase three clinical trial, we aimed to explore the current variation in medical and neurosurgical management amongst neurologists and neurosurgeons in the Netherlands, using an online questionnaire. In addition, we assessed which patient and haemorrhage characteristics would influence treatment decisions.

Methods

We designed two separate questionnaires, one for neurologists and one for neurosurgeons, using the web survey tool SurveyMonkey (http://www.surveymonkey.com). Questionnaires consisted of three parts (Online Appendix 1). The first part comprised six questions about the respondent. Part two comprised questions about the management in supratentorial sICH in general: the use of prognostic tools for decisions on treatment, the preferred surgical approach and the administration of dexamethasone, hypertonic saline and platelet transfusion. In the third part we asked questions about the initial treatment strategy, the treatment strategy in case of clinical deterioration, the preferred surgical approach and optional placement of an external ventricular drain, and the administration of dexamethasone, hypertonic saline and a platelet transfusion in six cases of patients who had presented with a supratentorial sICH (Table 1). We selected cases that differed regarding age, Glasgow Coma Scale score on admission, use of antiplatelets or anticoagulants at the time of admission, haematoma volume and location, and presence of intraventricular blood and a spot sign on CT-angiography (Table 1). These six cases were selected because they led to controversy about the right treatment strategy within our study team. Additionally, we asked the respondents about the case-specific factors that influenced their treatment decisions, the certainty about the chosen treatment strategy and whether they would randomise this patient in a clinical trial, assessing the effect of minimally-invasive surgery on functional outcome. The survey was open for response between December 2018 and March 2019. We sent the questionnaire for neurosurgeons to all Dutch neurosurgeons (n = 140; mean age 47 years, 89% male) via The Netherlands Society for Neurosurgery. We sent the questionnaire for neurologists (n = 999; mean age 49 years, 48% male) to a selection of five neurologists from each of the Dutch hospitals (378 neurologists from 73 hospitals). We specifically selected neurologists who were a member of the Neurovascular Workgroup of The Netherlands Society of Neurology or who had stroke as their area of interest as mentioned on the hospital website, totalling 378 potential respondents. We sent reminders after four and twelve weeks. Two weeks later, the survey was closed. All data were analysed anonymously. We included all received answers in our analysis, and did

Table 1. Cases with supratentorial spontaneous intracerebral haemorrhages.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age (years)	80	68	31	67	54	58
Medication	None	Acenocoumarol, HCT	None	Metformin	None	Clopidogrel, Lisinopril
GCS score	$E4M5V_{aphasia}$	E2M5V1	E4M6V3	E1M3V2	E1M5V2	E3M4V2
Pupillary reflex (right/left)	PEARL	PEARL	PEARL	Wide and not reactive/ normal and reactive	PEARL	PEARL
Location ICH	Lobar	Deep	Lobar	Deep	Lobar	Deep
Volume ICH (mL)	36	18	36	45	42	32
IVH	None	Minimal	None	Present	Minimal	Present
Spot sign[a]	No	No	No	No	Present	No

GCS = Glasgow Coma Scale, HCT = hydrochlorothiazide, ICH = Intracerebral haemorrhage, IVH = intraventricular haemorrhage, PEARL = pupils equal and reactive to light.
[a]None of the CT- angiographies showed an underlying (macrovascular) cause.

not restrict to fully completed surveys, in order to reduce selection bias. Descriptive statistics were used as appropriate. Differences between neurologists and neurosurgeons were compared using the χ^2-test, Fisher's exact test or Mann-Whitney U test as appropriate.

Results

A total of 121 (23%) persons responded, of whom 29 (21%) neurosurgeons and 92 (24%) neurologists. Mean age and median duration since completion of training were similar (Table 2). Neurosurgeon respondents more often worked in a university hospital (76%) than neurologist respondents (16%) and less often reported stroke as their specific field of interest (41% versus 65%; Table 2). Mean age and percentage males of respondents were similar to the those of all neurosurgeons and to those of all neurologists.

General questions

The neurosurgeons completed 97% of the general questions and the neurologists 100%. Less than half of the neurosurgeons and neurologists (31% versus 47%; $p = 0.125$) used a prognostic instrument to determine outcome after sICH. Those who did, most frequently used the ICH-score (63% of neurosurgeons and 79% of neurologists) or the ICH-GS score (25% of neurosurgeons and 19% of neurologists). If neurosurgeons decided to treat a patient with surgery, the preferred approach was craniotomy with evacuation of the haematoma (78%). The vast majority of neurosurgeons (75%) would never prescribe dexamethasone perioperatively, although some (14%) would occasionally. Neurosurgeons more frequently than neurologists considered administration of hypertonic saline if a patient with supratentorial sICH would deteriorate (57% versus 16%; $p = 0.000$). Neurosurgeons more frequently than neurologists advised platelet transfusion prior to surgery when a patient uses clopidogrel (64% versus 13%; $p = 0.000$) or acetylsalicylic acid (61% versus 11%; $p = 0.000$; Online Appendix 2)

Physicians with vascular expertise (both neurosurgeons and neurologists) more frequently used a prognostic instrument to determine outcome after supratentorial sICH than physicians without specific vascular expertise (57% versus 23%; $p = 0.000$). They advised platelet transfusion prior to surgery less frequently than physicians without vascular expertise, when a patient uses clopidogrel (17% versus 38%; $p = 0.003$) or acetylsalicylic acid (15% versus 33%; $p = 0.013$). For the other questions in this second part of the survey, there were no differences between physicians (both neurosurgeons and neurologists) with or without vascular expertise (Online Appendix 2).

Case-specific questions

Neurosurgeons completed 86% of the questions about the initial treatment strategy, and neurologists completed 84% (Online Appendix 3). For all six cases together, neurosurgeons and neurologists were similar in their choice for surgery as initial treatment (24% and 31%; Online Appendix 3). Neurosurgeons proposed conservative treatment as initial strategy more often than neurologists (69% versus 59%; $p = 0.04$). In initially conservatively treated patients who deteriorate, neurosurgeons would more often than neurologists decide to operate (58% versus 41%; $p = 0.004$).

In case of medical treatment, neurosurgeons would admit patients to the ICU rather than to the stroke-unit more frequently than neurologists (34% versus 19%; $p = 0.002$).

Neurosurgeons and neurologists were similar in their choice for palliative care as initial treatment (7% and 10%; $p = 0.29$), and in these situations both

Table 2. Characteristics of the respondents.

	Neurosurgeons N = 29	Neurologist N = 92	P-value
Age (years), mean (SD)	46 (7.9)	46 (9.6)	0.961[a]
Males, n (%)	23 (79)	55 (60)	0.055[b]
Years since finishing residency, median (IQR)	10 (6;21)	11 (5;21)	0.763[a]
University hospital (current location), n (%)	22 (76)	15 (16)	0.000[b]
Specific expertise in neurovascular diseases, n (%)	12 (41)	60 (65)	0.023[b]

IQR = interquartile range; SD = standard deviation.
[a]Mann Whitney U test.
[b]Chi-squared test.

would often consult a palliative care team (neurosurgeons 73% and neurologists 54%; p = 0.33; Online Appendix 3). In one case (case 4) palliative care was chosen by most physicians, but with large variation both amongst neurosurgeons and amongst neurologists: 38% of neurosurgeons and 58% of neurologists chose palliative care, whereas surgical treatment was preferred by 58% of neurosurgeons and 27% of neurologists. Conservative but active treatment would be advised by 4% of neurosurgeons and 15% of neurologists (Online Appendix 3). In the 31-year-old patient (case 3) with a lobar hematoma (36 mL; GCS score E4M6V3), 8% of neurosurgeons chose surgery as the preferred treatment, compared to 43% of neurologists (p = 0.001; Online Appendix 3). In the 80-year-old patient (case 1) with a lobar hematoma (36 mL, GCS score E4M5Vaphasia) none of the neurosurgeons chose surgical treatment, whereas 13% of the neurologists would consult a neurosurgeon (p = 0.06; Online Appendix 3). In cases 5 and 6, the proportion of neurosurgeons and neurologists who chose surgery as initial treatment were similar, but amongst these specialists there was large variation. As an example, in a 54-year-old patient with lobar hematoma (42mL, spot sign on CT-a, case 5), half of the neurosurgeons and neurologists would recommend surgery, whereas no neurosurgeon or neurologist would start palliative care initially (Online Appendix 3).

Neurosurgeons preferred craniotomy with haematoma evacuation in the majority of decisions (74%), above decompressive (hemi)craniectomy with (6%) or without (15%) haematoma evacuation and minimally invasive techniques (5%; Online Appendix 3). In case 6 (58-year-old patient using clopidogrel) 33% of the neurosurgeons who recommended surgery, advised platelet transfusion preoperatively. Many (47%) neurologists would leave the decision for a preoperative platelet transfusion to the neurosurgeon (Online Appendix 3).

Hypertonic saline was recommended in only a minority of the decisions by either neurosurgeons or neurologists (7% and 6%; Online Appendix 3). In patients for whom surgery was recommended, either initially or after neurological deterioration, neurosurgeons more frequently than neurologists advised dexamethasone, but only in a minority of cases (9% versus 2%; p = 0.006; Online Appendix 3).

Neurosurgeons were more frequently than neurologists very, or extremely, certain about their decision for a specific treatment (41% versus 29%; p = 0.006), whereas neurosurgeons less often than neurologists expressed that they were uncertain or very uncertain about their decision for a specific treatment (7% versus 17%; p = 0.003) (Online Appendix 3 and 5).

Factors influencing decision-making

Overall, neurologists and neurosurgeons regarded GCS score, age and haematoma location as the most important factors that influenced their decision for a chosen treatment strategy. Factors that were regarded less important were intraventricular extension of the haemorrhage, the use of medication, pupillary response to light and the side of the haemorrhage (Figure 1). The most important factors to choose for a palliative treatment were age and initial GCS score (Online Appendix 4). In case 5, for who 91% of neurosurgeons and 46% of neurologist preferred a surgical approach, the presence of a spot sign was not considered important by most (Figure 1 and Online Appendix 4).

Randomisation in a trial

The majority of neurosurgeons and neurologists were willing to randomise patients into a randomised controlled trial investigating the effectiveness of minimally invasive surgery for ICH, although neurologists were more likely than neurosurgeons to randomise patients (neurosurgeons 69% versus neurologist 80% of treatment decisions in the 6 cases; p = 0.006; Online Appendix 3). The largest variation between neurosurgeons and neurologists was present in case 2: 46% of neurosurgeons and 84% of neurologists would randomise this patient into a trial (p = 0.000), whereas 4% of neurosurgeons and 27% of neurologists preferred surgical treatment in this case (p = 0.013).

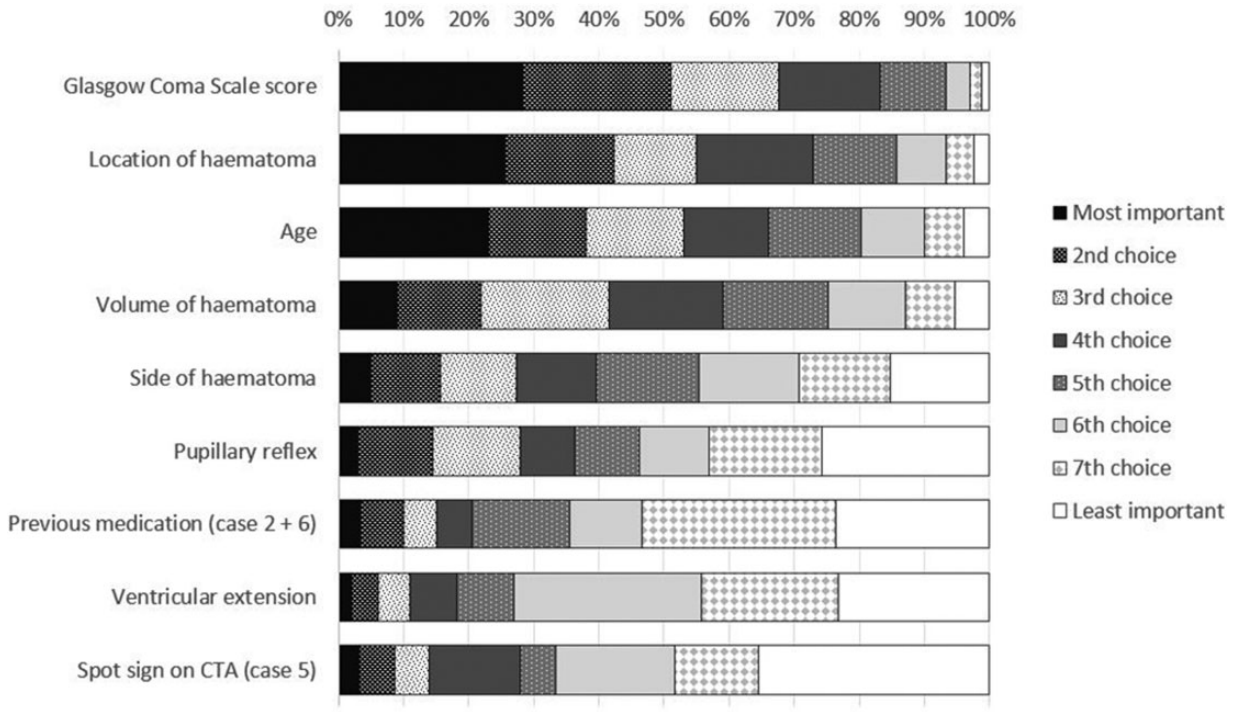

Figure 1. Factors that influenced decision making (all six cases together).

In case 4, 52% of neurosurgeons and 49% of neurologists would randomise this patient into a randomised trial ($p = 0.81$), whereas 58% of neurosurgeons and 27% of neurologists preferred surgery as initial treatment in this case ($p = 0.005$).

Discussion

This study shows variation amongst Dutch neurosurgeons and neurologists, and between these specialists, in treatment decisions whether or not to perform surgery in patients with supratentorial sICH. In case neurosurgeons opt for surgery, most prefer craniotomy over minimally-invasive procedures or hemicraniectomy. GCS score, age and location of the ICH were considered the most important factors for decisions on treatment. In patients on antiplatelet therapy, neurosurgeons are more likely to administer a platelet transfusion preoperatively than neurologists. A large majority of both neurosurgeons and neurologists would be willing to randomize patients in a trial evaluating the effect of minimally-invasive surgery on functional outcome.

Previous studies showed large variation between countries in the percentage of patients with supratentorial sICH who are treated with surgery (2–74%).[8] A recent survey amongst German neurosurgeons and neurologists also found variation in the treatment of intracerebral haemorrhage amongst neurosurgeons and neurologists. However, in this study there were no statistically significant differences between neurologists and neurosurgeons regarding the decision for a surgical or conservative treatment strategy for patients with supratentorial sICH.[27] An important difference with our survey is that in the German study the survey was sent only to neurosurgeons, neurointensivists and neurologists within neurosurgical centres, and did not include neurologists in general hospitals. Furthermore, they excluded 12% of the surveys because they were not fully completed. Finally, in this German study surgical treatment did not distinguish between haematoma evacuation and placement of an external ventricular drain.[27] In a survey amongst 742 American neurologists and neurosurgeons, presenting one moderately severe and one severe case of ICH, treatment intensity recommendations varied widely between and amongst physicians.[28]

Our finding that less than half of neurosurgeons and neurologists use a prognostic instrument to determine clinical outcome, may contribute to the observed variation in treatment recommendations. The aforementioned American survey showed that the use of a prognostic score decreases variation in treatment intensity recommendations for patients with supratentorial sICH.[28] Nevertheless, it is important to note that commonly used prognostic scores vary widely in their ability to predict outcome accurately, with a c-statistic varying from 0.62-0.88 for the prediction of 3- and

12-month mortality,[22] and may be particularly less reliable for the highest scores that predict poor outcome.[24] Only few of these scores can predict functional outcome beyond 30 days after symptom onset.[22] Although our study showed a relatively low percentage of physicians using a prediction tool, the factors age and GCS score, which are important components in all prediction scores, were considered important factors to influence decision-making. A previous study in 1,364 ICH cases in the United Kingdom found that GCS score alone was equivalent to the ICH-score, ICH-GS score or modified ICH score for prediction of 30-day mortality.[29] In contrast, age alone was not equivalent to any of these scores.[29] A Finnish study in 882 ICH cases showed similar results, with a weak association between age and mortality.[22] A Chinese study that randomised patients with basal ganglia sICH (10–100 mL) between endoscopic surgery and conservative treatment, found that GCS score, ICH volume and intraventricular extension were the only significant predictors of mortality at 6 months and good functional outcome at 12 months, and age was not a predictor.[30]

CT-angiography spot sign did not affect the decision for surgery in our study, and was not valued as an important factor that influenced the decision-making. This reflects the limited added value in prediction of prognosis when added to the ICH-score.[31,32] However, the importance of a spot sign for the indication for surgical treatment is contradictory. Some have suggested a decrease in mortality after surgery in spot sign-positive sICH patients compared to spot-sign positive patients that received conservative care.[33] Others found an increased risk of intraoperative bleeding,[34] recurrent postoperative haemorrhage[34,35] and larger residual ICH volumes[34] in spot sign-positive patients, compared to surgical patients without a spot sign. Some authors argue that the absence of a spot sign can be used to indicate that ultra-early stereotactic aspiration can be performed safely.[36] All these studies were small, not randomised and included either spot sign-negative patients only,[33,36] or surgically treated patients only.[34,35]

We found variation amongst physicians regarding preoperative platelet transfusion in patients on antiplatelet therapy. Data on the effect on outcome after platelet transfusion in patients with sICH undergoing surgery are currently lacking. In a randomised trial in 190 patients with sICH on antiplatelet therapy, patients had a two times higher chance on poor functional outcome (mRS 4-6) at three months after platelet transfusion, than after standard care.[13] However, this trial excluded patients with planned surgical evacuation, or patients with infratentorial or intraventricular haemorrhage, because they are more likely to undergo surgical procedures.[13] In daily practice, especially in the acute setting, platelet transfusions are commonly used to reverse coagulopathy preoperatively in neurosurgical patients on antiplatelet therapy.[14]

In our study, the finding that dexamethasone is prescribed only in a minority of cases is in line with the absence of evidence to support routine use of glucocorticoids in patients with sICH,[3,11,15] and that use of dexamethasone may be associated with increased risk of adverse effects.[11,15] Hypertonic saline was infrequently prescribed in our study, even in a patient who deteriorates. This is in line with previous studies[7] and meta-analysis[16] that have shown no benefit of treatment with mannitol.[9] However, particularly in Asia, patients with raised intracranial pressure are commonly treated with osmolar therapy.[3,37]

The observed variation in treatment recommendations and the variation in certainty about the decisions that were made in our cases reflect the lack of evidence about the right treatment strategy and the controversial influence of the CT-a spot sign. Recent narrative[9,37] and systematic reviews[12,38,39] emphasise the lack of high quality evidence and the need for high quality studies of treatment strategies, in particular surgery. In this light, it is reassuring that the majority of neurosurgeons and neurologists were willing to randomise patients with supratentorial sICH in a trial assessing the effect of minimally-invasive surgery on functional outcome.

Strengths of our study are that we included neurologists and neurosurgeons from tertiary referral centres as well as from general hospitals and did not restrict our survey to physicians specialised in neurovascular diseases. In daily practice, all neurologists or neurosurgeons, and not only those specialised in neurovascular diseases, will have to decide on the treatment strategy for patients with supratentorial sICH in the acute phase. To try to reduce selection bias, we included all received answers, despite the fact that some respondents had not fully completed our survey. Our survey was set up as a standardised, case-related questionnaire, with cases that differed regarding age, clinical state and haemorrhage characteristics, to resemble daily clinical practice. In contrast with previous studies, we also assessed determinants of treatment decisions and investigated the certainty of the physicians about the treatment strategy they proposed.

Our study also has limitations. The response rate of 23% was relatively low, although similar to that in previous surveys on ICH,[27,28] and traumatic brain injury.[40] However, our sample of neurosurgeons and neurologists was representative for these groups in

the Netherlands with respect to their mean age and sex distribution. Another limitation of our study is that treatment decisions on cases presented in a survey are never completely representative of clinical practice. Wishes and distress of family members, pressure exerted on physicians in an acute care setting, or logistical arguments that may play a role in clinical practice, may influence treatment decisions in clinical practice. Finally, our survey was conducted within the Netherlands, and results may not all be generalizable to other healthcare settings.

Conclusions

The large variability in treatment decision regarding surgery for spontaneous supratentorial ICH in this study indicates that new high quality evidence is needed to guide physicians in their treatment decisions in these patients. The willingness of both neurosurgeons and neurologists to randomise patients into a clinical trial that assesses whether minimally-invasive surgery improves functional outcome after sICH, contributes to the feasibility of such studies in the future.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

All participants in the survey consented to participate by replying to the survey. No informed consent was obtained from the patient(s) that represented the cases. Information was fully anonymized. Approval of the ethics committee was not obtained.

Guarantor

CJMK.

Contributorship

All authors reviewed and edited the manuscript and approved the final version of the manuscript.: LS, FHBMS, and CJMK designed the project and wrote the protocol. The survey was designed by LS, FAEJ, FHBMS, CJMK, and RD. Data collection was performed by LS and FAEJ with oversight of FHBMS and CJMK. LS and FAEJ processed the data and performed the data analyses, with oversight from FHBMS, RD, and CJMK. Data interpretation was performed by all authors: LS, FAEJ, FHBMS, HDB, RD, WPV, and CJMK. The draft of the manuscript was written by LS, FHBMS, and CJMK. FAEJ, HDB, RD, and WPV contributed to the writing of the manuscript and critically revised the work for important intellectual content where required, approved the final version to be published and agreed to be accountable for all aspects of the work.

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Supplemental material

Supplemental material for this article is available online.

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