Evacuation of Intracerebral Hematoma Is Likely to Be Beneficial

Kazuo Minematsu, MD, PhD

A new era has begun for acute ischemic stroke since the success of a clinical trial of hyperacute thrombolytic therapy. By contrast, there is yet time before daybreak in the management of acute intracerebral hematoma (ICH). Although many therapeutic options, including surgical evacuation, are described in stroke textbooks and guidelines for patients with acute ICH, nothing has yet been proven in large-scale randomized clinical trials. Only a few subgroups of patients with ICH are listed as candidates for surgical treatment. They are patients with large (>3 cm) cerebellar hematoma and young patients with a lobar hematoma who are clinically deteriorating. Patients with small hematoma and with deep coma should not be treated surgically. For all other ICH patients, the best therapeutic option remains unclear.

In the first and largest controlled trial by McKissock et al, no benefit from surgical evacuation was demonstrated in regard to either mortality or morbidity. However, many patients with ICH have been treated surgically since this negative study. For example, more than 7000 patients with ICH per year are estimated to receive surgical treatment for hematoma evacuation in the United States. The situation is similar in Japan.

In a retrospective, nonrandomized study in Japan, Kanayama and Kuroda compared the effects of surgical evacuation on mortality and morbidity in 3638 patients with putaminal hemorrhage to those of medical management in 3372. On the basis of the results, they recommended surgical treatment if the hematoma is larger than 30 mL in extent and the level of consciousness is somnolent to semicomatose. They also found that functional outcome was better in patients undergoing stereotaxic aspiration than in those with conventional evacuation, if the patient’s preoperative consciousness was normal or stuporous. Most of neurosurgeons and neurologists in Japan accept their opinion that hematoma evacuation can reduce the early mortality. The conclusion of this study, particularly concerning the beneficial effect of surgical evacuation on functional outcome, has been criticized, mainly because of the lack of randomized comparisons.

Recently, results of several randomized clinical trials were published. Their sample sizes were small, and therefore their results were inconclusive. In a systematic review by Hankey and Hon, the pooled results of the 3 randomized trials of open craniectomy and 1 trial of endoscopic evacuation for supratentorial ICH indicated a nonsignificant increase in odds of death and dependency at 6 months for patients treated surgically. More recent meta-analysis excluded the study by McKissock et al and a Chinese trial, because of problems of quality.

The Surgical Trial in Intracerebral Hemorrhage (STICH), a multicenter, randomized controlled trial, is in progress to evaluate the role of surgery in a total of 1000 patients with spontaneous supratentorial ICH. Unfortunately, the study protocol is rather ambiguous. A patient can be included when the surgeon is uncertain about the need for surgical evacuation. The neurosurgeon can use the method preferred for surgical evacuation. The study may have a danger of surgeon’s or institutional bias.

It is a reasonable concept that brain damage due to ICH may be minimized by removal of the hematoma. It may reduce the mass effect, block the release of toxic products from the hematoma, and prevent early hematoma enlargement occurring early after onset of ICH. I believe that hematoma evacuation can reduce not only mortality but also morbidity if several critical conditions are optimized. They are clinical and neurological conditions of patients, the extent and site of hematoma, the method of hematoma evacuation (conventional versus stereotaxic or endoscopic evacuation), the time window of surgery, and additional medications to facilitate complete evacuation (use of thrombolytic agents). In order to establish the best therapeutic option for acute ICH patients, further studies will be needed even after the STICH study.

References
Evacuation of Intracerebral Hematoma Is Likely to Be Beneficial—Against

Graeme J. Hankey, MBBS, MD, FRCP, FRCP (Edin), FRACP

The 4 recognized surgical procedures to evacuate an intracerebral hematoma (ICH) are simple aspiration, craniotomy with open surgery, endoscopic evacuation, and stereotactic aspiration. Their use in clinical practice is inconsistent. In some countries (eg, the Netherlands) they are rarely performed; in others (eg, the United States) they are undertaken in about 20% of patients with ICH; and in others (eg, some centers in Germany and Japan) they are offered to 50% or more of patients. Such wide variation in practice reflects uncertainty about the effectiveness and risks of surgery, due to a lack of appropriate evidence. The required evidence is evaluation by large randomized controlled trials (RCTs), because RCTs minimize systematic biases and random errors that can otherwise falsely exaggerate or completely mask any real modest overall treatment effect of surgery (favorable and unfavorable).

What Is the Evidence for Surgical Evacuation of Supratentorial Hematoma?

Simple Aspiration
Simple aspiration was abandoned before it was properly evaluated because only small amounts of clot could be removed, and it could precipitate “blind” re-bleeding.

Craniotomy With Open Surgery
A systematic review of 5 RCTs in a total of 305 patients indicates that craniotomy and open surgery combined with best medical therapy is associated with a nonsignificant increase in odds of death or dependency by 1.46 (95% CI: 0.87 to 2.45) compared with best medical therapy alone (surgery, n = 114/147 [77.6%]; control, n = 111/158 [70.2%]). After excluding the largest trial, because it was undertaken before CT brain scan, the 4 trials showed a modest nonsignificant decrease in death or dependency (odds ratio [OR] 0.90, 95% CI: 0.40 to 2.03) (surgery, 43/58 [74.1%]; control, 51/67 [76.1%]).

Endoscopic Evacuation
One RCT indicates that endoscopic evacuation by stereotactic methods is associated with a statistically nonsignificant, but substantial, 54% (95% CI: −4% to 80%) reduction in odds of death or dependency (surgery, 28/50 [56%]; control, 37/50 [74%]). The absolute risk reduction was 18% (95% CI, −3% to 36%).

Stereotactic Aspiration
Despite reports of stereotactic aspiration without endoscopy, usually combined with installation of fibrinolytic agents, in more than 500 patients with supratentorial intraparenchymal or intraventricular hemorrhage, this technique has not been evaluated by RCTs (but needs to be).

What Is the Evidence for Surgical Evacuation of Infratentorial Hematoma?

Cerebellar Hematomas
Because observational studies suggest that surgical evacuation of a cerebellar hematoma by suboccipital craniotomy has more than a modest favorable effect in saving the lives of patients with clinical features of progressive brain stem compression, and with surprisingly few adverse neurological sequela, a RCT is unlikely to be ethically approved and undertaken. The relative merits of conventional suboccipital craniotomy and stereotactic aspiration, with or without installation of fibrinolytic drugs, in this group of patients is uncertain.

Not all cerebellar hematomas require evacuation. The selection criteria for surgery ignite controversy, but probably include impaired consciousness with preserved brain stem reflexes, and perhaps large hematomas (>3 to 4 cm in diameter) and vermis hematomas distorting the quadrigeminal cistern, even in alert patients, because delayed decline in consciousness and death can be extremely rapid.
Pontine Hematoma

Despite a case-fatality rate of about 60%, most patients with pontine hematoma are managed conservatively. Apparently successful stereotactic aspiration has been reported in uncontrolled case series, but the effect on the prognosis remains uncertain.

Conclusion

It is sobering that surgical evacuation of intracerebral hematoma has been undertaken for nearly half a century on the basis of plausibility and general acceptance by the surgical community, without formal evaluation by the same regulatory standards that are applied to medical therapies. Although “surgical studies with controls have tended to lack enthusiasm, and surgical studies with enthusiasm have tended to lack controls” (David Sackett, MD, MSc, 1985), such double standards are no longer acceptable. If the standards for medical therapies are applied to surgical procedures for evacuation of intracerebral hematoma, surgical procedures would be not approved or funded. This does not mean they are not effective and safe; it means they have not been shown to be effective and safe, and it is our responsibility to do so before they are widely practiced.

What can be deduced from the available evidence is that surgery, and particularly endoscopic evacuation, may be effective and relatively safe, but it may also be ineffective and harmful, and the overall magnitude of the effectiveness and hazards of surgery is substantially uncertain, let alone for a particular technique, and for patients with different prognostic factors, and for hematomas in different sites of the brain (eg, lobar, deep, infratentorial).

However, the data from RCTs are about to treble with the forthcoming results of the International Surgical Trial in Intracerebral Hemorrhage (ISTICH), which randomized 1033 patients within 72 hours of supratentorial hematoma to immediate surgery versus no surgery, and which closed recruitment on February 25, 2003. The trial should refine the precision of the above estimates of effectiveness, generate more hypotheses, and hopefully generate more RCTs of surgery for intracerebral hematoma with improved patient outcome.

References


Key Words: intracerebral hematoma ■ randomized controlled trials ■ surgery

Surgery for Intracerebral Hemorrhage: An Evidence-Poor Zone

Geoffrey A. Donnan, MD, FRACP; Stephen M. Davis, MD, FRACP

Why do we know so little about the acute treatment of intracerebral hemorrhage (ICH)? Although it is a less common cause of stroke, with a frequency of 10% to 15%, it is at least double in Asian countries. Further, its higher mortality rate than ischemic stroke should have attracted more attention from investigators than has been the case. Based on a simple MEDLINE search of the last decade of publications concerning hemorrhagic versus ischemic stroke, we found that the proportions were 3% and 97%, respectively. Why is this such a grossly under-researched area? Perhaps there is a lack of appeal to basic researchers because of the absence of a well-understood pathophysiological mechanism for ICH in contrast to the better-documented ischemic cascade and penumbra. In addition, clinical research in ICH may have been hampered by an even greater nihilistic attitude by investigators than for ischemic stroke. Even when nihilism is overcome and interventions such as hematoma evacuation are contemplated, we find it quite remarkable that there is so little evidence from clinical trials in 2003.

Both our discussants also agree that the number of patients in randomized trials of surgery of hematoma evacuation is...
very small. Hankey has emphasized that this lack of evidence has translated into enormous national and regional variations in the proportion of patients treated surgically and, indeed, the very nature of the surgical procedure. The STICH Trial\(^1\) (Surgical Trial in Intracerebral Hemorrhage) has randomized more than 1000 patients and is nearly completed. While this will yield further important information, it is likely to raise more questions about patient selection, timing, and technique.

For supratentorial hemorrhage, we share Hankey’s uncertainty about surgery. Interestingly, in Japan Minematsu confirms the view that hematoma evacuation is probably more commonly performed than in most other parts of the world. Perhaps this is because of the magnitude of the problem in Japan as well as their pioneering work concerning concept of early bleeding—hence, the logic of acute evacuation of the hematoma and establishment of hemostasis.\(^2\) We do agree that those with small bleeds and those with large devastating hemorrhages are not appropriate candidates. Like Minematsu, our own surgeons consider evacuations in younger patients with moderately sized lobar hematomas who are not comatose, but are clinically deteriorating. However, even in our own institutions, surgical practices vary enormously, thus reflecting the wider uncertainties. We certainly agree with both Minematsu and Hankey that the benefits of evacuation of selected patients with cerebellar hematomas are widely accepted and unlikely to be tested in a clinical trial setting. This, at least, is clear.

Clinical trials in ischemic stroke have been catalyzed by the concept of the ischemic penumbra. Unfortunately, this has been shown to be unlikely to exist in ICH.\(^3,4\) One important advance, however, has been the demonstration of early hematoma growth in more than one third of ICH patients.\(^5\) This has generated interest in strategies to attenuate this expansion, one example being a trial of a hemostatic compound, activated recombinant factor VII.\(^6\) In addition, there has been renewed interest in blood pressure–lowering in acute ICH as another management strategy.

To return to our original theme concerning the paucity of knowledge and research in the area: there are encouraging signs that may suggest that we are, at last, emerging from one of the most evidence-poor zones in clinical medicine.

References
1. STICH Website. www.ncl.ac.uk/stich.

Key Words: intracerebral hemorrhage \[\text{randomized controlled trials} \[\text{surgery} \]