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Editorial

Surgery for Spontaneous Intracerebral Hemorrhage: Current Concept

Partha S. Ray[1]

[1]Department of Neurology and Clinical Neurophysiology, The Walton Centre for Neurology, National Health Service, Liverpool, United Kingdom

Address for correspondence Partha S. Ray, MD, DNB, FICP, FRCP, MRCP, CCST, Department of Neurology and Clinical Neurophysiology, The Walton Centre for Neurology, National Health Service, Liverpool, United Kingdom; National Professor of Neurology, India (e-mail: partha_ray@hotmail.com).

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Spontaneous intracerebral hemorrhage (ICH) into the brain parenchyma and into the ventricles presents as a severe stroke with high mortality,[1] with uncontrolled hypertension, cerebral amyloid angiopathy, and more recently the anticoagulant-induced cerebral bleeds representing the main risk factors.[2-5] Unfortunately, interventions to stop hematoma expansion by rapid reduction of blood pressure, the use of recombinant activated factor eight, or the administration of tranexamic acid have not shown improvement in functional outcome.[6-8]

The theoretical advantages of evacuating the hematoma and preventing the acute effects of the blood products on the surrounding healthy brain tissue are counterbalanced by the risks of reaching out to the location of the bleeds in the deep basal ganglia structures and the thalamus through healthy cerebral tissue and the additional burden of postsurgical complications.[9]

There is the need for emergency lifesaving surgical evacuation of large lobar hemorrhages and hematomas in the posterior fossa to avoid cerebral or brainstem herniation, and in such situations comparison of best medical management with surgical interventions does not lend itself to a randomized clinical trial (RCT) opportunity for an evidence-based assessment.

In about two-thirds of patients, acute hemorrhage into the brain parenchyma results in stoppage of bleeding through disruption and mass effect within the cerebral tissue. In the remaining one-third, hematoma expansion results in midline shift and an adverse outcome.[10] The best medical management and neuro intensive care with interventions of recombinant activated factor eight reduced hematoma growth but did not decrease mortality or improve functional outcome. The use of tranexamic acid reduced hematoma expansion but did not improve the functional outcome at 90 days. Two large trials of blood pressure lowering—INTERACT-2[11] and ATACH-II[6]—demonstrated that maintaining a systolic blood pressure around 120 to 130 mm Hg in the first 24 hours might result in improved functional outcome.[12]

Hematoma volume greater than 30 mL had statistically unfavorable outcome and a volume greater than 60 mL with Glasgow Coma Scale (GCS) score lower than 8 had greater than 90% predicted 30-day mortality. A volume greater than 150 mL through abrupt increase in intracranial pressure (ICP) and critical reduction of cerebral perfusion pressure (CPP) leads to death.[13,14] Much smaller hematoma volumes in the posterior fossa due to obvious limitations of space to expand leads to brainstem herniation/compression with hydrocephalus and clinical deterioration when hematoma evacuation is of lifesaving consequence.[15,16]

Additional adverse effects of the blood products from the hematoma and secondary inflammation and edema resulting from the same would compound the mass effect, midline shift and decreasing cerebral perfusion consequent to rising ICP.[17,18]

Availability of Surgical Treatment Alternatives

Several surgical treatment alternatives are available, as discussed below.

First, insertion of external ventricular drain (EVD) for intraventricular hemorrhage (IVH) management and ICP monitoring (in ICH): IVH occurs in 45% of patients with ICH, and interfering with normal cerebrospinal fluid (CSF) flow causes acute hydrocephalus and independently predicts an unfavorable outcome.[19] The urgent placement of an EVD with drainage of CSF and ICP monitoring (target less than 20 mm Hg and CPP more than 60 mm Hg) is the goal.[20] In the CLEAR

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III[21] trial, low-dose intraventricular recombinant tissue plasminogen activator (r-tPA) was compared with placebo in small spontaneous ICH with volume less than 30 mL and IVH obstructing the third and fourth ventricles. The targets were: opening of the third and fourth ventricles, the relief of the IVH mass effect, or 80% clot removal. A favorable outcome was defined as a 6-month modified Rankin scale (mRS) score of 0 to 3; this was not significantly different in the r-tPA and saline groups. In the r-tPA group, 11% lower case fatality was noted, which balanced against an 8% increase in patients in a vegetative state. Only a third of patients in the treatment arm had the desired end point of 80% of intraventricular clot removal. The 6-month functional outcome compared with placebo was no better.

Clot removal by neuro endoscopy in combination with EVD placement in a meta-analysis of 11 studies (out of which only 5 RCTs were included) found that neuro endoscopy with EVD was superior than EVD and tPA in terms of mortality, effective IVH evacuation, favorable functional outcome, and the need for ventricular peritoneal shunt. These preliminary results need to be followed through with further studies including comparisons between EVD and neuro endoscopy.[22-24]

Second, craniotomy for supratentorial hemorrhage drainage: The first controlled study from the early 1960s by McKissock[25] compared hematoma evacuation to conservative management when no benefit from surgery was noted in regard to mortality or morbidity. The surgical trial in intracerebral hemorrhage (STICH)[26] was the first well-powered multicenter multinational RCT (1,033 patients) to compare the benefits of early hematoma drainage with initial conservative management. No overall benefit in functional outcome was found with early hematoma drainage and the mortality rate was similar in both groups. Further subgroup analysis including age, hematoma volume, hemorrhage location, anticoagulation- or thrombolytic-associated hemorrhage, severity of neurological deficit, type of intended operation, hematoma side, depth from the cortical surface, and country showed no benefit of early surgery across all subgroups except for a possible benefit in the patients with superficial hematoma. This led to the STICH II[27] trial (601 patients) with superficial hematomas within 1 cm from the cortical surface. No overall benefit in functional outcome or mortality benefit was detected. The STICH trials were combined in a meta-analysis with 13 other studies when potential survival benefit in the intervention group was difficult to analyze as multiple surgical strategies, like craniotomy, endoscopic surgery, and stereotactic with/without plasminogen activator, limited the validity of the meta-analysis. Thus, the STICH RCTs did not show functional outcome or mortality benefit with early hematoma evacuation, particularly in deep hemorrhages and in small lobar hemorrhages with preserved level of consciousness. In large hematomas with mass effect and midline shift leading to altered levels of consciousness or when delayed neurological deterioration occurs through hematoma expansion as an important lifesaving measure, craniotomy and hematoma drainage are recommended. Ideal patient selection criteria for hematoma evacuation needs further determination.

Third, minimally invasive surgical techniques: Since the first trial of minimally invasive surgery in the 1980s comparing the use of endoscopic hematoma evacuation with conservative management using neuro endoscopy by Auer et al[28] (which showed a lower mortality and higher rate of favorable outcome after 6 months in patients with subcortical hemorrhages who were alert and somnolent but not in patients who were stuperose/comatose, and neither in putaminal nor thalamic hemorrhages), the recent ICES—intraoperative computed tomography guided endoscopic surgery for brain hemorrhage—trial[29] tested effectiveness of computed tomography (CT)-guided endoscopic drainage of ICH. The study was not powered to assess functional outcome and mortality, although compared with the medical group from the MISTIE—minimally invasive catheter evacuation followed by thrombolysis—trial (see below), the surgical group of ICES trial showed a nonsignificant favorable neurological outcome on mRS at 12 months.

Stereotactic surgery: In the MISTIE trials,[30] further data and experience were obtained for surgical management of ICH by stereotactic or image-guided placements with thrombolysis and clot evacuation. In the phase 2 MISTIE study performed in 26 centers across North America and Europe, adults with spontaneous ICH and hematoma volume more than 20 mL were allocated to conservative management or MISTIE and tPA with the goal of a clot size reduction to less than 15 mL. In this phase 2 study, accurate and safe drainage of the ICH was established followed by serial thrombolysis through a stereotactically targeted catheter that led to the phase 3 study. The MISTIE-III[31] trial performed at 78 hospitals in North America, Europe, Australia, and Asia involving 506 patients (255 MISTIE group versus 251 for conservative management) measured an mRS score of 0 to 3 at 12 months. Despite a significant reduction in hematoma size, no outcome benefit was found. Adverse events were similar in the two groups. Thus, the MISTIE technique confirmed safety although did not improve long-term functional outcome.[32,33]

The SCUBA—stereotactic intracerebral hemorrhage underwater blood aspiration[34]—technique performed in 47 patients in two phases—the first phase under dry field conditions and the second using a wet field strategy, where the surgeon is able to see the residual clot during hematoma drainage facilitating cauterization of possible bleeding vessels—has not been compared with other existing approaches.

Other ongoing RCTs—early minimally invasive removal of ICH, minimally invasive endoscopic surgical treatment with Apollo/Artemis in patients with brain hemorrhage, and a prospective multicenter study of Artemis in minimally invasive neuro evacuation device—use different strategies for both patient inclusion criteria and evacuation methodology.[35]

Fourth, patients in coma with GCS score less than 8, midline shift, and large hematomas or patients with refractory ICP based on only class III evidence showed that decompressive craniectomy with or without hematoma evacuation had a better outcome. In the study by Fung et al,[36] decompressive craniectomy without hematoma evacuation in supratentorial ICH showed less mortality and better outcome at 6 months

compared with the control group. The use of decompressive craniectomy with hematoma drainage was compared with hematoma drainage by craniotomy. Decompressive craniectomy in putaminal hemorrhage was associated with a significant improvement in midline shift and a trend toward better outcome. In the subgroup of patients with lobar ICH, decompressive craniectomy did not reveal a benefit.[37]

Fifth, posterior fossa hemorrhage: In ~5 to 13% of all ICH cases, a severe life-threatening bleeding occurs in the cerebellum or brainstem.[38] Due to the life-threatening nature of this condition, no randomized controlled clinical trial comparing early surgical evacuation with/without occipital decompressive craniectomy versus conservative management is available or likely possible. Only class III evidence is therefore available for suboccipital decompressive craniectomy, EVD insertion for hydrocephalus, or conservative management. These suggest cerebellar hemorrhage greater than 3 cm in diameter; cerebellar hemorrhage compressing the brainstem or causing acute hydrocephalus may be better managed with early ("early" not well defined) surgery. Patients with preserved levels of consciousness with cerebellar hematomas may be initially managed conservatively with urgent suboccipital craniectomy with/without hematoma drainage for acute neurological deterioration (GCS score ≤ 13).[39,40] In a multicenter retrospective study in 22 Italian hospitals, mortality was 38% for cerebellar hematomas versus 57% for brainstem hematomas (155 cerebellar and 50 brainstem hematomas). Level of consciousness 3 hours after initial hemorrhage and size of hemorrhage less than 3 cm were associated with better outcome. In brainstem hemorrhage, initial loss of consciousness and hematoma size were the main outcome determinants irrespective of hydrocephalus. This group proposed medical treatment for brainstem hematomas, and for larger lesions greater than 1.8 cm the outcome was uniformly fatal.

Kirollos et al[38] developed a grading system based on the fourth ventricle size, configuration and location found in the CT scan. With GCS score greater than 13 and normal or compressed/distorted fourth ventricle, conservative management was proposed. With neurological deterioration and evolving hydrocephalus, EVD insertion followed by hematoma evacuation was advised. With complete effacement of the fourth ventricle, hematoma evacuation and CSF drainage are recommended.

Kuramatsu et al[41] evaluated functional outcome of evacuation of cerebellar hematomas. In this meta-analysis of 4 observational ICH studies in 64 hospitals in the USA and Germany. The primary outcome was the proportion of patients with favorable outcome (mRS = 0–3) at 3 months. Secondary outcomes included the following: survival at 3 months, dichotomized functional outcome (mRS = 0–3 vs 4–6) at 12 months, and survival at 12 months. Hematoma evacuation was not associated with better functional outcome at 3 months although hematoma evacuation was significantly associated with improved survival at 3 and 12 months. The surgical evacuation of hematomas less than 12 mL was found to be harmful while the evacuation of hematomas more than 15 mL was associated with improved survival without a beneficial effect on functional outcome.

International Guideline Recommendations

American Heart Association/American Stroke Association guidelines[42] for the management of spontaneous ICH and the European Stroke Organization[43] guidelines for spontaneous ICH recommend for the majority of patients that with spontaneous supratentorial hemorrhage the benefit of surgical evacuation is not well established (class IIb; level of evidence A),[42] with no supporting evidence for routine surgery (moderate quality, weak recommendation).[42] For patients with a GCS score of 9–12, surgery may be lifesaving (moderate quality, weak recommendation) as well as for patients with delayed neurological deterioration (class IIb; level of evidence C).[42]

Decompressive craniectomy with/without hematoma evacuation may reduce mortality in patients with putaminal ICH, especially in comatose patients with large hematomas leading to significant midline shift and in patients with refractory intracranial hypertension (class IIb; level of evidence C).[42]

The effectiveness of the use of minimally invasive surgical approaches, such as stereotactic or endoscopic aspiration with or without thrombolysis, remains uncertain (class IIb; level of evidence B).[42]

In patients with posterior fossa hemorrhage with acute hydrocephalus, brainstem compression, or worsening in neurological status, surgery is to be performed as soon as feasible (class I; level of evidence B).[42]

Downsides of Surgical ICH Trials (So Far)

Neurosurgical patients requiring urgent procedures are difficult to recruit and the ideal candidate and the optimal timing of surgery have not been determined.[44] The perspective of clinicians considering hematoma drainage as a lifesaving measure comes in the way of randomization of these patients in these interventional studies. There is a significant crossover from medical management to the surgical arm of these studies, thereby concealing the otherwise higher rates of an unfavorable outcome and death in the conservative management arm. Problems of study design, sample size, and number of excluded patients affect conclusions. Very restrictive inclusion protocols[45] have resulted in slow recruitment as evidenced by only 9.5% of lobar ICH without IVH and only 3.7% of all ICH patients meeting inclusion criteria in the STICH II trial, a population-based study. These restrictions may have limited our understanding so far on the evidence base for spontaneous ICH surgical intervention procedures. We should endeavor to address the above, gather further evidence, and change management/surgical practice wherever necessary for the benefit of the patient.

Conflict of Interest
None declared.

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