Pharmaceutical management of hemorrhagic stroke: Optimizing outcomes following intracranial hemorrhage evacuation

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ABSTRACT

Stroke can be mainly categorized into hemorrhagic and ischemic stroke. Intracerebral hemorrhage (ICH) is a subtype of hemorrhagic stroke that is caused due to unconstrained bleeding within the parenchyma of the brain. ICH is one of the major conditions that have a high rate of disease and a high rate of death in a given population. Risk factors for ICH emerged to be age, male gender, hypertension, and intake of alcohol in huge quantities. The frequency of ICH is increased where hypertension is mainly untreated. To improve the prognosis and outcomes of an ICH patient, we need to perform emergent evacuation of blood from the brain parenchyma and prevent edema formation while restricting further neuronal damage due to surgical intervention. Evidence-based guidelines exist for ICH and form the basis for a care framework. The pharmaceutical management of ICH from current literature includes an aggressive reduction in blood pressure, tranexamic acid use, and recombinant activated factor VII administration. In addition, advanced imaging, surgical evacuation of ICH, and minimally invasive surgery techniques for hematoma evacuation could provide great benefits to patients with a large ICH.

Keywords: intracerebral hemorrhage; intracranial hemorrhage evacuation; neurosurgery; surgical management of stroke; ICH evacuation

1. Introduction

Intracerebral hemorrhage (ICH) is a hemorrhagic stroke due to spontaneous nontraumatic hemorrhage into the brain’s parenchyma[1]. This subtype of stroke accounts for about 15% to 20% of all types of strokes. However, it is accompanied by extremely high rates of disability and mortality[2]. Cerebral amyloid angiopathy and systemic hypertension are the two risk factors of ICH[3,4]. The clinical presentations of ICH typically consist of sudden onset of a focal neurologic deficit (FND), diminished levels of consciousness, seizures, vomiting, headache, and very high blood pressure (BP). These symptoms could direct the physician towards an ICH[5,6]. Noncontract computerized tomography (NCCT) is an extremely fast and excellent imaging technique with great accuracy for identifying a sudden ICH. The availability of NCCT is common and is therefore considered the gold standard for diagnosing ICH in the emergency department[7]. NCCT is also useful in distinguishing between a hemorrhagic stroke and an ischemic stroke and is therefore considered a first investigation of choice for patients presenting with a sudden FND. Other than the diagnosis of ICH, NCCT can also provide many valuable insights, such as the area of ICH, the presence of hydrocephalus, whether there is an
intraventricular extension, the presence and degree of edema, and midline shift or brainstem compression caused secondary to the mass effect from the hematoma\textsuperscript{[8]}. The volume of blood in an ICH is a brilliant predictor of prognosis for survival, and it depends on the early management of BP control, reversal of coagulopathy, and surgical evacuation of hematoma for appropriate patients\textsuperscript{[1]}. Unfortunately, no definite treatment has been shown to increase positive outcomes. Certain therapies that target and prevent the enlarging of hematoma, such as the assertive reduction in BP and maintaining a target systolic BP of <140 mmHg\textsuperscript{[9,10]}, using tranexamic acid, and administration of recombinant activated factor VII\textsuperscript{[11,12]}, were not found to improve functionality and prognosis in patients of ICH.

Improving the outcomes of ICH patients mainly requires the emergent evacuation of blood from the brain parenchyma and preventing the development of edema, along with restricting further neuronal damage caused by surgical interventions\textsuperscript{[13]}. Some surgical techniques include craniopuncture, minimally invasive catheter evacuation followed by thrombolysis, and auriscope\textsuperscript{[2,13]}. Surgical hemorrhage evacuation mainly benefits the patient by preventing mass-like effects and further preventing cerebral herniation according to the Monro-Kellie doctrine, reducing intracranial pressure by removal of the extra volume of blood caused by ICH, and decreasing excitotoxicity and neurotoxicity\textsuperscript{[2]}. Therefore, in addition to discuss the pharmaceutical management of ICH, this article reviews the surgical management of ICH.

2. Pharmaceutical management of intracranial hemorrhage

Sudden, nontraumatic intracerebral hemorrhage (ICH) remains an important cause of patient death worldwide\textsuperscript{[7]}. The clinical presentation of ICH typically involves a sudden onset of focal neurologic deficit\textsuperscript{[14]}. Noncontract computerized tomography (NCCT) has proven to be a fast and excellent technique with great accuracy for diagnosing a spontaneous ICH\textsuperscript{[4]}. The Glasgow Coma Scale reports show that a noteworthy percentage of patients with ICH exhibit a decrease by two points during an evaluation after an acute episode\textsuperscript{[7,15]}. The management to be given before reaching the hospital mainly aims at securing the airway and maintaining resuscitative measures for unstable patients. The meticulous restoration of onset of symptoms, history of previous admissions, history of medicines taken before, and medications currently taken by the patient\textsuperscript{[14]}. Early admission and assessment of the patient will lessen the time taken to do a NCCT scan and allows a quicker diagnosis\textsuperscript{[14]}. 

Class I recommendations by American Heart Association (AHA) and American Stroke Association (ASA) are listed in Table 1.

<table>
<thead>
<tr>
<th>Sections</th>
<th>Class I recommendations by AHA and ASA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency diagnosis and assessment</td>
<td>After initial assessment and resuscitation, NCCT is recommended to allow recognition of ICH.</td>
</tr>
<tr>
<td>Hemostasis and coagulopathy, antiplatelet agents</td>
<td>Factor replacement therapy for patients who have a severe coagulation factor deficiency or thrombocytopenia. Patients taking vitamin K antagonists like Warfarin should receive injectable vitamin K-dependent factors and correct the INR. Intermittent pneumatic compression is recommended for patients with ICH for the prevention of venous thromboembolism.</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>BP to be lowered and maintained no more than SBP of 140 mmHg.</td>
</tr>
<tr>
<td>General monitoring and nursing care</td>
<td>Initial management and routine vital examinations should begin in specialized stroke units or the ED.</td>
</tr>
<tr>
<td>Glucose management</td>
<td>Blood glucose levels should be checked and included in routine vital monitoring. Both hypoglycemia and hyperglycemia should be avoided in such patients. Dextrose normal saline should be immediately started for hypoglycemic patients. Intravenous Insulin should be started for patients with hyperglycemia.</td>
</tr>
<tr>
<td>Seizures and antiseizure drugs</td>
<td>Antiseizure drugs like Lorazepam should be used to treat seizures diagnosed clinically. Patients with an abnormal EEG should be treated with antiseizure drugs.</td>
</tr>
</tbody>
</table>
**Table 1. (Continued).**

<table>
<thead>
<tr>
<th>Sections</th>
<th>Class I recommendations by AHA and ASA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management of medical complications</td>
<td>Before resuming back to oral feeding and removal of nasogastric tube, the patient should be assessed for dysphagia. This will prevent the risk of developing pneumonia.</td>
</tr>
<tr>
<td>Surgical treatment of ICH</td>
<td>Surgical evacuation of hemorrhage is required for patients who have a deteriorating trend neurologically, have brainstem compression, hydrocephalus.</td>
</tr>
<tr>
<td>Prevention of recurrent ICH</td>
<td>BP to be lowered and controlled in all ICH patients. Regular follow ups to maintain BP and adjust medications.</td>
</tr>
<tr>
<td>Rehabilitation and recovery</td>
<td>Multidisciplinary rehabilitation to prevent a serious disability.</td>
</tr>
</tbody>
</table>

2.1. Blood pressure control

In the acute phase, the greater part of patients with ICH present with an elevated BP. This elevated BP can cause the growth of hematoma and result in a bad prognosis\(^1\). The most full-bodied data on BP management came from the INTERACT2 study, which is a large clinical trial with randomization of patients to either a BP control group of \(SBP < 140\) mmHg, or into a BP control group of \(SBP < 180\) mmHg for the first 24 h. Unfortunately, the study could not reach the goal and was not able to definitively demonstrate the improved outcomes with an intensive BP treatment of controlling systolic \(BP < 140\) mmHg\(^9\).

Accordingly, some authors mention that the evidence from studies favors the maintenance of \(SBP < 140\) mmHg as soon as the patient presents to the ED. However, this study had quite a few fallbacks, some of them being the inconsistent inclusion of those with small ICH, difficulty controlling the target \(BP\) quickly in the acute phase, and a various range of pharmacological agents used\(^{16,17}\). The current AHA/ASA guidelines are mentioned in Table 1. Short half-life agents such as Labetalol or Nicardipine should be used in the setting of an elevated BP. The shorter half-life agents do not cause sudden hypotension and are therefore avoided. Hydralazine and Nitroprusside should be avoided, as they can potentially cause an increase in ICP\(^{16}\). In a trial that involved patients with intracranial hemorrhage, they were able to find that an early intensive lowering and controlling of \(BP\), as compared to the more conservative level of blood-pressure control currently recommended in guidelines, was not able to significantly reduce the mortality or major disability\(^9\). However, in another study in which, they enriched the statistical power for the evaluation of physical functioning, they found significantly better results in the group treated with intensive lowering and control of \(BP\) compared to the group treated with the guideline-recommended treatments\(^{18,19}\). They also found that the patients treated with intensive lowering and control of \(BP\) were noticeably well physically as well as psychologically when compared to the patients who received guideline-recommended treatments. These results are constant with the observational epidemiologic findings that associated high BP levels with bad outcomes in patients with ICH\(^{20-24}\) and indicate that an early intensive lowering and control of \(BP\) in this patient population is safe and beneficial.

2.2. Use of tranexamic acid and factor VII

Tranexamic acid is used to reduce mortality due to bleeding in cases of post-partum hemorrhage and after trauma. A study was conducted that aimed to evaluate if tranexamic acid can diminish the expansion of hematoma and improve prognosis in adults with stroke due to ICH. They conducted a randomized controlled trial in adults with ICH and found a noteworthy increase in positive prognosis in patients, lesser incidence of hematoma expansion, and other major complications. These results were along the antifibrinolytic effects of tranexamic acid\(^{25}\). Tranexamic acid use results in a small but significant reduction in the expansion of hematoma and a smaller volume of hematoma formation. These are the major factors that influence the prognosis of the patient after an ICH\(^{26,27}\). The small reduction in hematoma was of a volume of about 1.4 mL lesser in the patients receiving tranexamic acid compared to the patients that received the placebo treatment\(^{25}\).
Recombinant activated factor VII (rFVIIa) is being used to reduce the expansion of the hematoma and improve survival and functional outcomes\cite{12,28}. In a study performed on patients with ICH, they randomly assigned patients to receive a placebo or recombinant activated factor VII. They found that rFVIIa reduced hematoma growth but still could not reduce the mortality rate or the occurrence of a severe disability after ICH\cite{12}. Another study found that treatment with rFVIIa within four hours after the onset of ICH limits the growth of the hematoma and reduces mortality and is shown to improve prognosis at 90 days. Although, it has been noticed that there is a slight chance of the occurrence of thromboembolic adverse events in patients on rFVIIa therapy\cite{29}.

2.3. Antioxidants

Edaravone is a hopeful therapeutic agent that can be used for the treatment of ICH. The beneficial effects of its use remain questionable, and its chronic use has an uncertain prognosis despite its benefits seen in patients with ICH\cite{30}. Edaravone is a powerful free radical scavenger\cite{31–35}, and it was firstly approved for the treatment of acute ischemic stroke (AIS) in Japan\cite{36,37}. The similarities in the mechanism of the processes of AIS and ICH led to the idea of testing Edaravone in ICH patients. It has been shown to improve neurological deficits in ICH models through anti-inflammatory and antiapoptotic mechanisms, decreasing the edema caused by ICH, and oxidative injury, and reducing iron-induced and thrombin-induced brain injury\cite{7,38–40}. This neuroprotective effect is the reason for its use in patients with ICH\cite{36,41}. Edaravone has been widely used in China and has become a part of the Chinese guidelines for the treatment of acute ICH as a result of its protective nature in preventing neurological impairment and improving prognosis\cite{42–44}.

NXY-059 is a free radical-trapping neuroprotectant that was created for use in AIS. A study studied the safety of NXY-059 in patients with ICH, and they found that NXY-059, if given within 6 hours of acute ICH, has a good safety index and tolerability profile, with a good prognosis\cite{45}.

N-hydroxy-N’-(4-n-butyl-2-methylphenyl)-formamidine (HET0016) inhibits the synthesis of the arachidonic acid metabolite 20-hydroxyeicosatetraenoic acid (20-HETE) and has been shown to have a protective effect after ICH. In a study, they studied if 20-HETE contributes to ICH-induced cell ferroptosis and found that 20-HETE inhibitors can enhance Hemoglobin-treated organotypic hippocampal slice cultures (OHSCs), 20-HETE induces ferroptosis in OHSCs, and inhibition of 20-HETE synthesis improves prognosis and decreases Glutathione peroxidase 4 (GPx4)\cite{46}. These findings point towards the fact that 20-HETE partakes in ICH-induced acute brain injury and neurotoxicity by facilitating ferroptosis, which can be used for the prevention of ICH-induced neurotoxicity. This could be a new target for medical innovations for ICH\cite{46}.

The pharmaceutical management of intracranial hemorrhage have been summed up in Figure 1.

**Figure 1.** Pharmaceutical management of intracranial hemorrhage.
3. Surgical management

3.1. Intracranial hemorrhage evacuation

For the most part, ICH has been controlled with medical management or surgical craniotomy. Several surgical techniques have now been considered, some of which include Craniopuncture, performing thrombolysis after aspirating the hematoma stereotactically, hematoma evacuation using an endoport, open craniotomy, craniectomy, neuroendoscopy, and evacuation and thrombolysis after catheter insertion by the minimally invasive method. The International Surgical Trial in Intracerebral Hemorrhage (STICH I) and STICH II trials evaluated the superiority of surgery to medical management but were not able to conclusively reach a conclusion on whether surgery would lead to a positive prognosis. The conclusions of STICH trials should not be generalized as there was a crossover of patients from medical management to the surgical management group. Without these crossovers, the prognosis in conservative management would have been poor. Furthermore, patients in a coma and patients at risk of cerebral herniation were not included and, in such patients, surgery could have been a potentially lifesaving procedure and prevented those patients from being enrolled in the trials, further potentially changing the results.

3.2. Craniopuncture

Craniopuncture has been the standard of care for the treatment of ICH in China. Craniopuncture uses a YL-1 needle. This has a hollow cannula of 3 mm diameter that contains the needle. The needle is then used to drill through the skull of the patient and into the hematoma. After the aspiration process, a lysis fluid (recombinant tissue plasminogen activator (rtPA) or urokinase) is injected. This fluid is injected into the hematoma 6–12 hourly. Another CT scan is performed around 2 days after the initial drainage to calculate the amount of blood present after the procedure. The drainage catheter remains in the brain for around 4 days. In a paper in which they compared outcomes between craniopuncture and conservative management in 377 patients who suffered a basal ganglia hemorrhage, they found significant improvement in neurological function in the patients that underwent craniopuncture by the end of two weeks with no variance in the rates of rebleeding and there was no notable difference in the mortality of patients. In a study on craniopuncture versus craniotomy, they demonstrated that craniopuncture convalesced outcomes over conventional craniotomy. At three months there was no positive progress in neurological function, but there was a significant decrease in the mortality and the rebleed rate (8.8% vs. 21.4%) for craniopuncture.

3.3. Thrombolysis after hematoma aspiration stereotactically

In Stereotactic aspiration with thrombolysis, the patient is sent for a repeat CT scan to estimate the stable nature of the clot after at least 5–6 h following their CT used for diagnosis. If the clot reveals to be a stable clot, a course trajectory is chosen, and the surgeon then drills a 1 cm burr hole at the most appropriate site. The surgeon uses image guidance and a 4.8 mm (14F) diameter sheath is stereotactically inserted into the hematoma. It is then aspirated using a syringe until resistance is felt, a drainage catheter is placed in and the sheath is removed. The catheter can be connected to a three-way cannula for the administration of thrombolitics and normal saline in addition to drainage. Next CT scan is done to establish the postprocedural stable nature of the clot and injections of rtPA start after six hours. rtPA is then injected eight hourlies, and up to nine injections can be given. Injections can be stopped after the clot has reduced to less than 15 mL or after the ninth administration. The catheter is allowed to drain for 1 day after the reduction of the clot or 1 day after the last dose of rtPA.

Three phases of the MISTIE trials (Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation) compared the stereotactic hematoma aspiration with thrombolysis with medical management. The initial data that was published suggested that the MISTIE protocol achieved greater clot
volume reduction over medical management\textsuperscript{54}. Another study published during the same time frame clarified that the administration of a thrombolytic agent did not worsen perihematoma brain edema (PHE), which had been a significant area of interest\textsuperscript{55}. MISTIE-II trial results displayed that this technique had comparable safety outcomes as medical management and that MISTIE may enhance Modified Rankin Score outcomes at 6 months, due to a greater hematoma reduction\textsuperscript{55}. However, the amount of rebleed at 72 h was significantly higher in the patients treated with the MISTIE technique. The results of MISTIE-III were published in 2019\textsuperscript{53}, and they found that there was significant positive progress in decreasing death at 1 year for the patients treated with surgical for those who achieved a hematoma volume evacuation to less than 15 mL\textsuperscript{53,56}.

3.4. Hematoma evacuation with endoport

The evacuation of hematoma with the endoport method requires a 3 cm craniotomy and a successive 2 cm opening in the dura. The sheath is placed in through the access point along with the inner obturator to the innermost part of the clot. The sheath provides the surgeons with direct access to the clot for removal\textsuperscript{57}. Bleeding is stopped by coagulation and the cavity is irrigated with normal saline\textsuperscript{58}. When the procedure is completed, the endoport is instantaneously removed.

In a study that performed an analysis of 11 patients, they found that the endoport enables 75% volume reduction of hematoma, which bettered the mass effect, but conclusions were not compared to a control group\textsuperscript{58}. Another study in which 18 ICH patients were followed over two years found that this technique was successful but also was not compared to a control group\textsuperscript{57}. In a review of 39 patients, they published evacuation of hematoma with the endoport method removed over 90% of the hematoma in 72% of patients\textsuperscript{59}.

3.5. Neuroendoscopy and evacuation

The neuroendoscopy and evacuation technique combines an endoscope with an aspiration cannula. The endoscope delivers visualization and the cannula is used to aspirate the clot, irrigate the cavity, and cauterize blood vessels. The procedure is carried out after a craniectomy of about 18 mm in diameter is performed\textsuperscript{49,51}. The instruments and sheath are removed towards the end of the procedure and a drainage catheter can be left in place\textsuperscript{60}.

In a study, they found that endoscopic evacuation managed to significantly lower poor prognosis in patients than the patients treated with medical management\textsuperscript{61}. In a study, they reviewed 23 ICH patients who had endoscopy against 20 patients who underwent craniotomy. Their published data pointed an increased efficacy in evacuation and improved Glasgow Coma Scale (GCS) by day 7 for the patients in the endoscopy group. 1 patient treated with craniotomy and 0 patient treated with endoscopy suffered from rebleeding\textsuperscript{60}. In a study review of 82 endoscope procedures and 69 craniotomies, they found that surgery with endoscopy resulted in a better evacuation and greater 6-month mRS outcomes\textsuperscript{62}. It was also associated with a good prognosis and a lesser rebleeding rate of 2% compared to the craniotomy group of 8%. However, a similar study was not able to show improved results at the 6-month time point\textsuperscript{63}. Another study was not able to find a difference in the prognosis for endoscopy in comparison to craniotomy or stereotactic aspiration, although endoscopy was found to have a higher evacuation rate\textsuperscript{64}. Another study comparing these methods found that endoscopy and stereotactic aspiration had better prognosis than craniotomy. It also concluded that endoscopy was an outstanding technique for patients who suffered a large bleed of >60 mL\textsuperscript{65}.

4. Novel method

A report on a case with a large ICH was evacuated using a novel DTI-guided (diffusion tensor imaging) parafascicular Brain Path/Myriad technique, concluded that it is a superior method to decrease the hematoma quickly\textsuperscript{66}.
5. Craniotomy

The function of surgery in treating patients with ICH remains debatable, but the use of craniotomy for draining hematoma is the most common technique used in hospitals\textsuperscript{[67,68]}. The Surgical Trial in Intracerebral Hemorrhage (STICH)\textsuperscript{[48]} was the preliminary well-driven, multifocal, international, randomized clinical trial to evaluate the upsides of immediate hematoma drainage with initial conservative management. 1033 patients with ICH were enrolled from 83 centers in 27 countries to undertake immediate hematoma drainage or receive conservative management. Delayed hematoma evacuation was permitted in the conservative group, if necessary. No overall benefit in prognosis was noticed with immediate hematoma drainage since 122 (26\%) patients had a favorable result in the surgical group against 118 (24\%) patients in the conservative treatment group\textsuperscript{[48]}. Another study was performed by the same team of researchers to test the hypothesis that patients with superficial hematomas within 1 cm from the cortical surface could gain benefit from early hematoma drainage\textsuperscript{[47]}. No overall gain in functional outcome (62\% unfavorable outcome in the surgical group vs. 59\% in the initial conservative treatment group), and neither mortality benefit was found.

An immediate craniotomy cannot be recommended as routine care for patients suffering from supratentorial ICH, more importantly in deep hemorrhages and in small lobar hemorrhages with well-maintained levels of consciousness. A craniotomy is a vital life-saving measure in situations such as large hematomas producing a mass effect with midline shift which can lead to an altered level of consciousness or when neurological deterioration appears due to hematoma expansion\textsuperscript{[69]}. The surgical management options for intracranial hemorrhage have been summed up in Figure 2.

![Figure 2. Surgical management of intracranial hemorrhage.](image)

5.1. Post-stroke complications and management: Orthotics and physical therapy

For many stroke patients, an acute episode of stroke is just the commencing of a long battle with physical impairment and disability\textsuperscript{[70]}. With time, the aftermaths of a stroke are complicated by a range of lesser-known medical, musculoskeletal, and psychosocial difficulties. These complications and their treatments are listed in Table 2.

![Table 2. Post stroke complications and treatment.](image)
Table 2. (Continued).

<table>
<thead>
<tr>
<th>Late medical complications</th>
<th>Musculoskeletal complications</th>
<th>Psychosocial complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary incontinence-rule of exacerbating and precipitating risk factors. Oxybutynin in certain patients. Urinary catheter considered last.</td>
<td>Hemiplegic shoulder pain-proper positioning, physiotherapy consult, analgesics, transcutaneous electrical nerve stimulation in selected patients.</td>
<td>Emotional/Mood changes-support groups, counselling.</td>
</tr>
<tr>
<td>Cognitive impairment-control of risk factors along with cognitive stimulation exercises.</td>
<td>Wrist and hand flexion-physiotherapy, splints.</td>
<td>-</td>
</tr>
</tbody>
</table>

The physician should optimize chronic disease control and lessen the risk of complications after a stroke. Therefore, early screening of patients and providing appropriate management are crucial.

One of the major concerns is the formation of musculoskeletal complications. Recuperation of arm function in patients after a stroke is proportional to the severity of impairment at stroke onset \[71\]. Those patients who have severe impairment of the arm at onset and do not recover useful arm function soon are most likely to form contractures \[72,73\]. In a study, they found that in the section of patients who had no arm function within the first six weeks of stroke, spasticity was seen early, and contractures were more prone to form in patients who did not recover arm function \[74-76\]. Therefore, it can be hypothesized that the lack of movement due to paralysis, in addition to the fixed positioning due to spasticity, accelerates the development of contractures \[77\]. Contractures are characterized by the grouping together of increased stiffness and loss of range of movement at a joint. Contractures can usually fully develop within four weeks after a stroke, and it was seen that 52% of stroke survivors had developed a contracture at six months post-stroke \[74-78\]. Multiple studies demonstrated the prevalence of spasticity in post-stroke patients within the first 18 months by using the Modified Ashworth scale, which divides the severity into normal, mild, moderate, severe, and extreme \[79-83\].

In a study to determine if shoulder orthoses prevent glenohumeral subluxation and hemiplegic shoulder pain, they found that in 186 participants, orthoses lessened shoulder pain in most stroke patients when it was worn for four weeks continuously after stroke. There was no rise in the development of contracture, spasticity, or hand edema when compared to participants with no orthosis. Orthoses were well-tolerated, and the reviews given were that it was comfortable to wear by most patients \[84\]. In another study that used functional electrical stimulation (FES) as a part of the rehabilitation program, they found that the FES program was effective in reducing the severity of shoulder subluxation, spasticity, and pain and possibly facilitating recovery of arm function \[85\]. To slow contracture development, physical therapy should include intensive mobilization by using cyclical electrical stimulation. This has been displayed previously in stroke patients prone to the development of wrist flexion contractures \[86\]. The aim of the study was to explore if avoiding the fixed positioning associated with spasticity using treatment with \textit{Botulinum} toxin could reduce both, the onset of contractures and the rate at which contractures were formed. The use of \textit{Botulinum} is toxic, led to the expected reduction in spasticity, and the effects lasted for about four to six weeks \[87\]. A combination of the above tailored to the patient’s needs could prevent the formation of contractures and ensure good functioning of the affected limb.

5.2. Weaning patient from ventilator and transition toward recovery

Patients with ICH are controlled in the emergency department, but a large part of the population requires higher care and admission to the intensive care unit. Mechanical ventilation (MV) is a widely used procedure in these patients because the patients are nonresponsive and are at great risk of aspiration from swallowing their own saliva further adding to the respiratory insufficiency. The location of the stroke is one of the most relevant factors related to the need for MV \[88,89\]. Table 3 mentions the locations of the brain along with the functions it performs that are impaired if involved.
Table 3. The locations of the brain which perform specific functions that determine the chances of respiratory failure if involved in a stroke.

<table>
<thead>
<tr>
<th>Functions</th>
<th>Location of the brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consciousness</td>
<td>Thalamus, limbic system, reticular formation in the brainstem.</td>
</tr>
<tr>
<td>Breathing</td>
<td>Respiratory centers-cortex, pons, and medulla.</td>
</tr>
<tr>
<td>Swallowing</td>
<td>Medulla and Brainstem.</td>
</tr>
</tbody>
</table>

Pulmonary complications such as respiratory failure, pneumonia, pleural effusion, acute respiratory distress syndrome, pulmonary edema, and pulmonary embolism from venous thromboembolism may occur in such patient brackets and are associated with a poor prognosis\textsuperscript{90,91}. Stroke-associated pneumonia is declared as a separate risk factor for unfavorable outcomes\textsuperscript{92,93}.

The different types of ventilation that can be used for such patients are supplemental oxygen therapy via nasal prongs/masks and Invasive intubation. The decisiveness to intubate is often prompted by neurological deficits, such as a Glasgow Coma Score (GCS) < 9, signs of increased intracranial pressure, generalized tonic-clonic seizures, and the presence of a midline shift on imaging\textsuperscript{94}.

Neurosurgical patients who experience prolonged ICU stay, especially after ICH with mechanical ventilation, have a higher incidence of ventilator-associated pneumonia compared to other patients\textsuperscript{90}. Even though MV is life-saving, it is associated with many complications that increase poor prognosis\textsuperscript{95}.

That is why weaning from mechanical ventilation should happen as early as possible after ensuring the patient’s safety. Expectation of successful extubation is important, as both delayed and premature extubation increase complication rates and a need for tracheostomy, increasing duration of ICU stay, and death\textsuperscript{96}.

In a meta-analysis precisely looking for predictors of extubation failure in neurocritical care patients, a low GCS (7–9) was identified as a risk factor, with nearly 5 times increased risk of reintubation and or complications\textsuperscript{97}. Other factors for the prediction of successful extubation include the orientation to obey directions and commands, and the presence of a gag reflex. In a retrospective study, they found that a composite GCS score of 8 with an eye sub score of 4 was found to be associated with successful extubation\textsuperscript{98}. A clinical score developed to predict extubation failure in patients with brain injury with a GCS < 12 before intubation, intubated for neurological reasons, and ventilated for about more than 48 h, it includes upper airway functions and neurological status which is evaluated through the visual subscale of the coma recovery scale-revised\textsuperscript{95}. A multicenter study found that patients <40 years, with visual searching, attempts at swallowing on their own, and a GCS > 10 were found to be predictors of successful extubation\textsuperscript{99}. Based on these items, the VISAGE score was constructed, which mentions if three or more items are positive, an extubation success rate of 90% could be expected. Visual pursuit and preserved upper airway reflexes, young age, negative fluid balance, and cough are described as positive signs of extubation success by other observational studies\textsuperscript{100}. Further trials are required to conclude the data of the newest research on neurological patients in general and stroke in particular. Figure 3 mentions the procedure for extubation.

![Figure 3. Extubation procedure.](image-url)
6. Conclusion

ICH still remains a devastating disease and continues to have high mortality. Pharmaceutical management with blood pressure control, Use of tranexamic acid, Factor VII, and antioxidants have a limited role in ICH management and cannot manage the complications such as hematoma expansion and increase in intracranial pressure due to mass effect.

This highlights the need for improved interventions for timely ICH treatment in emergencies. Surgical interventions like craniopuncture, stereotactic aspiration with thrombolysis, endoport-mediated evacuation method, endoscope-assisted evacuation technique, craniotomy, and open craniotomy. Minimally invasive surgery techniques are predicted to achieve the most beneficial outcomes on mortality and reduce complications, but the largest clinical trials have yet to demonstrate definitive effects of surgical intervention on mortality and functional outcomes.

One of the major complications of ICH is the formation of contractures in patients who remain in bed due to paralysis. These patients develop spasticity, which further leads to the development of contractures. Orthoses should be used as a part of post-stroke management of all patients who are unable to mobilize to prevent the development of contractures and functional electrical stimulation to be used for reducing the severity of limb subluxation, spasticity, pain and possibly facilitating recovery of the limb function.

Weaning of neurosurgical patients after long ICU stays should be done with care as they are at high risk for developing complications and might need tracheostomy if extubated prematurely. Predictors for successful extubation should be used to initiate the process of recovery in such patients.

Author contributions

Conceptualization, SS and BLW; methodology, SS; software, SS; validation, SS and BLW; formal analysis, SS and BLW; investigation, SS and BLW; resources, SS; data curation, SS; writing—original draft preparation, SS; writing—review and editing, SS; visualization, SS; supervision, SS and BLW; project administration, SS and BLW; funding acquisition, SS and BLW. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

References


