8 Intensive Care Management of Stroke

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8.1 Introduction

Ischemic stroke is a social problem and a strong challenge to both healthcare system and providers. Nearly, 12 million cases of ischemic stroke are registered worldwide annually [1, 2]. Ischemic stroke is a predominant kind of vascular brain injury. Outcomes of ischemic stroke are usually much better in comparison to hemorrhagic stroke, and results of treatment have been considerably improved during last decades due to progress in intensive care, endovascular technologies, and implementation of aggressive neurosurgical approach [3]. However, mortality and rate of invalidation are still high, especially in some groups of patients with ischemic stroke, for example, in cases with malignant stroke, when almost 90% have unfavorable outcomes [4].

Pathophysiologically, ischemic stroke presents infarct of the brain due to arterial thrombosis and further events, developing in the core zone, penumbra, and surrounding tissues. Intensive care management of stroke is based on the understanding of pathophysiological mechanisms. Therefore, following treatment directions will be discussed below: (a) recanalization, (b) prevention of thrombosis enlargement and early recurrent stroke, and (c) intensive care and management of complications.

8.2 Recanalization

Recanalization is the cornerstone of intensive care management of stroke, and it should be performed as early as possible [5–8]. Shortening of time between stroke onset and recanalization significantly improves outcomes. Recanalization is achieved with intravenous thrombolysis and endovascular treatment. Stroke onset 3–4.5 h, absence of contraindications for recombinant tissue plasminogen activator (rt-PA), and blood pressure less than 185/110 mmHg are strong indications for intravenous thrombolysis. Thrombolysis in Cerebral Infarction (TICI) scale reflects visual success of the treatment on angiograms, where TICI 2a is partial recanalization, TICI 2b is near complete recanalization,

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and TICI 3 is complete recanalization. TICI 2b and TICI 3 are being perceived as a successful result [9].

Zeumer et al. first reported successful recanalization of basilar artery occlusion after intra-arterial administration of streptokinase in 1983 [10]. A number of experimental studies of 1980s led to establishing safe and effective regimens of intravenous thrombolytic therapy. Thus, the biggest randomized clinical trials of 1990s concerning intravenous thrombolytic therapy of acute stroke were based on intravenous administration of recombinant tissue plasminogen activator (rt-PA). The dosage of rt-PA was reduced from 1.1 mg/kg in ECASS I to 0.9 mg/kg in all other trials without loss of its efficacy.

Results of ECASS I were published in 1995. It was randomized as 1.1 mg/kg of rt-PA vs placebo in 511 patients [11]. Outcomes in thrombolytics group were significantly better; however, 30-day mortality was equal. National Institute of Neurological Disorders and Stroke Trial (NINDS trial) showed 50% higher probability of good outcome in 3 months after stroke onset comparing to the control group [12]. In this trial, randomization was between groups of 0.9 mg/kg of rt-PA and placebo in 624 patients. NINDS trial established safe 3-h therapeutic window for intravenous thrombolysis in acute stroke. ECASS II study, whose results were reported in 1998, contained an attempt to enlarge therapeutic window up to 6 h in randomization between groups of rt-PA 0.9 mg/kg and placebo in 800 patients [13]. The rates of hemorrhagic complications were significantly higher in treatment group, and therapeutic window remained unchanged after this study. In 2008, ECASS III study demonstrated safe enlargement of therapeutic window for 0.9 mg/kg intravenous administration of rt-PA up to 4.5 h [14]. IST—III study accounted 3035 patients, 1617 of which were older than 80, and there were no significant differences in outcomes [15].

Comparing guidelines for early management of patients with acute ischemic stroke from the American Heart Association/American Stroke Association (AHA/ASA), published in 2013 and in 2015, shows liberalization of rt-PA use [16, 17]. History of ischemic or hemorrhagic stroke, and gastrointestinal or gastrourinary bleeding in anamnesis are no longer contraindications for rt-PA use. These changes were based on the experience of rt-PA safety in patients with complicated anamnesis. Seizures at onset with postictal neurologic impairment, hypoglycemia at the presentation, and the severity of stroke are no longer contraindication for intravenous thrombolysis according to recent guidelines. These changes are very interesting. Previous position was based on the concept that thrombolysis in stroke mimics leads to complications. However, recent studies demonstrated safety of thrombolysis in patients with stroke-like symptoms, and worsening outcomes in patients with stroke, whose symptoms were incorrectly interpreted as stroke mimics, and thrombolysis was avoided [18]. NIHSS 4 or less is not a guarantee of favorable outcomes, and some patients even with minimal NIHSS can have poor outcomes [19–21]. The matter is that the NIHSS predominantly assesses anterior circulation, and the scale can miss some kinds of posterior circulation infarction. Moreover, NIHSS at presentation cannot exclude patient's deterioration.

Besides CT data regarding volume of brain infarct, and laboratory data regarding hemostasis abnormalities, like platelet count, international normalized ratio (INR), prothrombin time (PT), and anamnesis data of use of heparin or new oral anticoagulants (NOA), were removed from recent AHA/ASA guidelines in comparison to 2013 edition. Age greater than 77 years is no longer contraindication for rt-PA use, because intravenous thrombolysis has showed benefit in elderly patients, in spite of increased risk of intracranial hemorrhage in comparison to younger groups [16, 17]. In accordance with recent guidelines, uncontrolled arterial hypertension is still a contraindication for intravenous thrombolysis; however, there are in the literature some examples of successful off-label rt-PA use in patients with blood pressure, exceeding 200/110 mmHg [22].

The only permitted drug for intravenous thrombolysis in patients with stroke rt-PA is Alteplase, which was approved in North America in 1996 and in Europe in 2002. Alteplase is

administrated via peripheral IV line. Before thrombolysis, two peripheral IV lines should be placed. Central vein and arterial catheterization as well, as placement of nasogastric tubes and urinal catheters is strictly prohibited. These manipulations should be postponed for, at least, 2–4 h after thrombolysis. Dose of Alteplase is 0.9 mg/kg of actual body mass, not to exceed 90 mg. The initial 10% of the dose is injected during 1 min, and the remaining 90% is infused over 1 h. Use of both anticoagulants and antiplatelet drugs starts in 24 h after thrombolysis, and this approach distinguishes cerebral thrombolysis from other kinds of systemic thrombolysis.

Alteplase is not without side effects and complications. Most dangerous of them are intracranial hemorrhage and angioedema with following airway obstruction. Uncontrolled arterial hypertension, volume of infarction area, and age are strong risk factors of intracranial hemorrhage during and immediately after intravenous thrombolysis. In the case with suspicion to intracranial hemorrhage, Alteplase infusion is stopped, and emergent CT is indicated with the following neurosurgical consultation. Management of hemostasis is a difficult issue, and mainstream of treatment is the use of cryoprecipitate or fibrinogen concentrate with or without platelet transfusion. Conventional laboratory tests include fibrinogen, prothrombin time (PT), and complete blood count. However, such global method of hemostasis investigation as rotational thromboelastometry (ROTEM) is a much more precise method. Analysis of maximum clot firmness in FibTEM and ExTEM (FibTEM-MCF, ExTEM-MCF) allows to make a correct decision regarding the use of fibrinogen donators and platelets [23, 24].

Angioedema after Alteplase use represents a type of anaphylactoid reaction, which develops much more rarely in comparison to the rates of anaphylaxis after streptokinase administration [25, 26]. Angioedema during Alteplase infusion develops in 0.02–1.9% of patients (Fig. 8.1) [27–29]. Interestingly, angioedema appears more frequently in cases with cerebral thrombolysis in comparison to other kinds of systemic thrombolysis. The cause of angioedema is complement and kinin cascades activation [30]. There are several important clinical issues that deserve discussion. First, angioedema can rapidly lead to upper airway obstruction, and hypoxia, which is a strong factor of secondary brain injury in patients with cerebral catastrophe. Second, cases with stroke frequently have dysphagia and consciousness alterations, and even mild upper airways obstruction can rapidly decompensate patient's condition. Third, management of airways in cases with angioedema and intravenous thrombolysis is an extremely difficult challenge, because both laryngoscopy during tracheal intubation and emergent cricothyrotomy would be complicated with bleeding in the upper airways. Therefore, timely tracheal intubation is the only safe and effective decision in stroke patients with angioedema.

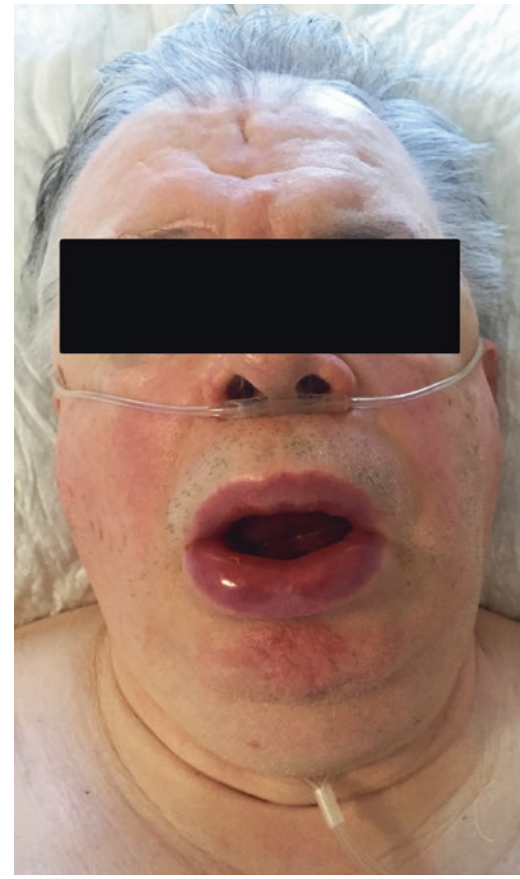

Fig. 8.1 Angioedema after rt-PA use

Despite the approved efficiency of rt-PA, the outcomes after intravenous thrombolysis in patients with large vessel occlusion (LVO: intracranial segment of internal carotid artery (ICA), proximal segment (M1) of middle cerebral artery (MCA), vertebral artery (VA), and basilar artery (BA)) still remain poor, and recanalization does not exceed 40% in this cohort [31–34]. Outcomes are strongly linked with recanalization, and endovascular treatment is an important option for recanalization.

Real renaissance of endovascular treatment for acute stroke therapy started only in 2015 with technological development of mechanical thrombectomy. However, first generation of thrombextractors did not show any benefits in comparison to systemic thrombolytic therapy. Moreover, in 2013 three trials showed poorer results of mechanical thrombectomy in comparison to systemic thrombolysis: SYNTHESIS [35], MR RESCUE [36], and IMS-III [37]. Second generation of clot retrievers was a game changer. On March 3, 2008, Dr. Hans Henkes in Stuttgart performed first thrombectomy with intracranial self-expandable stent Solitaire, a device originally engineered as assistance for brain aneurysms coiling. It was the start of stent-retrievers era in the treatment of stroke. This safe and effective method is widely spread around the globe. Several prospective randomized trials were ended and reported in 2015. Published in January 2015, MR CLEAN study, or Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands, randomized 233 patients with endovascular thrombectomy and standard therapy vs 267 patients with standard intravenous thrombolytic therapy [38]. Patients with stroke in anterior circulation were included, 90% of them received rt-PA intravenously in both groups. Stent retriever was used in 97% of endovascular procedures. Results showed significant prevalence of favorable outcomes in endovascular group.

ESCAPE trial, or Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke, compared also endovascular and standard treatment randomized groups of 165 and 150 patients with anterior circulation stroke; however, therapeutic window for thrombectomy was as large as 12 h [39]. Patients with big core or poor collaterals on CTA were excluded. The study was stopped earlier than planned. Results were reported on February 2015 with better outcomes in endovascular arm compared to standard. EXTEND-IA, or Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection, trial was also stopped in advance after randomization of 70 patients due to clinical success of an endovascular arm [40]. This study was designed for patients with stroke in anterior circulation with core of brain infarction <70 ml and timing to start endovascular treatment within 6 h since symptoms onset. Trial showed better outcomes in endovascular arm in comparison to medical treatment. Similar results were achieved in industry—sponsored SWIFT PRIME, or SOLITAIRE FR with the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke trial [41]. Another industry funded trial, REVASCAT, or Endovascular Revascularization with Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 h, with extended therapeutic window for thrombectomy, showed twice superiority of an endovascular method regarding outcomes without significant difference in safety [42]. In June 2015, American Heart Association published special focused update to the guidelines concerning inclusion of endovascular therapy in the early stroke management, based on the data of the randomized controlled trials published earlier in 2015 [43].

Despite the recent success of stent retrievers, it is not the exclusive type of devices for intracranial thrombectomy. Contact aspiration technique, mostly conducted by Penumbra with its catheters and aspiration system, also appeared to be safe and effective. Lapergue et al. reported slight superiority of thrombaspiration in a prospective nonrandomized trial whose results were published in June 2016 [44]. However, randomized controlled trial ASTER (Direct Aspiration First Pass Technique for Thrombectomy Revascularization of Large Vessel Occlusion in Acute Ischemic Stroke) did not

show any significant difference in recanalization rates between ADAPT and stentretreiver groups with rates of achievement of TICI 2b–3 85.4% and 83.1%, respectively [45]. In practice, most cath labs use both methods for acute stroke therapy and often combine them. Distal access catheters, like Sofia by Microvention or Fargo by Balt, appeared to be suitable for aspiration simultaneously with stentreiver thrombectomy.

In January 2018, Society of Neurointerventional Surgery (SNIS) published a standard for neuroendovascular management of stroke and summarized some important statements [46]. Successful mechanical thrombectomy, as defined by TICI grade 2b/3 reperfusion, should be an angiographic goal to be achieved. Despite the fact that intravenous thrombolysis is insufficiently effective in LVO, there is no evidence for harm from IV rt-PA administration. Because of the possibility of benefit and the lack of clear evidence of harm, candidacy for thrombectomy should not preclude patients, receiving full-dose IV rt-PA. In agreement with AHA guidelines, patients who meet the criteria for on-label use of IV rt-PA should receive it, irrespective of whether endovascular treatments are being considered or not [47, 48]. The role of intra-arterial thrombolysis remains unclear. There is no evidence of its effectiveness.

The type of anesthesia for performing mechanical thrombectomy is an important question. Randomized controlled trial Sedation vs Intubation for Endovascular Stroke TreAtment (SIESTA) and meta-analysis did not find significant differences between sedation and general anesthesia [46, 49]. Moreover, another recent randomized trial AnStroke (Anesthesia During Stroke) resulted with equal percentage of good outcomes at 3 months between sedation and general anesthesia groups [50]. Thus, both types of anesthesia are acceptable and may be individualized on the basis of patient's condition or stroke team habits.

Recently published DAWN trial showed the possibility of safety and effectiveness of endovascular treatment far beyond 6-h window [51]. It is a prospective randomized multicenter trial, focused on patients with severe clinical condition, relatively small core of brain infarction, and stroke onset between 6 and 24 h. One arm received standard care and the other arm combination of standard care and thrombectomy with Trevo device. Infarct volume was assessed with the use of DWI MRI or perfusion CT and was measured with the use of automated software (RAPID, iSchemaView). Results showed impressive difference with significantly better outcomes in the combined therapy arm. One month later, New England Journal of Medicine published the results of NIH funded DEFUSE-3 randomized trial (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke) [52]. This trial compared endovascular treatment within 6–16-h therapeutic window vs standard medical therapy. Patient's selection was based on CTP data and included those with volume of brain infarction less than 70 ml and a ratio of ischemic tissue on perfusion imaging to infarct volume 1.8 or more. Any thrombectomy device could be used. Results showed superiority of endovascular treatment not only in terms of good outcomes but also in mortality rate.

Therefore, state-of-the-art strategy of recanalization in patients with stroke comprises intravenous thrombolysis with immediately following mechanical thromboectomy with stent retriever devices in eligible for this procedure candidate. All manipulations are required to be performed as fast as possible without any time delay; however, the most recent data show safety and effectiveness of aggressive recanalization, performed during first 24 h of acute ischemic stroke.

8.3 Prevention of Thrombosis Enlargement and Early Recurrent Stroke

Stroke is an arterial thrombosis, and thus all patients obligatorily require antiaggregants. Adequate antiplatelet therapy prevents thrombosis enlargement and early recurrent stroke. There are some possible clinical scenarios, and therapeutic tactics is different from case to case (Table 8.1).

Table 8.1 Clinical scenarios of antiaggregants administration

	No antiaggregants before stroke	Antiaggregants before stroke
No intravenous thrombolysis	A: Immediately antiaggregants	B: Continue antiaggregants
Intravenous thrombolysis	C: Antiaggregants in 24 h after thrombolysis	D: Discontinue antiaggregants and resume in 24 h after thrombolysis
Endovascular mechanical thromboectomy	E: Antiaggregants perioperatively	F: Antiaggregants perioperatively

Clinical Scenario A: No Antiaggregants Before Stroke, No Intravenous Thrombolysis Patient should receive antiplatelet therapy immediately. This recommendation is based on the two large RCTs, and demonstrated significant reduction of morbidity and mortality due to administration of antiplatelet agents within 2 days after stroke [53, 54]. Despite the 48 h, mentioned in trials as a time of antiplatelet therapy beginning, antiaggregants should be given as early after stroke onset as possible in cases with missed intravenous thrombolysis. Choice of aspirin, COX-1 inhibitor, as a first line of antiplatelet therapy is still a commonly accepted approach. Monotherapy with clopidogrel, P2Y12 receptor inhibitor, is hypothetically possible, but did not demonstrate any benefit in comparison to aspirin [55]. Ticagrelor, another P2Y12 receptor inhibitor, works without metabolic activation. Comparison of aspirin and ticagrelol showed some nonsignificant benefit of ticagrelor, for example, in preventing stroke, myocardial infarction, and death within 3 months (Acute Stroke or Transient Ischemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes trial (SOCRATES)) [56]. This trial focused on non-severe stroke, and therefore further studies are needed for drawing any definite conclusions regarding comparison of aspirin and ticagrelor. Eptifibatide, glycoprotein IIb/IIIa inhibitor, is a promising antiplatelet agent, and the results of ongoing studies are forthcoming.

Dual antiplatelet therapy in patients with stroke is the controversial issue. Pathophysiologically, benefit of dual therapy can be explained with several arguments. First, different antiaggregants inhibit different pathways of platelets activation. Second, rate of nonresponders to COX and P2Y12 receptor inhibitors is not low in the population, and sometimes that is not easy to timely verify this phenomenon [57]. The most investigated and cited combination of antiaggregants is aspirin and clopidogrel. Moreover, this regimen demonstrated significant benefit in comparison to monotherapy in RCTs and meta-analysis (Clopidogrel plus Aspirin for Infarct Reduction in patients with acute stroke/TIA with large artery stenosis and microembolic signal (CLAIR), Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS)) [58, 59]. However, some important remarks have to be made. All above-mentioned studies, that showed benefit of dual antiplatelet therapy over monotherapy, had involved patients with TIA, or mild stroke. There are no trials that included patients with severe stroke, and thus we cannot extrapolate demonstrated evidence to severe stroke. The next extremely important remark, limited enthusiasm of administration of dual antiplatelet therapy in severe stroke, is the strong necessity of co-administration of anticoagulants. Low molecular weight heparin (LMWH) is not indicated for treatment of cerebral infarction, but anticoagulants are strongly recommended for the prevention of thromboembolic complications [16, 17]. Simultaneous use of dual antiplatelet therapy and LWMH in patients with stroke is very risky and dangerous, because even combination of aspirin and LWMH increases the rate of intracranial hemorrhage [60]. Therefore, in patients with severe stroke antiaggregant therapy should be presented to monotherapy with aspirin.

Clinical Scenario B: Antiaggregants Before Stroke, No Intravenous Thrombolysis Antiplatelet therapy should be continued. There are two main questions that should be answered before antiaggregant administration. First, if patient received antiplatelet monotherapy before stroke, should this therapy be continued, or should it be changed

to another antiaggregant? There is no any evidence, which could be used as a basis for the answer to this question. Hypothetically, it would be reasonable to perform aggregometry [61]. Second, if patient received antiplatelet dual therapy before stroke, should this therapy be continued, or should it be switched to monotherapy? It is also a disputable issue. In severe stroke, it is reasonable to switch to the monotherapy, as we discussed above. Aggregometry can help to choose the antiplatelet agent, which should be cancelled, and which should be kept. Further antiaggregant and anticoagulant therapy has to be managed under ROTEM [24].

Clinical Scenario C: No Antiaggregants Before Stroke, and Intravenous Thrombolysis In accordance to recent guidelines, antiplatelet agent should be started not earlier than in 24 h after intravenous thrombolysis and only after controlled CT. In severe stroke, LMWH should be co-administrated for prevention of thromboembolic events also, at least, in 24 h after thrombolysis [16, 17].

Clinical Scenario D: Antiaggregants Before Stroke, and Intravenous Thrombolysis Similar to the previous scenario, antiaggregants can be begun on the next day and after CT only. Tactics regarding the choice of antiplatelet agent is similar to scenario B.

Clinical Scenario E: No Antiaggregants Before Stroke, Endovascular Mechanical Thromboectomy If intravenous thrombolysis was missed, antiplatelet therapy is administrated perioperatively. Aspirin should be started as early as possible, before endovascular thromboectomy, and should be continued postoperatively [16, 17]. Indications can appear for intraoperative use of glycoprotein IIb/IIIa inhibitors. An indication for postoperative dual antiplatelet therapy is controversial and very risky in severe stroke.

Clinical Scenario F: Antiaggregants Before Stroke, Endovascular Mechanical Thromboectomy If intravenous thrombolysis was missed, antiplatelet therapy is administrated perioperatively. It is reasonable to stop dual antiaggregant therapy, and to begin monotherapy with choice like in scenario B. Intraoperatively, surgeon can face with the necessity of glycoprotein IIb/IIIa inhibitors. Postoperatively, antiaggregant monotherapy is continued under control of ROTEM. Intravenous thrombolysis, performed before endovascular therapy, is a strong contraindication for perioperative use of antiplatelet agents in both scenario E and F.

8.4 Intensive Care and Management of Complications

8.4.1 Blood Pressure Management

The majority of patients with stroke have arterial hypertension during acute stage of illness [62]. Rapid decrease of blood pressure is not indicated, and this can be dangerous, because the curve of cerebral autoregulation shifts to the right in most cases with stroke. This means that elevated level of blood pressure is required for adequate cerebral blood flow, especially in penumbra. Permissive hypertension is a commonly accepted practice. In cases without intravenous thrombolysis, or endovascular treatment blood pressure should not be lowered until 220/120 mmHg. As it was discussed above, blood pressure should be less than 180/105 after recanalization for the minimization of the risk of intracranial hemorrhage.

Arterial hypotension develops much more rarely in the acute stage of the stroke in comparison to the rate of arterial hypertension; however, decreased blood pressure is much more dangerous for the injured brain, and especially, for the penumbra zone [63]. Therefore, arterial hypotension should be corrected immediately. The target value of blood pressure for patient with stroke is a disputable question. According to the pathophysiology of the stroke, blood pressure should be maintained at the high level of patient's habitual blood pressure, or a little bit higher [16, 17]. Crystalloids compose the basis of volume resuscitation, whose aim is achievement and maintenance of euvolemia. Solution of 25% albumin can be also successfully used for the volume resuscitation. Simultaneously with volume effects, high dose of albumin demonstrates neuroprotective effects [64]. If arterial

hypotension persists, infusion of sympathomimetics starts without delay. Alpha-sympathomimetics are preferable, and norepinephrine is the sympathomimetic of choice. Beta-sympathomimetics should be avoided, especially in patients with cardioembolic type of stroke, because of high risk of cardiac rhythm abnormalities.

8.4.2 Airways Management

Patients in coma with the absence of protective reflexes due to severe dysphagia, and with hypoxic or hypercarbic respiratory failure are intubated immediately, because all these conditions represent absolute and classical indications for tracheal intubation and mechanical ventilation. There are some specific neurological indications for tracheal intubation: signs of increased intracranial pressure, infarct size >2/3 of MCA territory, and midline shift with compression of basal cisterns [65, 66]. In clinical practice, the spectrum of conditions between normal breathing and absolute indications for intubation and mechanical ventilation is extremely wide, and making decision regarding intubation is almost totally a subjective process. Today, there are no commonly accepted scales, which would objectify this making decision.

Previously, my group created Burdenko Respiratory Insufficiency Scale (BRIS: Table 8.2) [67]. The scale evaluates mental status with Richmond agitation sedation scale (RASS); swallowing, cough, and airway patency with previously reported protocols [68], and pO_2/FiO_2 index. Scoring is increased by 1 point with obesity because it has negative impact on the respiratory function [69]. Minimal total score is 0 (healthy person), maximal total score is 12 in a patient with normal weight, and 13 in an obese patient. BRIS parts begin with a normal criterion and ends with absolute indication for the intubation and mechanical ventilation. Therefore, patient must be intubated and ventilated immediately, if there is BRIS scoring 4 in any part of the scale ("Mental status", or "Swallowing, cough, and airway patency", or "Index pO_2/FiO_2"), or BRIS score of 5 or more as a sum. A BRIS score of 3 or less means that the patient can breathe spontaneously. A BRIS score of 4 as sum points of all three parts of BRIS is still a gray zone.

8.4.3 Deep Venous Thrombosis Prophylaxis

Stroke is a prothrombotic state, and larger half of patients with stroke have such risk factors, which considerably increase the risk of thromboembolic complications, such as hemiparesis and immobilization. Therefore, deep venous thrombosis prophylaxis should be performed in all cases, and needs intensive care. Prophylaxis can be started at least in 24 h and after brain CT, confirmed absence of bleeding, in cases with intravenous thrombolysis, and immediately after patient's admission and brain CT, if patient missed intravenous thrombolysis. Heparins either

Table 8.2 Burdenko Respiratory Insufficiency Scale (BRIS)

	Score 0	Score 1	Score 2	Score 3	Score 4
Mental status	RASS 0 or consciousness	RASS −1/+1 or hypersomnia	RASS −2/+2 or obtundation	RASS −3−4/+3+4 or stupor	RASS −5 or coma
Swallowing, cough, and airway patency	Independent swallowing. Effective cough. Normal airway patency	Independent swallowing. Ineffective cough. Normal airway patency	Slight aspiration of liquids. Effective cough. Normal airway patency	Aspiration for 2 or more food constituents. Ineffective cough. Normal airway patency	Aspiration for 2 or more food constituents. Ineffective cough. Impaired airway patency
Index pO_2/FiO_2	>300	250–300	220–250	200–220	<200

Scoring is increased by 1 in patients with obesity (body mass index > 30)
RASS Richmond agitation sedation scale

unfractionated or LMWH can be used for prophylaxis; however, LMWH are more effective in comparison to unfractionated heparin in preventing deep venous thrombosis [70].

It is difficult to choose correct dose of LMWH, because conventional hemostatic tests do not reflect influence of LMWH to hemostasis. The gold standard for this purpose is Anti-Xa-activity [71]. However, this test does not assess antiaggregants' influence on hemostasis, and has limited accuracy in cases with multi-organ dysfunction and sepsis. Therefore, ROTEM is a preferable laboratory method for choosing adequate dose of LMWH in cases with severe stroke, because different parameters of this test are influenced with both anticoagulants and antiaggregants [23].

8.4.4 Malignant Cerebral Infarction

W. Hacke and coauthors coined the term "malignant cerebral infarction" (MCI) in 1996 [72]. MCI is a space-occupying brain edema, developed in patients with ICA or MCA occlusion on the third-to-fifth day after stroke onset. CT and MRI show infarct of, at least, 1/2 of the MCA territory with midline shift and basal cisterns effacement. MCI is the most difficult and severe type of stroke with extremely high morbidity and mortality. Notwithstanding comprehensive patient management with timely use of state-of-the-art methods of recanalization and advanced intensive care give the chance for functional independence to 40–45% of patients with MCI in MCA territory, and to 22–45% of patients with thrombosis of BA [73].

MCI is a unique neurocritical care condition. There is no any other pathology, which would have brain herniation with nearly normal intracranial pressure [74]. This phenomenon is explained with Monro–Kellie doctrine, which postulates that increased volume of brain edema compensates with decreased volume of blood in case of LVO. Therefore, MCI is the only state when routine monitoring of intracranial pressure is not indicated, and when decision-making regarding decompressive hemicraniectomy is solely based on the clinical picture and CT data [74]. Decompressive hemicraniectomy with durotomy decreases mortality, and improves functional outcomes if it performs during 45 h after neurological deterioration. This statement is based on several RCTs [75–78]. For routine clinical practice, this means that decompressive hemicraniectomy should be performed in every patient with MCI regardless of the age, damage of dominant hemisphere, level of consciousness after deterioration, instability of blood pressure, and severity of patient's condition.

In MCI, temperature management is recommended in two regimens: induced normothermia in case of fever, and induced normo- or hypothermia in case of resistant intracranial hypertension after decompressive hemicraniectomy. Prophylactic induced normo- or hypothermia did not show benefit to outcomes [16, 17]. Hypothetically, that is an illogical fact, because decompressive hemicraniectomy and temperature management are most effective maneuvers for intracranial pressure reduction, and their effectiveness is comparable [79–81]. Commonly accepted explanation of the absence of approved efficacy of temperature management is wide spectrum of possible complications of induced hypothermia, which can worsen outcomes [82]. However, decompressive hemicraniectomy has also a lot of possible complications, including fatal [83]. At the same time, there is precise protocol of decompressive hemicraniectomy with description of all details of surgical technique. As a result, effective brain decompression is achieved. Surgical protocol is standardized and implemented into routine clinical practice [84]. Diametrically opposite situation existed with temperature management. Today, there is no single standardized temperature management protocol in MCI, which would be based on RCT. It is difficult to create design and perform high-quality RCT, because temperature management has a lot of details and nuances. We believe that standardized temperature management started in perioperative period of decompressive hemicraniectomy and continued during relatively long period, enough for brain edema dissolving would prove its effectiveness and benefit for outcomes. Further studies are strongly desirable.

8.5 Conclusion

Management of stroke is a hard teamwork, when well-organized cooperation between neurologist, intensive care specialist, and neurosurgeon increases the chance of survival and functional independence. Timely performed recanalization, correct prevention of recurrent early thrombosis, and adequate intensive care are obligatory conditions for patient's recovery.

Key Points

- Recanalization is the cornerstone of stroke management, and it should be performed as early as possible, because shortening of time between stroke onset and recanalization significantly improves outcomes. Recanalization is achieved with intravenous thrombolysis and endovascular treatment.
- Stroke is an arterial thrombosis, and thus all patients obligatorily require antiaggregants. Dual antiplatelet therapy with aspirin and clopidogrel is reasonable in selected subpopulations.
- Permissive arterial hypertension is a commonly accepted practice, because rapid decrease of blood pressure can be detrimental. Arterial hypotension is dangerous for the injured brain, and it should be corrected immediately.
- Malignant cerebral infarction is a unique neurocritical care condition, and requires decompressive hemicraniectomy with durotomy. Timely and adequate surgery improves outcomes in patients with malignant cerebral infarction.
- Hemostasis management is a real challenge for intensivists, because critically ill patients with stroke receive antiaggregants and anticoagulants. Traditional methods of hemostasis assessment frequently miss dangerous abnormalities. Global method of hemostasis investigation, such as rotational thromboelastometry (ROTEM) or thromboelastography (TEG), can be useful in intricate clinical situations.

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