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HEMORRHAGIC TRANSFORMATION OF ISCHEMIC STROKE: RISK FACTORS, EARLY OUTCOMES AND REHABILITION OF MOTOR DISORDERS

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Abstract: Objective: Hemorrhagic transformation (HT) after reperfusion therapy for acute ischemic stroke often predicts a poor prognosis. This systematic review and meta-analysis aimed to identify risk factors for HT and how they are modified by hyperacute treatment [intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT)].

Research Methods: PubMed and EMBASE electronic databases were used to search for relevant studies. Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated.

Results : A total of 120 studies were included. Atrial fibrillation and NIHSS scores were overall predictors of any intracerebral hemorrhage (ICH) after reperfusion therapy (IVT and EVT), hyperdense artery sign (OR = 2.605, 95% CI 1.212-5.599, I %) and number 2 = 0.000. Thrombectomy (OR = 1.151, 95% CI 1.041-1.272, I 2 = 54.3% were predictors of any ICH after IVT and EVT, respectively. The common predictors for symptomatic ICH (sICH) after reperfusion therapy were age and serum glucose level. Atrial fibrillation (OR = 3.867, 95% CI 1.970-7.591, I 2 = 29.1%), NIHSS score (OR = 1.082, 95% CI 1.060-1.105, I 2 = 54.5%), and time to onset (OR-TO) = 1.003, 95% CI 1.001-1.005, I 2 = 0.0%) were predictors of sICH after IVT. Alberta Stroke Program Early CT Score (ASPECTS) (OR = 0.686, 95% CI 0.565-0.833, I 2 = 77.6%) and number of thrombectomy passes (OR = 1.374, 95% CI 1.012-1.012-1.6 %) = 1.866, I 2 = 1.866. were predictors of sICH after EVT.

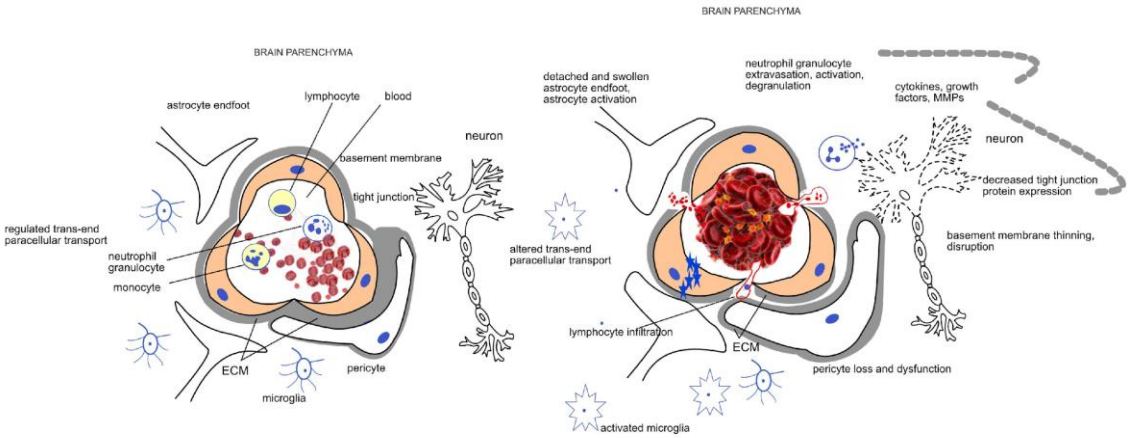
Conclusion : Several predictors of ICH have been identified, which differ depending on the type of treatment. Studies based on larger and multicenter data sets should be prioritized to confirm the results.

Ischemic stroke, which results from a lack of blood supply to the brain, is one of the leading causes of death and disability worldwide. Hemorrhagic transformation (HT), a potentially serious complication of the disease itself or its treatment aimed at restoring optimal blood flow, increases morbidity and mortality. Detailed conclusions can be found in the literature on the pathophysiological background of hemorrhagic transformation, potential clinical risk factors that increase its likelihood, and various biomarkers that are expected to help predict it and contribute to clinical outcome. Clinicopathological studies also contribute to improving our knowledge of hemorrhagic transformation. We summarized the clinical risk factors for hemorrhagic transformation of ischemic stroke in terms of risk reduction and collected the most promising biomarkers in the field. Also, adjuvant treatment options in reperfusion therapy were reviewed and summarized. We emphasized the importance of the optimal timing of revascularization treatment for carefully selected patients and the individual treatment of underlying diseases and comorbidities. Another important conclusion is that more intensive clinical follow-up, including serial cranial CT, may be recommended for selected patients, as clinicopathological examinations indicated that HT was more common than clinically suspected.

Keywords: ischemic stroke, hemorrhagic transformation, clinical risk factors, pathophysiology, biomarkers, clinicopathological studies, antithrombotic treatment

Introduction

Ischemic stroke (IS) is usually caused by occlusion of arteries in the central nervous system. It is a leading cause of death and disability worldwide [1]. Hemorrhagic transformation (HT), i.e. extravasation of blood into ischemic tissues, is a serious complication that worsens outcomes and increases mortality. HT can develop spontaneously or after reperfusion therapy [2]. HT occurs at different rates, ranging from 3 to 40% depending on the definition used in different studies [3]. According to the European Collaborative Acute Stroke Study (ECASS), HT on computed tomography is divided into two stages: radiologically detectable petechiae can be called hemorrhagic infarction (HI), and more severe forms are called parenchymal hematoma (PH), or without mass effect [4]. The National Institutes of Neurological Disorders and Stroke (NINDS) have classified HT into asymptomatic and symptomatic forms [5]. The SITS-MOST criteria define symptomatic intracranial hemorrhage (sICH) as a local or distant type 2 parenchymal hematoma, occurring within 22–36 hours after thrombolysis on CT, and associated with a four-point increase in NIHSS score from baseline or resulting in death [6]. Based on the pathophysiology, we aimed to collect key factors contributing to hemorrhagic transformation, including clinical risk factors, laboratory parameters, and biomarkers. We also sought prospective experimental data on potential future treatment options.



(a) (b)

Ischemic stroke is a sudden neurological deficit resulting from focal cerebral ischemia with persistent cerebral infarction (e.g., positive findings on diffusion-weighted MRI). The most common causes are: atherothrombotic occlusion of large arteries; embolism of cerebral vessels (embolic infarction); nonthrombotic occlusion of small, deep cerebral arteries (lacunar infarction); and proximal arterial stenosis with hypotension that reduces cerebral blood flow in arterial bifurcations (hemodynamic stroke). In one-third of ischemic strokes, the cause is not identified when the patient is discharged from the hospital; such strokes are classified as cryptogenic. The diagnosis is made on the basis of clinical findings, but CT or MRI is performed to exclude hemorrhage and to confirm the infarct size and extent. In some patients, thrombolytic therapy is effective in the acute phase. Depending on the cause of the stroke, carotid endarterectomy or stenting, as well as the use of antiplatelet or anticoagulant drugs, can help reduce the risk of subsequent strokes.

Embolic stroke of unknown source (ESUS), a subcategory of cryptogenic stroke, is diagnosed when the source is not identified after adequate diagnostic evaluation has excluded lacunar stroke, primary cardioembolic sources, and ipsilateral stenotic-occlusive disease (>50% occlusion). Recent evidence suggests that asymptomatic carotid artery disease with less than 50% occlusion may be an important cause of stroke (1).

Mechanical circulatory support devices (e.g., left ventricular assist devices or LAVA [2]). Other sources of embolism may include blood clots formed during open-heart surgery and atheroma of extracranial vessels - the aortic arch and jugular veins. Less common embolisms include fat (with fractures of tubular bones), gas (with decompression sickness), and venous thrombi passing from the right side of the heart to the left through the patent foramen ovale (paradoxical embolism). Embolism may resolve spontaneously or after invasive manipulation of the heart and blood vessels (e.g., during catheterization). Rarely, embolic stroke develops as a result of subclavian artery thrombosis, in which case the vertebral arteries and their branches are embolized.

Ischemic stroke can also be associated with the formation of lacunar infarcts. These small (≤ 1.5 cm) infarcts are caused by obstruction of the small perforating arteries that supply deep cortical structures. The cause of the obstruction of these vessels is believed to be lipoalveolar degeneration (degeneration of the wall of small arteries and their replacement by lipids and collagen). Lacunar infarcts can be caused by embolism. Lacunar infarcts larger than 1.5 cm in patients without cardiovascular risk factors (eg, hypertension, diabetes, smoking) indicate a central source of embolism. Neuroimaging with CT or MRI is performed primarily to exclude intracerebral hemorrhage, subdural or epidural hematoma, as well as rapidly growing, bleeding, or suddenly symptomatic tumors. Even with a large ischemic stroke in the carotid artery, CT signs may be insignificant in the first few hours. Changes may include loss of sulcus or insular cortex, loss of gray-white matter junction between cortex and white matter, and increased middle cerebral artery density. Within 6–12 hours after ischemia, medium- to large-sized infarcts are visible as areas of decreased density. Small infarcts (e.g., lacunar) can only be detected with MRI.

The electronic databases PubMed and EMBASE were used to identify relevant studies. Reference lists of relevant studies and systematic reviews were also checked, and a hand search was completed to find additional relevant studies. The following search terms, including synonyms and existing MeSH terms, were used to retrieve relevant studies: Acute ischemic stroke, hemorrhagic transformation, endovascular thrombectomy, intravenous thrombolysis. The primary search terms were combined using the logical operators "and" and "or" to obtain search results. The databases were searched from their inception to August 2021.

Eligibility criteria

To be eligible for inclusion, studies had to meet the following criteria: (1) Full-text publications in English. (2) Patients were diagnosed with acute ischemic stroke. (3) Patient cohort aged 18 years and older. (4) HT confirmed by CT/MRI scan within 48 hours of treatment. (5) The study included at least 50 patients. (6) Clinical or imaging data were measured before or during reperfusion therapy. (7) The type of treatment of the enrolled patients was IVT or EVT or bridging therapy (IVT plus EVT). (8) HT predictors were based on multivariate analysis and expressed as odds ratios (OR) with 95% CI.

Study screening and data acquisition

Studies retrieved from the search results were screened using three steps. First, duplicate studies from different databases were removed. Second, the titles and abstracts of the search results were screened for consistency by two independent reviewers (JS and CL), with disagreements resolved through discussion and, if necessary, checked with a third reviewer (LC). Finally, the relevant full texts were screened by the same independent reviewers (JS and CL), with disagreements resolved through discussion and, if necessary, with a third reviewer.

Method

For data extraction, two reviewers independently extracted data using a pre-specified data extraction spreadsheet. Data were extracted from selected studies based on the CHARMS checklist (20), including authors and years, journal of publication, study type (randomized controlled trial or observational cohort), single-center or multicenter study, baseline characteristics of participants such as age, sex, time to treatment initiation, NIHSS score, reported intracerebral hemorrhage (ICH) definitions, and number of patients with HT, time since HT treatment was confirmed, type of treatment

(intravenous or endovascular therapy), identified risk factors and their type (continuous or categorical), regions, and sample size. Odds ratios and 95% confidence intervals (CIs) were obtained for prognostic factors for performance measures, and confounding variables adjusted in multivariate analysis.

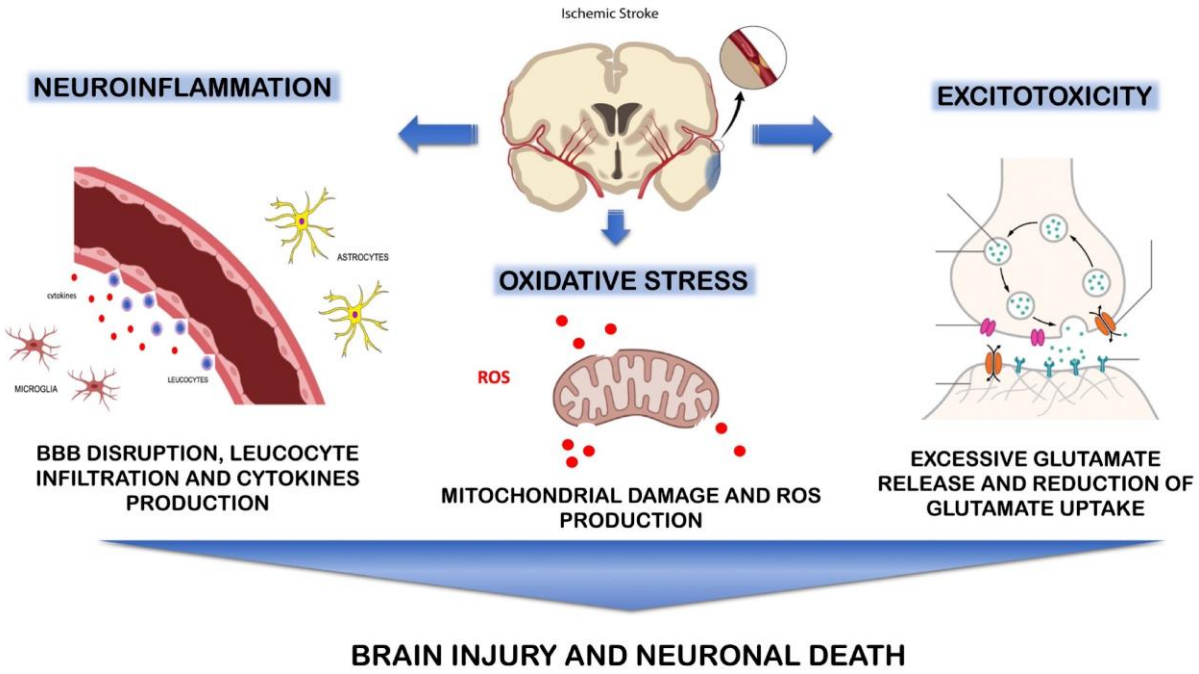
Quality assessment

Two reviewers independently assessed the risk of bias in the included studies. Any disagreements were resolved by discussion between the two reviewers and, if necessary, with a third reviewer until consensus was reached.

To assess the risk of bias in the included studies, the Quality of Prognostic Studies (QIPS) tool was used to assess validity and bias in six areas: participation, attrition, measurement of prognostic factors, measurement and accounting of confounders, outcome measurement and analysis, and reporting (21).

Statistical analysis

Combined hemorrhagic transformation rates with 95% CIs were calculated for symptomatic ICH (sICH) and any ICH, respectively. If a risk factor was reported in at least two studies, a meta-analysis of risk factors was performed using ORs with 95% CIs extracted from the individual studies. Odds ratios are an appropriate measure for categorical outcomes (22) and are the preferred reporting measure in meta-analyses of outcome prediction models (23). As the most common odds ratio reported in the included studies, we only reported odds ratios adjusted for confounding factors, which is preferable to analyses based on aggregate statistics in accordance with Cochrane guidelines (24).)



The I 2 test was used to assess heterogeneity among included studies (25). The cutoffs for the I 2 statistic were 25, 50, and 75% for low, moderate, and high heterogeneity, respectively. t 2 was used to assess the variance of the distribution of true effect sizes (26), and confidence intervals around t 2 were calculated to quantify the uncertainty of heterogeneity (27). Based on the available evidence (28), prediction intervals were calculated to estimate the effect size of future studies. A random-effects model was used to analyze the data regardless of heterogeneity. Begg's funnel plots were used to test for potential publication bias in the results for studies with more than 10 studies. Sensitivity analyses were performed by removing included studies one by one to determine the impact of individual studies on the overall effect estimate. All statistical analyses were performed with the Stata software package (V.13.1; Stata, College Station, Texas, USA) and R 4.1.2 (R Foundation), with a p -value of $p < 0.05$ considered statistically significant.

Results

The literature search and screening processes are shown in Figure 1. The initial search results included 5742 articles after removing duplicates. After title and abstract screening, 482 articles remained. After full-text screening, 107 studies were included based on the search results, and a further 13 relevant studies were identified through hand searching. A total of 120 studies (5, 6, 16–19, 29–142) were included in the meta-analysis.

Among the 120 studies, 67 patients were treated with IVT and 53 patients were treated with EVT. Table 1 shows the characteristics of the included studies. The number of participants ranged from 71 (44) to 88,094 (55), with an overall median sample size of 414 (interquartile range: 204.5–1,125). Additional information on the characteristics of the included studies is summarized in the Supplementary Table ('General characteristics').

The overall study quality was good, with ~48% of the included studies (58 out of 120) reporting a lack of reporting in the "Study Confounding" domain. The results of the quality assessment for each study are presented in the Supplementary Table ("Quality Assessment – QUIPS") and Supplementary Figures 1, 2 (143).

ICH and sICH event rates

Any ICH and sICH events were reported for any treatment type. In total, there were 32 IVT-based studies and 26 EVT-based studies reporting any ICH rates. Among the reported studies, the rate of any ICH ranged from 6.45% (106) to 49.55% (65), with a pooled rate of any ICH of 22.0% (95% CI 20.0–24.1%). The number of studies reporting sICH rates was 48 for IVT and 41 for EVT, respectively. The sICH rate ranged from 1.27% (55) to 20.89% (129), with a pooled rate of 5.2% (95% CI 4.8–5.6%). Four main sICH criteria were used in the included studies: the Stroke Monitoring Study of Safe Implementation of Thrombolysis (SITS-MOST) criteria (144), the European Collaborative Acute Stroke Study (ECASS) criteria (145), the National Institute of Neurological Disorders and Stroke (NINDS) criteria (7), and the Heidelberg Bleeding Classification (HBC) (146). The proportion of studies using each sICH criterion is shown in Supplementary Figure 3 . In cases where multiple sICH criteria were available, the SITS-MOST criteria were used to calculate the sICH rate; if the SITS-MOST criteria were not reported, the ECASS criteria were used.

HT risk factors

In total, more than 100 risk factors were reported in 113 prognostic factor studies. Because many risk factors were reported in only one study, the meta-analysis included 24 risk factors contributing to any ICH and 32 risk factors contributing to sICH. A summary of the risk factors reported in the included studies is provided in the Supplementary Table ("Study Results").

Meta-analysis of risk factors associated with ICH

Figures 2 and 3 show forest plots of risk factors for any ICH (147). A total of 16 risk factors for any ICH after IVT and 14 risk factors for any ICH after EVT were included in the meta-analysis. The meta-analysis showed that early ischemic changes, atrial fibrillation, hypertensia artery sign, hypertension, and NIHSS score were predictive factors for any ICH after IVT, while atrial fibrillation, Merci device use, diabetes mellitus, NIHSS score, and number of thrombectomy procedures were predictive factors for any ICH after EVT. Intraarterial tirofiban was associated with a lower risk of any ICH after EVT. Table 4 lists the predictors for any ICH.

Sensitivity analysis

To assess whether any particular study had a disproportionate impact on the results of the meta-analysis, heterogeneity was assessed for outcomes with a study size ≥3 and an I 2 ≥50%. A further sensitivity analysis was performed by removing one study at a time for outcomes with a non-zero confidence interval around the t 2 . Three outcomes showed a statistically significant association between prior IVT and any ICH after EVT, but with very high heterogeneity (I 2 ranged from 74 to 81%). The upper limit of the sensitivity analysis showed a statistically significant association between

prior stroke and any ICH after IVT, with low to moderate heterogeneity but very wide confidence intervals (OR = 13.06, 95% CI 1.08-

Pathology of the cardiovascular system

Cardiac evaluation typically includes ECG, telemetry or Holter monitoring, serum troponin levels, and transthoracic or transesophageal echocardiography. Implantable cardiac monitors are useful in identifying underlying atrial arrhythmias in patients with cryptogenic stroke (1).

Lacunar infarctions are more common in patients with diabetes mellitus or inadequately controlled hypertension.

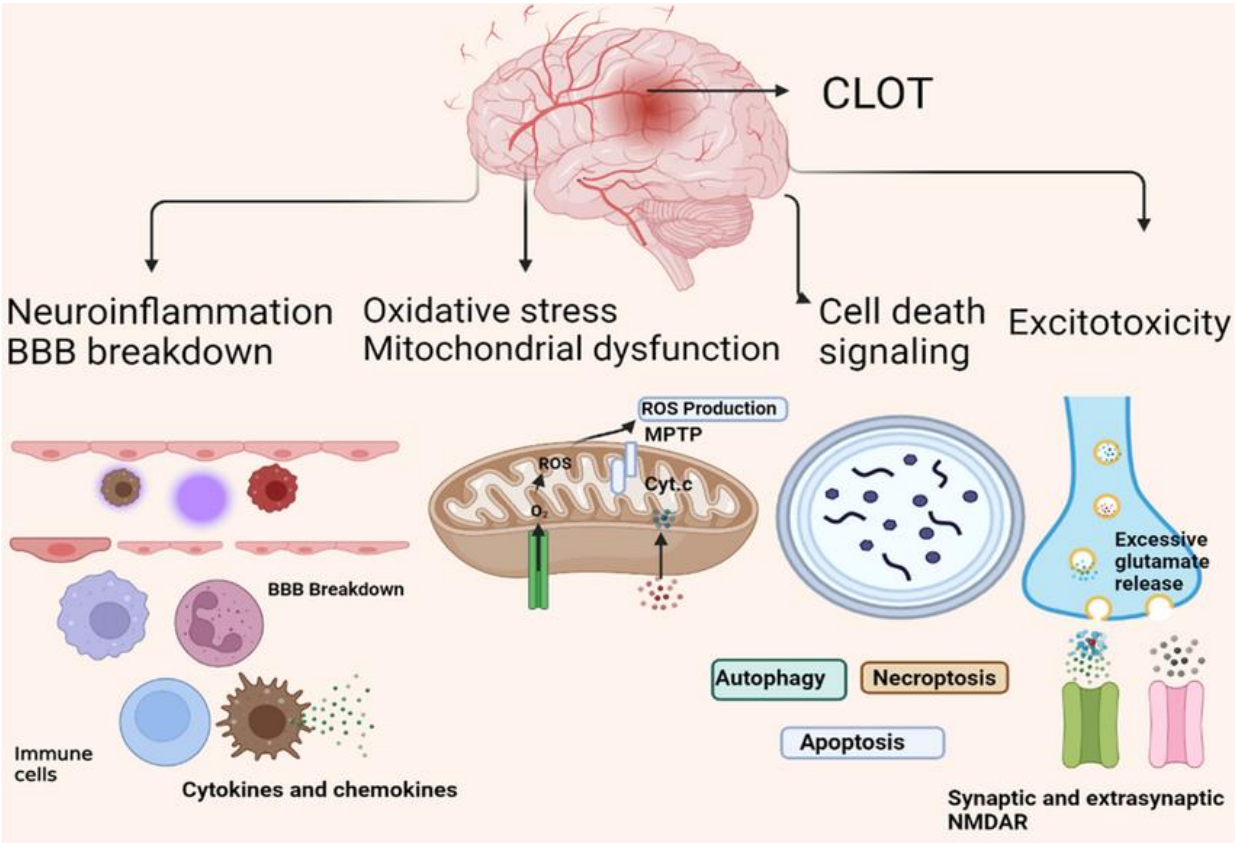
Atherosclerosis of large vessels

Large vessel atherosclerosis can affect intracranial or extracranial arteries.

Atherosclerotic plaque, especially ulceration, is a source of thrombus formation. Atherosclerotic plaque formation is possible in any large cerebral artery, but is more common in areas of turbulent blood flow, especially in the area of the carotid artery bifurcation. Most often, incomplete thrombosis or thrombotic occlusion occurs in the main trunk of the middle cerebral artery and its branches, as well as in the large arteries of the base of the brain, deep perforating arteries, and small cortical branches. The basilar artery and the supraclinoid part of the internal carotid artery are most often affected, that is, its segment between the cavernous sinus and the supraclinoid process.

Other reasons

Rare causes of stroke include vascular inflammation due to acute or chronic meningitis, vasculitis, and syphilis; dissection of the cerebral arteries or aortic wall; diseases accompanied by hypercoagulability (e.g., antiphospholipid syndrome, hyperhomocysteinemia, presence of a concomitant malignancy); increased blood viscosity (e.g., polycythemia, thrombocytosis, hemoglobinopathy, plasma cell pathology); and rare diseases (e.g., fibromuscular dysplasia, moyamoya disease, Binswanger disease).



Sickle cell disease is a common cause of ischemic stroke in children.

Any factor that compromises the circulatory system (e.g., carbon monoxide toxicity, severe anemia or hypoxia, polycythemia, hypotension) increases the risk of all types of ischemic stroke. Strokes can occur in border areas, between the blood flow of individual arteries; blood supply to such areas is usually poor, especially if the patient is hypotensive and/or has narrowed major cerebral vessels.

Most often, ischemic stroke develops due to spasm of blood vessels (for example, after migraine, subarachnoid hemorrhage, use of sympathomimetic drugs or drugs such as cocaine or amphetamines) or thrombosis of venous sinuses (for example, intracranial infection, after surgery, childbirth, secondary hypercoagulability).).

Pathophysiology of ischemic stroke

Insufficient blood flow in a single cerebral artery can often be compensated for by the efficient functioning of the collateral system, especially between the carotid and vertebral arteries through anastomoses in the circle of Willis and, to a lesser extent, between the large cerebral arteries. hemispheres. However, anatomical changes in the diameter of the circle of Willis and collateral vessels, atherosclerosis, and other acquired arterial lesions can interrupt collateral flow, increasing the likelihood that occlusion of a single artery will cause cerebral ischemia.

Results observed: Some neurons die when cerebral perfusion is reduced by 5% of normal for more than 5 minutes, and the size of the lesion depends on the severity of ischemia. With mild ischemia, the process of damage to neural tissue proceeds slowly. Thus, if perfusion is reduced to 40% of normal values, it may take 3-6 hours for all neurons in the ischemic zone to die. If severe ischemia lasts > 15-30 minutes, all affected tissue dies (infarcts). Damage progresses more rapidly under hyperthermia and more slowly under hypothermia. If tissues are ischemic but still damaged, rapid restoration of blood flow can prevent tissue necrosis or reduce its size. For example, interventions are often able to restore viability to moderately ischemic tissue (penumbra) surrounded by areas of severe ischemia; The penumbra exists due to collateral blood flow.

The mechanisms of ischemic injury include:

a) Swelling

b) Microvascular thrombosis

c) Programmed cell death (apoptosis)

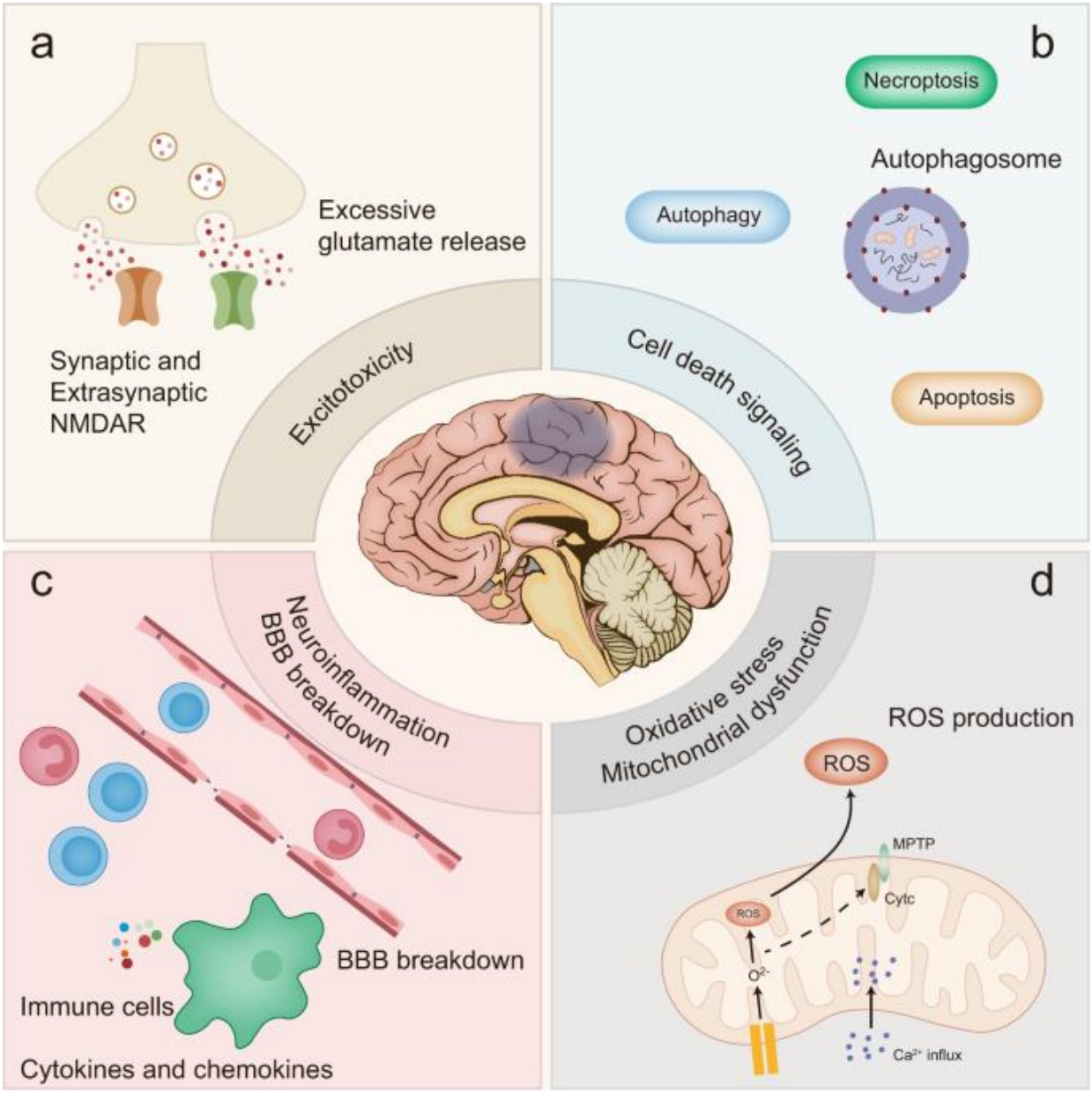
d) Infarction with cell necrosis

Inflammatory mediators (e.g., interleukin-1-beta, tumor necrosis factor-alpha) contribute to the development of microvascular edema and thrombosis. The edema, if acute or extensive, can increase intracranial pressure.

Many factors can lead to cell death: depletion of adenosine triphosphate (ATP) stores, disruption of ionic homeostasis (including intracellular calcium accumulation), lipid peroxidation by free radicals with damage to cell membranes (an iron-mediated process), exposure to excitatory neurotoxins (e.g. glutamate), and intracellular acidosis due to lactate accumulation.

Signs and symptoms of ischemic stroke

The signs and symptoms of ischemic stroke depend on the area of the brain affected. The clinical picture often allows us to determine which artery is affected (see table. Selected vascular syndromes), but, as a rule, there is no complete correspondence. The most severe neurological deficit can usually develop within a few minutes in the case of an embolism. Less often, the failure develops slowly, usually within 24-48 hours (the so-called "developmental stroke"), usually in atherothrombotic stroke.



In most of these strokes, unilateral neurological symptoms (often starting in one arm and spreading ipsilaterally) develop without headache, fever, or pain in the affected body parts. The development of symptoms is usually gradual, alternating with periods of stabilization.

A stroke is considered subtotal if there is residual function in the affected area, which implies the presence of viable tissue at risk of injury.

Embolic strokes often occur during the day, and the onset of neurological symptoms often precedes the headache. Blood clots usually form at night and are therefore first noticed upon awakening.

Lacunar infarctions may result in one of the classic lacunar syndromes (e.g., pure motor hemiparesis, pure sensory hemianesthesia, combined hemiparesis and hemianesthesia, ataxic hemiparesis, dysarthria, and awkward hand syndrome); there are no signs of cortical dysfunction (e.g., aphasia). The consequence of recurrent lacunar infarctions may be the development of postinfarction dementia.

When a stroke occurs, an embolic stroke is more likely to occur than a thrombotic stroke. Seizures may occur months or years later; late attacks result from scarring or hemosiderin deposition at the site of ischemia.

Sometimes there is a fever.

Increasing neurological deficit, especially impaired consciousness in the first 48-72 hours, is often associated with increasing brain edema, but may also be associated with an expansion of the infarct zone. If the infarct is small, functional improvement is noticeable in the first days of the disease; further recovery occurs gradually up to 1 year.

a) Diagnosis of ischemic stroke

b) Initial clinical examination

c) Neuroimaging and blood glucose level determination using test strips

d) Test to determine the cause of a stroke

The diagnosis of ischemic stroke should be suspected when there is a sudden onset of neurological symptoms that are localized to the area of blood supply to one of the cerebral arteries. Ischemic stroke should be distinguished from other causes of similar focal deficits (sometimes called stroke mimics, which are non-cerebral vascular disorders that cause focal neurological signs (e.g., hypoglycemia), e.g.

a) seizures (e.g., with postictal paralysis)

b) Infectious lesion of the central nervous system

c) Functional neurological disorders (usually diagnosed by exclusion)

d) Migraine (e.g., hemiplegic migraine)

e) Headache, coma or stupor, and vomiting are more likely with a hemorrhagic stroke than with an ischemic stroke.

When a stroke is suspected, doctors can use standardized criteria to assess severity and track changes over time. This approach can be particularly useful as an outcome measure in efficacy studies. The National Institutes of Health Stroke Scale (NIHSS) is a 15-point scale that assesses a patient's level of consciousness, speech function, and motor and sensory impairment by asking the patient to answer questions and perform physical and mental tasks. It is also useful for selecting appropriate treatment and predicting outcome.

Evaluation of a patient with ischemic stroke requires assessment of the brain parenchyma, blood vessels (including the heart and major arteries), and blood.

It is not clear how to differentiate the different types of stroke based on clinical presentation; however, some guidelines based on the progression of symptoms, time of onset, and type of impairment can aid in diagnosis.

Although the initial diagnosis is made by clinical signs, neuroimaging and blood glucose level determination using test strips are considered urgent measures.

Clinical differentiation between lacunar, embolic, and thrombotic stroke based on history, examination, and neuroimaging is not always reliable, so additional testing is routinely performed to identify common or preventable causes and risk factors for stroke. Patients should be evaluated for the following causes and risk factors:

Vascular diseases

Vascular imaging may include magnetic resonance angiography (MRA), computed tomography angiography (CTA), bilateral carotid and transcranial duplex ultrasound, and conventional angiography. The choice and sequencing of imaging tests are individualized based on clinical findings. MRA, CT-A, and carotid ultrasound provide equally good visualization of the anterior cerebral circulation (carotid area); however, MRA and CT-A provide better visualization of the posterior cerebral circulation than carotid ultrasound. In general, CTA is preferred over MRA because it avoids

motion artifacts. In general, CTA or MRA should be performed promptly, but treatment with IV tissue plasminogen activator (tPA) should not be delayed if indicated.

Blood-related causes

Blood tests are performed to identify causes related to blood disorders (such as thrombotic pathologies), to assess the contribution of these pathologies and the contribution of other causes. Routine testing usually includes a complete blood count (CBC), blood chemistry panel, prothrombin time/partial thromboplastin time (PT/PTT), fasting glucose, hemoglobin A1C, and lipid profile.

Depending on the clinically suspected cause, additional tests may be performed, including homocysteine levels, thrombotic pathologies (antiphospholipid antibodies, protein S, protein C, antithrombin III, factor V Leiden), tests for rheumatic diseases (e.g., antinuclear antibodies, rheumatoid factor, erythrocyte sedimentation rate), serological analysis for syphilis, hemoglobin electrophoresis, and urine screening tests for cocaine and amphetamine.

Conclusion

Based on the provided file, here's a concise and academically-toned conclusion:

This study highlights the significant risk factors and outcomes associated with hemorrhagic transformation (HT) in ischemic stroke, emphasizing the complex interplay of clinical and pathophysiological elements. Key findings include the identification of predictors such as atrial fibrillation, NIHSS scores, and serum glucose levels, which vary depending on the treatment type—intravenous thrombolysis (IVT) or endovascular thrombectomy (EVT). These results underline the critical need for targeted interventions and vigilant clinical monitoring to mitigate HT risk and improve patient outcomes. The implications of this research extend to enhancing therapeutic strategies, refining patient selection criteria, and advancing neuroimaging protocols. However, gaps remain in understanding the long-term impact of HT and the efficacy of emerging biomarkers. Future research should focus on larger multicenter studies, novel biomarkers, and integrative therapeutic approaches to optimize stroke management and reduce the burden of complications like HT. These efforts will contribute to the evolution of personalized medicine in stroke care

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