

# Acute ischemic stroke

Acute [ischemic stroke](#) (AIS) AKA [cerebral infarction](#). Obsolete term: [cerebrovascular accident](#) (CVA).

Acute ischemic [stroke](#) is a potentially devastating condition and the leading cause of morbidity and mortality, affecting an estimated 800 000 people per year in the USA.

The natural history of untreated or un revascularized large vessel occlusions in acute stroke patients results in mortality rates approaching 30%, with only 25% achieving good neurologic outcomes at 90 days.

Endovascular therapy (ET) is typically not considered for patients with large baseline ischemic cores (irreversibly injured tissue). Computed tomographic perfusion (CTP) imaging may identify a subset of patients with large ischemic cores who remain at risk for significant infarct expansion and thus could still benefit from reperfusion to reduce their degree of disability <sup>1)</sup>.

## Pathophysiology

see [Cerebral ischemia pathophysiology](#).

## Diagnosis

Raabe and Seidel, discuss imaging and neurophysiological tools that may help the surgeon to detect intraoperative ischemia. The strength of intraoperative [digital subtraction angiography](#) (DSA) is the full view of the arterial and venous vessel. DSA is the gold standard in complex and giant aneurysms, but due to certain disadvantages, it cannot be considered standard of care.

[Intraoperative microvascular Doppler sonography](#) is probably the fastest diagnostic tool and can quickly aid diagnosis of large vessel occlusions.

Intraoperative [indocyanine green videoangiography](#) is the best tool to assess flow in perforating and larger arteries, as well as occlusion of the aneurysm sac.

[Intraoperative neurophysiological monitoring](#) with [somatosensory evoked potentials](#) and [motor evoked potentials](#) indirectly measures [blood flow](#) by recording neuronal function. It covers all causes of intraoperative ischemia, provided that ischemia occurs in the brain areas under surveillance. However, every method has advantages and disadvantages. No single method is superior to the others in every aspect. Therefore, it is very important for the neurosurgeon to know the strengths and weaknesses of each tool in order to have them available, to know how to use them for each individual situation, and to be ready to apply them within the time window for reversible cerebral ischemia <sup>2)</sup>.

During [cerebral ischemia](#) induced by severe hemorrhagic shock, intravascular microdialysis of the draining venous blood will exhibit changes of the [Lactate to Pyruvate Ratio](#) (LP ratio) revealing the deterioration of global cerebral oxidative energy [metabolism](#). In neurocritical care, this technique might be used to give information regarding global cerebral energy metabolism in addition to the regional information obtained from intracerebral microdialysis catheters. The technique might also be

used to evaluate cerebral energy state in various critical care conditions when insertion of an intracerebral microdialysis catheter may be contraindicated, e.g., resuscitation after cardiac standstill, open-heart surgery, and multi-trauma<sup>3)</sup>.

## Treatment

see [Cerebral ischemia treatment](#).

## Epidemiology

Of the approximately 795 000 [strokes](#) in the United States annually, 87% are from [ischemia](#) and result in significant morbidity and mortality.

[Acute ischemic stroke in COVID-19 pandemic](#)

## Etiology

[Acute ischemic stroke Etiology](#)

## Diagnosis

[Acute ischemic stroke diagnosis](#).

## Differential diagnosis

A cerebral [infarction](#) is a type of [ischemic stroke](#) resulting from a blockage in the blood vessels supplying blood to the brain. It can be atherothrombotic or embolic.

Stroke caused by cerebral infarction should be distinguished from two other kinds of stroke: cerebral hemorrhage and subarachnoid hemorrhage.

A cerebral infarction occurs when a blood vessel that supplies a part of the brain becomes blocked or leakage occurs outside the vessel walls. This loss of blood supply results in the death of that area of tissue. Cerebral infarctions vary in their severity with one third of the cases resulting in death.

## Treatment

see [Acute ischemic stroke treatment](#).

## Complications

Liu et al. explored the mechanism of [P2RX7](#) in reducing hemorrhagic transformation [pathogenesis](#) after [acute ischemic stroke](#) by regulating [endotheliocyte Ferroptosis](#). Male SD rats were performed to establish [middle cerebral artery occlusion](#) (MCAO) model injected with 50% high [glucose](#) (HG) and HUVECs were subjected to OGD/R treated with high glucose (30 mM) for establishing HT model in vivo and in vitro. P2RX7 inhibitor (BBG), and P2RX7 small interfering [RNAs](#) (siRNA) were used to investigate the role of P2RX7 in BBB after MCAO in vivo and OGD/R in vitro, respectively. The [neurological deficits](#), [infarct](#) volume, degree of [intracranial hemorrhage](#), the integrity of the BBB, [immunoblotting](#), and [immunofluorescence](#) were evaluated at 24 h after MCAO. The study found that the level of P2RX7 was gradually increased after MCAO and/or treated with HG. The results showed that treatment with HG after MCAO can aggravate neurological deficits, infarct volume, oxidative stress, iron accumulation, BBB injury in the HT model, and HG-induced HUVECs damage. The inhibition of P2RX7 reversed the damaging effect of HG, significantly downregulated the expression level of [P53](#), HO-1, and p-ERK1/2, and upregulated the level of SLC7A11 and GPX4, which implicated that P2RX7 inhibition could attenuate oxidative stress and [Ferroptosis](#) of the [endothelium](#) in vivo and in vitro. The data provided [evidence](#) that the P2RX7 plays an important role in HG-associated [oxidative stress](#), endothelial damage, and BBB disruption, which regulates HG-induced HT by [ERK1/2](#) and [P53](#) signaling pathways after MCAO <sup>4)</sup>.

## Outcome

[Acute ischemic stroke outcome](#).

## Randomized, noninferiority trial

A randomized, [noninferiority trial](#) enrolled patients at 25 [North American](#) centers from May 19, 2012, through November 19, 2015, with follow-up for 90 days. Adjudicators of the [primary endpoints](#) were masked to treatment allocation. Patients with intracranial [large vessel occlusion acute ischemic stroke](#) presenting with a National Institutes of Health Stroke Scale (NIHSS) score of at least 8 within 8 hours of onset underwent 1:1 randomization to 3-D [stent retriever](#) with [aspiration](#) or aspiration alone. The primary analyses were conducted in the [intention-to-treat](#) population.

Interventions: Mechanical thrombectomy using intracranial aspiration with or without the 3-D stent retriever.

Main outcomes and measures: The primary effectiveness endpoint was the rate of a modified Thrombolysis in Cerebral Infarction (mTICI) grade of 2 to 3 with a 15% noninferiority margin. Device- and procedure-related serious adverse events at 24 hours were the primary safety endpoints.

Results: Of 8082 patients screened, 198 patients were enrolled (111 women [56.1%] and 87 men [43.9%]; mean [SD] age, 66.9 [13.0] years) and randomized, including 98 in the 3-D stent retriever with aspiration group and 100 in the aspiration alone group; an additional 238 patients were eligible but not enrolled. The median baseline NIHSS score was 18.0 (interquartile range, 14.0-23.0). Eighty-two of 94 patients in the 3-D stent retriever and aspiration group (87.2%) had an mTICI grade of 2 to 3 compared with 79 of 96 in the aspiration alone group (82.3%; difference, 4.9%; 90% CI, -3.6% to

13.5%). None of the other measures were significantly different between the 2 groups. Device-related serious adverse events were reported by 4 of 98 patients in the 3-D stent retriever with aspiration group (4.1%) vs 5 of 100 patients in the aspiration only group (5.0%); procedure-related serious adverse events, 10 of 98 (10.2%) vs 14 of 100 (14.0%). A 90-day modified Rankin Scale score of 0 to 2 was reported by 39 of 86 patients in the 3-D stent retriever with aspiration group (45.3%) vs 44 of 96 patients in the aspiration-only group (45.8%).

This [Randomized, noninferiority trial](#) provides [Class I](#) evidence for the noninferiority of the 3-D stent retriever with aspiration vs aspiration alone in [acute ischemic stroke](#). Future [trials](#) should evaluate whether these results can be generalized to other [stent retrievers](#) <sup>5)</sup>

## Retrospective cohort studies

Elawady et al. included [acute ischemic stroke](#) patients who underwent mechanical thrombectomy for [anterior circulation large vessel occlusion](#) with failed [recanalization](#) (modified treatment in cerebral ischemia [mTICI] score  $\leq 2A$ ). Patients who received IVT before MT were compared to those who received MT alone. [Propensity score matching](#) used demographic, clinical, radiographic, and procedural variables to match patients with and without IVT. The primary outcome was a favorable 90-day good functional outcome (defined as a modified Rankin scale of 0-2), and secondary outcomes included intracranial hemorrhage (ICH), symptomatic ICH (sICH), and 90-day mortality.

A total of 610 AIS patients with unsuccessful MT were included. After propensity matching, 219 patients were identified in each group. Median age was 70 years and 73 years in the IVT + MT and MT alone groups, respectively. In the IVT + MT group, final mTICI scores of 0, 1, and 2A were achieved in 92 (42.0%), 33 (15.1%), and 94 (42.9%) patients, respectively, versus 76 (34.7%), 29 (13.2%), and 114 (52.1%) in the MT alone group. The IVT + MT group had greater odds of a 90-day good functional outcome (adjusted odds ratio 2.54, 95% confidence interval 1.53-4.32). There were no significant differences in secondary outcomes.

[Intravenous thrombolysis](#) is associated with improved [functional outcomes](#) in AIS patients with LVO despite unsuccessful MT <sup>6)</sup>.

## Case series

[Acute ischemic stroke case series.](#)

## Case reports

A 70-year-old man was admitted to the hospital due to sudden inability to speak and inability to move his right limb for 3 h. Imaging confirmed a diagnosis of a [tandem occlusion](#) in the left carotid artery with a left [M1](#) occlusion. Carotid artery incision thrombectomy combined with stent [thrombectomy](#) was performed. The operation was successful, and 24 h later the patient was conscious and mentally competent but had motor aphasia. His bilateral limb muscle strength level was 5, and his neurologic severity scores score was 2.

Carotid artery incision thrombectomy combined with stenting for carotid artery plus cerebral artery

tandem embolization is clinically feasible. For patients with a complicated aortic arch and an extremely tortuous carotid artery, carotid artery incision can be chosen to establish the interventional path <sup>7)</sup>.

1)

Rebello LC, Bouslama M, Haussen DC, Dehkharghani S, Grossberg JA, Belagaje S, Frankel MR, Nogueira RG. Endovascular Treatment for Patients With Acute Stroke Who Have a Large Ischemic Core and Large Mismatch Imaging Profile. *JAMA Neurol*. 2016 Nov 7. doi: 10.1001/jamaneurol.2016.3954. [Epub ahead of print] PubMed PMID: 27820620.

2)

Raabe A, Seidel K. Prevention of ischemic complications during aneurysm surgery. *J Neurosurg Sci*. 2015 Nov 24. [Epub ahead of print] PubMed PMID: 26606432.

3)

Jakobsen R, Halfeld Nielsen T, Granfeldt A, Toft P, Nordström CH. A technique for continuous bedside monitoring of global cerebral energy state. *Intensive Care Med Exp*. 2016 Dec;4(1):3. doi: 10.1186/s40635-016-0077-2. Epub 2016 Jan 20. PubMed PMID: 26791144.

4)

Liu C, Tian Q, Wang J, He P, Han S, Guo Y, Yang C, Wang G, Wei H, Li M. Blocking **P2RX7** Attenuates **Ferroptosis** in Endothelium and Reduces HG-induced Hemorrhagic Transformation After MCAO by Inhibiting ERK1/2 and P53 Signaling Pathways. *Mol Neurobiol*. 2022 Oct 25. doi: 10.1007/s12035-022-03092-y. Epub ahead of print. Erratum in: *Mol Neurobiol*. 2022 Nov 23;; PMID: 36282438.

5)

Nogueira RG, Frei D, Kirmani JF, Zaidat O, Lopes D, Turk AS 3rd, Heck D, Mason B, Haussen DC, Levy EI, Mehta S, Lazzaro M, Chen M, Dörfler A, Yoo AJ, Derdeyn CP, Schwamm L, Langer D, Siddiqui A; Penumbra Separator 3D Investigators. Safety and Efficacy of a 3-Dimensional Stent Retriever With Aspiration-Based Thrombectomy vs Aspiration-Based Thrombectomy Alone in Acute Ischemic Stroke Intervention: A Randomized Clinical Trial. *JAMA Neurol*. 2018 Mar 1;75(3):304-311. doi: 10.1001/jamaneurol.2017.3967. PMID: 29296999; PMCID: PMC5885851.

6)

Elawady SS, Kasem RA, Matsukawa H, Cunningham C, Sowlat MM, Nawabi NL, Orscelik A, Venegas JM, Isidor J, Loulida H, Maier I, Jabbour P, Kim JT, Wolfe SQ, Rai A, Starke RM, Psychogios MN, Samaniego EA, Goyal N, Yoshimura S, Cuellar H, Howard B, Alawieh A, Alaraj A, Ezzeldin M, Romano DG, Tanweer O, Mascitelli J, Fragata I, Polifka A, Siddiqui F, Osbun J, Grandhi R, Crosa R, Matouk C, Park MS, Levitt MR, Brinjikji W, Moss M, Daglioglu E, Williamson R Jr, Navia P, Kan P, De Leacy R, Chowdhry S, Altschul DJ, Spiotta AM, Al Kasab S. The effect of intravenous thrombolysis in stroke patients with unsuccessful thrombectomy. *Interv Neuroradiol*. 2024 Sep 12;15910199241279009. doi: 10.1177/15910199241279009. Epub ahead of print. PMID: 39262342.

7)

Zhang M, Hao JH, Lin K, Cui QK, Zhang LY. Combined surgical and interventional treatment of tandem carotid artery and middle cerebral artery embolus: A case report. *World J Clin Cases*. 2020 Feb 6;8(3):630-637. doi: 10.12998/wjcc.v8.i3.630. PubMed PMID: 32110676; PubMed Central PMCID: PMC7031835.

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