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Acute revascularization in ischemic stroke: Updated Swiss guidelines

Patrik Michel[1], Michael Diepers[2], Pasquale Mordasini[3], Tilman Schubert[4], David Bervini[5], Jean-Daniel Rouvé[6], Yvan Gasche[7], Guido Schwegler[8], Christophe Bonvin[9], Krassen Nedeltchev[10], Emmanuel Carrera[11], Georg Kägi[12], Carlo Cereda[13], Thomas Nyffeler[14], Stephan Wetzel[15], Susanne Wegener[16], Henrik Gensicke[17], Stefan Engelter[17], Marcel Arnold[18], and on behalf of the Swiss Stroke Society.

Abstract

In acute ischemic stroke, intravenous thrombolysis (IVT) and acute endovascular therapy (EVT) have been shown to reduce long-term disability in randomized trials. International guidelines are partially not up to date and may not address situations for which there is limited scientific evidence. The goals of the present guidelines are to summarize the current scientific data for acute revascularization treatments to make sure that all Swiss Centers apply a similar, evidence, or consensus-based treatment standard. A multidisciplinary working group of the Swiss Stroke Society (SSS) searched and reviewed the literature on new randomized controlled trials (RCTs), large case series, meta-analyses, and other guidelines since the previous recommendations in 2009 to elaborate the consensus guidelines. The new RCTs have confirmed the effectiveness of IVT in various populations up to 4.5 h and proven the benefit of acute EVT up to approximately 8 h. For patients with unknown onset (including wake-up stroke), IVT and EVT can be effective up to 24 h after last proof of good health if patients are selected with advanced neuroimaging. Multiple

[1] Neurology Service, Lausanne University Hospital, Lausanne, Switzerland
[2] Neuroradiology Division, Cantonal Hospital Aarau, Aarau, Switzerland
[3] Institute for Diagnostic and Interventional Neuroradiology, Inselspital Bern and University of Bern, Berne, Switzerland
[4] Diagnostic and Interventional Neuroradiology, Department of Radiology and Nuclear Medicine, University Hospital Basel, Basel, Switzerland
[5] Department of Neurosurgery, Inselspital Bern and University of Bern, Berne, Switzerland
[6] Anesthesiology Service, Lausanne University Hospital, Lausanne, Switzerland
[7] Department of Anesthesiology, Pharmacology, Intensive Care & Emergency Medicine, University of Geneva, Geneva, Switzerland
[8] Division of Neurology, Hospital Limmattal, Schlieren, Switzerland
[9] Division of Neurology and Stroke Unit, Hôpital du Valais, Sion, Switzerland
[10] Department of Neurology, Cantonal Hospital Aarau, Aarau, Switzerland
[11] Neurology Service, University Hospitals of Geneva, Geneva, Switzerland
[12] Department of Neurology, Cantonal Hospital, St. Gallen, Switzerland
[13] Department of Neurology, Neurocentro della Svizzera Italiana, Lugano Civic Hospital, Lugano, Switzerland
[14] Neurozentrum, Cantonal Hospital Lucerne, Lucerne, Switzerland
[15] Neuroradiology, Hirslanden Clinic, Zürich, Switzerland
[16] Department of Neurology, University Hospital Zurich, Zurich, Switzerland
[17] Department of Neurology and Stroke Centre, University Hospital Basel, Basel, Switzerland
[18] Department of Neurology, Inselspital Bern and University of Bern, Bern, Switzerland

Corresponding author:
Patrik Michel, Service de Neurologie, Centre Hospitalier Universitaire Vaudois, 1011 Lausanne, Switzerland.
Email: patrik.michel@chuv.ch

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case series and meta-analyses allow narrowing down the indications and relative and absolute contraindications to optimize the benefit–risk ratio of acute revascularization.

Keywords
Stroke, revascularization, thrombolysis, thrombectomy, guidelines, Swiss

Background and methods

Randomized controlled trials (RCTs) have shown long-term benefit for acute acetylsalicylic acid, intravenous thrombolysis (IVT), acute endovascular therapy (EVT), neurorehabilitation, and decompressive craniectomy in selected ischemic stroke patients if they are treated in Stroke Units or Stroke Centers. Most of these treatments can be used in combination.

Treatment in Stroke Units and Stroke Centers is effective for all stroke patients, but IVT can only be offered to approximately 20–30% and EVT to 10–20% of patients arriving at the hospital within 24 h.[1] This restricted treatment rate for acute revascularization stems from the need to select patients with specific clinical and radiological criteria to obtain the treatment benefit.

The multidisciplinary working group "Acute Stroke Treatment" of the Swiss Stroke Society (SSS) has now updated the previous guidelines from 2009[2] in face-to-face reunions and by email. Representatives of the Swiss Neurological Society, the Swiss Society of Neuroradiology, the Swiss Society of Neurosurgery, the Swiss Society for Anesthesiology and Intensive Care, and the Swiss Society of Intensive Care Medicine participated actively in their elaboration. The working group performed a literature review in Pubmed/MEDLINE (2008–2020) for the combination of "stroke" and "randomised" or "meta-analysis" with any one of the following: "thrombolysis," "thrombectomy," "endovascular treatment," "endovascular therapy," and "anesthesia." In addition to retrieved phase III studies, we also considered large case series combining the latter five search terms with "minor stroke," "pediatric," "preexisting disability," "pregnancy," "mismatch," "antithrombotics," "anticoagulation," "platelet inhibitor," "blood pressure," "hemorrhage," "bleeding," and "craniectomy." Retrieved articles and other national and international guidelines were also scanned to identify further case series, in particular dealing with conditions potentially including the bleeding risk with IVT. The working group then reviewed these new publications to develop the consensus guidelines. The strength of our recommendations was expressed by the wording rather than a classification system.

Since 2014, the SSS maintains the Swiss Stroke Registry[3] for quality improvement and research purposes. The registry follows international recommendations for quality control of acute revascularization treatments.[4]

The goals of the present guidelines are to summarize the current scientific data for acute revascularization treatments in acute ischemic stroke. This should allow all Swiss Stroke Centers to apply a similar, evidence or consensus-based treatment to optimize the benefit–risk ratio for such patients. The author affiliations and potential conflicts of interest are listed in Appendix I, Table IA.

New scientific data

Since the third Swiss guidelines for acute treatment of ischemic stroke in 2009,[2] RCTs have

- confirmed the effectiveness of IVT with recombinant tissue plasminogen activator (rtPA) (alteplase, Actilyse®) within the 4.5 h window (up to 5 h in the meta-analysis)[5]; Patients over 85 years, with small vessel strokes, and patients with minor disabling and severe strokes seem to have similar benefit as all other patients[6];
- shown the effectiveness of EVT, in particular with stent retrievers[7–13] and/or aspiration techniques,[14,15] in combination with IVT up to about 8 h after stroke onset[16];
- confirmed the major prognostic importance of rapid treatment for both IVT and EVT ("time is brain")[5,17];
- shown the effectiveness of direct EVT for unknown onset or late-arriving patients between 6 h and 24 h in the presence of certain neuroradiological selection criteria (computed tomography (CT)- or magnetic resonance (MR)-based perfusion imaging or a combination of clinical deficit and radiological core measures)[18,19];
- shown the effectiveness of direct IVT for unknown onset or late-arriving patients beyond 4.5 h since last proof of good health if certain neuroradiological selection criteria are present (CT- or MR-based perfusion imaging[20–22] or fluid-attenuated inversion recovery diffusion-weighted imaging (FLAIR-DWI) mismatch on magnetic resonance imaging (MRI))[23];
- not shown the equivalence of low-dose IVT (with rtPA 0.6 mg/kg) with the usual dose (0.9 mg/kg), despite reduced bleeding risk with the lower dose[24];
- shown the probable ineffectiveness of IVT for patients with *non*disabling stroke[25];
- shown the ineffectiveness of ultrasound-assisted IVT[26];
- shown the probable superiority of IVT with tenecteplase (Metalyse®) 0.25 mg/kg over rtPA 0.9 mg/kg before EVT[27,28];
- shown the ineffectiveness of EVT within 8 h for basilar artery occlusion in two RCT.[29,30] A secondary on-

treatment analysis of one of these studies showed potential effectiveness,[29] whereas the analysis of patients with the National Institutes of Health Stroke Scale (NIHSS) >10 showed potential effectiveness in the other[30];
- shown noninferiority of IVT preceding the EVT in patients with proximal intracranial occlusions in two studies[31,32] but not in another[33];
- shown that short general anesthesia during EVT was not harmful[34–36] and potentially even beneficial.[37]

Furthermore, several international societies have updated their recommendations for treatment of acute ischemic stroke,[38–42] and rtPA for ischemic stroke treatment was accepted by the World Health Organization in their 21st List of Essential Medicines.[43,44]

Ongoing RCTs

Current RCTs are investigating the effectiveness of

- early EVT in patients with a minor neurological deficit (IN EXTREMIS) or with a large core (TENSION and IN EXTREMIS);
- EVT with or without preceding IVT (SWIFT-DIRECT, MR-CLEAN-no-IV, and DIRECT-SAFE);
- acetylsalicylic acid before/during early EVT (MR-CLEAN-MED);
- EVT based on simple CT-based selection criteria for unknown onset or late-arriving patients of up to 24 h (MR-CLEAN-LATE);
- IVT within 4.5 h after awakening with stroke based on simple CT-based selection criteria (TWIST)[45];
- IVT with tenecteplase (Metalyse®)[46–48] compared to rtPA;
- general anesthesia compared to conscious sedation during EVT (COMET, GASS, AMETIS, and CANVAS).

Efficacy and complications of revascularization treatment

IVT within 3 h reduced long-term disability and death in about one in four patients and within 4.5 h in about one in six.[49] Early IVT avoids completely long-term disability and death in about 1 out of 10 stroke patients.[5,6] The risk of symptomatic intracranial bleeding as defined by the Safe Implementation of Thrombolysis in Stroke-Monitoring Study definition[50] of 3–4% is already included in these long-term benefits.

After IVT, long-term mortality is neither increased nor decreased, despite an initial elevated risk of death.[5,6] Orolingual edema after IVT with rtPA occurs in 1–3% of patients, particularly if pretreated with angiotensin-converting enzyme inhibitors and with insular infarct localization.[51] Despite a mostly benign course, this situation provoked by a local release of bradykinin may require immediate intensive care measures. It is unknown whether treatment by bradykinin-receptor antagonists such as Icatibant (Firazyr®) reduces the need for intensive care measures.

EVT within 6 h reduces the long-term disability in one out of two treated patients and completely avoids disability in one out of four patients.[16,17] There is no increase in hemorrhage or early mortality, and long-term mortality is probably decreased.[16]

General recommendations

Given its narrow therapeutic window, we recommend that IVT be given in hospitals equipped with Stroke Units or Stroke Centers certified according to Swiss recommendations.[52] Similarly, we recommend that EVT is performed only by Stroke Centers mandated by the Inter-cantonal Agreement on Highly Specialized Medicine,[53] which fulfill the Swiss certification criteria.[52,54] In remote hospitals without a Stroke Unit, IVT may be offered in direct collaboration with a Stroke Unit or Stroke Center (e.g. via telemedicine) and should be documented in the national stroke registry for quality control.[3]

IVT based on simple neuroradiological criteria is effective within at least 4.5 h (in the meta-analysis up to about 5 h) after symptom onset[5,55–57] and EVT up to about 8 h.[17] Thereafter, patients need to be selected by specific neuroradiological criteria (see details below). Figure 1 shows the indications for different types of revascularization treatments in acute ischemic stroke, depending on delays and neuroradiological criteria.

Based on current scientific data, we recommend IVT within 4.5 h than EVT (bridging therapy) for proximal intracranial occlusions unless there are IVT contraindications as mentioned above. Several RCTs are currently studying this recommendation.

The effectiveness of both revascularization methods decreases minute-by-minute with increasing time from symptoms onset.[5,17] For this reason, we recommend speedy interventions for treatable patients, independently of prehospital delays. To shorten treatment delays, we recommend

- standardized prehospital and transfer protocols aiming at defining and shortening triage and transport delays (see the simultaneously published guidelines on this topic)[59];
- standardized management protocols in all emergency departments of hospitals with Stroke Units and Stroke Centers offering IVT and EVT, integrating neuroradiology and urgent laboratory assessment;
- to initiate IVT in the diagnostic imaging facility while applying clinical and vital sign surveillance.

We recommend that the choice of the revascularization method for a given situation should be based on all available clinical, neuroradiological, and laboratory data while trying to avoid additional delay.

Specific recommendations

Indications and contraindications for IVT and EVT are listed in Tables 2–9. We recommend performing an

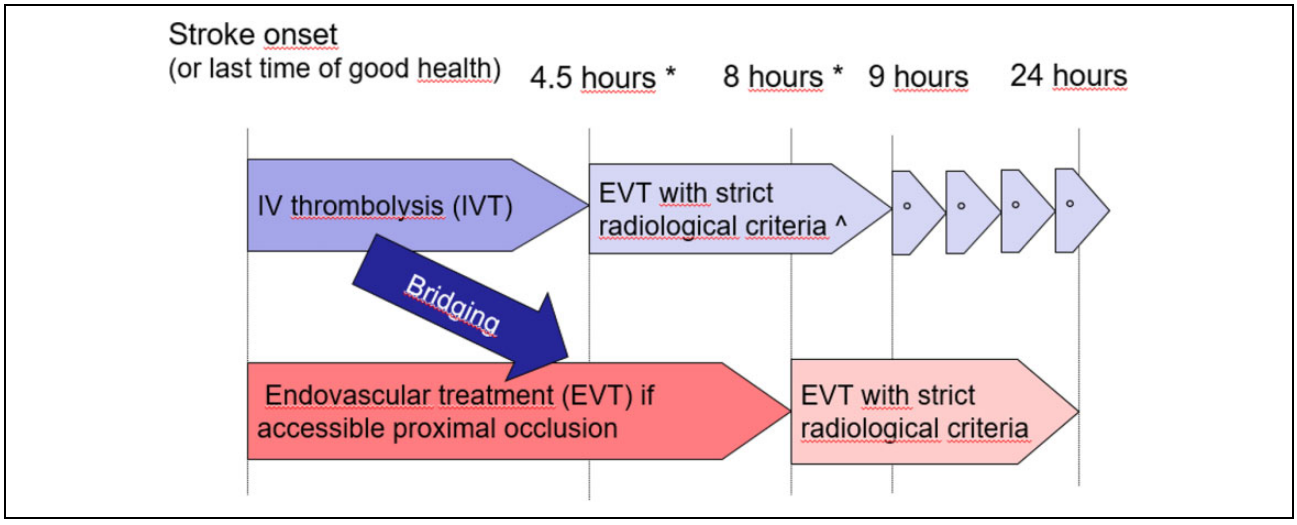

Figure 1. Overview of basic indications for revascularization treatment in acute stroke, considering time from onset (or last time of good health) and neuroradiological criteria. Stroke onset is defined as the last time free of stroke symptoms. See text and tables for further details. *In meta-analyses: IVT up to 5 h,[5] EVT up to 7.3 h.[17] ^Unknown stroke onset and neuroradiological mismatch: up to 9 h after the mid-time between symptom-free and stroke discovery.[58] °Unknown stroke onset and FLAIR/DWI-mismatch (MRI): IVT without upper time limit.[23] IVT: intravenous thrombolysis; EVT: endovascular therapy; FLAIR: fluid-attenuated inversion recovery; DWI: diffusion-weighted imaging; MRI: magnetic resonance imaging.

individualized benefit-risk estimation in the presence of *relative* contraindications (Table 8); such contraindications can also be regarded as additional outcome modulators.

Stroke onset is defined as the last time point when the patient was in his/her usual state of health, that is, the last proof of being without stroke symptoms. The NIHSS allows quantification of the clinical neurological deficit in stroke patients. We recommend that the NIHSS is used by medical personnel with appropriate instruction, exercise, and experience.

Given that IVT, and probably of EVT, are effective across all severities of a disabling stroke, we do not recommend to limit the treatments to a specific NIHSS window. We do recommend, however, that a disabling deficit (IVT and EVT) and/or a proven arterial occlusion within the ischemic territory (EVT) are present before initiation of treatment. For nondisabling deficits without major occlusions, IVT is may not be effective.[25]

If a major occlusion is not treated initially because of mild symptoms, in the case of worsening during continuous clinical surveillance, a "rescue" revascularization may be considered.

For patients with basilar artery occlusion, we recommend applying similar revascularization criteria and time windows as for the anterior circulation. MR-based imaging can help determine the "core" and, therefore, subsequent decision-making (see Table 2). However, measurement of the penumbra for decisions in the late time window is not recommended in basilar artery occlusions.

In patients with significant preexisting disability, there is little data on the effect of IVT and EVT[60] and safety concerns are the same as in nondisabled patients. In such patients, an individual estimation of the risk–benefit ratio may be used, which also considers the patient's personal values (if known).

There are no acute revascularization RCTs on children and adolescents up to 18 years. In this population, IVT and/or EVT may be considered along the criteria used in adult patients, if possible after a consensus discussion between neuropediatricians, adult stroke specialists, and parents.[61]

Pregnancy is a relative contraindication for IVT, and potential treatment effect on the mother should be balanced by the risk of harm to the fetus. Again, we recommend a discussion with all concerned persons if this does not cause significant treatment delay. The risk for the fetus is probably minor, in particular with EVT. The usual radioprotective measures in pregnancy should be applied.[62]

Neuroradiological selection of late patients

The irreversible ischemia ("core," in general, defined by diffusion or perfusion imaging) and the reversible ischemia ("penumbra," in general, defined by perfusion imaging or estimated from the neurological deficit) can be determined with sufficient precision for clinical decision-making. Rapid recanalization becomes more effective with a small "core" and an increasing "mismatch" between "penumbra" and "core." Another type of "mismatch" is based on acute MRI on the presence of a DWI and absence of a FLAIR lesion; this kind of mismatch indicates the short duration of ischemia (such as <4.5–6 h) and not the direct presence of a penumbra. Different concepts of mismatch are described in Table 1.

There is also potential for a mismatch between the core and neuroradiolocially defined (good) collateral circulation, but current RCTs have not yet used this concept.

Table 1. Mismatch definitions as used in RCTs.

Mismatch type and examples of RCTs	Mismatch definition in trials	Comments
Pure neuroradiological mismatch (PCT or MRI)[20,21]	Mismatch ratio $\geq$ 1.8 (in some studies > 1.2)[58,63]	Thresholds not validated for posterior circulation. Penumbra estimation is clinical rather than neuroradiological.
Clinical–neuroradiological mismatch (PCT or MRI)[18]	NIHSS $\geq$10 and core $\leq$30 ml NIHSS $\geq$20 and core 31–50 ml	Thresholds not validated for posterior circulation. Use of contrast medium not mandatory if using MRI.
FLAIR-DWI mismatch (MRI)[23]	Acute DWI lesion that is not visible on FLAIR sequences	Corresponds to stroke onset <4–6 h. Also applicable for posterior circulation. Use of contrast medium not mandatory if using MRI.

RCT: randomized controlled trial; PCT: Perfusion computed tomography; MRI: magnetic resonance imaging; NIHSS: National Institutes of Health Stroke Scale; FLAIR: fluid-attenuated inversion recovery; DWI: diffusion-weighted imaging; rCBV: regional cerebral blood volume.
Definition of penumbra and core: see text.
Mismatch ratio = (penumbra and core)/core.
If only raw perfusion images are available (without thresholding software), the following visual estimations can be used as follows:
- Core = clearly decreased rCBV.
- Penumbra = clearly slowed regional perfusion (rMTT or rTTP) blood flow (after subtraction of the rCBV volume).

In the absence of automated calculations of penumbra and core volumes, these can be estimated from the formula (a * b * c)/2. The letters stand for the largest diameter of the lesion in each plane.

We can summarize neuroradiological findings in acute ischemia as follows:

- A large core volume increases the risk of a poor outcome and bleeding, independent of whether acute recanalization is achieved or not.
- A larger "mismatch" between penumbra and core leads to more treatment benefit if acute recanalization is achieved rapidly.

Regarding treatment decisions and its benefits, the presence of a mismatch is as follows:

- Of minor importance in the very early time window.
- More important in late time windows and in patients with unknown stroke unset.

We, therefore, recommend that neuroradiological findings are used in *late* decisions for IVT/EVT; they may also be used in borderline situations in the early time windows.

We recommend following the revascularization criteria described in Tables 2–9 corresponding to inclusion and exclusion criteria used in RCTs, data from case series, other stroke treatment guidelines[37–44] and the consensus opinion of the authors.

Table 2. General indications and exclusion criteria for acute revascularization by IVT and/or EVT.

Indications
• Clinical diagnosis of ischemic stroke (neuroradiological proof desirable but not mandatory).
• New, disabling deficit at the time of treatment.
• Consider treatment also in a nondisabling deficit if there is an acute occlusion of a proximal intracranial artery (such as M1, carotid siphon, and basilar artery) and/or fluctuating symptoms.
Relative contraindications
• Severe preexisting disability, very poor quality of life, and life expectancy <3 months.
• For late EVT and late IVT >4.5 h: neuroradiological core concerning the major part of the ischemic territory. If brainstem ischemia: neuroradiological extensive transverse core (based on MRI if possible, especially if high NIHSS).

IVT: intravenous thrombolysis; EVT: endovascular therapy; MRI: magnetic resonance imaging; NIHSS: National Institutes of Health Stroke Scale.

Table 3. Indications for early IVT.

Cf. Table 2 and:
• Treatment onset <4.5 (maximally 5) hours.[5]
• For early IVT, perfusion imaging and/or demonstration of an arterial occlusion are not needed.

IVT: intravenous thrombolysis.

Additional measures during and after revascularization

Regarding the anesthesiology management during EVT:

- We do not make a recommendation regarding the type of anesthesia (general anesthesia vs. conscious sedation). Arguments in favor of general anesthesia are as follows:
    - Decreased level of consciousness (Glasgow Coma Scale $\leq$ 8).
    - Difficult communication, agitation, and excessive movements.
    - Cardiac and respiratory instability.
    - Potentially long-lasting or complex interventions.
- We recommend to elaborate institutional standardized operating procedures for anesthesiology management, aiming to

Table 4. Indications for early EVT.

Cf. Table 2 and:
- Treatment onset < 8 h.[17]
- In middle cerebral artery strokes: usually CT-ASPECTS $\geq$ 6 and/or MRI-DWI < 100 ml.
- Acute occlusion of an intracranial artery that is accessible with acceptable risk.
- If arterial imaging not possible: diagnostic cerebral angiography followed, if needed, by EVT, if indirect neuroradiological signs for arterial occlusion,[a] or if a proximal occlusion is clinically likely (stroke severity).
- If near-complete arterial occlusion, or if isolated extracranial occlusion: consider EVT in the presence of a neuroradiological or clinical–neuroradiological mismatch (cf. Table 1).

EVT: endovascular therapy; MRI: magnetic resonance imaging; DWI: diffusion-weighted imaging; CT: computed tomography.
[a]Noncontrast CT: "dense artery sign." MRI-SWI: "susceptibility vessel sign."

Table 5. Indications for EVT for wake-up stroke, unknown stroke onset, or late hospital arrival.

Cf. Tables 2 and 4 and:
- Treatment onset 8–24 h after last proof of good health maybe even later.[18,19]
- Additional criteria for supratentorial strokes.
- Core in general <70 ml
- Neuroradiological or clinical–neuroradiological mismatch (cf. Table 1).

EVT: endovascular therapy.

Table 6. Indications for IVT for wake-up stroke, unknown stroke onset, or late hospital arrival.

Attention: If criteria for late EVT are fulfilled (Table 5), direct EVT without IVT is recommended.
Cf. Table 2 and:
- Treatment onset beyond 4.5 (or maximally 5) hours, and
- Acute MRI: IVT without upper time limits[23] if
  - DWI-FLAIR mismatch
  - DWI in general <70 ml
- Or acute perfusion imaging on CT or MRI: IVT up to 9 h from the mid-time between last proof of good health and symptoms discovered[20,21] if
  - Neuroradiological mismatch (cf. Table 1).
  - Core in general <30 ml.

  Attention: demonstration of an arterial occlusion is not needed for late IVT.

IVT: intravenous thrombolysis; EVT: endovascular therapy; MRI: magnetic resonance imaging; FLAIR: fluid-attenuated inversion recovery; DWI: diffusion-weighted imaging; CT: computed tomography.

  - reduce preinterventional delays,
  - enhance patient safety,
  - respect general principles of neuroanesthesia, including pathophysiology-based blood pressure management.

Table 7. Contraindications for IVT.

In the presence of contraindications for IVT, the patient should be immediately evaluated for direct EVT according to Tables 3 and 5.
- Acute or subacute intracranial hemorrhage on acute neuroimaging.
- Rapid regression of symptoms to a degree not fulfilling the above indications for acute revascularization treatment.
- Symptoms or signs highly suggestive of a current subarachnoid hemorrhage.
- History of subarachnoid hemorrhage with unknown or incompletely treated bleeding source.
- Intracranial giant aneurysm >25 mm, large arteriovenous malformation with/without meningeal fistula, large cavernoma, any incompletely treated cavernoma with previous hemorrhage, and multiple cavernomas.
- Active malignant intracranial tumors (e.g. glioblastoma and metastasis).
- Intracranial or intraspinal intervention within <14 days (except lumbar puncture).
- Moderate or severe traumatic brain injury within <6 weeks.
- Known INR >1.7 or aPTT >40 s (spontaneously or from anticoagulants).
- Anticoagulation (inform the laboratory about the drug and time since last dose): if plasma levels not immediately available or if levels above the following limits → direct EVT. Otherwise, respect the following upper limits for IVT:
  - Any anticoagulant INR >1.7 and aPTT >40 s.
  - Therapeutic doses of heparin (unfractionated or low molecular): anti-Xa >0.2 units/ml.
  - Apixaban, rivaroxaban, and edoxaban: anti-Xa >100 ng/ml.[a]
  - Dabigatran: TT > 80 s or anti-IIa (=Hemoclot®=dTT) >100 ng/ml → Consider IVT 10 min after Praxbind® 5 mg IV (without rechecking coagulation).
- Endocarditis, pericarditis, and vasculitis of the central nervous system (known or high suspicion).
- Symptomatic aortic aneurysm (unless completely treated).

IVT: intravenous thrombolysis; EVT: endovascular therapy; aPTT: activated partial thromboplastin time; TT: thrombin time.
[a]No recommendation can be made regarding treatment with Andexxa® before IVT in patients with therapeutic levels of anti-Xa oral anticoagulants, because the efficacy and safety of such a pretreatment are not yet known.

Like in all strokes, we recommend that patients with revascularization treatments are admitted and continuously monitored for at least 24 h in a Stroke Unit or Stroke Center.[52,54] Treatment in intensive care in a hospital with a Stroke Unit or Stroke Center is recommended if admission criteria for intensive care are present.

We recommend that a platelet inhibitor is administered before, during, or immediately after a direct EVT, for example, with acetylsalicylic acid at a loading dose of 250–500 mg. Exceptions are patients who are already fully anticoagulated at the time of stroke. It is recommended to continue preexisting antiplatelet therapy should be continued and adapted, if needed.

We recommend avoiding antithrombotic drugs during the first 12–24 h after IVT, with justified exceptions. Prevention of deep vein thrombosis is recommended with intermittent

Table 8. Relative contraindications for IVT.

- In the presence of relative contraindications, IVT may be used after an individualized benefit-risk estimation taking into consideration other information on the patient, discussion among specialists, consideration of other factors that influence the cost-benefit ratio of IVT, and discussion with the patient and their legal representative (if possible). Consider direct EVT.
- Important prestroke disability (such as a modified Rankin score $\geq$4) and/or severe comorbidities.
- Subacute clinical ischemic stroke (< 6 weeks, with or without previous IVT/EVT).
- Silent (purely neuroradiological) subacute ischemic stroke.
- History of hypertensive intracerebral hemorrhage (consider IVT if blood pressure now well controlled).
- History of or current subdural hematoma.
- Asymptomatic intracranial aneurysm of 10–25 mm.
- Small intracranial arteriovenous malformations, meningeal fistula, isolated small cavernoma, and intracranial dissection (discuss with neuroradiologist).
- Large number of asymptomatic microbleeds (risk starts to increase from about 10) or extensive chronic nontraumatic superficial hemosiderosis.
- Malignant intracranial tumor in remission.
- Epileptic seizure at symptom onset (we recommend IVT if simultaneous acute ischemia proven by neuroimaging).
- Glycemia <2.7 or >22.2 mmol/l (we recommend IVT if simultaneous acute ischemia proven by neuroimaging).
- Known thrombocytompenia <100,000/mm^3 (we recommend not to delay IVT while awaiting laboratory tests, unless in patients with recent hemorrhages).
- Treatment with ticagrelor or prasugrel in combination with other antithrombotics.
- High blood pressure clearly above 185/110 mmHg at time of intended IVT.
- Important surgical intervention within <14 days (discuss with specialist).
- Ophthalmological intervention within <14 days (discuss with ophthalmologist).
- Diseases with increased bleeding risk (discuss with specialist).
- Internal bleeding (gastrointestinal, urological, active metrorrhagia, etc.) or biopsy of an internal organ within <14 days (discuss with specialist).
- Severe body trauma within <6 weeks (discuss with specialist).
- Pregnancy (balance potential effectiveness for the mother with risk for the fetus).

IVT: intravenous thrombolysis; EVT: endovascular therapy.

Table 9. Not contraindications for IVT.

- Antiplatelet agents in monotherapy or combination of acetylsalicylic acid and clopidogrel.
- Vitamin-K-antagonists if INR $\leq$ 1.7.
- Direct oral anticoagulants if
  - last dose at >48 h (>24 h if normal kidney function);
  - and/or plasma levels below certain thresholds (e.g. anti-Xa $\leq$100 ng/ml or anti-IIa $\leq$100 mg/ml);
  - and/or administration of a specific antidote[a] before IVT.
- History of subarachnoid hemorrhage with known and completely treated bleeding source (e.g. completely treated cerebral aneurysm).
- Preceding transient ischemic attack.
- Hygroma (asymptomatic not caused by subdural hematoma).
- Small number of (asymptomatic) microbleeds (e.g. <10) or (asymptomatic) superficial hemosiderosis.
- Asymptomatic intracranial aneurysm <10 mm.
- Benign intracranial tumors.
- Active extracranial oncological disease (if gastrointestinal participation: discuss with specialist).
- Known asymptomatic aortic aneurysm.
- After small surgical interventions in an easily accessible location.
- After cerebral or coronary angiography or percutaneous coronary revascularization (if taking aggressive antithrombotics: cf. contraindications in Tables 7 and 8).
- After lumbar puncture or arterial puncture (even if a few hours ago).
- History of sufficiently treated and controlled internal bleedings (gastrointestinal, urological, etc.)
- Menstruation.

IVT: intravenous thrombolysis.
[a]The efficacy and safety of IVT after Andexxa® in patients on anti-Xa oral anticoagulants is not yet known.

pneumatic compression and with early mobilization of the patient. The latter may start within the first 24 h with intermittent sitting at the edge of the bed or in a chair, if the neurological deficit and collaboration permit.[64,65]

According to the current evidence, acute blood pressure treatment seems to have little influence on long-term outcome. Still, the following upper blood pressure limits may be used as follows:

- During and after IVT: 185/110 mmHg (mean arterial pressure (MAP) 135 mmHg);
- After successful EVT resulting in a Thrombolysis in Cerebral Ischemia Score 2b or 3: 160/90 mmHg (MAP 115 mmHg);
- After successful revascularization of a chronic carotid stenosis during EVT: 140/70 mmHg (MAP 95 mmHg).

Worsening symptoms during blood pressure reduction and internistic comorbidities may also be considered in the acute blood pressure management.

We recommend offering craniectomy for ischemic mass effect after IVT for large hemispheric or cerebellar infarcts according to published criteria of the SSS[66] (and may also in selected patients above age 60[67]) after IVT and/or EVT if the clotting status (including fibrinogen levels) is within normal limits. This intervention may also be offered in the case of hemorrhagic transformation after IVT and/or EVT.

Patient information and consent for acute revascularization treatments

In an emergency medical situation in Switzerland, a patient's consent is not required for acute treatments such as IVT and/or EVT if they are offered within scientifically proven indications. If a clear expression of treatment refusal is known (e.g. in a living will) at the time of treatment decision, we recommend that this decision is honored. Refusal of a scientifically proven therapy can only be considered valid if expressed by a patient with sufficient decisional capacity regarding the intended treatment. In noncompetent patients, we recommend that the next of kin is informed concisely about risks and benefits of the planned intervention (including anesthetic management) if this does not lead to significant time loss. Deliberations should be documented in the medical chart. If a legal representative declines a scientifically proven therapy, we recommend that the treating physician follows this advice if it corresponds to a previously expressed wish or the patient's presumed will.

Author's note

The guidelines were elaborated and approved by the Swiss Stroke Society, the Swiss Neurological Society, the Swiss Society of Neuroradiology, the Swiss Society of Neurosurgery, the Swiss Society for Anesthesiology and Resuscitation, and the Swiss Society of Intensive Care Medicine. The German version of this guideline is published elsewhere and is the legally binding text.

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ORCID iD

Patrik Michel https://orcid.org/0000-0003-4954-7579
Christophe Bonvin https://orcid.org/0000-0002-9058-8105
Susanne Wegener https://orcid.org/0000-0003-4369-7023

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Appendix 1

Table 1A. Author affiliations, and potential past or current conflicts of interest regarding IVT and EVT.

Name	Institution	Potential conflicts of interest
Patrik Michel	Service de Neurologie, Center Hospitalier Universitaire Vaudois, Lausanne	Boehringer-Ingelheim, Medtronic, PROMISE steering committee (Penumbra). All payments go to the employer and are used for research and education.
Michael Diepers	Neuroradiologische Abteilung, Kantonsspital Aarau	RAPID Medical, Microvention. All payments go to the employer and are used for research and education.
Pasquale Mordasini	Universitätsinstitut für Diagnostische und Interventionelle Neuroradiologie, Inselspital Bern	Medtronic. Honoraria for presentations and courses go directly to the employer and are used for research and education. Steering committee of the SWIFT-DIRECT trial.
Thilman Schubert	Diagnostische und Interventionelle Neuroradiologie Klinik für Radiologie und Nuklearmedizin Universitätsspital Basel	None
David Bervini	Universitätsklinik für Neurochirurgie, Inselspital Bern	None. Honoraria for presentations and courses go directly to the employer and are used for research and education.
Jean-Daniel Rouvé	Service d'Anesthésiologie, Center Hospitalier Universitaire Vaudois, Lausanne	None
Yvan Gasche	Département d'Anesthésiologie, Pharmacologie, Soins Intensifs, & Urgences, Faculté de Médecine, Université de Genève	None
Guido Schwegler	Neurologie, Spital Limmattal	None
Christophe Bonvin	Service de Neurologie, Hôpital du Valais, Sion	Boehringer-Ingelheim: honoraria for presentations and advisory boards
Krassen Nedeltchev	Klinik für Neurologie, Kantonsspital Aarau	Boehringer-Ingelheim, Medtronic: honoraria for presentations and advisory boards
Emmanuel Carrera	Service de Neurologie, Hôpitaux Universitaires de Genève	None
Georg Kägi	Klinik für Neurologie, Stroke Center, Kantonsspital St.Gallen	Boehringer-Ingelheim, Zambon: honoraria for presentations and advisory boards
Carlo Cereda	Servizio di Neurologia, Neurocentro della Svizzera Italiana, Ospedale Civico di Lugano	None
Thomas Nyffeler	Neurozentrum, Luzerner Kantonsspital	None
Stephan Wetzel	Neuroradiologie, Hirslanden Klinik, Zürich	None
Susanne Wegener	Klinik für Neurologie, Universitätsspital Zürich und Universität Zürich	Boehringer-Ingelheim: for research projects
Henrik Gensicke	Klinik für Neurologie und Stroke Center, Universitätsspital Basel und Universität Basel	None
Stefan Engelter	Klinik für Neurologie und Stroke Center, Universitätsspital Basel und Universität Basel	None
Marcel Arnold	Universitätsklinik für Neurologie, Inselspital Bern	Boehringer-Ingelheim, Covidien, and Medtronic: honoraria for presentations and advisory boards.

IVT: intravenous thrombolysis; EVT: endovascular therapy.