Endovascular treatment for acute ischemic stroke

- Endovascular Stent Placement for Acute Ischemic Cerebral Infarction Secondary to Longsegment Internal Carotid Artery Dissection
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Do not wait for a patient with suspected stroke from large vessel occlusion to 'improve' after IV tPA initiation (possible harm ¹). Once the IV tPA drip is started, the patient should be immediately taken to the angiography suite or transported to a center with neuroendovascular capabilities, preferably a comprehensive stroke center. An ongoing debate is whether IV tPA is 'futile' in cases with large vessel occlusion given the low chance of large clot lysis, increased risk profile with the use of systemic tPA, and time delay to the initiation of thrombectomy. Trials to address this issue are currently underway in Europe.

Data have demonstrated that early endovascular recanalization of large vessel occlusions results in better outcomes than medical therapy alone. However, the majority of patients in these studies were treated with a stent retriever-based approach. The purpose of COMPASS is to evaluate whether patients treated with a direct aspiration first pass (ADAPT) approach have non-inferior functional outcomes to those treated with a stent retriever as the first line (SRFL) approach ².

For eligible patients with large vessel occlusions, mechanical thrombectomy is a highly effective treatment. It involves the use of a catheter to physically remove or break up the clot. This procedure is typically performed within 6-24 hours after symptom onset, depending on the specific case.

Intraarterial recombinant human tissue plasminogen activator for ischemic stroke treatment

Mechanical thrombectomy for acute ischemic stroke treatment

General information

Endovascular intervention is extremely safe and effective when performed up to 24 hours from stroke symptom onset, including "wake-up" strokes. The number needed to treat (NNT) (the number of patients to which treatment must be administered before either a single patient achieves a benefit or one adverse event is prevented) with thrombectomy is 2–4, compared to 3–19 for IV tPA in acute ischemic stroke (AIS).

Indications and case selection for intra-arterial tPA (IA-tPA)

see Intraarterial recombinant human tissue plasminogen activator for ischemic stroke treatment.

Unclassified

In 2015, the American Heart Association (AHA) made major changes to the guidelines for the endovascular treatment of acute ischemic stroke. The Class IA indications for endovascular therapy of stroke patients include symptom onset within 6 hours, proven large vessel occlusion of an artery in the anterior circulation, and the use of a stent retriever as part of the mechanical thrombectomy. Advanced perfusion imaging helps identify patients with a low ratio of ischemic core to salvageable penumbra. Equally important to overall clinical outcome is the organization of comprehensive stroke centers and the recent advent of the mobile stroke unit. Future clinical endovascular stroke trials will help us to better understand the role of endovascular interventions ³⁾.

Endovascular treatment (ET) of acute ischemic stroke (AIS) in the setting of carotid artery dissection (CAD) is a feasible, safe, and promising strategy ⁴⁾.

The treatment has been revolutionized by the introduction of several interventions supported by class I evidence-care on a stroke unit:

Thrombolysis with recombinant tissue plasminogen activator within 4.5 hours of stroke onset, aspirin commenced within 48 hours of stroke onset, and decompressive craniectomy for supratentorial malignant hemispheric cerebral infarction. There is new class I evidence also demonstrating benefits of endovascular therapy on functional outcomes in those with anterior circulation stroke. In addition, the importance of the careful management of key systemic physiological variables, including oxygenation, blood pressure, temperature, and serum glucose, has been appreciated. In line with this, the role of anesthesiologists and intensivists in managing AIS has increased ⁵⁾.

Anesthetic management

Debate continues about the optimal anesthetic management for patients undergoing endovascular treatment (ET) of acute ischemic stroke due to emergent large vessel occlusion.

Goyal et al., performed a systematic review and meta-analysis of all available studies that involved the use of stent retrievers for ET (stentriever group). Additionally, we included studies that were

published in 2015 and later, and compared the clinical outcomes among the studies using stentrievers or no stentrievers (pre-stentriever group). Outcome variables included functional independence (FI; modified Rankin Scale scores of 0-2), symptomatic hemorrhage, mortality, procedure duration, and vascular and respiratory complications. We calculated pooled odds ratios and 95% Cls using random-effects models.

Complications

Complications of endovascular treatment for acute ischemic stroke.

Randomized Controlled Trials

Amini et al. used data from the MR CLEAN (Multicenter Randomized Controlled Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) Registry, a large multicenter prospective cohort study including 3279 patients with acute ischemic stroke undergoing EVT. Random effect linear and proportional odds regression were used to analyze the effect of case mix on betweenhospital differences in 2 early outcomes: the National Institutes of Health Stroke Scale (NIHSS) score at 24 to 48 hours and the expanded thrombolysis in cerebral infarction score. Between-hospital variation in outcomes was assessed using the variance of random hospital effects (tau2). In addition, we estimated the correlation between hospitals' EVT-patient volume and (case-mix-adjusted) outcomes. Both early outcomes and case-mix characteristics varied significantly across hospitals. Between-hospital variation in the expanded thrombolysis in cerebral infarction score was not influenced by case-mix adjustment (tau 2=0.17 in both models). In contrast, for the NIHSS score at 24 to 48 hours, case-mix adjustment led to a decrease in variation between hospitals (tau 2 decreases from 0.19 to 0.17). Hospitals' EVT-patient volume was strongly correlated with higher expanded thrombolysis in cerebral infarction scores (r=0.48) and weakly with lower NIHSS score at 24 to 48 hours (r=0.15). Conclusions Between-hospital variation in NIHSS score at 24 to 48 hours is significantly influenced by case-mix but not by patient volume. In contrast, between-hospital variation in expanded thrombolysis in cerebral infarction score is strongly influenced by EVT-patient volume but not by case-mix. Both outcomes may be suitable for comparing hospitals on guality of care, provided that adequate adjustment for case-mix is applied for NIHSS score ⁶⁾

Trials favor rapid endovascular intervention in AIS with anterior circulation proximal vessel occlusion, small infarct core, and moderate-to-good collateral circulation ^{7) 8) 9) 10) 11) 12)}

Meta-analysis of these randomized trials shows that even large core infarcts or more distal occlusions still benefit from thrombectomy ¹³⁾.

Studies have established the effectiveness and relative safety of endovascular intervention. These trials favor rapid endovascular intervention in acute ischemic stroke with proximal vessel occlusion, small infarct core and moderate to good collateral circulation ^{14) 15) 16) 17)}.

Aspirin and unfractionated heparin are often used during endovascular stroke treatment to improve reperfusion and outcomes. However, the effects and risks of antithrombotics for this indication are unknown. van der Steen et al. therefore aimed to assess the safety and efficacy of intravenous aspirin, unfractionated heparin, both, or neither started during endovascular treatment in patients with ischemic stroke.

They did an open-label, multicentre, randomised controlled trial with a 2 × 3 factorial design in 15 centres in the Netherlands. They enrolled adult patients (ie, \geq 18 years) with ischaemic stroke due to an intracranial large-vessel occlusion in the anterior circulation in whom endovascular treatment could be initiated within 6 h of symptom onset. Eligible patients had a score of 2 or more on the National Institutes of Health Stroke Scale, and a CT or MRI ruling out intracranial haemorrhage. Randomisation was done using a web-based procedure with permuted blocks and stratified by centre. Patients were randomly assigned (1:1) to receive either periprocedural intravenous aspirin (300 mg bolus) or no aspirin, and randomly assigned (1:1:1) to receive moderate-dose unfractionated heparin (5000 IU bolus followed by 1250 IU/h for 6 h), low-dose unfractionated heparin (5000 IU bolus followed by 1250 IU/h for 6 h), low-dose unfractionated heparin (5000 IU bolus followed by 1250 IU/h for 6 h), low-dose unfractionated heparin (5000 IU bolus followed by 300 IU/h for 6 h), or no unfractionated heparin. The primary outcome was the score on the modified Rankin Scale at 90 days. Symptomatic intracranial haemorrhage was the main safety outcome. Analyses were based on intention to treat, and treatment effects were expressed as odds ratios (ORs) or common ORs, with adjustment for baseline prognostic factors. This trial is registered with the International Standard Randomised Controlled Trial Number, ISRCTN76741621.

Between Jan 22, 2018, and Jan 27, 2021, we randomly assigned 663 patients; of whom, 628 (95%) provided deferred consent or died before consent could be asked and were included in the modified intention-to-treat population. On Feb 4, 2021, after unblinding and analysis of the data, the trial steering committee permanently stopped patient recruitment and the trial was stopped for safety concerns. The risk of symptomatic intracranial haemorrhage was higher in patients allocated to receive aspirin than in those not receiving aspirin (43 [14%] of 310 vs 23 [7%] of 318; adjusted OR 1.95 [95% CI 1.13-3.35]) as well as in patients allocated to receive unfractionated heparin than in those not receiving unfractionated heparin (44 [13%] of 332 vs 22 [7%] of 296; 1.98 [1.14-3.46]). Both aspirin (adjusted common OR 0.91 [95% CI 0.69-1.21]) and unfractionated heparin (0.81 [0.61-1.08]) led to a non-significant shift towards worse modified Rankin Scale scores.

Periprocedural intravenous aspirin and unfractionated heparin during Endovascular treatment for acute ischemic stroke are both associated with an increased risk of symptomatic intracranial hemorrhage without evidence for a beneficial effect on functional outcome ¹⁸.

Sixteen studies (three randomized controlled clinical trials (RCTs) and 13 non-randomized studies) were identified comprising 5836 patients. Although non-GA was associated with higher odds of 3-month FI (OR=1.57; 95% CI 1.17 to 2.10; P=0.003) and lower odds of 3-month mortality (OR=0.62; 95% CI 0.47 to 0.82; P=0.0006, substantial heterogeneity was noted across included trials. Sensitivity analyses of RCTs showed that non-GA was inversely associated with FI (OR=0.55; 95% CI 0.34 to 0.89; P=0.01; I2=15%), while no association was noted with mortality (OR=1.36; 95% CI 0.79 to 2.34; P=0.27; I2=0%).

The updated meta-analysis demonstrates favorable results with non-GA, probably owing to inclusion of non-randomized studies. Recent single-center RCTs indicate that GA is associated with higher odds

of FI at 3 months, while other outcomes are similar between the two groups ¹⁹.

Observational cohort studies

Zhang et al. enrolled patients between January 2015 and December 2022 in a prospective database. Eligible patients with occlusions in the anterior circulation were given endovascular treatment and achieved successful reperfusion. The primary outcome was functional independence (modified Rankin Scale (mRS) score 0-2). Propensity score (PS)-weighted multivariable logistic regression analyses were adjusted and were repeated in subsequent 1:1 PS-matched cohorts.

732 patients, 516 without any intracranial hemorrhage (ICH) and 216 with aICH, were included. 418 and 348 patients were identified after matching in the aICH substudy and hemorrhagic infarction type aICH substudy, respectively. In the postmatched population, patients with aICH had worse functional outcomes (mRS score 0-2) at 90 days than patients without any ICH (37.8% vs 55.5%: P<0.001). Worse functional outcomes were seen in patients with aICH who were older (OR=5.59 (95% CI 2.91 to 10.74)), had higher baseline National Institutes of Health Stroke Scale score (OR=6.80 (95% CI 3.72 to 12.43)), lower baseline Alberta Stroke Program Early CT Score (OR=2.08 (95% CI 1.23 to 3.51)), and who received general anesthesia (OR=3.37 (95% CI 1.92 to 5.90)).

This matched control study largely confirmed that asymptomatic ICH after EVT is associated with worse functional outcomes, and the harmful effect is more significant in older patients and those with severe baseline clinical and radiological features ²⁰

A matched case-control study of patients with proximal occlusion after stroke (intracranial internal carotid artery and/or middle cerebral artery M1 and/or M2) on computed tomography angiography and baseline ischemic core greater than 50 mL on CT Perfusion (CTP) at a tertiary care center from May 1, 2011, through October 31, 2015. Patients receiving ET and controls receiving medical treatment alone were matched for age, baseline ischemic core volume on CTP, and glucose levels. Baseline characteristics and outcomes were compared.

The primary outcome measure was the shift in the degree of disability among the treatment and control groups as measured by the modified Rankin Scale (mRS) (with scores ranging from 0 [fully independent] to 6 [dead]) at 90 days.

Fifty-six patients were matched across 2 equally distributed groups (mean [SD] age, 62.25 [13.92] years for cases and 58.32 [14.79] years for controls; male, 13 cases [46%] and 14 controls [50%]). Endovascular therapy was significantly associated with a favorable shift in the overall distribution of 90-day mRS scores (odds ratio, 2.56; 95% CI, 2.50-8.47; P = .04), higher rates of independent outcomes (90-day mRS scores of 0-2, 25% vs 0%; P = .04), and smaller final infarct volumes (mean [SD], 87 [77] vs 242 [120] mL; P < .001). One control (4%) and 2 treatment patients (7%) developed a parenchymal hematoma type 2 (P > .99). The rates of hemicraniectomy (2 [7%] vs 6 [21%]; P = .10) and 90-day mortality (7 [29%] vs 11 [48%]; P = .75) were numerically lower in the intervention arm. Sensitivity analysis for patients with a baseline ischemic core greater than 70 mL (12 pairs) revealed a significant reduction in final infarct volumes (mean [SD], 110 [65] vs 319 [147] mL; P < .001) but only a nonsignificant improvement in the overall distribution of mRS scores favoring the treatment group (P = .18). All 11 patients older than 75 years had poor outcomes (mRS score >3) at 90 days.

In properly selected patients, ET appears to benefit patients with large core and large mismatch

profiles. Future prospective studies are warranted ²¹⁾.

Retrospective cohort studies

A study evaluates endovascular thrombectomy safety and efficacy in patients with acute large-vessel occlusion with tandem lesions, stratified by baseline ASPECTS.

Methods and results: We conducted a retrospective analysis of data from 16 centers. Inclusion criteria included the following: age \geq 18 years, anterior circulation tandem lesions, endovascular thrombectomy <24 hours of symptom onset, and \geq 70% internal carotid artery stenosis/occlusion. Patients were categorized into low (0-5) and high (6-10) ASPECTS. Inverse probability of treatment weighting matching was used to balance the groups. Primary outcomes included the following: 90-day modified Rankin Scale (mRS) score 0 to 2 and symptomatic intracranial hemorrhage. Secondary outcomes included the following: ordinal mRS, mRS 0 to 3, modified Thrombolysis in Cerebral Infarction \geq 2b and 2c-3, petechial hemorrhage, parenchymal hematoma (1/2), early neurologic improvement, and mortality. Of 691 patients, 44 had ASPECTS 0 to 5 and 505 had ASPECTS 6 to 10. Patients with low ASPECTS had lower odds of 90-day mRS 0 to 2 (adjusted odds ratio [OR], 0.48; P=0.036) and higher odds of symptomatic intracranial hemorrhage (adjusted OR, 3.78; P=0.014). Additional significant differences were found in mRS shift, mRS 0 to 3, parenchymal hematoma 2, and mortality. In interaction analysis, the association between low ASPECTS and functional outcome persisted only in the internal carotid artery occlusion subgroup, with no significant interaction indicating no reason to suppose a difference between the effect of both subgroups.

Conclusions: Endovascular thrombectomy in patients with tandem lesions with low ASPECTS is associated with reduced odds of functional recovery and increased symptomatic intracranial hemorrhage risk, when compared with patients with high ASPECTS. However, 30% of patients with low ASPECTS achieved 90-day functional independence, suggesting potential benefit for a nonnegligible proportion of patients²².

Interdisciplinary management

Interventional cardiologists adequately trained to perform Endovascular treatment for acute ischemic stroke could complement stroke teams to provide the 24/7 on call duty and thus to increase timely access of stroke patients to endovascular treatment. The training requirements for interventional cardiologists to perform endovascular therapy are described in details and should be based on two main principles: (i) patient safety cannot be compromised, (ii) proper training of interventional cardiologists should be under supervision of and guaranteed by a qualified neurointerventionist and within the setting of a stroke team. Interdisciplinary cooperation based on common standards and professional consensus is the key to the quality improvement in stroke treatment²³⁾.

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