PRESS RELEASE

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Endovascular thrombectomy for large ischemic strokes: is there still an equipoise?

Is endovascular thrombectomy (EVT) effective and safe in patients with large ischemic strokes up to 24 hours after last known well? Yes, according to the randomised controlled trials RESCUE Japan Limit, SELECT-2, and ANGEL ASPECT. But what are the latest insights and clinical implications after combining the individual patient data (IPD) from these three trials?

With the expansion of the treatment window for patients with acute ischemic stroke, the selection process for EVT has shifted towards a more imaging-driven decision process.

Especially for patients in later treatment windows (>6 hours after last seen well), unfavourable parenchymal and perfusion imaging criteria, such as low ASPECT scores (indicating large infarction) or small penumbras, may result in withholding EVT in these patients. This persisting equipoise can be partly explained by the fact that patients with large ischemic strokes have mostly been excluded from previous clinical EVT trials. However, three recent randomised controlled trials have addressed the safety and efficacy of EVT for large ischemic strokes. In the current study, the investigators performed an IPD meta-analysis of these three published trials.[1]

The RESCUE Japan Limit trial was conducted in Japan, the SELECT-2 trial in North America, Europe, Australia and New Zealand and the ANGEL ASPECT trial in China. All trials compared EVT to standard medical care in patients with large ischemic strokes of the anterior circulation up to 24 hours of last known well and used imaging criteria to define stroke magnitude. For the current IPD meta-analysis, the ischemic core was considered large if ASPECTS was ≤5 on non-contrast CT or MRI-scan, or if the core was 50ml or more. The primary efficacy outcome was the distribution of scores on the modified Rankin Scale (mRS) at 90-day follow-up. Secondary outcomes included functional independence (mRS 0-2), independent ambulation (mRS 0-3), symptomatic intracranial haemorrhage (sICH), and mortality.

In total 1009 patients were included, of whom 412 (41%) were female, 506 (50%) received EVT and 503 (50%) received medical management (MM). EVT improved functional outcomes, (adjusted Generalized Odds Ratio (aOR): 1.78 (95%CI: 1.48-2.14; p<0.001), functional independence (23% vs 9%, adjusted risk ratio (aRR): 2.62 (2.31-2.97), p<0.001) and independent ambulation (41% vs 24%, aRR: 1.76 (1.30-2.38), p<0.001) compared to MM, but with more frequent early neurological worsening (aRR: 1.42 (1.09-1.84), p=0.010). No difference in mortality was identified between EVT (27%) and MM (28%), aRR: 0.90

(0.80-1.01), p=0.063 or sICH (EVT: 1.8% vs MM: 1.6%, aRR: 1.14 (0.36-3.12), p=0.83). Subgroup analyses consistently favoured EVT.

Professor Amrou Sarraj, first author of this meta-analysis, concludes: “The MAGNA IPD meta-analysis provides strong evidence for clinically meaningful benefit in reducing disability for patients with extensive ischemic injury on non-contrast CT, CTP or MRI.”

He adds: “The results from the previously published large core trials and from this pooled dataset provide unequivocal evidence on the efficacy and safety of EVT in patients with large core infarcts. The benefit persists across the spectrum of age, clinical severity and time with clear benefit up to an estimated ischemic core volume of 150mL.”

The investigators look forward to the upcoming results from the other, yet to be published, large core trials from TESLA, TENSION and LASTE and plan on updating the results of the MAGNA meta-analysis upon the publication of these trials. “This will increase the accuracy of the estimation of the treatment effect and will give even more power to look further into the details related to subgroups and selection imaging modalities”, Professor Sarraj added. The research team hopes that this joint effort will eventually set the pathway for selection algorithms and treatment boundaries in patients with large vessel occlusion.

ENDS

References:

1. Sarraj A *et al.* Mechanical thrombectomy for large brain infarctions (MAGNA) – An individual patient-level data (IPD) meta-analysis of SELECT-2, RESCUE Japan Limit and ANGEL ASPECT trials. Presented at the European Stroke Organisation Conference; 26 May 2023; Munich, Germany.

Effect of individualised versus standard blood pressure management during endovascular stroke treatment under procedural sedation (INDIVIDUATE) on clinical outcome: A randomised clinical trial[1]

Does an individualised approach to blood pressure management work better than standard strategy in stroke patients undergoing endovascular treatment?

The optimal strategy for management of blood pressure during endovascular treatment of cerebral stroke is not established. The INDIVIDUATE study is a prospective, randomised, open-label, blinded end-point study. The study aimed to evaluate if an individualised approach to blood pressure management is superior in achieving a favourable functional outcome compared to the standard blood pressure management strategy.

Patients with anterior circulation stroke and a National Institutes of Health Stroke Scale (NIHSS) score of 8 or higher were included. The primary endpoint of a favourable functional outcome was defined as a modified Rankin Scale score of 0 to2 after 90 days. The secondary endpoints included mortality, short term outcome as measured by NIHSS score and safety measures such as critical hypo- or hypertension, cerebral haemorrhage and use of vasopressors or vasodepressors.

During the study period, 123 patients were treated with individualised BP management and 127 with standard blood pressure management. The rate of favourable functional outcome after 3 months, defined as modified Rankin Scale 0 to 2, was not significantly different between the individualised and the standard blood pressure management groups (25% vs 24%). Among patients treated with endovascular stroke treatment due to an acute ischemic stroke of the anterior circulation, no significant difference was seen between an individualised and standardised blood pressure management.

ENDs

View a summary presentation by the Principal Investigator here

References:

1. Schönenberger S *et al*. Effect of individualised versus standard blood pressure management during endovascular stroke treatment under procedural sedation (INDIVIDUATE) on clinical outcome. Presented at the European Stroke Organisation Conference; 26 May 2023; Munich, Germany.

The PERFEQTOS randomized trial: studying the implementation of performance feedback on quality of stroke care one step at a time

We all know that it is important to act fast when a patient with an ischemic stroke arrives at the hospital. But can performance feedback make healthcare providers even faster? The PERFEQTOS randomized trial implemented performance feedback in 13 Dutch hospitals step-by-step and assessed its effect on time from arrival at the hospital to initiation of endovascular thrombectomy (EVT).[1]

The timing of acute treatment in patients with ischemic stroke is crucial, as time to reperfusion is strongly associated with functional outcome. Providing performance feedback to healthcare providers about process indicators may be an attractive strategy to improve quality of stroke care. However, it can be challenging to study the effects of feedback on quality of care, as variation in outcomes between or within hospitals may also be explained by case-mix differences, stroke logistics, and time trends.

The investigators of the PERFEQTOS trial assessed the extent to which performance feedback to healthcare providers could reduce time from arrival at the hospital to initiation of EVT (door-to-groin time). They used a stepped-wedge cluster randomized trial design and included 13 Dutch hospitals providing EVT for ischemic stroke. All hospitals started with a non-exposed period, after which clusters of 3-4 hospitals were randomised in steps of six months to cross from the control to the intervention group. The intervention consisted of the installation of a local quality intervention team that had access to a dashboard containing quality of care measures of its own hospital, benchmarked against the other participating hospitals for the same period as well as their own performance over time. Based on these measures, the dashboard gave a clear recommendation for action: improvement needed yes or no.

In total, 4747 EVT-treated acute stroke patients were included, of which 2431 contributed to the intervention group and 2316 to the control group. Performance feedback significantly reduced the door-to-groin time by almost 5 minutes, which corresponds with more than 9%.

Daniël Hansen, the lead author of this study, concluded: “This trial is the first methodologically rigorous approach to show that performance feedback in acute stroke care works. Ideally, such feedback should become part of daily practice.”

ENDS

View a summary presentation by the Principal Investigator here

References:

1. Hansen D *et al.* Performance feedback to improve time to thrombectomy for ischemic stroke: A stepped wedge cluster randomized trial (PERFEQTOS). Presented at the European Stroke Organisation Conference; 26 May 2023; Munich, Germany.

Sonolysis in prevention of brain infarctions during internal carotid endarterectomy (SONOBIRDIE): The results of a randomised controlled trial[1]

Does sonolysis reduce peri-procedural stroke risk after carotid endarterectomy?

Carotid endarterectomy (CEA) is a well-established surgical procedure to remove a build-up of fatty deposits, which cause narrowing of a carotid artery. However, the risk of stroke during or immediately after the procedure is not negligible and novel approaches to reduce such risk is needed.

Transcranial Doppler (TCD) uses ultrasound beam with a specific frequency and is a non-invasive procedure which has been shown to have some potential effect on accelerating spontaneous or induced reopening of otherwise occluded arteries. This novel therapeutic procedure is also referred to as sonolysis. The SONOBIRDIE trial is a multi-centre, randomised, double-blinded, sham-controlled study to evaluate if sonolysis is safe and effective during CEA in reducing risks of stroke, mini-stroke or any infarction detected on brain imaging.

Patients from 16 European centres were recruited between 2015 and 2022. All patients had severe internal carotid artery stenosis (≥70%) with a clinical indication for CEA and were aged between 40–85 years. They were randomised either to sonolysis or to a sham procedure. Neurological exams and magnetic resonance imaging (MRI) were performed both before and after CEA to detect any stroke, mini-stroke or death within 30 days.

Overall, the study recruited 1004 patients with a mean age of 68 years, 31% of which were women. 507 of the 1004 were randomised to the sonolysis group. The investigators found that sonolysis during CEA was associated with a significant reduction in risks of stroke, mini-stroke or death at 30 days (2.2% vs. 7.6%). The same was seen for both symptomatic strokes (1.8% vs. 7.5%) and new ischaemic lesions on MRI (8.6% vs. 17.4%).

“The randomised clinical trial confirmed the results of pilot studies that sonolysis using diagnostic 2-MHz probe is save and significantly reduce the risk of stroke, [transient ischemic stroke] (TIA) and silent brain infarctions detected using brain MRI. In clinical practice, this could mean not only an increase in the safety of carotid endarterectomy, but also an expansion of indications for this procedure,” commented Dr David Školoudík, principal investigator of SONOBIRDIE.

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References:

1. Skoloudik D *et al*. Sonolysis in prevention of brain infarctions during internal carotid endarterectomy (SONOBIRDIE): The results of a randomised controlled trial. Presented at the European Stroke Organisation Conference; 26 May 2023; Munich, Germany.

Intensive Statin and Antiplatelet Therapy for Acute High-risk Intracranial or Extracranial Atherosclerosis (INSPIRES)

Is immediate intensive antiplatelet and statin therapy initiated within 72 hours after onset effective in reducing the risk of recurrent and progressive stroke compared to standard antiplatelet and delayed intensive statin among patients with acute mild ischemic stroke or transient ischemic attack (TIA) from isolated intracranial or extracranial artery atherosclerosis?

INSPIRES is a randomised, double-blind, placebo-controlled and 2-by-2 factorial trial involving 6100 patients with acute mild ischemic stroke or high-risk TIA of isolated intracranial artery atherosclerosis disease (ICAD) or extracranial artery atherosclerosis disease (ECAD) origin.[1] Within 72 hours of symptom onset, patients were randomly assigned in a 1:1 ratio to receive either a combination therapy of clopidogrel and aspirin (for the first 21 days) or placebo and aspirin, and immediate intensive atorvastatin or 3-day delayed intensive atorvastatin.

A new stroke occurred within 90 days in 7.3% versus 9.2% in the clopidogrel-aspirin and aspirin group (p=0.007) and 8.1% versus 8.5% in the immediate and delayed intensive statin group, respectively (hazard ratio, 0.95). The interaction between clopidogrel-aspirin and intensive statin was not significant. Poor functional outcome (mRS score 2-6) occurred in 9.8% in the immediate statin group and 11.4% in the delayed statin group (P=0.04). 0.9% of the patients on clopidogrel-aspirin had moderate-to-severe bleeding compared with 0.4% on placebo-aspirin (p=0.03). There was no difference between groups for the intensive statin safety outcomes.

The study's author, Yilong Wang, concluded that among patients with acute mild ischemic stroke or TIA from ICAD/ECAD, the combination of clopidogrel and aspirin initiated within 72 hours of onset is superior to aspirin alone in reducing the risk of new stoke occurrence at 90 days. This combination was, however, associated with an increased risk of moderate to severe bleeding. In contrast, immediate intensive statin initiated within 72 hours of onset was not found to reduce the risk of stroke recurrence at 90 days compared to intensive statin with a 3-day delay. However, immediate statin therapy significantly improved the poor functional outcome without increasing the risk of moderate to severe bleeding.

ENDS

View a summary presentation by the Principal Investigator here

References:

1. Wang Y *et al.* Immediate intensive statin versus delayed intensive statin for patients with acute mild ischemic stroke or TIA with intracranial or extracranial atherosclerosis. Presented at the European Stroke Organisation Conference; 26 May 2023; Munich, Germany.