

PRESS RELEASE

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ESOC 2024 Plenary Highlights (Closing Ceremony & Large Clinical Trials 2): Friday, 17 May 2024

Remote ischemic preconditioning offers potential breakthrough in stroke treatment

(Friday, 17 May 2024, Basel, Switzerland) A group of scientists from Spain investigated the potential use of remote ischemic preconditioning during ambulance transportation towards the hospital for acute ischemic stroke treatment. Their findings, presented today at the European Stroke Organisation Conference (ESOC) 2024, showed that this intervention may increase favourable outcome and functional status after stroke in specific patient subgroups, supporting further investigation on the technique.¹

In the relentless quest to improve outcomes for acute ischemic stroke patients, a groundbreaking study has emerged, shedding light on the potential of remote ischemic preconditioning (RIPerC) as a novel neuroprotective strategy. The REMOTE-CAT project, conducted across multiple centres in Catalonia, marks a significant milestone in stroke research and offers new hope for patients and clinicians alike.

Acute ischemic stroke stands as a leading cause of disability and mortality worldwide, underscoring the urgent need for innovative therapeutic interventions. Remote ischemic preconditioning, involving the application of brief episodes of transient limb ischemia, has garnered attention as a promising approach to mitigate cerebral damage during stroke onset. Despite encouraging preclinical evidence, its efficacy in clinical settings remained uncertain until now.

The REMOTE-CAT project employed a multicentre, double-blind study design to investigate the impact of RIPerC on acute ischemic stroke patients. Notably, the primary outcome focused on the proportion of patients achieving a modified Rankin Scale (mRS) score of 2 or less at 90 days post-stroke, while secondary outcomes examined reductions in infarct volume. The findings unveiled a potential association between RIPerC and improved functional outcomes, particularly among lower NIHSS cases and those without large vessel occlusion.

Conducted across four centres in Catalonia, the study enrolled patients diagnosed with suspected clinical stroke within 8 hours of symptom onset. RIPerC, comprising five cycles of electronic tourniquet inflation and deflation, was initiated in the ambulance before hospital admission. Despite facing an interruption caused by the COVID-19 pandemic, the study proceeded in two phases, concluding after 200 patients were randomised due to funding constraints. Analyses focused on 122 patients with ischemic stroke. Notably, the primary outcome of mRS 0-2 was achieved by 64.9% of patients receiving RIPerC compared to

47.3% in the sham stimulation group, a result at the very margin of statistical significance suggesting a potential benefit of RPerC in improving functional recovery post-stroke.

The findings of the REMOTE-CAT project represent a significant advancement in stroke research, offering a glimmer of hope for patients facing the debilitating consequences of acute ischemic stroke. If further validated, RPerC could emerge as a safe, simple, and low-cost adjunctive therapy in stroke management, revolutionizing current treatment paradigms and enhancing patient outcomes. This study underscores the importance of ongoing research efforts in unlocking new avenues for stroke prevention and treatment.

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References:

1. REMOTE ISCHEMIC PERCONDITIONING AMONG ACUTE ISCHEMIC STROKE PATIENTS IN CATALONIA: REMOTE-CAT PROJECT. Presented at the European Stroke Organisation Conference; 17 May 2024; Basel, Switzerland.

Remote ischemic conditioning does not improve outcomes after intracerebral haemorrhage, new study shows

(17 May 2024, Basel, Switzerland) In the randomised controlled trial RICH-2, which was conducted in China, patients presenting with intracerebral haemorrhage received either remote ischemic conditioning (RIC) or sham RIC. The study showed no difference in functional outcome between groups at 90 days.¹

The RICH-2 trial, presented today at the European Stroke Organisation Conference (ESOC) 2024, included 458 patients presenting with acute intracerebral haemorrhage. Patients were randomised in a 1:1 manner into either receiving RIC or sham RIC and the treatment was continued for seven consecutive days. The primary outcome was functional independence, defined as a modified Rankin Scale score of 0–2, at 90 days.

The results showed that the two groups of 229 patients each were well balanced. At 90 days, 68.1% in the RIC group and 71.2% in the sham RIC group achieved functional independence and there was no statistical difference between groups (adjusted p-value=0.69). Mortality was 3% in both groups, and RIC was not associated with any safety concerns.

Dr Wenbo Zhao, one of the lead authors from Xuanwu Hospital, Capital Medical University, Beijing, China, commented, “The neutral results of the trial may be mainly attributed to the mild severity of ICH and the relatively small size of the hematoma, as the subgroup analysis showed that patients with hematoma volume of 21-30 ml favored RIC treatment. In addition, whether the other RIC protocol could benefit this patient population also needs to be investigated.”

Intracerebral haemorrhage is associated with high mortality and morbidity. Advancements in treatments have been much slower than for ischemic stroke. In animal models, remote ischemic conditioning has been shown to accelerate hematoma absorption and improve neurological outcomes, but these results have not yet been translated into clinical benefits in humans. Most previous trials were confined to patients with ischemic stroke, but the RICH-2 is the first large trial that aimed to determine whether RIC could improve outcomes after intracerebral haemorrhage.

Dr Zhao continued, “Although the clinical effects of RIC have not been proven, the RICH-2 study provided new insights into the investigation of ICH, especially in patients who did not undergo surgical treatment. This trial determined the safety of RIC in patients with ICH, so more work should be done to investigate whether RIC could benefit patients with severe ICH, especially other RIC protocols, such as 14 days’ bilateral RIC. More recently, a large trial has determined the efficacy of hematoma evacuation in patients with ICH, therefore, hematoma evacuation-based RIC neuroprotection is also a very promising research direction.”

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[Watch a recorded summary from the author](#)

References:

1. SAFETY AND EFFICACY OF REMOTE ISCHEMIC CONDITIONING FOR SPONTANEOUS INTRACEREBRAL HAEMORRHAGE (RICH-2): A MULTICENTER RANDOMISED CONTROLLED TRIAL. Presented at the European Stroke Organisation Conference; 17 May 2024; Basel, Switzerland.

Tenecteplase not superior to non-thrombolytic standard of care in minor ischaemic stroke treatment: The TEMPO2 trial

(Friday, 17 May 2024, Basel, Switzerland) In the pursuit of improved outcomes for individuals with minor ischaemic stroke and intracranial occlusion, a trial led by Professor Coutts, from the University of Calgary, is sparking new debates in stroke management.¹ Indeed, tenecteplase, a clot busting treatment, has been shown futile and potentially harmful compared to antiplatelet treatment only in the context of minor stroke with confirmed vessel occlusion. These results, presented today at the European Stroke Organisation Conference (ESOC) 2024, pave the way to treatment tailoring and optimisation.

Minor ischaemic stroke, characterised by minimal neurological deficits, still poses substantial risks, especially when caused by a demonstrable intracranial occlusion. The use of thrombolytic agents, such as Tenecteplase, holds promise in enhancing outcomes by swiftly restoring blood flow to affected brain regions. However, rigorous evaluation of its efficacy is essential to guide clinical practice effectively.

The multicentre, prospective, randomised controlled TEMPO-2 trial was conducted across various global sites to establish the superiority of intravenous tenecteplase in patients with minor ischaemic stroke and intracranial occlusion compared to standard care. The study was halted prematurely due to futility, revealing no significant benefit from tenecteplase over standard care. Moreover, concerns arose regarding potential harm, as the tenecteplase group exhibited a higher mortality rate and more symptomatic intracranial hemorrhage.

A total of 886 patients were enrolled in the trial between April 27, 2015, and Jan 19, 2024, with 369 (42%) being female and 517 (58%) male. The primary outcome, defined as a return to baseline functioning at 90 days, was reported in 338 (75%) of 452 patients in the control group and 309 (72%) of 432 in the tenecteplase group. The primary outcome rate was not different between groups. The incidence of symptomatic intracranial hemorrhage, a critical safety concern, was higher in the tenecteplase group. Eight patients (2%) in the tenecteplase arm experienced symptomatic intracranial hemorrhages, while only two (<1%) such cases were observed in the control group. This was an expected finding, low in incidence and not significantly different between groups.

These findings underscore the complexities and potential risks associated with thrombolytic therapy in minor ischaemic stroke patients with intracranial occlusion. The study did not reveal a significant benefit from intravenous tenecteplase over standard care in achieving the primary outcome, diverging from prior evidence from a meta-analysis but entirely concordant with the recent PRISMS and ARAMIS trials. Although there was numerically increased symptomatic intracranial hemorrhage, this did not account for the lack of benefit. A higher mortality rate was observed in the tenecteplase arm, due to what appears to a series of late deaths biologically unrelated to the tenecteplase.

The findings of this trial challenge the conventional wisdom surrounding thrombolytic therapy in minor ischaemic stroke with intracranial occlusion. Despite hopes for a breakthrough, the lack of benefit and the possibility of harm associated with tenecteplase underscore the

complexities of acute stroke management. Antiplatelet therapy should be favoured over thrombolytic therapy for most patients with minor ischemic stroke.

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References:

1. A RANDOMIZED CONTROLLED TRIAL OF TENECTEPLASE VERSUS STANDARD OF CARE FOR MINOR ISCHEMIC STROKE WITH PROVEN OCCLUSION (TEMPO-2). Presented at the European Stroke Organisation Conference; 17 May 2024; Basel, Switzerland.

Patients with severe hypodensity within their large core ischemic stroke benefit less from thrombectomy

(Friday, 17 May 2024, Basel, Switzerland) The randomised controlled trial SELECT 2 recently showed that patients with large core ischemic stroke benefit from thrombectomy compared to medical management.¹ A secondary analysis of the data shows that in patients with severe hypodensity of ≥ 26 ml within their ischemic lesions, the benefit from thrombectomy is uncertain and the risk of hemicraniectomy is increased.

The secondary analysis from the SELECT 2 trial¹, presented today at the European Stroke Organisation Conference (ESOC) 2024, used imaging and outcome data from the 322 large core ischemic stroke patients included in the trial. The authors hypothesised that the occurrence of severe hypodensity, indicative of more evolved tissue injury, may modify the effect of thrombectomy. Researchers defined severe hypodensity as an attenuation in the ischemic lesion of less than 26 Hounsfield Units, and a favourable outcome as a modified Rankin Scale score of 0–3.

The results showed that, with increasing volume of severe hypodensity, the odds of a favourable outcome decreased. At a cut-off of ≥ 26 ml of severe hypodensity, thrombectomy was no longer associated with a favourable outcome compared to medical management. Also, the odds of requiring hemicraniectomy, a life-saving decompressive neurosurgical treatment, were increased.

During the last decade, thrombectomy has revolutionised the treatment of acute ischemic stroke. The indications for thrombectomy have continued to expand, including the recent evidence of treatment benefit in patients presenting with large ischemic core.

Dr Vignan Yogendrakumar, one of the lead authors of the study, from Melbourne, Australia, commented, “This study provides evidence supporting the concept that the gradient of tissue injury can influence clinical outcomes and the treatment effect of endovascular therapy. It is, however, important that these findings be validated with independent data as the techniques used in this analysis are relatively novel. If validated, the prognostic value of assessing CT hypodensity could be used to assist with bedside decision making, accelerate innovations in automated imaging processing, and could even be used as a biomarker for trial recruitment of new therapies designed to limit reperfusion injury.

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[Watch a recorded summary from the author](#)

References:

1. ASSOCIATION OF ISCHAEMIC CORE HYPODENSITY ON ENDOVASCULAR THERAPY TREATMENT EFFECT IN LARGE CORE ISCHAEMIC STROKE. Presented at the European Stroke Organisation Conference; 17 May 2024; Basel, Switzerland.

Intra-arterial tenecteplase shows no superiority in posterior circulation stroke treatment, new trial finds

(Friday, 17 May 2024, Basel, Switzerland) A team of researchers from China examined intra-arterial tenecteplase post-endovascular therapy for posterior circulation stroke.¹ Contrary to expectations, it found no significant difference in functional outcomes, mortality, or intracranial hemorrhage compared to standard care. These results challenge assumptions, emphasizing the need for continued research in stroke management.

In a groundbreaking multicentre randomised controlled trial, presented today at the European Stroke Organisation Conference (ESOC) 2024, researchers sought to determine the efficacy of intra-arterial tenecteplase (a clot-busting drug) following successful recanalisation in patients suffering from acute posterior circulation arterial occlusion. Despite hopes for a breakthrough, the findings present a surprising revelation regarding the treatment's effectiveness.

Posterior circulation stroke, affecting critical arteries in the back of the brain, pose significant challenges in treatment and management. While techniques like endovascular therapy (EVT) have shown promise, the optimal approach post-recanalisation remains uncertain.

The ATTENTION-IA trial, conducted across 31 centres in China, randomised patients after successful EVT (defined as TIC1 2b50 or higher) for posterior circulation stroke into receiving either intra-arterial tenecteplase or standard care. The study included all cases of occlusion of the vertebral, basilar, or posterior cerebral artery, with all patients being randomly allocated in a 1:1 fashion to receive intra-arterial tenecteplase or standard of care.

Contrary to expectations, the study found no significant advantage in functional outcomes at 90 days between the tenecteplase group and the control group. Mortality rates and incidences of symptomatic intracranial hemorrhage also showed no meaningful difference between the two groups.

Between January 2023 and August 2024, 208 participants were enrolled, evenly split between the tenecteplase group and the control group. At the 3-month mark, 34.6% of the tenecteplase group achieved a modified Rankin Score of 0-1 compared to 26.0% in the control group, though the difference did not reach statistical significance. Mortality rates at 90 days were comparable between the groups, as were incidences of symptomatic intracranial hemorrhage.

These findings challenge the assumption that intra-arterial tenecteplase would offer superior outcomes in posterior circulation stroke management post-successful EVT. While the results suggest equipoise between the two treatment approaches, they underscore the complexity of stroke care and the need for continued research to optimise therapeutic strategies. The study's implications extend beyond clinical practice, emphasising the importance of rigorous trials in guiding evidence-based interventions for stroke patients.

The ATTENTION-IA trial sheds new light on the management of acute posterior circulation arterial occlusion, highlighting the need for further exploration and refinement of treatment protocols in this challenging clinical scenario.

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References:

1. INTRA-ARTERIAL TENECTEPLASE AFTER EVT IN ACUTE POSTERIOR CIRCULATION ARTERIAL OCCLUSION-A MULTICENTER RANDOMIZED CONTROLLED TRIAL. Presented at the European Stroke Organisation Conference; 17 May 2024; Basel, Switzerland.

Implementation of sleep apnea screening post-stroke: results of the ASAP trial

(17 May 2024, Basel, Switzerland) The Addressing Sleep Apnea Post-Stroke/TIA (ASAP) trial, a pioneering initiative aimed at enhancing the early diagnosis of obstructive sleep apnea (OSA) among ischemic stroke and transient ischemic attack (TIA) patients, has presented its interim results today at the European Stroke Organisation Conference (ESOC) 2024.¹

OSA is associated with ischemic stroke recurrence and poor outcome after stroke. Screening for OSA and appropriate treatment, including weight reduction and continuous positive airway pressure (CPAP) ventilation is therefore recommended by current guidelines for stroke and TIA patients. Nonetheless, diagnostic rates remain alarmingly low.

The stepped-wedge cluster randomised ASAP trial seeks to address this gap by evaluating the effectiveness and implementation of a quality improvement intervention to enhance OSA diagnosis rates. The trial was conducted across six U.S. Department of Veterans Affairs hospitals and 30 control sites. Over three study phases – baseline, active implementation, and sustainability – the trial assessed the impact of a comprehensive quality improvement intervention on OSA diagnostic rates and implementation outcomes. Notably, no acute sleep service existed at baseline at any of the intervention or control sites.

A total of 952 patients were included in ASAP. The investigators reported a significant increase in OSA diagnostic testing within 30 days from 2.2% at baseline to 28.5% at ASAP intervention sites, compared to a range of 0.7-2.2% at control sites. Moreover, four of the six ASAP sites achieved a Group Organization (GO) Score of ≥ 6 , indicating the establishment of comprehensive, facility-wide acute sleep services. Sites with higher GO Scores demonstrated engaged champions, effective networks, and communications, contributing to the success of the intervention despite external challenges such as the COVID-19 pandemic and global ventilation device recall.

Dr. Jason Sico, lead investigator of the ASAP trial commented, "By implementing comprehensive acute sleep services and fostering strong champions, we have demonstrated the feasibility and effectiveness of increasing OSA testing rates in this vulnerable patient population. These results underscore the transformative potential of the ASAP trial in improving post-stroke and TIA care."

Awaiting final results, the insights gleaned from ASAP have the potential to inform future guidelines and protocols, ultimately enhancing the quality of care for stroke/TIA patients worldwide.

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1. LATE BREAKING – RESULTS FROM THE ADDRESSING SLEEP APNEA POST-STROKE/TIA (ASAP) STEPPED-WEDGE CLUSTER RANDOMIZED TRIAL. Presented at the European Stroke Organisation Conference; 17 May 2024; Basel, Switzerland.

Stenting plus medical therapy fails to outperform medical therapy alone in long-term stroke prevention for symptomatic intracranial stenosis: 7-year results of CASSISS TRIAL

(17 May 2024, Basel, Switzerland) The CASSISS trial investigators presented the 7-year results of their study today at the European Stroke Organisation Conference (ESOC) 2024 comparing the efficacy of stenting plus medical therapy (MT) versus MT alone for symptomatic severe intracranial atherosclerotic stenosis (ICAS), shedding new light on the long-term benefits and risks of these treatment modalities.¹

Severe symptomatic ICAS is known to confer a significant risk of ischemic stroke. The CASSISS trial aimed to determine whether the addition of stenting to MT could reduce the risk of stroke, outweighing the associated perioperative risks, compared to MT alone.

Conducted as a multicentre, open-label, randomised trial across 8 centres in China, the CASSISS trial enrolled patients with transient ischemic attack (TIA) or ischemic stroke attributed to severe ICAS (70%-99%). Patients were randomised in a 1:1 ratio to receive either stenting plus MT or MT alone.

The primary outcome, a composite of stroke or death within 30 days or ipsilateral ischemic stroke beyond 30 days, showed no difference between the two groups over the 7-year follow-up period (HR, 1.02 [95% CI, 0.58-1.77]; P = .97). Additionally, there were no differences in secondary outcome measures including ipsilateral ischemic stroke, disabling stroke or death, and death after enrollment between the two treatment arms.

This study provides compelling evidence that, even in the long-term, stenting does not confer additional benefits to medical therapy alone in patients with symptomatic severe ICAS. These results underscore the importance of medical therapy as the cornerstone of long-term stroke prevention in this patient population.

[Watch a recorded summary from the author](#)

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References:

1. STENTING PLUS MEDICAL THERAPY VS MEDICAL THERAPY ALONE FOR SYMPTOMATIC INTRACRANIAL STENOSIS: 7-YEAR RESULTS OF A RANDOMIZED CONTROL TRIAL. Presented at the European Stroke Organisation Conference; 17 May 2024; Basel, Switzerland.

Screening for emotional and cognitive problems in stroke patients discharged home improves quality of life and reduces fear

(17 May 2024, Basel, Switzerland) A team of researchers from the Netherlands have discovered that screening for emotional and cognitive problems in patients who are discharged home after stroke improves quality of life and reduces fear.¹ The screening intervention improves quality of life outcomes at three months and one year, indicating its potential as rehabilitation tool for patients with less severe strokes.

The research team presented their multicentre, cluster randomised controlled trial today at the European Stroke Organisation Conference (ESOC) 2024, which assigned 12 Dutch hospitals to a screening intervention or usual care. The intervention, six weeks post-stroke, included screening for emotional and cognitive problems, participation restrictions, self-management support and referral to rehabilitation services. The researchers primarily focused on restrictions in societal participation at one year, but also assessed quality of life (QoL), symptoms of anxiety and depression, cognitive and emotional complaints, self-efficacy, and disability at three months and one year.

In total, 531 patients were included in the trial: 264 from hospitals randomised to the intervention and 267 from usual care hospitals. The intervention group did not differ from the usual care group in terms of restrictions in societal participation one-year post-stroke but reported lower levels of anxiety (mean difference [MD] on the HADS-A questionnaire score - 0.86; 95% confidence interval [CI] -1.33 - -0.39) and higher levels of QoL (EQ-5D-5L index score; MD 0.04; 95% CI 0.02 – 0.07) at three months. The QoL improvement in the screening cohort persisted at one year (EQ-5D-5L; MD 0.04; 95% CI 0.02 – 0.06).

Dr. Jos Slenders, one of the lead authors on the study from the OLVG hospital in Amsterdam, is enthusiastic about these findings. “It is great to see that such an inexpensive and simple intervention might improve important QoL outcomes.”

He believes that the positive screening effect may, at least partially, be explained by reassurance. “From previous research we know that appropriate education can reassure patients. In addition, we think it is very important for patients to feel seen and acknowledge the emotional and cognitive challenges that are so meaningful to them.”

Despite various advances in acute stroke care, ischemic stroke remains a major cause of adult disability, with a global increase in disability-adjusted life years of 32% from 1990 to 2019. Post-stroke rehabilitation aims to reduce this disability but is dependent on stroke severity and various QoL aspects. For patients discharged home after stroke, such QoL factors and unmet needs in their hospital-to-home transition have been reported to challenge the trajectory of poststroke rehabilitation and recovery.

Dr. Vincent Kwa, the principal investigator of the study, also from Amsterdam, added, “Patients with less severe strokes who can ‘walk and talk’ also deserve our full attention. Research aimed at improving post-stroke recovery and QoL in this specific group of patients is very fulfilling. Our next step towards implementation will be an economic evaluation to investigate if this screening intervention is cost-effective.”

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1. SCREENING FOR EMOTIONAL AND COGNITIVE PROBLEMS IN PATIENTS DISCHARGED HOME AFTER STROKE: A MULTICENTER, CLUSTER RANDOMIZED CONTROLLED TRIAL. Presented at the European Stroke Organisation Conference; 17 May 2024; Basel, Switzerland.