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Joint European and World Stroke Organisation (ESO-WSO) conference highlights-2020

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Abstract

Despite a difficult year focusing on the COVID-19 pandemic, from 7 November to 8 November, stroke clinicians and researchers experienced a great opportunity to learn about the latest research results and developments across the entire care spectrum. This year's European and World Stroke Organisation Conference was not only the first joint conference but also the first virtual experience of this magnitude in the field. More than 5000 participants were registered worldwide. Many interesting studies and impactful large trial results were presented giving rise to lively controversies (live sessions and chats). This article will focus on a few selected studies that were presented at the conference, ranging from insights into pre-hospital triage, acute interventions, to secondary prevention, rehabilitation and the impact of the current pandemic on stroke care.

Keywords

Stroke, conference highlights, triage, thrombolysis, secondary prevention

Where to go with a LVO?

Pre-hospital stroke rescue chain needs to be streamlined to enable timely delivery of highly effective endovascular therapies in selected patients. 'Time is brain', so referral strategies could impact greatly on patient outcomes. However, it can be anticipated that no single referral model will fit all healthcare settings. Well-designed randomised controlled trials (RCTs) are needed to evaluate different models of referral. The RACECAT trial[1] assessed whether stroke patients meeting criteria for large vessel occlusion (LVO) on the 'Rapid Arterial oCclusion Evaluation (RACE) Score' have a better functional outcome when transferred directly to an Endovascular Center (EC; mothership paradigm), as compared to transfer to the closest Local Stroke Center (LSC; drip and ship paradigm). Seven thousand four hundred seventy-five patients were screened by the emergency medical services using the RACE score. A cut off >5 points indicated a likely LVO. One thousand four hundred one patients were randomised to either the LSC or EC group. Two-thirds of patients identified by the RACE score had ischaemic stroke and two-thirds of these had LVO. The proportion of patients receiving IV thrombolysis was higher in the LSC than in the EC group (60.4% vs. 47.5%, $p < 0.001$), whereas the proportion of patients receiving thrombectomy was higher in the EC group (50.0% vs. 40.9%, $p = 0.003$). 'Time from symptom onset to thrombolysis' was faster in the LSC group (120 vs. 155 min), and 'Time from symptom onset to groin puncture' was faster in the EC group (214 vs. 270 min). There was no difference in 90-day disability between the two groups based on shift analysis of the modified Rankin Scale (mRS) and this was consistent across various subgroups. This trial shows that pre-hospital triage in

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patients using the RACE score is feasible and that both transfer protocols performed equally well in the region of Catalonia, Spain (data to be published).

Imaging-based decision for thrombolysis in stroke of unknown time of onset – Go for it!

Thrombolysis has been, in the last decades, the standard therapy for acute ischaemic stroke with time from symptom onset up to 4.5 h. Patients with unknown time of symptom onset, who account for about 20% of all ischaemic stroke cases, were excluded from the landmark RCTs. In the past years, several clinical studies have tried to identify the group of patients with unknown time of symptom onset who might benefit from IV thrombolysis. A new individual patient data meta-analysis from the 'Evaluation of unknown Onset Stroke thrombolysis trials collaborators' supports the use of advanced neuroimaging to select patients of unknown time of symptom onset for IV thrombolysis.[2] The meta-analysis used individual patient data ($n = 843$) from four published major RCTs – WAKE-UP, EXTEND, THAWS and ECASS-IV, where patient selection was done using perfusion–diffusion MRI, perfusion CT or MRI diffusion-weighted imaging–fluid-attenuated inversion recovery mismatch. A favourable treatment outcome (mRS 0–1) occurred in 199 out of 420 patients (47%) who had undergone thrombolysis, compared to 160 out of 409 patients (39%) in the placebo group. This benefit was statistically significant (adjusted odds ratio (OR) 1.49 [95% confidence interval (CI) 1.10–2.03]; $p = 0.011$) and heterogeneity across studies was low ($I^2 = 11\%$). Regarding safety, the 90-day death or severe disability (mRS 4–6) occurred in 21% in the thrombolysis group and 25% in the placebo group (adjusted OR 0.76 [0.52–1.11]; $p = 0{\cdot}15$).[2] While more advanced imaging techniques are needed, this high-quality evidence is a welcome advance for treating patients experiencing stroke with unknown time of onset, such as 'wake-up' stroke.

Endovascular therapy for basilar artery occlusion within 6 h may not be as effective as previously thought

Patients with basilar artery occlusion could potentially suffer devastating outcomes, but there has been a lack of RCT evidence to guide its treatment. The Basilar Artery International Collaboration Study assessed the efficacy and safety of endovascular therapy (EVT) plus best medical management (BMM) compared to BMM alone within 6 h from symptom onset.[3] The study enrolled 300 patients, randomised in a 1:1 ratio, stratified by National Institute of Health Stroke Sceale (NIHSS) score, use of IV thrombolysis and treatment centre. At 90 days, the primary end point of good functional outcome, defined by mRS score of <3 points, was similar between two groups (1.18 RR, 95% CI 0.92–1.5). Secondary clinical outcomes showed no statistically significant differences between groups, with only one subgroup analysis suggesting that patients with a milder stroke (NIHSS <10 points) might benefit from BMM and those with more severe symptoms (NIHSS >10 points) might benefit from EVT. Safety outcomes did not differ. This trial suggests that basilar artery occlusion may be a more diverse entity than occlusions in the anterior circulation, and there is currently not a simple answer to guide treatment in this patient group (data to be published).

In selected patients with high-risk TIA and minor stroke, we have a new treatment option

In the search to reduce the risk of recurrent stroke after transient ischemic attack (TIA) and minor stroke (i.e. 5–10%), the SOCRATES trial[4] did not show any superiority of ticagrelor over aspirin in preventing stroke recurrence. The strategy of dual antiplatelets was more fruitful as has been shown in the POINT[5] and CHANCE[6] trials, examining the combination of aspirin with clopidogrel (once daily). The THALES trial[7] examined if dual antiplatelet therapy with aspirin (300–325 mg on the first day followed by 75–100 mg daily) plus ticagrelor (300–325 mg on the first day followed by 75–100 mg daily) for 30 days after high-risk TIA (ABCD2 $\geq$6 or >50% symptomatic arterial stenosis) or minor non-cardioembolic stroke (NIHSS $\leq$ 5) would result in a net clinical benefit on stroke recurrence compared to aspirin alone, when given within 24 h of symptom onset. A total of 1106 patients were randomly allocated to either combination therapy or aspirin alone (1:1). Those in the combination therapy arm had a lower risk of recurrent stroke or death at 30 days compared to the group on aspirin alone (hazard ratio of 0.83 [0.71–0.96]). In a subgroup analysis, the combination therapy saw a reduction in disability of the recurrent stroke (OR, 0.77; 95% CI, 0.65–0.91; $p = 0.002$).[7] The bleeding risk was higher in the combination group but did not exceed the benefit (number needed to treat =92; number needed to harm =263). Ticagrelor plus aspirin can now be considered as an effective option in secondary prevention following TIA and minor stroke, especially in patients for whom clopidogrel is unsuitable (CYP2C19 loss-of-function carrier status).

BP lowering in ICH – Still an unsolved problem

The evidence for intensive blood pressure (BP) lowering in patients with an acute intracerebral haemorrhage (ICH), particularly over the timing and type of strategy remained unclear. A systematic review and meta-analysis conducted by the 'Blood pressure in Acute Stroke Collaboration' analysed individual patient data from 16 RCTs ($n = 6221$) on

BP management within 7 days of onset in adult patients with acute ICH (mean age of 64 years, 36% females, median time at enrolment 3.8 h after symptom onset).[8] Intensive antihypertensive therapy lowered the median BP to 158.6 mmHg systolic within an hour of starting treatment (control arm: 166 mmHg) and a median of 144.3 mmHg within 24 h (control arm: median of 156.4 mmHg).[8] However, the difference between treatment arms was small in the period between 2 days and 7 days (median systolic BP 143.7 mmHg in the intensive treatment arm and 151 mmHg in the control arm). The primary outcome was functional status, defined by the mRS at 90 days after acute ICH. The authors also evaluated the proportional change in haematoma growth. Early BP lowering in acute ICH was not accompanied by a statistically significant improvement in functional outcome at day 90 after the acute insult (OR: 0.97; $p = 0.503$). However, patients in the intensive BP treatment arm did show reduced haematoma volume growth in the first 24 h (OR: 0.75; $p = 0.007$)[8] (data to be published). Further studies are needed to understand why reduction in haematoma growth did not translate into functional benefit and to define the optimal approach to treatment by agent and time.

VNS: A new player in chronic stroke rehabilitation

A pivotal phase III study has shown promising results in improving upper limb function after ischaemic stroke by pairing electrical vagus nerve stimulation (VNS) with intensive physical therapy. The VNS-Rehab study investigated the effectiveness of pairing VNS using an implanted device with an intensive physical rehabilitation programme. The trial included 108 patients with moderate-to-severe upper extremity impairment in the chronic phase of ischaemic stroke.[9] All participants received 6 weeks of in-clinic physical rehabilitation, followed by a home exercise programme. Fifty-three participants were randomly allocated to receive VNS (VNS group), and 55 participants were randomly allocated to receive sham VNS (control group). The primary outcome was upper limb function, measured by the Fugl-Meyer Assessment Upper Extremity (FMA-UE) score on day 1 post-completion of the in-clinic therapy. The FMA-UE scale ranges in value from 0 for non-functional to 66 for fully functional. At day 1 post-completion of the 6 weeks of in-clinic therapy, the mean FMA-UE score had increased by 5.0 points in the VNS group compared to 2.4 points in the control group ($p = 0.001$). At day 90 post-completion of the in-clinic therapy, a larger proportion of patients in the VNS group (47%) showed a statistically significant and clinically meaningful response in motor function than the control group (24%) on the FMA-UE ($p = 0.01$) (data to be published). The VNS device has been submitted for approval by the U.S. Food and Drug Administration (FDA) and for CE mark for clinical use.

Global effects of COVID-19 pandemic on stroke services

COVID-related strokes have a more severe course result in poorer outcome and lead to higher mortality than non-COVID-related strokes.[10] The COVID-19 pandemic has seen a drop in acute stroke presentations and the provision of essential stroke treatments across the globe. The numbers of thrombolysis and thrombectomy for ischaemic strokes fell by about 12% in a global registry (Nguyen T, data presented at the ESO/WSO 2020, to be published) and even by 20–30% in specific regions.[11–13] Time from symptom onset to acute treatment was delayed in many cases of thrombolysis[13] and thrombectomy.[11,12] This could lead to adverse consequences such as patients receiving insufficient care and appropriate treatment, leading to higher long-term disability, recurrent stroke and death. Stroke services across the globe are urged to reinforce the message to the public that 'time is brain' and to ensure revascularization therapy is delivered in a timely fashion.

Author contributions

All three authors drafted and reviewed the manuscript.

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