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Library Current Awareness Bulletin Stroke – December 2021

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News

New clot busting drug could improve stroke treatment
British Heart Foundation, November 2021
[The researchers found that the drug they've developed, called caADAMTS13, was effectively able to break down blood clots in the brains of mice who had had a stroke. They also found signs that it may have a beneficial effect on the immune response that a stroke triggers.]

Thousands spared strokes thanks to new NHS drug agreements
National Health Executive, November 2021
[More than 20,000 strokes and 5,000 deaths could be averted after NHS England struck new agreements to expand life-saving blood thinning drugs, Chief Executive Amanda Pritchard has announced.]

Complications

Associations between Upper Extremity Motor Function and Aphasia after Stroke: A Multicenter Cross-Sectional Study.
Xu S; Yan Z; Pan Y; Yang Q; Liu Z; Gao J; Yang Y; Wu Y; Zhang Y; Wang J; Zhuang R; Li C; Zhang Y; Jia J
Behavioural Neurology
November 2021

[**Methods**: Patients with stroke were compared and correlated from overall and three periods (1-3 months, 4-6 months, and >6 months). Fugl-Meyer assessment for the upper extremity (FMA-UE) and action research and arm test (ARAT) were used to compare the UE motor status between patients with PSA and without PSA through a cross-sectional study among 435 patients. Then, the correlations between the evaluation scale scores of UE motor status and language function of patients with PSA were analyzed in various dimensions, and the language subfunction most closely related to UE motor function was analyzed by multiple linear regression analysis. **Results**: We found that the scores of FMA-UE and ARAT in patients with PSA were 14 points ((CI) 10 to 18, $p < 0.001$) and 11 points lower ((CI) 8 to 13, $p < 0.001$), respectively, than those without PSA. Their FMA-UE ($r = 0.70$, $p < 0.001$) and ARAT ($r = 0.62$, $p < 0.001$) scores were positively correlated with language function. Regression analysis demonstrated that spontaneous speech ability may account for UE motor function ($R2 = 0.51$, $p < 0.001$; $R2 = 0.42$, $p < 0.001$). Consistent results were also obtained from the analyses within the three time subgroups. **Conclusion**: Stroke patients with PSA have worse UE motor performance. UE motor status and language function showed positive correlations, in which spontaneous speech ability significantly accounts for the associations.]

Effect of early enteral nutrition on critical care outcomes in patients with acute ischemic stroke.
Mizuma A; Netsu S; Sakamoto M; Yutani S; Nagata E; Takizawa S
The Journal of International Medical Research, vol. 49(11)
November 2021
[**Objective**: Stroke-associated pneumonia (SAP) is a comorbidity of ischemic stroke related to clinical outcomes. Early enteral nutrition (EEN; within 48 hours) reduces the incidence of infection and length of intensive care unit (ICU)/hospital stay. The relationship between EEN and critical care outcomes, including SAP, in patients with ischemic stroke has been insufficiently studied. **Methods**: We recruited 499 patients in this retrospective observational study. We evaluated SAP incidence within 14 days from admission. Patients were divided into an EEN group and a late EN group (LEN; start later than EEN). We compared groups regarding background and length of ICU/hospital stay. **Results**: EN was started within 48 hours in 236 patients. SAP was diagnosed in 94 patients (18.8%), with most in the LEN group (28.1% vs. 8.5%). Median [interquartile range] lengths of hospitalization (22 [12-30] days vs. 35 [20-45] days) and ICU stay (4 [2-5] days vs. 6 [3-8] days) were longer in the LEN group. EEN reduced the incidence of SAP. By contrast, consciousness disturbance and worsening consciousness level increased the SAP incidence. Increased age and National Institutes of Health Stroke Scale score were associated with start of prolonged EN. **Conclusions**: We found that EEN may reduce SAP risk.]

Screening for aspiration risk associated with dysphagia in acute stroke.
Boaden E, Burnell J, Hives L, Dey P, Clegg A, Lyons MW, Lightbody CE, Hurley MA, Roddam H, McInnes E et al
Cochrane Database of Systematic Reviews 2021, Issue 10. Art. No.: CD012679.
October 2021
[**Background**: Stroke can affect people's ability to swallow, resulting in passage of some food and drink into the airway. This can cause choking, chest infection, malnutrition and dehydration, reduced rehabilitation, increased risk of anxiety and depression, longer hospital stay, increased likelihood of discharge to a care home, and increased risk of death. Early identification and management of disordered swallowing reduces risk of these difficulties. **Primary objective**: To determine the diagnostic accuracy and the sensitivity and specificity of bedside screening tests for detecting risk of aspiration associated with dysphagia in people with acute stroke.]

Drug Therapy / Stroke Prophylaxis

Anticoagulants for acute ischaemic stroke.
Wang X, Ouyang M, Yang J, Song L, Yang M, Anderson CS.
Cochrane Database of Systematic Reviews 2021, Issue 10. Art. No.: CD000024.
October 2021
[**Background**: Stroke is the third leading cause of early death worldwide. Most ischaemic strokes are caused by a blood clot blocking an artery in the brain. Patient outcomes might be improved if they are offered anticoagulants that reduce their risk of developing new blood clots and do not increase the risk of bleeding. This is an update of a Cochrane Review first published in 1995, with updates in 2004, 2008, and 2015. **Objectives**: To assess the effectiveness and safety of early anticoagulation (within the first 14 days of onset) for people with acute presumed or confirmed ischaemic stroke. Our hypotheses were that, compared with a policy of avoiding their use, early

anticoagulation would be associated with: reduced risk of death or dependence in activities of daily living a few months after stroke onset; reduced risk of early recurrent ischaemic stroke; increased risk of symptomatic intracranial and extracranial haemorrhage; and reduced risk of deep vein thrombosis and pulmonary embolism.]

Gliflozins for the prevention of stroke in diabetes and cardiorenal diseases: A meta-analysis of cardiovascular outcome trials.
Zhao LM; Huang JN; Qiu M; Ding LL; Zhan ZL; Ning J
Medicine, vol. 100(39)
October 2021
[**Background**: Individual randomized trials are not powered to assess the relationship between use of sodium-glucose transporter 2 inhibitors and risk of stroke. We sought to explore this issue by a meta-analysis incorporating relevant trials including several latest trials. **Methods**: Cardiovascular outcome trials of gliflozins were included. Primary outcome was stroke, while secondary outcome was major adverse cardiovascular events (MACE), which was a composite of stroke, myocardial infarction, or cardiovascular death. Meta-analysis was conducted stratified by with/without chronic kidney disease (CKD), with/without heart failure (HF), and with/without atherosclerotic cardiovascular disease (ASCVD), and stratified by different gliflozins. **Results**: We included 9 trials in this meta-analysis. Compared with placebo, gliflozins significantly lowered stroke (hazard ratio [HR] 0.68, 95% confidence interval [CI] 0.55-0.84) and MACE (HR 0.77, 95% CI 0.69-0.86) in type 2 diabetes (T2D) patients with CKD, but did not significantly affect stroke (HR 1.00, 95% CI 0.86-1.16) and MACE (HR 0.94, 95% CI 0.86-1.02) in T2D patients without CKD. Gliflozins had no significant effects on the stroke risk (HR 0.94, 95% CI 0.82-1.07) in T2D patients regardless of HF status (Psubgroup = .684) and ASCVD status (Psubgroup = .915), but significantly lowered MACE (HR 0.89, 95% CI 0.83-0.96) in T2D patients regardless of HF status (Psubgroup = .428) and ASCVD status (Psubgroup = .423). Canagliflozin (HR 0.84, 95% CI 0.69-1.01) showed the trend of a reduction in the stroke risk versus placebo, and sotagliflozin (HR 0.73, 95% CI 0.54-0.98) significantly lowered the stroke risk; whereas the other 3 gliflozins did not significantly affect that risk. Ertugliflozin (HR 0.97, 95% CI 0.85-1.11) had no significant effects on the MACE risk, whereas the other 4 gliflozins significantly lowered that risk. **Conclusions**: Gliflozins, especially canagliflozin and sotagliflozin, should be recommended in T2D patients with CKD to prevent stroke. Most gliflozins lower the risk of MACE in T2D patients regardless of HF status and ASCVD status, whereas ertugliflozin is not observed to lower that risk.]

Post-stroke Health

A randomized controlled trial to explore the efficacy and safety of transcranial direct current stimulation on patients with post-stroke fatigue.
Dong XL; Sun X; Sun WM; Yuan Q; Yu GH; Shuai L; Yuan YF
Medicine, vol. 100(41)
October 2021
[**Background**: Post-stroke fatigue seriously affects the quality of life for stroke patients. There is no effective treatment at present. transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation which may have therapeutic effect on post-stroke fatigue. This study will explore about this. **Method**: A total of 60 patients with post-stroke fatigue were randomly divided into the control group and the treatment group with 30 patients each by minimization randomization. Both groups received basic treatment and conventional rehabilitation. In the treatment group, patients were treated with active tDCS, while in the control group, sham tDCS. Both active and sham tDCS were administered 6 times a week for 4 weeks. Before and after the trial, the Fatigue Severity Scale (FSS), Fugl-Meyer Assessment (FMA) and Modified Barthel Index (MBI) were evaluated and analyzed. And comparisons were made among groups. And there were an 8-week follow-up after the intervention. **Result**: Before the intervention, there were no significant differences in baseline data and assessment scores between the groups ($P > 0.05$). After 4 weeks of intervention, FSS scores in the treatment group were significantly lower than those in the control group ($P = 0.012$), and FMA and BMI scores were significantly higher than those in the control group ($P < 0.05$). There was no significant change in FSS scores after 8 months of follow-up ($P > 0.05$). **Discussion**: TDCS is a safe treatment that can effectively reduce the degree of fatigue after stroke, improve the motor function and daily activity ability of patients after stroke, and the efficacy is better than only routine rehabilitation training.]

Higher fasting C-peptide is associated with post-stroke depression: a multicenter prospective cohort study.
Wang Y; Sun W; Miao J; Qiu X; Lan Y; Pan C; Li G; Zhao X; Zhu Z; Zhu S
BMC Neurology, vol. 21(1)
October 2021
[**Background**: Fasting C-peptide (FCP) has been shown to play an important role in the pathophysiology of mood disorders including depression and schizophrenia, but it is unknown whether it also predicts post-stroke depression (PSD). This study examined the association between FCP and PSD at 6 months after acute ischemic-stroke onset among Chinese subjects. **Methods**: A total of 656 stroke patients were consecutively recruited from three hospitals of Wuhan city, Hubei province. Clinical and laboratory data were collected on admission. PSD status was evaluated by DSM-V criteria and 17-item Hamilton Rating Scale for Depression (HAMD-17) at 6 months after acute ischemic stroke. The χ2-test, Mann-Whitney U-test, and t-test were used to check for statistical significance. Multivariate logistic regression model was used to explore independent predictor of PSD. **Results**: In the univariate analysis, significant differences were found between the PSD and non-PSD groups in terms of FCP level (p = 0.009). After multivariate adjustments, FCP remained a significant independent predictor of PSD, with an adjusted odds ratio of 1.179 (95%CI: 1.040-1.337, p = 0.010). **Conclusions**: Higher FCP levels on admission were found to be associated with PSD at 6 months after acute ischemic-stroke onset. For stroke patients, doctors should pay attention to the baseline FCP for screening high-risk PSD in clinical practice.]

Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery.
Legg LA, Rudberg A-S, Hua X, Wu S, Hackett ML, Tilney R, Lindgren L, Kutlubaev MA, Hsieh C-F, Barugh AJ, et al.
Cochrane Database of Systematic Reviews 2021, Issue 11. Art. No.: CD009286.
November 2021
[**Background**: Selective serotonin reuptake inhibitors (SSRIs) might theoretically reduce post-stroke disability by direct effects on the brain. This Cochrane Review was first published in 2012 and last updated in 2019. **Objectives**: To determine if SSRIs are more effective than placebo or usual care at improving outcomes in people less than 12 months post-stroke, and to determine whether treatment with SSRIs is associated with adverse effects.]

Rehabilitation

Environmental enrichment for stroke and other non-progressive brain injury
Qin H, Reid I, Gorelik A, Ng L.
Cochrane Database of Systematic Reviews, 2021, Issue 11. Art. No.: CD011879.
November 2021
[**Background**: Rehabilitation is effective for recovery after stroke and other non-progressive brain injuries but it is unclear if the rehabilitation environment itself, outside of limited therapy hours, is maximally conducive to recovery. Environmental enrichment is a relatively new concept within rehabilitation for humans. In this review, this is defined as an intervention designed to facilitate physical (motor and sensory), cognitive and social activity by the provision of equipment and organisation of a structured, stimulating environment. The environment should be designed to encourage (but not force) activities without additional specialised rehabilitation input. **Objectives**: To assess the effects of environmental enrichment on well-being, functional recovery, activity levels and quality of life in people who have stroke or non-progressive brain injury.]

The effect of time spent in rehabilitation on activity limitation and impairment after stroke.
Clark B, Whitall J, Kwakkel G, Mehrholz J, Ewings S, Burridge J.
Cochrane Database of Systematic Reviews 2021, Issue 10. Art. No.: CD012612.
October 2021
[Stroke affects millions of people every year and is a leading cause of disability, resulting in significant financial cost and reduction in quality of life. Rehabilitation after stroke aims to reduce disability by facilitating recovery of impairment, activity, or participation. One aspect of stroke rehabilitation that may affect outcomes is the amount of time spent in rehabilitation, including minutes provided, frequency (i.e. days per week of rehabilitation), and duration (i.e. time period over which rehabilitation is provided). Effect of time spent in rehabilitation after stroke has been explored extensively in the literature, but findings are inconsistent. Previous systematic reviews with meta-analyses have included studies that differ not only in the amount provided, but also type of rehabilitation.]

The Use of Cardiac Autonomic Responses to Aerobic Exercise in Elderly Stroke Patients: Functional Rehabilitation as a Public Health Policy.
Raimundo RD; Zangirolami-Raimundo J; Leone C; de Carvalho TD; da Silva TD; Bezerra IMP; de Almeida AD Jr et al
International Journal of Environmental Research and Public Health, vol. 18(21)
October 2021
[**Background and Purpose**: The development of public policies must be guided by full knowledge of the health-disease process of the population. Aerobic exercises are recommended for rehabilitation in stroke patients, and have been shown to improve heart rate variability (HRV). Our aim was to compare the cardiac autonomic modulation of elderly stroke patients with that of healthy elderly people during and after an acute bout of aerobic exercise. **Methods**: A total of 60 elderly people participated in the study (30 in the control group, mean age of 67 ± 4 years; 30 in the stroke group, mean age of 69 ± 3 years). HRV was analyzed in rest-10 min of rest in supine position; exercise-the 30 min of peak exercise; and recovery-30 min in supine position post-exercise. **Results**: Taking rest and exercises together, for SDNN, RMSSD, pNN50, RRTri, and TINN, there was no difference between the stroke and control groups ($p = 0.062$; $p = 0.601$; $p = 0.166$; $p = 0.224$, and $p = 0.059$, respectively). The HF (ms 2) was higher and the LF/HF ratio was lower for the stroke group than the control group ($p < 0.001$ and $p = 0.007$, respectively). The SD2 was lower for the stroke group than for the control group ($p = 0.041$). **Conclusion**: Stroke patients present reduced variability at rest, sympathetic predominance during exercise, and do not return to baseline after the 30 min of recovery, with similar responses found in the healthy elderly group.]

Risk of Stroke

Coffee consumption and the risk of cerebrovascular disease: a meta-analysis of prospective cohort studies.
Chan L; Hong CT; Bai CH
BMC Neurology, vol. 21(1)
October 2021
[**Background**: Stroke is a crucial health threat to adults worldwide. Despite extensive knowledge of risk-factor mitigation, no primary prevention exists for healthy people. Coffee is a widely consumed beverage globally. Health benefit of coffee for several neurological diseases has been identified; however, the association between stroke risk and coffee consumption in healthy people has not been determined. We investigated the effect of coffee on stroke risk by conducting a meta-analysis of prospective cohort studies. **Methods**: Electronic databases, namely PubMed, BioMed Central, Medline, and Google Scholar, were searched using terms related to stroke and coffee. Articles that described clear diagnostic criteria for stroke and details on coffee consumption were included. The reference lists of relevant articles were reviewed to identify eligible studies not shortlisted using these terms. Enrolled studies were grouped into three outcome categories: overall stroke, hemorrhagic stroke, and ischemic stroke. **Results**: Seven studies were included and all of them were large-scale, long-term, follow-up cohort studies of a healthy population. Upon comparing the least-coffee-consuming groups from each study, the meta-analysis revealed a reduction in the risk of overall stroke during follow-up (hazard ratio [HR] for overall stroke = 0.922, 95% confidence interval [CI] = 0.855-0.994, P = 0.035). In studies with a clear definition of hemorrhagic and ischemic stroke, coffee consumption reduced the risk of ischemic stroke more robustly than that of hemorrhagic stroke (hemorrhagic, HR = 0.895, 95% CI = 0.824-0.972, P = .008; ischemic, HR = 0.834, 95% CI = 0.739-0.876, P < .001). No obvious dose-dependent or U-shaped effect was observed. **Conclusions**: Coffee consumption reduces the risk of overall stroke, especially ischemic stroke. Further investigation is required to identify beneficial components in coffee, including caffeine and phenolic acids, to develop preventive medication for stroke.]

Risk for ischemic stroke and coronary heart disease associated with migraine and migraine medication among older adults.
McKinley EC; Lay CL; Rosenson RS; Chen L; Chia V; Colantonio LD; Muntner P; Urman R; Farkouh ME
The Journal of Headache and Pain, vol. 22(1)
October 2021
[Background: Migraine has been associated with cardiovascular disease (CVD) events among middle-aged adults. The objective of this study was to determine the risk for ischemic stroke and coronary heart disease (CHD) events among older adults with versus without migraine. **Methods**: This retrospective cohort study was conducted using data from US adults ≥66 years of age with Medicare health insurance between 2008 and 2017. After stratification by history of CVD, patients with a history of migraine were matched 1:4 to those without a history of migraine, based

on calendar year, age, and sex. Patients were followed through December 31, 2017 for ischemic stroke and CHD events including myocardial infarction or coronary revascularization. All analyses were done separately for patients with and without a history of CVD. **Results**: Among patients without a history of CVD (n = 109,950 including n = 21,990 with migraine and n = 87,960 without migraine), 1789 had an ischemic stroke and 3552 had a CHD event. The adjusted hazard ratio (HR) among patients with versus without migraine was 1.20 (95% confidence interval [95%CI], 1.07-1.35) for ischemic stroke and 1.02 (95%CI, 0.93-1.11) for CHD events. Compared to patients without migraine, those with migraine who were taking an opioid medication had a higher risk for ischemic stroke (adjusted HR 1.43 [95%CI, 1.20-1.69]), while those taking a triptan had a lower risk for CHD events (adjusted HR 0.79 [95%CI, 0.67-0.93]). Among patients with a history of CVD (n = 79,515 including n = 15,903 with migraine and n = 63,612 without migraine), 2960 had an ischemic stroke and 7981 had a CHD event. The adjusted HRs (95%CI) for ischemic stroke and CHD events associated with migraine were 1.27 (1.17-1.39) and 0.99 (0.93-1.05), respectively. Patients with migraine taking an opioid medication had a higher risk for ischemic stroke (adjusted HR 1.21 [95%CI, 1.07-1.36]), while those taking a triptan had a lower risk for CHD events (adjusted HR 0.83 [95%CI, 0.72-0.95]), each versus those without migraine. **Conclusions**: Older adults with migraine are at increased risk for ischemic stroke. The risk for ischemic stroke among older adults with migraine may differ by migraine medication classes.]

Traditional risk factors and combined genetic markers of recurrent ischemic stroke in adults.
M'barek L; Sakka S; Megdiche F; Farhat N; Maalla K; Turki D; Feki S; Rebai A; Dammak M; Kallel C; Mhiri C
Journal of Thrombosis and Haemostasis, vol. 19(10)
October 2021
[**Background**: The involvement of traditional risk factors and combined genetic markers of recurrent arterial ischemic stroke (AIS) in adults remains unclear. **Objective**: This study aims to determine significant clinical and genetic factors of AIS recurrence, and to investigate the combined effect of genotypes on the occurrence of a second cerebral ischemic attack. **Methods**: We investigated a cohort study of AIS patients (18-50 years old) followed in the neurology department over 5 years. Traditional and genetic risk factors were carried through a multivariable logistic regression model. We used a Cox proportional hazard model for identifying predictors of recurrence. **Results**: Two hundred and seventy patients were enrolled in our study. The risk of AIS recurrence was 36.2% within 5 years. The potential risk of recurrence of AIS increased with traditional and genetic risk factors such as hypertension, diabetes mellitus, heart failure, and family history of cerebrovascular diseases. This risk increased with increasing number of genetic factors. The hazard ratio (HR) was 0.66 (95% confidence interval [CI] 0.97-2.67) for the subject with one genetic factor, 1.61 (95% CI 0.97-2.25) for combined methylenetetrahydrofolate reductase (MTHFR) polymorphisms, and 2.57 (95% CI 1.32-4.99) for combined factor V Leiden (FVL) and MTHFR polymorphisms (677 or 1298). The HR for the three polymorphisms combined was 6.04 (95% CI 2.40-15.16). **Conclusions**: Our findings suggest that cumulative effect of both traditional and common genetic risk factors was associated with recurrence of ischemic stroke. We demonstrated for the first time that a combined genotype FVL/MTHFR profile increase the risk of a second cerebral ischemic attack.]

Trends, risk factors, and outcomes of post-operative stroke after heart transplantation: an analysis of the UNOS database.
Alvarez P; Kitai T; Okamoto T; Niikawa H; McCurry KR; Papamichail A; Doulamis I; Briasoulis A
ESC Heart Failure, vol. 8(5)
October 2021
[**Background**: Post-operative stroke increases morbidity and mortality after cardiac surgery. Data on characteristics and outcomes of stroke after heart transplantation (HTx) are limited. **Methods and Results**: We conducted a retrospective analysis of the United Network for Organ Sharing (UNOS) database from 2009 to 2020 to identify adults who developed stroke after orthotropic HTx. Heart transplant recipients were divided according to the presence or absence of post-operative stroke. The primary endpoint was all-cause mortality. A total of 25,015 HT recipients were analysed, including 719 (2.9%) patients who suffered a post-operative stroke. The stroke rates increased from 2.1% in 2009 to 3.7% in 2019, and the risk of stroke was higher after the implantation of the new allocation system [odds ratio 1.29, 95% confidence intervals (CI) 1.06-1.56, P = 0.01]. HTx recipients with post-operative stroke were older (P = 0.008), with higher rates of prior cerebrovascular accident (CVA) (P = 0.004), prior cardiac surgery (P < 0.001), longer waitlist time (P = 0.04), higher rates of extracorporeal membrane oxygenation (ECMO) support (P < 0.001), left ventricular assist devices (LVADs) (P < 0.001), mechanical ventilation (P = 0.003), and longer ischaemic time (P < 0.001). After multivariable adjustment for recipient and donor characteristics, age, prior cardiac surgery, CVA, support with LVAD, ECMO, ischaemic time, and mechanical ventilation at the time of HTx were

independent predictors of post-operative stroke. Stroke was associated with increased risk of 30 day and all-cause mortality (hazard ratio 1.49, 95% CI 1.12-1.99, P = 0.007). **Conclusions**: Post-operative stroke after HTx is infrequent but associated with higher mortality. Redo sternotomy, LVAD, and ECMO support at HTx are among the risk factors identified.]

Thrombectomy / Endovascular Treatment

Differential effect of mechanical thrombectomy and intravenous thrombolysis in atrial fibrillation associated stroke.
Akbik F; Alawieh A; Cawley CM; Howard BM; Tong FC; Nahab F; Saad H; Dimisko L; Mustroph C; Samuels OB et al
Journal of Neurointerventional Surgery, vol. 13(10)
October 2021
[**Background**: Atrial fibrillation (AF) associated ischemic stroke has worse functional outcomes, less effective recanalization, and increased rates of hemorrhagic complications after intravenous thrombolysis (IVT). Limited data exist about the effect of AF on procedural and clinical outcomes after mechanical thrombectomy (MT). **Objective**: To determine whether recanalization efficacy, procedural speed, and clinical outcomes differ in AF associated stroke treated with MT. **Methods**: We performed a retrospective cohort study of the Stroke Thrombectomy and Aneurysm Registry (STAR) from January 2015 to December 2018 and identified 4169 patients who underwent MT for an anterior circulation stroke, 1517 (36.4 %) of whom had comorbid AF. Prospectively defined baseline characteristics, procedural outcomes, and clinical outcomes were reported and compared. **Results**: AF predicted faster procedural times, fewer passes, and higher rates of first pass success on multivariate analysis (p<0.01). AF had no effect on intracranial hemorrhage (aOR 0.69, 95% CI 0.43 to 1.12) or 90-day functional outcomes (aOR 1.17, 95% CI 0.91 to 1.50) after MT, although patients with AF were less likely to receive IVT (46% vs 54%, p<0.0001). **Conclusions**: In patients treated with MT, comorbid AF is associated with faster procedural time, fewer passes, and increased rates of first pass success without increased risk of intracranial hemorrhage or worse functional outcomes. These results are in contrast to the increased hemorrhage rates and worse functional outcomes observed in AF associated stroke treated with supportive care and or IVT. These data suggest that MT negates the AF penalty in ischemic stroke.]

Duration of symptomatic stroke and successful reperfusion with endovascular thrombectomy for anterior circulation large vessel occlusive stroke.
de Havenon A; Alexander MD; Nogueira RG; Haussen DC; Castonguay AC; Linfante I; Johnson MA; Nguyen TN et al
Journal of Neurointerventional Surgery, vol. 13(12)
December 2021
[**Background**: It has been reported that longer time intervals from stroke onset to endovascular therapy are associated with lower rates of successful reperfusion in acute ischemic stroke patients with large vessel occlusion. However, procedural variables and potential mechanisms of this association have not been fully elucidated. Methods: We performed a secondary analysis of individual patient data from the North American Solitaire Stent Retriever Acute Stroke (NASA) and Trevo Stent-Retriever Acute Stroke (TRACK) registries. We included patients with occlusion of the internal carotid artery or middle cerebral artery (M1 and M2 segments) who were treated by mechanical thrombectomy within 24 hours of last known normal. The primary outcome was reperfusion, defined as a Thrombolysis In Cerebral Infarction (TICI) score ≥2b. The secondary outcome was reperfusion on the first pass. The primary predictor was duration of symptomatic stroke, defined as time from last known normal to time of final pass. Adjusted logistic regression models were utilized to determine associations between variables and outcome. Results: We included 506 patients, of which 401 (79.3%) achieved successful reperfusion (TICI 2b/3). The mean (SD) duration of symptomatic stroke was 6.8 (3.5) hours and in the adjusted logistic regression model the duration of symptomatic stroke was associated with reperfusion (OR 0.90, 95% CI 0.84 to 0.96) and reperfusion on the first pass (OR 0.89, 95% CI 0.83 to 0.95). In that model, the predicted probability of reperfusion was 88% (95% CI 0.83 to 0.92) at 1 hour, 81% (95% CI 0.78 to 0.84) at 6 hours, 70% (95% CI 0.63 to 0.77) at 12 hours, and 42% (95% CI 0.17 to 0.67) at 24 hours (p trend =0.001). Reperfused patients were significantly younger, more likely to be male, and to have had a balloon guide catheter used during the procedure. Conclusion: In a real-world cohort of acute ischemic stroke patients with anterior circulation occlusion treated with endovascular therapy, longer duration of symptomatic stroke is associated with lower rates of successful reperfusion and reperfusion on the first pass.]

Health economic impact of first-pass success among patients with acute ischemic stroke treated with mechanical thrombectomy: a United States and European perspective.
Zaidat OO; Ribo M; Mattle HP; Saver JL; Bozorgchami H; Yoo AJ; Ehm A; Kottenmeier E; Cameron HL et al
Journal of Neurointerventional Surgery, vol. 13(12)
December 2021
[Background: First-pass effect (FPE), restoring complete or near complete reperfusion (modified Thrombolysis in Cerebral Infarction (mTICI) 2c-3) in a single pass, is an independent predictor for good functional outcomes in the endovascular treatment of acute ischemic stroke. The economic implications of achieving FPE have not been assessed. **Objective**: To assess the economic impact of achieving complete or near complete reperfusion after the first pass. **Methods**: Post hoc analyses were conducted using ARISE II study data. The target population consisted of patients in whom mTICI 2c-3 was achieved, stratified into two groups: (1) mTICI 2c-3 achieved after the first pass (FPE group) or (2) after multiple passes (non-FPE group). Baseline characteristics, clinical outcomes, and healthcare resource use were compared between groups. Costs from peer-reviewed literature were applied to assess cost consequences from the perspectives of the United States (USA), France, Germany, Italy, Spain, Sweden, and United Kingdom (UK). **Results**: Among patients who achieved mTICI 2c-3 (n=172), FPE was achieved in 53% (n=91). A higher proportion of patients in the FPE group reached good functional outcomes (90-day modified Rankin Scale score 0-2 80.46% vs 61.04%, p<0.01). The patients in the FPE group had a shorter mean length of stay (6.10 vs 9.48 days, p<0.01) and required only a single stent retriever, whereas 35% of patients in the non-FPE group required at least one additional device. Driven by improvement in clinical outcomes, the FPE group had lower procedural/hospitalization-related (24-33% reduction) and annual care (11-27% reduction) costs across all countries. **Conclusions**: FPE resulted in improved clinical outcomes, translating into lower healthcare resource use and lower estimated costs.]

Optimal thresholds to predict long-term outcome after complete endovascular recanalization in acute anterior ischemic stroke.
Neuberger U; Vollmuth P; Nagel S; Schönenberger S; Weyland CS; Gumbinger C; Ringleb PA; Bendszus M; et al
Journal of Neurointerventional Surgery, vol. 13(12)
December 2021
[**Background**: Despite complete endovascular recanalization, a significant percentage of patients with acute anterior stroke do not achieve a good clinical outcome. We analyzed optimal thresholds of relevant parameters to discern functional independence after successful endovascular recanalization and test their predictive performance. **Methods**: Patients with acute anterior ischemic stroke undergoing endovascular treatment between April 2015 and November 2019 were retrospectively analyzed. Only patients with premorbid modified Rankin Scale (mRS) score <3 and complete recanalization (modified Thrombolysis In Cerebral Infarction 2c/3) were included. Optimal thresholds of the most important variables predicting functional independence (mRS 0-2 after 90 days) were calculated using receiver operating characteristic curves and their predictive performance was tested in an independent dataset using machine learning algorithms. Results: Overall, 371 patients met the inclusion criteria. Optimal thresholds for the overall most important variables to predict functional independence were (1) National Institutes of Health Stroke Scale (NIHSS) score ≤5 after 24 hours (area under the curve (AUC) 0.88 (95% CI 0.84 to 0.92)); (2) Alberta Stroke Program Early CT Score (ASPECTS) ≥7 on follow-up CT (AUC 0.72 (95% CI 0.68 to 0.77)); and (3) change in NIHSS score ≥8 after 24 hours (AUC 0.70 (95% CI 0.65 to 0.74)). The performance of these thresholds to predict a good outcome using machine learning in the independent dataset was evaluated for (1) NIHSS score ≤5 after 24 hours (AUC 0.76 (95% CI 0.71 to 0.81)); (2) follow-up ASPECTS ≥7 (AUC 0.64 (95% CI 0.58 to 0.70)); (3) change in NIHSS score ≥8 after 24 hours (AUC 0.61 (95% CI 0.55 to 0.67)); and (4) the combination of all three parameters (AUC 0.84 (95% CI 0.80 to 0.88)). **Conclusions**: After complete recanalization in acute anterior circulation ischemic stroke, a good long-term outcome could be accurately predicted reaching NIHSS score ≤5 after 24 hours.]

Safety and efficacy of intra-arterial fibrinolytics as adjunct to mechanical thrombectomy: a systematic review and meta-analysis of observational data.
Kaesmacher J; Meinel TR; Kurmann C; Zaidat OO; Castonguay AC; Zaidi SF; Mueller-Kronast N et al
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[**Background**: Achieving the best possible reperfusion is a key determinant of clinical outcome after mechanical thrombectomy (MT). However, data on the safety and efficacy of intra-arterial (IA) fibrinolytics as an adjunct to MT with the intention to improve reperfusion are sparse. **Methods**: We performed a PROSPERO-registered

(CRD42020149124) systematic review and meta-analysis accessing MEDLINE, PubMed, and Embase from January 1, 2000 to January 1, 2020. A random-effect estimate (Mantel-Haenszel) was computed and summary OR with 95% CI were used as a measure of added IA fibrinolytics versus control on the risk of symptomatic intracranial hemorrhage (sICH) and secondary endpoints (modified Rankin Scale ≤2, mortality at 90 days). **Results**: The search identified six observational cohort studies and three observational datasets of MT randomized-controlled trial data reporting on IA fibrinolytics with MT as compared with MT alone, including 2797 patients (405 with additional IA fibrinolytics (100 urokinase (uPA), 305 tissue plasminogen activator (tPA)) and 2392 patients without IA fibrinolytics). Of 405 MT patients treated with additional IA fibrinolytics, 209 (51.6%) received prior intravenous tPA. We did not observe an increased risk of sICH after administration of IA fibrinolytics as adjunct to MT (OR 1.06, 95% CI 0.64 to 1.76), nor excess mortality (0.81, 95% CI 0.60 to 1.08). Although the mode of reporting was heterogeneous, some studies observed improved reperfusion after IA fibrinolytics. **Conclusion**: The quality of evidence regarding peri-interventional administration of IA fibrinolytics in MT is low and limited to observational data. In highly selected patients, no increase in sICH was observed, but there is large uncertainty.]

Toward a more inclusive paradigm: thrombectomy for stroke patients with pre-existing disabilities.
Regenhardt RW; Young MJ; Etherton MR; Das AS; Stapleton CJ; Patel AB; Lev MH; Hirsch JA; Rost NS et al
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[**Background**: Persons with pre-existing disabilities represent over one-third of acute stroke presentations, but account for a far smaller proportion of those receiving endovascular thrombectomy (EVT) and thrombolysis. This is despite existing ethical, economic, legal, and social directives to maximize equity for this vulnerable population. We sought to determine associations between baseline modified Rankin Scale (mRS) and outcomes after EVT. **Methods**: Individuals who underwent EVT were identified from a prospectively maintained database. Demographics, medical history, presentations, treatments, and outcomes were recorded. Baseline disability was defined as baseline mRS≥2. Accumulated disability was defined as the delta between baseline mRS and absolute 90-day mRS. Results: Of 381 individuals, 49 had baseline disability (five with mRS=4, 23 mRS=3, 21 mRS=2). Those with baseline disability were older (81 vs 68 years, P<0.0001), more likely female (65% vs 49%, P=0.032), had more coronary disease (39% vs 20%, P=0.006), stroke/TIA history (35% vs 15%, P=0.002), and higher NIH Stroke Scale (19 vs 16, P=0.001). Baseline mRS was associated with absolute 90-day mRS ≤2 (OR=0.509, 95%CI=0.370-0.700). However, baseline mRS bore no association with accumulated disability by delta mRS ≤0 (ie, return to baseline, OR=1.247, 95%CI=0.943-1.648), delta mRS ≤1 (OR=1.149, 95%CI=0.906-1.458), delta mRS ≤2 (OR 1.097, 95% CI 0.869-1.386), TICI 2b-3 reperfusion (OR=0.914, 95%CI=0.712-1.173), final infarct size (P=0.853, β=-0.014), or intracerebral hemorrhage (OR=0.521, 95%CI=0.244-1.112). **Conclusions**: While baseline mRS was associated with absolute 90-day disability, there was no association with accumulated disability or other outcomes. Patients with baseline disability should not be routinely excluded from EVT based on baseline mRS alone.]

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