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Library Current Awareness Bulletin
Stroke – March/April 2021

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News & Reports

Stroke Association and BASP write open letter to GPs after vaccine rollout concerns raised
Stroke Association
March 2021
[The Stroke Association has expressed concern regarding the rollout of the Covid-19 vaccine to survivors of stroke or mini-stroke. They cite examples of people, who should be in the first phase priority group six, being unable to get appointments.]

Stroke recoveries at risk – sharing lived experiences at the UK Stroke Forum 2020
Stroke Association
February 2021
[This article discusses the impact of the 'Stroke recoveries at risk' report and includes eight recommendations.]

Without Skipping a Beat
The Progressive Policy Think Tank (IPPR)
March 2021
[In the context of considering how the health and care system can recover from Covid-19 and 'build back better', this briefing considers the challenge in relation to cardiovascular disease (CVD) – the UK's leading cause of death.]

COVID-19: Impact on Stroke Services

[Impact of COVID-19 pandemic on acute stroke care: facing an epidemiological paradox with a paradigm shift.](#)
Paolucci M., Biguzzi S., Cordici F., Lotti, E.M., Morresi S., Romoli M., Strumia S., Terlizzi R., Vidale, S. et al
Neurological Sciences, vol. 42(2) pp. 399-406
February 2021
[**Background**: During the coronavirus disease 2019 (COVID-19) outbreak, a decrease of stroke's hospital admissions and reperfusion therapy has been reported worldwide. This retrospective observational study assessed the volume of stroke cases managed in the Emergency Department (ED) and reperfusion therapies in an Italian stroke network with a high incidence of COVID-19, particularly to evaluate if the in-hospital rerouting and the switch from a drip-and-ship to a mothership model could assure an adequate volume of acute treatments. **Methods**: We compared data from March 2020 with those from previous years and formulated five PICO questions regarding (1) incidence of stroke cases in the ED; (2) relation between stroke cases and COVID-19; (3) differences in the number of reperfusion therapies, (4) in the call-to-needle and door-to-needle times for intravenous thrombolysis, and (5) in the call-to-groin and door-to-groin times for thrombectomy. **Results**: We found (1) a 28% decrease of confirmed stroke cases managed in the ED, (2) a negative correlation between stroke cases in ED and COVID-19 progression (rs = - .390, p = .030), and (3) a similar number of treatments in March 2020 and March 2019. The adoption of the mothership model (4) did not delay alteplase infusion (median call-to-needle p = .126, median door-to-needle p = .142) but led to (5) a significant reduction in median call-to-groin (p = .018) and door-to-groin times (p = .010). **Conclusion**: The "hospital avoidance" of stroke patients during the "stay-at-home" appeals needs to be considered for future public health campaigns. A prompt reorganization of the stroke network can guarantee optimal performances at times of crisis.]

[Stroke and digital technology: a wake-up call from COVID-19 pandemic.](#)
Iodice F., Romoli M., Giometto B., Clerico M., Tedeschi G., Bonavita, S., Leocani, L., Lavorgna, L.
Neurological Sciences, vol. 42(3) pp. 805-809
March 2021
[**Introduction**: The pandemic has implemented the need for new digital technologies as useful tools during the emergency and the long recovery phase that will follow. SARS-CoV-2 has strongly impacted stroke care with significant contraction in a number of patients treated. **Methods**: This mini-review is an initiative of the "Digital Technologies, Web and Social Media Study Group" of the Italian Society of Neurology and briefly discusses digital tools for managing the acute phase and the rehabilitation after stroke, even considering the new apps that will improve the process of remote monitoring of patients after discharge at home. **Results**: Telemedicine and digital technologies could play a role in each of the three stroke-belt stages: hyperacute treatment and reperfusion, acute care, etiological classification and secondary prevention and rehabilitation. **Conclusion**: The global emergency represented by the COVID-19 pandemic can be the stimulus to accelerate the digitalization process in the field of stroke for the use of new methods on a large scale.]

Drug Therapy / Stroke Prophylaxis

[Healthcare costs before and after stroke in patients with non-valvular atrial fibrillation who initiated treatment with rivaroxaban or warfarin](#)
Milentijevic D.; Lin J.H.; Chen Y.-W.; Kogan E.; Sjoeland E.; Shrivastava S.; Alberts M.
Journal of Medical Economics, vol. 24(1) pp. 212-217
February 2021
[**Aims**: Rivaroxaban reduces stroke compared with warfarin in patients with non-valvular atrial fibrillation (NVAF). This study compared healthcare costs before and after stroke in NVAF patients treated with rivaroxaban or warfarin. **Material(s) and Method(s)**: Using de-identified IBM MarketScan Commercial and Medicare databases, this retrospective cohort study (from 2011 to 2019) included patients with NVAF who initiated rivaroxaban or warfarin within 30 days after initial NVAF diagnosis. Patients who developed stroke were identified, and stroke severity was determined by the National Institutes of Health Stroke Scale (NIHSS) score, imputed by a random forest method. Total all-cause per-patient per-year (PPPY) costs of care were determined for patients: (1) who developed stroke during the pre- and post-stroke periods and (2) who remained stroke-free during the follow-up period. Treatment groups were balanced using inverse probability of treatment weighting. **Result(s)**: A total of 13,599 patients initiated rivaroxaban and 39,861 initiated warfarin, of which 272 (2.0%) and 1,303 (3.3%), respectively, developed stroke during a mean follow-up of 28 months. Among patients who developed stroke, PPPY costs increased from the pre-

stroke to post-stroke period, with greater increases in the warfarin cohort relative to the rivaroxaban cohort. Overall, the costs increased by 1.78-fold for rivaroxaban vs 3.07-fold for warfarin; for less severe strokes (NIHSS < 5), costs increased 0.88-fold and 1.05-fold, respectively. Cost increases for more severe strokes (NIHSS >= 5) among rivaroxaban patients were half those for warfarin patients (3.19-fold vs 6.37-fold, respectively). Among patients without stroke, costs were similar during the follow-up period between the two treatment groups. **Conclusion(s)**: Total all-cause costs of care increased in the post-stroke period, and particularly in the patients treated with warfarin relative to those treated with rivaroxaban. The lower rate of stroke in the rivaroxaban cohort suggests that greater pre- to post-stroke cost increases result from more strokes occurring in the warfarin cohort.]

[Pre-treatment of Single and Double Antiplatelet and Anticoagulant With Intravenous Thrombolysis for Older Adults With Acute Ischemic Stroke: The TTT-AIS Experience](#)
Lin S.-F., Hu H.-H., Chan L., Ho B.-L., Chao A.-C., Chen C.-H., Lin H.-J., Sun Y., Lin Y.-Y., Chen P.-L., Lin S.-K. et al
Frontiers in Neurology, vol. 12
February 2021
[**Background**: This study aimed to investigate the safety and efficacy of single antiplatelet, anticoagulant and Dual Antiplatelet pre-treatment (DAPP) in older, moderate to high severity acute ischemic stroke patients treated with intravenous thrombolysis (IVT). **Method(s)**: A prospective cohort study was conducted to monitor the development of symptomatic intracranial hemorrhage (SICH) and functional outcomes at 90 days. Two different dosages of alteplase were used for IVT. Logistic regression models were used for analysis of the safety and efficacy outcomes. **Result(s)**: A total of 1,156 patients were enrolled and categorized into six groups based on their pre-treatment medications: (1) aspirin (n = 213), (2) clopidogrel (n = 37), (3) DAPP of aspirin + clopidogrel (n= 27), (4) warfarin (n = 44), (5) any of the above pre-medications (n = 331), and (6) none of these medications as controls (n = 825). The DAPP group showed significantly increased SICH by the NINDS (adjusted OR: 4.90, 95% CI 1.28-18.69) and the ECASS II (adjusted OR: 5.09, 95% CI: 1.01-25.68) standards. The aspirin group was found to significantly improve the favorable functional outcome of the modified Rankin Scale (mRS) of 0-1 (adjusted OR: 1.91, 95% CI, 1.31.2.78), but no significance for mRS of 0-2 (adjusted OR: 1.39, 95% CI, 0.97-1.99). The DAPP group also significantly increased mortality (adjusted OR: 4.75, 95% CI: 1.77-12.72). A significant interaction between different dosages for IVT and the functional status was noted. Compared to standard dose, the DAPP group showed higher proportions of disability and mortality with low dose of IVT. **Conclusion(s)**: For older adults with higher baseline severity of acute ischemic stroke, DAPP may increase the risk of SICH and mortality post IVT. However, DAPP is still not an indication to withdraw IVT and to prescribe low-dose IVT for older adults.]

[Trends in Stroke Prevention between 2014 and 2018 in Hospitalized Atrial Fibrillation Patients](#)
Bielecka B., Gorczyca I., Jelonek O., Wozakowska-Kaplon B.
Cardiology Research and Practice
February 2021
[In recent years, significant changes in stroke prophylaxis in patients with atrial fibrillation (AF) have been observed. Non-vitamin K antagonist oral anticoagulants (NOACs) are more commonly used in the prevention of thromboembolic complications in patients with AF. The aim of the study was to evaluate recommended stroke prophylaxis in patients with AF and to identify predictors of using NOACs in patients treated with anticoagulant therapy. The present study was a retrospective, observational, single-center study which included consecutively hospitalized patients in the reference cardiology center from January 2014 to December 2018. In the study group of 4027 patients with AF, to prevent thromboembolic complications, OACs were used in 3680 patients (91.4%), an antiplatelet drug(s) was used in 124 patients (3.1%), and 223 patients (5.5%) did not undergo any thromboembolic event prevention. In the group of 3680 patients treated with OACs, 2311 patients (62.8%) received NOACs and 1639 patients (37.2%), VKAs. Independent predictors of the use of NOACs were age (OR, 1.02; 95% CI, 1.01-1.03; P<0.001), a previous thromboembolic event (OR, 1.29; 95% CI, 1.01-1.65; P=0.04), nonpermanent AF (OR, 1.61; 95% CI, 1.34-1.93; P<0.001), and eGFR (OR, 1.22; 95% CI, 1.02-1.46; P=0.03). Between 2014 and 2018, an increase of patients treated with OACs, mainly with NOACs, was observed. Age, past thromboembolic complications, nonpermanent AF, and preserved renal function determined the choice of NOACs.]

[Quantitatively monitoring acute ischemic stroke patients post recombinant tissue plasminogen activator treatment](#)
Liu Y., Ma J., Shi Q., Xin S., Yu H., Liu Z., Pang C., Dong F., Wang J.
Health Science Reports, vol. 4(1)
March 2021

[**Background and aims**: Thrombolytic therapy is widely used to treat acute ischemic stroke (AIS) patients. As intracerebral hemorrhage is a life-threatening complication of this therapy, monitoring the fibrinolytic and coagulation systems is imperative. However, existing studies on plasmin inhibitor complex (PIC) and thrombin-antithrombin III complex (TAT) mostly apply the enzyme-linked immunosorbent assay (ELISA) method. The aim of this study is to establish the baseline of thrombolytic treatment for AIS patients; to monitor the fibrinolytic and coagulation system following alteplase administration; to ascertain the proper time point to predict intracerebral hemorrhage. **Method(s)**: The method used to assess a patient's intravascular situation, namely chemiluminescence, was used to quantitatively assess the PIC, TAT, and thrombomodulin (TM). Immuno-turbidimetric was used to assess the concentration of D-dimer, fibrin/fibrinogen degradation products (FDP), and the Von Willebrand factor (vWF). The Clauss clotting method was used to assay the activated partial thromboplastin time (APTT), prothrombin time (PT) and FIB. **Result(s)**: PIC increased to its peak concentration at 3 hours post intravenous (IV) alteplase infusion and decreased by nearly 50% every 3 hours thereafter. After 24 hours, PIC returned to its normal range, while D-dimer and FDP decreased 3 hours later compared to PIC. PT and APTT exhibited no obvious change during the 24-hour period. TM also exhibited no changes during the treatment. **Conclusion(s)**: PIC decreased 3 hours earlier than D-dimer and FDP. The combined test of PIC, D-dimer, and fibrinogen can be used to monitor the fibrinolytic system after the IV alteplase infusion. The use of IV alteplase had no impact on the endothelium. Creating a patient's individual data curve could assist in the prediction of hemorrhagic transformation (HT) and a stroke occurring.]

Neuroscience & Neuroimaging

[Long Non-coding RNAs as Promising Therapeutic Approach in Ischemic Stroke: a Comprehensive Review](#)
Wolska M., Jarosz-Popek J., Junger E., Wicik Z., Porshoor T., Sharif L., Czajka P., Postula M., Mirowska-Guzel D. et al
Molecular Neurobiology, vol. 58 (no. 4) pp. 1664-1682
April 2021
[In recent years, ischemic stroke (IS) has been one of the major causes of disability and mortality worldwide. The general mechanism of IS is based on reduced blood supply to neuronal tissue, resulting in neuronal cell damage by various pathological reactions. One of the main techniques for acute IS treatment entails advanced surgical approaches for restoration of cerebral blood supply but this is often associated with secondary brain injury, also known as ischemic reperfusion injury (I/R injury). Many researches have come to emphasize the significant role of long non-coding RNAs (lncRNAs) in IS, especially in I/R injury and their potential as therapeutic approaches. LncRNAs are non-protein transcripts that are able to regulate cellular processes and gene expression. Further, lncRNAs have been shown to be involved in neuronal signaling pathways. Several lncRNAs are recognized as key factors in the physiological and pathological processes of IS. In this review, we discuss the role of lncRNAs in neuronal injury mechanisms and their association with brain neuroprotection. Moreover, we identify the lncRNAs that show the greatest potential as novel therapeutic approaches in IS, which therefore merit further investigation in preclinical research.]

Post-Stroke Complications

[Blood Biomarker Panels for the Early Prediction of Stroke-Associated Complications](#)
Faura J., Bustamante A., Garcia-Berrocoso T., Ventura O., Montaner J., Millan M., Hernandez-Perez M. et al
Journal of the American Heart Association
February 2021
[**Background:** Acute decompensated heart failure (ADHF) and respiratory tract infections (RTIs) are potentially life-threatening complications in patients experiencing stroke during hospitalization. We aimed to test whether blood biomarker panels might predict these complications early after admission. **Methods and Results:** Nine hundred thirty-eight patients experiencing ischemic stroke were prospectively recruited in the Stroke-Chip study. Post-stroke complications during hospitalization were retrospectively evaluated. Blood samples were drawn within 6 hours after stroke onset, and 14 biomarkers were analyzed by immunoassays. Biomarker values were normalized using log-transformation and Z score. PanelomiX algorithm was used to select panels with the best accuracy for predicting ADHF and RTI. Logistic regression models were constructed with the clinical variables and the biomarker panels. The additional predictive value of the panels compared with the clinical model alone was evaluated by receiver operating characteristic curves. An internal validation through a 10-fold cross-validation with 3 repeats was performed. ADHF and RTI occurred in 19 (2%) and 86 (9.1%) cases, respectively. Three-biomarker panels were developed as predictors:

vascular adhesion protein-1 >5.67, NT-proBNP (N-terminal pro-B-type natriuretic peptide) >4.98 and d-dimer >5.38 (sensitivity, 89.5%; specificity, 71.7%) for ADHF; and interleukin-6 >3.97, von Willebrand factor >3.67, and d-dimer >4.58 (sensitivity, 82.6%; specificity, 59.8%) for RTI. Both panels independently predicted stroke complications (panel for ADHF: odds ratio [OR] [95% CI], 10.1 [3-52.2]; panel for RTI: OR, 3.73 [1.95-7.14]) after adjustment by clinical confounders. The addition of the panel to clinical predictors significantly improved areas under the curve of the receiver operating characteristic curves in both cases. **Conclusions:** Blood biomarkers could be useful for the early prediction of ADHF and RTI. Future studies should assess the usefulness of these panels in front of patients experiencing stroke with respiratory symptoms such as dyspnea.]

Rehabilitation

[Dysarthria and stroke. The effectiveness of speech rehabilitation. A systematic review and meta-analysis of the studies](#)
Chiaramonte R. and Vecchio M.
European Journal of Physical and Rehabilitation Medicine, vol. 57(1) pp. 24-43
February 2021
[**Introduction**: Speech difficulties, such as dysarthria or aphasia, in addition to motor impairments are frequently seen in post-stroke patients. **Evidence acquisition**: Literature searches with the keywords: "stroke" and "dysarthria" and "diagnosis" and "stroke" and "dysarthria" and "assessment" were conducted using PubMed, EMBASE, Cochrane Library, and Web of Science databases to perform the systematic review about the methods used to measure the severity of dysarthria in subjects post-stroke. The search was performed by two authors from 15 January to 22 February 2020. The research identified a total of 402 articles for the search using the keywords "stroke" and "dysarthria," and "diagnosis" and 84 references for the search using the keywords "stroke" and "dysarthria" and "assessment." Sixty-nine selected articles were analyzed by the reviewers. Thirty-seven publications met the inclusion criteria and were included in the systematic review. Thirty-two articles were excluded for several reasons: 1) 12 involved individuals with aphasia or other speech problems different from dysarthria; 2) 12 examined different topics from our aim; and 3) eight did not include post-stroke cases. **Evidence synthesis**: The systematic review identified methods for measuring the severity of post-stroke dysarthria. The meta-analysis showed the acoustic parameters affected in dysarthria secondary to stroke and the differences in these parameters after speech therapy. **Conclusion(s)**: The alternating and sequential motion rate (AMR- P, AMR-T, AMR-K, and SMR-PTK) and maximum phonation time were significantly improved after speech rehabilitation.]

[Economic evaluation of nurse-led stroke aftercare addressing long-Term psychosocial outcome: A comparison to care-As-usual](#)
Verberne D.P.J., Ponds R.W.H.M., Van Heugten C.M., Van Mastrigt G.A.P.G., Kroese M.E.A.L.
BMJ Open, vol. 11(2)
February 2021
[**Objective**: To examine the cost-effectiveness of nurse-led stroke aftercare addressing psychosocial outcome at 6 months post stroke, compared with care-As-usual. **Design:** Economic evaluation within a comparative effectiveness research design. **Setting:** Primary care (2016-2017) and community settings (2011-2013) in the Netherlands. **Participants:** Persons who suffered from ischaemic or haemorrhagic stroke, or a transient ischaemic attack and were discharged home after visiting the emergency department, hospitalisation or inpatient rehabilitation. **Interventions:** Nurse-led stroke aftercare at 6 months post stroke addressing psychosocial functioning by providing screening, psycho-education, emotional support and referral to specialist care when needed. Care-As-usual concerned routine follow-up care including secondary prevention programmes and a consultation with the neurologist at 6 weeks post stroke. **Primary and secondary outcome measures**: Main outcome measure of cost-effectiveness was quality-Adjusted life years (QALYs) estimated by the quality of life measured by the five-dimensional, three-level EuroQol. Costs were assessed using a cost-questionnaire. Secondary outcomes were mood (Hospital Anxiety and Depression Scale) and social participation (Utrecht Scale for Evaluation of Rehabilitation-Participation) restrictions subscale. **Results**: Health outcomes were significantly better in stroke aftercare for QALYs ("=0.05; 95% CI 0.01 to 0.09) and social participation ("=4.91; 95% CI 1.89 to 7.93) compared with care-As-usual. Total societal costs were 1208 higher in stroke aftercare than in care-As-usual (95% CI-3881 to 6057). Healthcare costs were in total 1208 higher in stroke aftercare than in care-As-usual (95% CI-3881 to 6057). Average costs of stroke aftercare were 91 (SD=3.20) per person. Base case cost-effectiveness analyses showed an incremental cost-effectiveness ratio of 24 679 per QALY gained. Probability of stroke aftercare being cost-effective was 64% on a 50 000 willingness-To-pay level.

Conclusions: Nurse-led stroke aftercare addressing psychosocial functioning showed to be a low-cost intervention and is likely to be a cost-effective addition to care-As-usual. It plays an important role by screening and addressing psychosocial problem, not covered by usual care.]

[Head-Mounted Display-Based Therapies for Adults Post-Stroke: A Systematic Review and Meta-Analysis.](#)
Palacios-Navarro, Guillermo; Hogan, Neville
Sensors, vol. 21(4)
February 2021
[Immersive virtual reality techniques have been applied to the rehabilitation of patients after stroke, but evidence of its clinical effectiveness is scarce. The present review aims to find studies that evaluate the effects of immersive virtual reality (VR) therapies intended for motor function rehabilitation compared to conventional rehabilitation in people after stroke and make recommendations for future studies. Data from different databases were searched from inception until October 2020. Studies that investigated the effects of immersive VR interventions on post-stroke adult subjects via a head-mounted display (HMD) were included. These studies included a control group that received conventional therapy or another non-immersive VR intervention. The studies reported statistical data for the groups involved in at least the posttest as well as relevant outcomes measuring functional or motor recovery of either lower or upper limbs. Most of the studies found significant improvements in some outcomes after the intervention in favor of the virtual rehabilitation group. Although evidence is limited, immersive VR therapies constitute an interesting tool to improve motor learning when used in conjunction with traditional rehabilitation therapies, providing a non-pharmacological therapeutic pathway for people after stroke.]

[International consensus recommendations for outcome measurement in post-stroke arm rehabilitation trials](#)
Duncan Millar J., Van Wijck F., Pollock A., Ali M.
European Journal of Physical and Rehabilitation Medicine, vol. 57(1) pp. 61-68
February 2021
[**Background**: Existing randomized controlled trials (RCTs) of arm rehabilitation interventions after stroke use a wide range of outcome measures, limiting ability to pool data to determine efficacy. Published recommendations also lack stroke survivor, carer and clinician involvement specifically about perceived relevance and importance of outcomes and measures. **Aim**: To generate international consensus recommendations for selection of outcome measures for use in future stroke RCTs in arm rehabilitation, considering outcomes important to stroke survivors, carers and clinicians. The recommendations are the Standardizing Measurement in Arm Rehabilitation Trials (SMART) Toolbox. **Design**: Two-round international e-Delphi Survey and consensus meeting. **Setting**: Online and University. **Population**: Fifty-five researchers and clinicians with expertise in stroke upper limb rehabilitation from 18 countries (e-Delphi); N.=13 researchers and clinicians, N.=2 stroke survivors, N.=1 carer (consensus meeting). **Method(s)**: Using systematically identified outcome measures from published RCTs, we conducted a two-round international e-Delphi Survey with researchers and clinicians to identify the most important measures for inclusion in the toolbox. Measures that achieved >=60% consensus were categorized using the International Classification of Functioning, Disability and Health Framework (ICF); psychometric properties were ascertained from literature and research resources. At a final consensus meeting, expert stakeholders selected measures for inclusion in the toolbox. **Result(s)**: e-Delphi participants recommended 28/170 measures for discussion at the final consensus meeting. Expert stakeholders (N.=16) selected the Visual Analogue Scale for pain/0-10 Numeric Pain Rating Scale, dynamometry, Action Research Arm Test, Wolf Motor Function Test, Barthel Index, Motricity Index and Fugl-Meyer Assessment (upper limb section of each), Box and Block Test, Motor Activity Log 14, Nine Hole Peg Test, Functional Independence Measure, EQ-5D, Canadian Occupational Performance Measure and Modified Rankin Scale for inclusion in the toolbox. **Conclusion(s)**: The SMART Toolbox provides a refined selection of measures that capture outcomes considered important by stakeholders for each ICF domain. **Clinical rehabilitation impact**: The toolbox will facilitate data aggregation for efficacy analyses thereby strengthening evidence to inform clinical practice. Clinicians can also use the toolbox to guide selection of measures ensuring a patient-centered focus.]

[Localized muscle vibration in the treatment of motor impairment and spasticity in post-stroke patients: a systematic review](#)
Avvantaggiato C., Cinone N., Facciorusso S., Turitto A., Stuppiello L., Ciritella C., Fiore P., Casale R., Picelli A. et al
European Journal of Physical and Rehabilitation Medicine, vol. 57(1) pp. 44-60
February 2021

[**Introduction**: During the last decades, many studies have been carried out to understand the possible positive effects of vibration therapy in post-stroke rehabilitation. In particular, the use of localized muscle vibration (LMV) seems to have promising results. The aim of this systematic review was to describe the use of LMV in post-stroke patients to improve motor recovery, reducing spasticity and disability in both upper and lower limb. **Evidence acquisition**: A search was conducted on PubMed, Scopus, Pedro and REHABDATA electronic database. Only randomized controlled trials have been included, excluding no-localized vibratory treatments and other pathological conditions. Fourteen studies met the inclusion criteria and were included in this review. **Evidence synthesis**: Collectively, the studies involved 425 stroke patients. Most studies included chronic stroke patients (ten) and treated only the upper limb (eleven). There is evidence that LMV therapy is effective in reducing spasticity and improving motor recovery, especially when associated with conventional physical therapy. **Conclusion(s)**: LMV may be a feasible and safe tool to be integrated into traditional and conventional neurorehabilitation programs for post-stroke patients to reduce spasticity. Analysis of the available clinical trials do not allow us to indicate vibration therapy as effective in functional motor recovery, despite some studies showed encouraging results. Further studies, with larger size of homogeneous patients and with a shared methodology are needed to produce more reliable data, especially on the lower limb.]

[The influences of Tai Chi on balance function and exercise capacity among stroke patients: A meta-analysis](#)
Evidence-based Complementary and Alternative Medicine
Zheng X., Liu Z., Wang X., Wu X., Wang J., Wang K., Yin J.
February 2021
[**Objective**: This study aims to explore the influences of Tai Chi on the balance function and exercise capacity among stroke patients. **Methods**: Databases including PubMed, Embase, WOS (Web of Science), the Cochrane Library, CNKI (China National Knowledge Infrastructure), Wanfang Data, VIP (VIP database), and CBM (China Biology Medicine disc) were retrieved to gather the figures of randomized controlled trials on the balance function and exercise capacity among stroke patients. Then relevant data were input and analyzed in Review Manager 5.3. **Results**: Nineteen papers were included and analyzed in this study. According to the combined effect size, the balance function of stroke patients improved significantly: the Berg Balance Function Scale score [MD = 7.67, 95% CI (3.44, 11.90)]; standing and walking test scores [MD = 3.42, 95% CI (4.22, -2.63)]; gravity swing area [MD = 0.79, 95% CI (1.48, 0.10)]; and gravity swing speed [MD = -5.43, 95% CI (-7.79, 3.08)]. In addition, the exercise capacity improved significantly as well: the FMA (Fugl-Meyer Assessment Scale) scale score [MD = 4.15, 95% CI (1.68, 6.63)]. There are no significant influences or changes of other related results. **Conclusions**: Stroke patients are able to improve their balance functions and exercise capacities prominently when they do Tai Chi exercise once or twice a week and >=5 times/week and >30 <= 60 min/time.]

Risk of Stroke

[Acute Ischemic Stroke and COVID-19: An Analysis of 27676 Patients](#)
Qureshi A.I., Huang W., Lobanova I., French B.R., Gomez C.R., Baskett W.I., Raju M., Shyu C.-R., Shyu D. et al
Stroke, vol. 52(3) pp. 905-912
March 2021
[**Background and purpose**: Acute ischemic stroke may occur in patients with coronavirus disease 2019 (COVID-19), but risk factors, in-hospital events, and outcomes are not well studied in large cohorts. We identified risk factors, comorbidities, and outcomes in patients with COVID-19 with or without acute ischemic stroke and compared with patients without COVID-19 and acute ischemic stroke. **Method(s):** We analyzed the data from 54 health care facilities using the Cerner deidentified COVID-19 dataset. The dataset included patients with an emergency department or inpatient encounter with discharge diagnoses codes that could be associated to suspicion of or exposure to COVID-19 or confirmed COVID-19. **Result(s):** A total of 103 (1.3%) patients developed acute ischemic stroke among 8163 patients with COVID-19. Among all patients with COVID-19, the proportion of patients with hypertension, diabetes, hyperlipidemia, atrial fibrillation, and congestive heart failure was significantly higher among those with acute ischemic stroke. Acute ischemic stroke was associated with discharge to destination other than home or death (relative risk, 2.1 [95% CI, 1.6-2.4]; P<0.0001) after adjusting for potential confounders. A total of 199 (1.0%) patients developed acute ischemic stroke among 19513 patients without COVID-19. Among all ischemic stroke patients, COVID-19 was associated with discharge to destination other than home or death (relative risk, 1.2 [95% CI, 1.0-1.3]; P=0.03) after adjusting for potential confounders. **Conclusion(s):** Acute ischemic stroke was infrequent in patients with COVID-19 and usually occurs in the presence of other cardiovascular risk factors. The risk

of discharge to destination other than home or death increased 2-fold with occurrence of acute ischemic stroke in patients with COVID-19.]

[Modifiable Lifestyle Factors and Risk of Stroke: A Mendelian Randomization Analysis](#)

Harshfield E.L., Markus H.S., Georgakis M.K., Malik R., Dichgans M.

Stroke, vol. 52(3) pp. 931-936

March 2021

[**Background and purpose**: Assessing whether modifiable risk factors are causally associated with stroke risk is important in planning public health measures, but determining causality can be difficult in epidemiological data. We evaluated whether modifiable lifestyle factors including educational attainment, smoking, and body mass index are causal risk factors for ischemic stroke and its subtypes and hemorrhagic stroke. **Method(s)**: We performed 2-sample and multivariable Mendelian randomization to assess the causal effect of 12 lifestyle factors on risk of stroke and whether these effects are independent. **Result(s)**: Genetically predicted years of education was inversely associated with ischemic, large artery, and small vessel stroke, and intracerebral hemorrhage. Genetically predicted smoking, body mass index, and waist-hip ratio were associated with ischemic and large artery stroke. The effects of education, body mass index, and smoking on ischemic stroke were independent. **Conclusion(s)**: Our findings support the hypothesis that reduced education and increased smoking and obesity increase risk of ischemic, large artery, and small vessel stroke, suggesting that lifestyle modifications addressing these risk factors will reduce stroke risk.]

[Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis](#)

Howard D.P.J., Gaziano, L., Rothwell, P.M.

The Lancet. Neurology, vol. 20(3) pp. 193-202

March 2021

[**Background**: There is uncertainty around which patients with asymptomatic carotid stenosis should be offered surgical intervention. Although stroke rates were unrelated to the degree of stenosis in the medical-treatment-only groups in previous randomised trials, this could simply reflect recruitment bias and there has been no systematic analysis of a stenosis-risk association in cohort studies. We aimed to establish whether there is any association between the degree of asymptomatic stenosis and ipsilateral stroke risk in patients on contemporary medical treatment. **Methods**: We did a prospective population-based study (Oxford Vascular Study; OxVasc), and a systematic review and meta-analysis. All patients in OxVasc with a recent suspected transient ischaemic attack or stroke, between April 1, 2002, and April 1, 2017, who had asymptomatic carotid stenosis were included in these analyses. We commenced contemporary medical treatment and determined ipsilateral stroke risk in this cohort by face-to-face follow-up (to Oct 1, 2020). We also did a systematic review and meta-analysis of all published studies (from Jan 1, 1980, to Oct 1, 2020) reporting ipsilateral stroke risk in patients with asymptomatic carotid stenosis. We searched MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials, and included both observational cohort studies and medical treatment groups of randomised controlled trials if the number of patients exceeded 30, ipsilateral stroke rates (or the raw data to calculate these) were provided, and were published in English. **Findings**: Between April 1, 2002, and April 1, 2017, 2354 patients were consecutively enrolled in OxVasc and 2178 patients underwent carotid imaging, of whom 207 had 50-99% asymptomatic stenosis of at least one carotid bifurcation (mean age at imaging: 77·5 years [SD 10·3]; 88 [43%] women). The 5-year ipsilateral stroke risk increased with the degree of stenosis; patients with 70-99% stenosis had a significantly greater 5-year ipsilateral stroke risk than did those with 50-69% stenosis (six [14·6%; 95% CI 3·5-25·7] of 53 patients vs none of 154; p<0·0001); and patients with 80-99% stenosis had a significantly greater 5-year ipsilateral stroke risk than did those with 50-79% stenosis (five [18·3%; 7·7-29·9] of 34 patients vs one [1·0%; 0·0-2·9] of 173; p<0·0001). Of the 56 studies identified in the systematic review (comprising 13 717 patients), 23 provided data on ipsilateral stroke risk fully stratified by degree of asymptomatic stenosis (in 8419 patients). Stroke risk was linearly associated with degree of ipsilateral stenosis (p<0·0001); there was a higher risk in patients with 70-99% stenosis than in those with 50-69% stenosis (386 of 3778 patients vs 181 of 3806 patients; odds ratio [OR] 2·1 [95% CI 1·7-2·5], p<0·0001; 15 cohort studies, three trials) and a higher risk in patients with 80-99% stenosis than in those with 50-79% stenosis (77 of 727 patients vs 167 of 3272 patients; OR 2·5 [1·8-3·5], p<0·0001; 11 cohort studies). Heterogeneity in stroke risk between studies for patients with severe versus moderate stenosis (phet<0·0001) was accounted for by highly discrepant results (pdiff<0·0001) in the randomised controlled trials of endarterectomy compared with cohort studies (trials: pooled OR 0·8 [95% CI 0·6-1·2], phet=0·89; cohorts: 2·9 [2·3-3·7], phet=0·54). **Interpretation**: Contrary to the assumptions of current guidelines and the findings of subgroup analyses of previous randomised controlled trials, the stroke risk reported in cohort

studies was highly dependent on the degree of asymptomatic carotid stenosis, suggesting that the benefit of endarterectomy might be underestimated in patients with severe stenosis. Conversely, the 5-year stroke risk was low for patients with moderate stenosis on contemporary medical treatment, calling into question any benefit from revascularisation. **Funding**: NIHR Oxford Biomedical Research Centre, Wellcome Trust, Wolfson Foundation, and the British Heart Foundation.]

[Stroke as a Neurological Complication of COVID-19: A Systematic Review and Meta-Analysis of Incidence, Outcomes and Predictors.](#)
Siow I., Lee K.S., Zhang J.J.Y., Saffari S.E., Ng A., Young B.
Journal of Stroke and Cerebrovascular Diseases, vol. 30(3)
March 2021
[**Introduction**: COVID-19 is a multi-system infection which predominantly affects the respiratory system, but also causes systemic inflammation, endothelialitis and thrombosis. The consequences of this include renal dysfunction, hepatitis and stroke. In this systematic review, we aimed to evaluate the epidemiology, clinical course, and outcomes of patients who suffer from stroke as a complication of COVID-19. **Methods**: We conducted a systematic review of all studies published between November 1, 2019 and July 8, 2020 which reported on patients who suffered from stroke as a complication of COVID-19. **Results**: 326 studies were screened, and 30 studies reporting findings from 55,176 patients including 899 with stroke were included. The average age of patients who suffered from stroke as a complication of COVID-19 was 65.5 (Range: 40.4-76.4 years). The average incidence of stroke as a complication of COVID-19 was 1.74% (95% CI: 1.09% to 2.51%). The average mortality of stroke in COVID-19 patients was 31.76% (95% CI: 17.77% to 47.31%). These patients also had deranged clinical parameters including deranged coagulation profiles, liver function tests, and full blood counts. **Conclusion**: Although stroke is an uncommon complication of COVID-19, when present, it often results in significant morbidity and mortality. In COVID-19 patients, stroke was associated with older age, comorbidities, and severe illness.]

[Stroke in COVID-19: A systematic review and meta-analysis](#)
Nannoni S., de Groot R., Bell S., Markus, H.S.
International Journal of Stroke, vol. 16(2) pp. 137-149
February 2021
[**Background**: Coronavirus disease 2019 (COVID-19) has become a global pandemic, affecting millions of people. However, the relationship between COVID-19 and acute cerebrovascular diseases is unclear. **Aims**: We aimed to characterize the incidence, risk factors, clinical-radiological manifestations, and outcome of COVID-19-associated stroke. **Methods**: Three medical databases were systematically reviewed for published articles on acute cerebrovascular diseases in COVID-19 (December 2019-September 2020). The review protocol was previously registered (PROSPERO ID = CRD42020185476). Data were extracted from articles reporting ≥5 stroke cases in COVID-19. We complied with the PRISMA guidelines and used the Newcastle-Ottawa Scale to assess data quality. Data were pooled using a random-effect model. **Summary of review**: Of 2277 initially identified articles, 61 (2.7%) were entered in the meta-analysis. Out of 108,571 patients with COVID-19, acute CVD occurred in 1.4% (95%CI: 1.0-1.9). The most common manifestation was acute ischemic stroke (87.4%); intracerebral hemorrhage was less common (11.6%). Patients with COVID-19 developing acute cerebrovascular diseases, compared to those who did not, were older (pooled median difference = 4.8 years; 95%CI: 1.7-22.4), more likely to have hypertension (OR = 7.35; 95%CI: 1.94-27.87), diabetes mellitus (OR = 5.56; 95%CI: 3.34-9.24), coronary artery disease (OR = 3.12; 95%CI: 1.61-6.02), and severe infection (OR = 5.10; 95%CI: 2.72-9.54). Compared to individuals who experienced a stroke without the infection, patients with COVID-19 and stroke were younger (pooled median difference = -6.0 years; 95%CI: -12.3 to -1.4), had higher NIHSS (pooled median difference = 5; 95%CI: 3-9), higher frequency of large vessel occlusion (OR = 2.73; 95%CI: 1.63-4.57), and higher in-hospital mortality rate (OR = 5.21; 95%CI: 3.43-7.90). **CONCLUSIONS**: Acute cerebrovascular diseases are not uncommon in patients with COVID-19, especially in those whom are severely infected and have pre-existing vascular risk factors. The pattern of large vessel occlusion and multi-territory infarcts suggests that cerebral thrombosis and/or thromboembolism could be possible causative pathways for the disease.]

[The Impact of SARS-CoV-2 on Stroke Epidemiology and Care: A Meta-Analysis.](#)
Katsanos A.H., Palaiodimou L., Zand, R., Yaghi S., Kamel H., Navi B.B., Turc G., Romoli M., Sharma V.K. et al
Annals of Neurology, vol. 89(2) pp. 380-388
February 2021

[**Objective**: Emerging data indicate an increased risk of cerebrovascular events with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and highlight the potential impact of coronavirus disease (COVID-19) on the management and outcomes of acute stroke. We conducted a systematic review and meta-analysis to evaluate the aforementioned considerations. **Methods**: We performed a meta-analysis of observational cohort studies reporting on the occurrence and/or outcomes of patients with cerebrovascular events in association with their SARS-CoV-2 infection status. We used a random-effects model. Summary estimates were reported as odds ratios (ORs) and corresponding 95% confidence intervals (CIs). **Results**: We identified 18 cohort studies including 67,845 patients. Among patients with SARS-CoV-2, 1.3% (95% CI = 0.9-1.6%, I2 = 87%) were hospitalized for cerebrovascular events, 1.1% (95% CI = 0.8-1.3%, I2 = 85%) for ischemic stroke, and 0.2% (95% CI = 0.1-0.3%, I2 = 64%) for hemorrhagic stroke. Compared to noninfected contemporary or historical controls, patients with SARS-CoV-2 infection had increased odds of ischemic stroke (OR = 3.58, 95% CI = 1.43-8.92, I2 = 43%) and cryptogenic stroke (OR = 3.98, 95% CI = 1.62-9.77, I2 = 0%). Diabetes mellitus was found to be more prevalent among SARS-CoV-2 stroke patients compared to noninfected historical controls (OR = 1.39, 95% CI = 1.00-1.94, I2 = 0%). SARS-CoV-2 infection status was not associated with the likelihood of receiving intravenous thrombolysis (OR = 1.42, 95% CI = 0.65-3.10, I2 = 0%) or endovascular thrombectomy (OR = 0.78, 95% CI = 0.35-1.74, I2 = 0%) among hospitalized ischemic stroke patients during the COVID-19 pandemic. Odds of in-hospital mortality were higher among SARS-CoV-2 stroke patients compared to noninfected contemporary or historical stroke patients (OR = 5.60, 95% CI = 3.19-9.80, I2 = 45%). **Interpretation**: SARS-CoV-2 appears to be associated with an increased risk of ischemic stroke, and potentially cryptogenic stroke in particular. It may also be related to an increased mortality risk.]

[The Modifiable Risk Factors of Uncontrolled Hypertension in Stroke: A Systematic Review and Meta-Analysis](#)
Upoyo A.S.; Setyopranoto I.; Pangastuti H.S
Stroke Research and Treatment
February 2021
[**Objective**: This review aimed at figuring out the risk factors of uncontrolled hypertension in stroke. **Method**: This study systematically analyzed the hypertension risk factors available in the ProQuest, EBSCO, and PubMed databases published between 2010 and December 2019. The risk factors' pooled odds ratio (POR) included in this research was calculated using both fixed and random-effect models. The meta-data analysis was processed using the Review Manager 5.3 (Rev Man 5.3). **Result**: Of 1868 articles, seven studies were included in this review searched using specific keywords. Based on the analysis results, there were 7 risk factors of uncontrolled hypertension in stroke: medication nonadherence (POR=2.23 [95% CI 1.71-2.89], p=0.342; I2=6.7%), use of antihypertensive drugs (POR=1.13 [95% CI 1.19-1.59, p=0.001; I2=90.9%), stage of hypertension (POR=1.14 [95% CI 1.02-1.27], p=<0.001; I2=97.1%), diabetes mellitus (POR=0.71 [95% CI 0.52-0.99], p=<0.001; I2=96.5%), atrial fibrillation (POR=1.74 [95% CI 1.48-2.04)], p=<0.001; I2=93.1%), triglycerides (POR=1.47 [95% CI 1.23-1.75], p=0.879; I2=0%), and age (POR=1.03 [95% CI 0.89-1.18], p=<0.001; I2=97.5%]. There were no bias publications among studies. Medication nonadherence and triglycerides had homogeneous variations, while the others had heterogeneous variations. **Conclusion**: Medication nonadherence, triglycerides, stage of hypertension, atrial fibrillation, and use of antihypertensive drugs significantly affect the uncontrolled hypertension in stroke.]

Thrombectomy

[Adverse Outcomes Associated With Higher Mean Blood Pressure and Greater Blood Pressure Variability Immediately After Successful Embolectomy in Those With Acute Ischemic Stroke, and the Influence of Pretreatment Collateral Circulation Status](#)
Liu D., Nie X., Pan Y., Pu Y., Wei Y., Cai Y., Ding Y., Lu Q., Zhang Z., Yang Z., Wen M., Wang P., Wang Y., Liu L. et al
Journal of the American Heart Association
March 2021
[**Background:** To investigate whether collateral status could modify the associations between post-thrombectomy blood pressure (BP) measures and outcomes. **Methods and Results:** Patients with anterior-circulation large-vessel-occlusion successfully recanalized in a multicenter endovascular thrombectomy registry were enrolled. Pretreatment collateral status was graded and dichotomized (good/poor) in angiography. Maximum, minimum, and mean systolic BP (SBP) and BP variability (assessed by the SD, coefficient of variation) during the initial 24 hours after endovascular thrombectomy were obtained. The primary outcome was unfavorable 90-day outcome (modified Rankin Scale score 3-6). Secondary outcomes included symptomatic intracranial hemorrhage and 90-day mortality. Adjusted odds ratios (aOR) of BP parameters over the outcomes were obtained in all patients and in patients with good/poor collaterals.

Among 596 patients (mean age 66 years; 59.9% males), 302 (50.7%) patients had unfavorable 90-day outcome. In multivariable analyses, higher mean SBP (aOR, 1.59 per 10 mm Hg increment; 95% CI, 1.26-2.02; P<0.001), mean SBP >140 mm Hg (versus <=120 mm Hg; aOR, 4.27; 95% CI, 1.66-10.97; P=0.002), and higher SBP SD (aOR, 1.08 per 1-SD increment; 95% CI, 1.01-1.16; P=0.02) were respectively associated with unfavorable 90-day outcome in patients with poor collateral but not in those with good collateral. A marginal interaction between SBP coefficient of variation tertiles and collaterals on 90-day functional outcome (P for interaction, 0.09) was observed. A significant interaction between SBP coefficient of variation tertiles and collaterals on 90-day mortality (P for interaction, 0.03) was observed. **Conclusions:** Higher postprocedural BP is associated with 90-day unfavorable outcomes after successful endovascular thrombectomy in patients with poor collateral.]

[Endovascular Thrombectomy of COVID-19-Related Large Vessel Occlusion: A Systematic Review and Summary of the Literature](#)
Al-Smadi A.S., Mach J.C., Abrol S., Abujudeh H., Luqman A., Chamiraju P.
Current Radiology Reports, vol. 9(4)
April 2021
[**Purpose**: Despite an overall reduction in the number of stroke cases presenting to hospitals during the COVID-19 pandemic, a remarkably high incidence of acute cerebrovascular disease associated with the infection has been reported. In this systematic review, we assess the neurological outcomes and complications of endovascular thrombectomy (EVT) for large vessel occlusions (LVO) in COVID-19 patients. **Method(s)**: A literature search was performed in PubMed from December 1, 2019 through September 1st, 2020 using different combinations of suitable keywords. Ten studies reporting EVT outcomes and complications were identified. Two studies that included non-LVO pathologies and COVID-19 negative patients with the outcomes analysis were excluded. Patient demographics, comorbidities, anatomic thrombus location, neurological and angiographic outcomes were assessed. **Result(s)**: A total of 8 studies, in addition to our institutional case series, were ultimately included in this review. The mean age was 62.2 years, of which 67.6% were males. M1 segment involvement was the most commonly reported (53.8%) thrombus location. The mean NIHSS at presentation was 20.4 with no significant change at 24 h. Successful revascularization (TICI >= 2b) was achieved in 89%. Early proximal cerebral re-occlusion was reported in 6 patients (11%) and cerebral hemorrhage in 3 patients (4%). In hospital mortality was reported in 15 patients (28.8%). **Conclusion(s)**: Despite angiographically successful EVT of LVOs in the majority of patients, this literature analysis demonstrates overall poor outcomes and high mortality in COVID-19 patients post EVT. An unusual incidence of early intracerebral proximal arterial re-occlusion was notable.]

[Machine-learning-based outcome prediction in stroke patients with middle cerebral artery-M1 occlusions and early thrombectomy](#)
Hamann J., Herzog L., Wehrli C., Luft A.R., Wegener S., Sick B., Bink A., Piccirelli M., Stippich C., Dobrocky T. et al
European Journal of Neurology, vol. 28(4) pp. 1234-1243
April 2021
[Background and purpose: Clinical outcomes vary substantially among individuals with large vessel occlusion (LVO) stroke. A small infarct core and large imaging mismatch were found to be associated with good recovery. The aim of this study was to investigate whether those imaging variables would improve individual prediction of functional outcome after early (<6 h) endovascular treatment (EVT) in LVO stroke. Method(s): We included 222 patients with acute ischemic stroke due to middle cerebral artery (MCA)-M1 occlusion who received EVT. As predictors, we used clinical variables and region of interest (ROI)-based magnetic resonance imaging features. We developed different machine-learning models and quantified their prediction performance according to the area under the receiver-operating characteristic curves and the Brier score. Result(s): The rate of successful recanalization was 78%, with 54% patients having a favorable outcome (modified Rankin scale score 0-2). Small infarct core was associated with favorable functional outcome. Outcome prediction improved only slightly when imaging was added to patient variables. Age was the driving factor, with a sharp decrease in likelihood of favorable functional outcome above the age of 78 years. Conclusion(s): In patients with MCA-M1 occlusion strokes referred to EVT within 6 h of symptom onset, infarct core volume was associated with outcome. However, ROI-based imaging variables led to no significant improvement in outcome prediction at an individual patient level when added to a set of clinical predictors. Our study is in concordance with current practice, where imaging mismatch or collateral readouts are not recommended as factors for excluding patients with MCA-M1 occlusion for early EVT.]

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