

Late-Breaking Science Posters I

Wednesday, February 11, 2015, 6:15 pm – 6:45 pm

LATE-BREAKING SCIENCE abstracts/studies presented at the INTERNATIONAL STROKE CONFERENCE 2015:

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Presentation Number: LB P1

Publishing Title: 5 Year Follow Up Results from the Pipeline for Uncoilable or Failed Aneurysms Trial

Author Block: **Waleed Brinjikji**, David F Kallmes, Mayo Clinic, Rochester, MN; Tibor Becske, NYU Medical Ctr, New York, NY

Abstract Body: Background and Purpose: Early and mid-term safety and efficacy of the aneurysm treatment with the Pipeline Embolization Device (PED) has been very well demonstrated in prior studies. In this study we report the 3-, and 5-year follow-up results for patients treated in the Pipeline for Uncoilable or Failed Aneurysms (PUFS) clinical trial.

Materials and Methods: In this prospective, multi-center trial, 110 large and giant wide-neck internal carotid artery aneurysms in 108 patients were treated with PED. Patients were followed per a standardized protocol at 6 months, 1, 3 and 5 years post implant. Aneurysm occlusion, in-stent stenosis, modified rankin scale (mRS), and complications were collected during this 5 year follow-up period. Delayed complications were defined as those occurring after 6 months.

Results: Results up to 6-months post-treatment have been previously published. At 3-years post treatment, 83 patients with 85 treated aneurysms had imaging follow-up and 84 patients had formal clinical follow-up. At 5-years post treatment 62 patients harboring 65 aneurysms underwent imaging follow-up, 53 (85.5%) with conventional angiography, and 81 patients had formal clinical follow-up. Complete occlusion rate was 91.8% (78/85) at 3 years and 95.3% (61/64) at 5 years. 94.0% (79/84) of patients had an mRS \leq 2 at 3 years and 93.8% (76/81) had an mRS \leq 2 at 5 years. There were no delayed neurological deaths or delayed device-related hemorrhagic or ischemic cerebrovascular events. Seven aneurysms (6.5%) were retreated for failure to occlude between 6 months and 3 years following initial treatment and no patients were retreated between 3 and 5 years post-treatment. No recanalization of previously completely occluded aneurysms was observed.

Conclusions: Our findings demonstrate that in the long term setting of 5 years, the PED is safe and effective treatment for complex, large and giant aneurysms of the intracranial internal carotid artery, with high rates of complete occlusion and low rates of adverse events.

Author Disclosure Block: **W. Brinjikji:** None. **D.F. Kallmes:** Research Grant; Modest; Covidien. Consultant/Advisory Board; Modest; Covidien. **T. Becske:** Consultant/Advisory Board; Modest; Covidien.

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Presentation Number: LB P2

Publishing Title: Improvement in Door-to-Needle Times and Neurological Outcomes when IV-tPA given by Neurological Emergency Department Physicians

Author Block: **Karen J Greenberg**, Christina Maxwell, Keisha Moore, Michael D'Ambrosio, Kenneth Liebman, Erol Veznedaroglu, Geri Sanfillippo, Cynthia Diaz, Mandy J. Binning, Capital Health System, Trenton, NJ

Abstract Body: Background and Purpose: Intravenous tissue plasminogen activator is considered the standard of care in certain patients with acute ischemic stroke. The neurological emergency department (neuro ED) at Capital Health Regional Medical Center is staffed by emergency medicine physicians who have specialized neuroscience training and give IV-tPA independently for acute ischemic stroke patients. Our neuro ED is staffed from 7 am to 6 pm. From 6 pm to 7 am, stroke patients are seen in the main ED and teleneurology is utilized to make decisions regarding IV-tPA administration. Door-to-needle times (DTN), discharge location, and discharge NIHSS were studied between the neurologic emergency department and the main emergency department with the hypothesis that all measures would be better in the neuro ED group. Methods: This is a retrospective study evaluating door-to-needle time, discharge outcomes and discharge location in acute stroke patients who received IV tPA at our comprehensive stroke center. These outcome measures were compared between patients who were evaluated and treated in our neurologic ED to those treated in our main ED.

Results: From 2012-2014, 67 acute stroke patients received IV tPA in our emergency department. 35 patients were evaluated in the neurologic ED and 32 in the main ED. There were no symptomatic intracranial hemorrhages in either group. Average DTN times were significantly faster in the neurologic ED at 35 minutes, compared to main ED DTN times of 83 minutes. No differences were found in mean admission NIHSS or MRS indicating that the patient populations were similar prior to intervention. Discharge NIHSS score was significantly lower and more patients were discharged to home in the neurologic ED group compared to the main ED group.

Conclusions: Trained neurological emergency room physicians can safely give IV tPA independently for stroke patients with improved DTN times, lower discharge NIHSS, and higher likelihood of being discharged to home compared to the main ED physicians who utilized teleneurology consultation. This suggests utility in training emergency medicine physicians to administer tPA independently based on clinical practice guidelines.

Author Disclosure Block: **K.J. Greenberg:** None. **C. Maxwell:** None. **K. Moore:** None. **M. D'Ambrosio:** None. **K. Liebman:** Consultant/Advisory Board; Modest; Stryker. **E. Veznedaroglu:** Consultant/Advisory Board; Modest; Cordis, Codman, Micrus, Microvention. **G. Sanfillippo:** None. **C. Diaz:** None. **M.J. Binning:** None.

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Presentation Number: LB P3

Publishing Title: Intraventricular Hemorrhage Recovery: Change in disability and function at Year 1

Author Block: **Gayane Yenokyan**, Johns Hopkins Biostatistics Ctr, Baltimore, MD; Wendy Ziai, Johns Hopkins Univ, Baltimore, MD; Richard Thompson, Johns Hopkins Biostatistics Ctr, Baltimore, MD; Steve Mayo, Emissary Intl, Austin, TX; Rachel Dlugash, Karen Lane, Nichol McBee, Johns Hopkins Univ, Baltimore, MD; Sayona John, Rush Univ, Chicago, IL; Sagi Harnof, Chaim Sheba Medical Ctr, Ramat Gan, Israel; George Lopez, Rush Univ, Chicago, IL; E. Francois Aldrich, Univ of Maryland, Baltimore, MD; Mark Harrigan, Univ of Alabama at Birmingham, Birmingham, AL; Jesse Dawson, Kennedy Lees, Univ of Glasgow, Glasgow, United Kingdom; Issam Awad, Univ of Chicago, Chicago, IL; Daniel Hanley, Johns Hopkins Univ, Baltimore, MD

Abstract Body: Data on recovery trajectory after intracerebral hemorrhage (ICH) complicated by intraventricular hemorrhage (IVH) are scarce and limited in period of follow-up.

We explore the natural history of recovery in the Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage Phase III trial (CLEAR III) where IVH patients are followed up to 365 days after stroke. Trained and monitored coordinators measured Modified Rankin Scale (MRS) & Barthel Index (BI) scores at 30, 90, 180, 270 and 365 days and Stroke Impact Scale (SIS) & NIH Stroke Scale (NIHSS) scores at 30, 180, and 365 days.

Generalized population-averaged models with Generalized Estimating Equations (GEE) and exchangeable working correlation structure were used to estimate trajectories of daily activities (BI score) and independence (MRS ≤ 2). Additional analyses looked at individual BI items, SIS domains and NIHSS change over time. The longitudinal analyses were stratified by ICH location, age at enrollment, gender, initial IVH volume and baseline Glasgow Coma Scale (GCS) and NIHSS scores.

We analyzed data from 274 patients across the two treatment arms who survived to 365-day follow-up with mean age 56.9 ± 10.9 ; 43% female; 27.2 ± 18.3 mL IVH volume; and median GCS 10, interquartile range 8-13. Results revealed continuous, statistically significant improvement in daily activities and independence at all time-points. Adjusted odds ratios of MRS score ≤ 2 were 2.9, 4.5, 4.7 and 4.9 at 90, 180, 270 and 365 days, respectively, compared to 30 days. Non-thalamic ICH location, younger age, smaller IVH volume, and higher GCS score predicted better outcomes. The more severe cases had lower scores at all time-points but their improvement was more pronounced (p-value for NIHSS ≥ 13 by visit interaction=0.017). Overall, mobility and chair-to-bed transfer domains showed greatest improvement at all visits; while bathing and grooming were slowest to improve. Time to recovery for SIS and MRS trajectories was similarly dependent on initial severity. The continuing improvements in BI, MRS, NIHSS and SIS up to one year has implications for clinical prognosis, intensity of care, and the design of future ICH trials.

Author Disclosure Block: **G. Yenokyan:** None. **W. Ziai:** None. **R. Thompson:** None. **S. Mayo:** None. **R. Dlugash:** None. **K. Lane:** None. **N. McBee:** None. **S. John:** None. **S. Harnof:** None. **G. Lopez:** None. **E.F. Aldrich:** None. **M. Harrigan:** None. **J. Dawson:** None. **K. Lees:** None. **I. Awad:** None. **D. Hanley:** Research Grant; Significant; CLEAR III U01 NS062851, MISTIE III U01 NS080824.

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Presentation Number: LB P4

Publishing Title: Idarucizumab, A Specific Antidote To Dabigatran, Prevents Hematoma Enlargement And Reduces Mortality In Experimental Intracerebral Hemorrhage In Mice

Author Block: **Roland Veltkamp**, Imperial Coll London, London, United Kingdom; Eva Mracsko, Univ Heidelberg, Heidelberg, Germany; Joanne vanRyn, Boehringer Ingelheim, Biberach, Germany; Shin-Young Na, Univ Heidelberg, Heidelberg, Germany

Abstract Body: Introduction: Intracerebral hemorrhage (ICH) is one of the most feared complications of long-term anticoagulation. The development of specific antidotes to direct oral anticoagulants including dabigatran etexilate (DE) may alleviate complications related to ICH. We investigated whether idarucizumab influences hematoma volume in a murine model of ICH under dabigatran anticoagulation.

Methods DE was injected to C57BL/6 mice at doses of 4.5 or 9.0mg/kg i.p. (7.16 or 14.32 μ mol/kg). ICH was induced by striatal collagenase injection under anesthesia. Anticoagulation reversal was started with 8 or 16 μ mol/kg idarucizumab or saline injected via the tail vein 30 min after ICH initiation. ICH volume and intracerebral blood content were quantified on brain cryosections and by hemoglobin spectrophotometry. Mortality over 7days was also assessed in separate experiments. Dabigatran plasma levels were determined by diluted thrombin time (dTT). Data expressed as mean \pm SD, n=9, significance was tested with t-test or ANOVA, p<0.05.

Results: Initial dabigatran plasma levels (dTT) were 1573 \pm 120 and 2831 \pm 136 ng/mL. Increasing DE doses significantly increased ICH after 24 hrs to 21 \pm 2mm³ and 25 \pm 4mm³, with 4.5 and 9mg/kg vs control (17 \pm 3mm³). Reversal of hematoma volume expansion was achieved in a dose-dependent manner with equimolar doses of idarucizumab. With 4.5mg/kg DE, the lower idarucizumab dose reduced hematoma volume to control. However with higher DE dosing, only the 16 μ mol/kg idarucizumab dose, which was equimolar to the DE dose (9mg/kg or 14.3 μ mol/kg) significantly reduced hematoma volume to baseline. This was associated with a return to baseline of dTT after dosing with idarucizumab. Mortality in DE-treated mice was 80% after 7 days with 9 mg/kg DE treatment, this was reduced to 40% in DE mice treated with 16 μ mol/kg idarucizumab (p<0.05).

Conclusions: This study shows that equimolar doses of the specific antidote, idarucizumab, can reduce the dabigatran-induced increase in hematoma volume and mortality when dosed soon after ICH occurrence in this murine model.

Author Disclosure Block: **R. Veltkamp:** Research Grant; Significant; Boehringer Ingelheim, Bayer. Honoraria; Significant; Boehringer Ingelheim, Bayer, BMS, Daiichi Sankyo. Consultant/Advisory Board; Significant; Boehringer Ingelheim, Bayer, Daiichi Sankyo. **E. Mracsko:** None. **J. vanRyn:** Employment; Significant; Boehringer Ingelheim. **S. Na:** None.

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Presentation Number: LB P5

Publishing Title: The Different Contribution to Vascular Events Between Day by Day Systolic Blood Pressure Variability and Diastolic Blood Pressure Variability in Ischemic/Transient Ischemic Attack Patients: The Boss Study

Author Block: Yilong Wang, **Jie Xu**, Xingquan Zhao, Liping Liu, Yuesong Pan, Dandan Yu, Yongjun Wang, Beijing Tiantan hospital, Beijing, China

Abstract Body: Background_The blood supply of brain depends on systolic blood pressure(SBP), while heart depends on diastolic blood pressure(DBP). It is therefore reasonable to hypothesize that SBP variability was more likely to be associated with stroke, but DBP variability may tend to develop pure cardiovascular events. Methods_The BOSS study was a longitudinal cohort study aiming to assess blood pressure parameters and clinical outcome in the ischemic(IS)/ Transient ischemic attack (TIA) patients aged more than 18 years old within 7 days after onset. Blood pressure was measured twice a day since the first day after hospitalization to 90 days after onset using semiautomatic omron blood pressure monitor. The BP variability was defined as the standard deviation and coefficient of variation of day-by-day measurements. The clinical outcome was collected at 90 days after onset, including nonfatal stroke recurrence (ischemic stroke, intracerebral hemorrhage) and cardiovascular events (myocardial infarction, angina, coronary artery stenting, heart failure, cardiovascular death). Cox proportional hazards model was used to test the association between BP variability and stroke recurrence, while logistic regression model used for BP variability and cardiovascular events. Results_Of 2608 patients with IS/TIA (mean age 62.5 years [SD,11.0]; 845 [32.4%] women), 103(3.95%) experienced a recurrent stroke and 67(2.57%) had cardiovascular events within 3 months. Day-by-day SBP variability within 90 days after IS/TIA was only associated with stroke recurrence (hazard ratio :1.531 , 95% CI :1.004- 2.333) , but not with cardiovascular events (odds ratio :0.866, 95% CI :0.528- 1.421). However, DBP variability seems to be related to both stroke and cardiovascular events: there was a trend of high DBP variability being related to cardiovascular events (odds ratio: 1.606 , 95% CI :0.975- 2.647), and a positive association with stroke recurrence (hazard ratio :1.510, 95% CI : 1.005- 2.271). Conclusion_For patients with IS/TIA , stroke recurrence was associated with both SBP variability and DBP variability, however, cardiovascular events seems to be only related to DBP variability.

Author Disclosure Block: **Y. Wang:** None. **J. Xu:** None. **X. Zhao:** None. **L. Liu:** None. **Y. Pan:** None. **D. Yu:** None. **Y. Wang:** None.

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Presentation Number: LB P6

Publishing Title: Cerebral Blood Flow Augmentation By External Counterpulsation Enhances Corticomotor Excitability In Subacute Stroke Patients: A Randomized Controlled Trial

Author Block: Jingyi LIU, The Chinese Univ of Hong Kong, Hong Kong, Hong Kong; Cathy STINEAR, Univ of Auckland, Auckland, New Zealand; Howan LEUNG, Hinglung IP, Sinying FAN, Yuklun LAU, Oiyen SOO, Kasing WONG, The Chinese Univ of Hong Kong, Hong Kong, Hong Kong

Abstract Body: Background: External counterpulsation (ECP) enhances cerebral blood flow in patients with subacute ischemic stroke but whether it changes corticomotor excitability, which is a powerful prognostic predictor for motor recovery, remains unknown.

Methods: We randomized 30 patients with subacute ischemic stroke within 4-21 days of onset (mean 6.23 days) in this sham-controlled clinical trial to either real ECP (n=15) or sham ECP (n=15). Treatment consisted of daily one hour sessions of ECP for ten days. Clinical measures included National Institutes of Health Stroke Scale (NIHSS); functional measures included Purdue Pegboard Test (PPT), Hand Grip (HG), Pinch Grip (PG); and cortical excitability measures included bilateral resting motor threshold (RMT) and motor evoked potential amplitude (MEP) at 130% of RMT. Measures were made at baseline, post-ECP day 1 (post 1), and post-ECP day 30 (post 30).

Results: There were no significant differences between groups at baseline. At post 30, there were significant differences between the real ECP group vs sham ECP group in normalized ipsilesional MEP amplitude (real: 2.35 vs sham: 1.08, $P=0.001$) and ipsilesional RMT (real: 0.89 vs sham: 0.96, $P=0.039$). The increase in HG and PPT were also significantly different between the groups at post 30 (HG: real 9.81 vs sham 4.83, $P=0.027$; PPT: real 4.73 vs sham 2.00, $P=0.014$), but no differences were found in the NIHSS and PG. No differences were found in the contralesional RMT or MEP amplitude.

Conclusion: ECP enhances ipsilesional corticomotor excitability in subacute stroke patients. This proof-of-principle study provides a mechanism of motor recovery facilitated by ECP treatment in ischemic stroke patients.

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Presentation Number: LB P7

Publishing Title: Telephone Assessment and Skill-Building Kit for Stroke Caregivers: A Randomized Controlled Clinical Trial

Author Block: **Tamilyn Bakas**, Joan K. Austin, Indiana Univ Sch of Nursing, Indianapolis, IN; Barbara Habermann, Univ of Delaware Sch of Nursing, Newark, DE; Nenette M. Jessup, Susan M. McLennon, Indiana Univ Sch of Nursing, Indianapolis, IN; Pamela H. Mitchell, Univ of Washington, Biobehavioral Nursing and Health Systems, Seattle, WA; Gwendolyn C. Morrison, Indiana Univ Dept of Economics, Indianapolis, IN; Ziyi Yang, Timothy E. Stump, Indiana Univ Dept of Biostatistics, Indianapolis, IN; Michael T. Weaver, Indiana Univ Sch of Nursing, Indianapolis, IN

Abstract Body: For approximately two-thirds of stroke survivors, family members are thrust into providing care with limited training. There are few evidence-based, easy-to-deliver programs for stroke caregivers post-discharge. The purpose of this study was to evaluate efficacy of the Telephone Assessment and Skill-Building Kit (TASKII), a nurse-led intervention enabling family members to build caregiving skills based on assessment of their own needs. **Methods:** Using an intent-to-treat design, 254 stroke caregivers were randomized to the TASKII intervention (n=123) or to an Information, Support, and Referral (ISR) group (n=131) to determine efficacy of the TASKII for reducing caregiver depressive symptoms (PHQ-9), life changes (BCOS), and unhealthy days. Both groups received 8 weekly telephone sessions, with a booster at 12 weeks. General linear models with repeated measures tested efficacy, controlling for patient hospital days and call minutes. **Results:** Caregivers who screened positive for depressive symptoms at baseline (PHQ-9 ≥ 5), and were randomized to the TASKII group, had a significantly greater reduction in depressive symptoms compared with those in the ISR group from baseline to 8 weeks (TASKII $W8-W0 = -3.34$, ISR $W8-W0 = -0.95$, $p = .0247$). Although change in BCOS from baseline to 8 weeks was not significantly different between the two groups ($p = .4239$), there was significant improvement within the TASKII group ($W8-W0 = 2.81$, $p = .0246$). Change within the ISR group was not significantly different ($W8-W0 = 1.41$, $p = .2554$). Change in the number of unhealthy days from baseline to 8 weeks was marginally different between TASKII and ISR groups ($p = .0508$). Although not significant, the TASKII group had a reduction in the number of unhealthy days (changes $W8-W0 = -0.85$, $p = .3539$). In contrast, the ISR group showed an increase in number of unhealthy days ($W8-W0 = 1.69$, $p = .0660$). **Conclusions:** The TASKII intervention produced positive results relative to the ISR control with respect to depressive symptoms and unhealthy days. There was also improvement in life changes within the TASKII group. Although further analyses are warranted to determine subgroups that would benefit most, the TASKII intervention was efficacious for stroke caregivers with depressive symptoms.

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Presentation Number: LB P8

Publishing Title: Sensory Deprivation Following Cortical Focal Ischemia Facilitates Remapping And Accelerates Behavioral Recovery

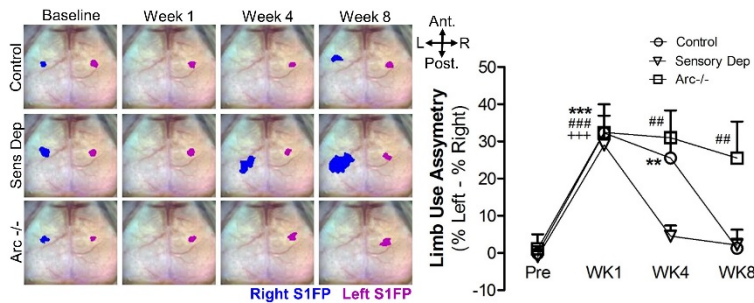
Author Block: Andrew W Kraft, Adam Q Bauer, Karen P Smith, Joseph P Culver, Jin-Moo Lee, Washington Univ Sch of Med, Saint Louis, MO

Abstract Body: Introduction: Recovery after focal cortical stroke, often unpredictable and incomplete, is associated with functional remapping to cortical regions adjacent to the lesion. We sought to determine if recovery could be accelerated by enhancing adjacent cortical plasticity using focal sensory deprivation; and if this remapping was dependent on mechanisms involved in synaptic plasticity.

Methods: Three cohorts of mice were subjected to focal photothrombosis (PT) of the right forepaw somatosensory (S1fp) cortex: 1) C57bl6 mice (control, n=11); 2) C57bl6 mice subjected to chronic whisker trimming (sensory deprivation, n=9); and 3) C57bl6 mice with Arc gene deletion (Arc, n=7), a gene critical for synaptic plasticity. S1fp remapping was assessed by electrical forepaw stimulation with optical intrinsic signal (OIS) imaging through the intact skull, and behavioral recovery was assessed using the cylinder rearing test prior to, and 1, 4, and 8 weeks following PT. ANOVA with repeated measures and Newman-Keuls' multiple comparisons was used to compare each timepoint to baseline.

Results: PT reproducibly infarcted S1fp in all cohorts, resulting in absent S1fp activation maps and reduced right forepaw use (30% more left paw use than right $P \leq 0.001$ in all groups) at wk 1 post-PT. In control mice, S1fp remapping was first observed at wk 8 in the motor area, and symmetric forepaw use improved along a similar time-course (26% asymmetry at wk 4; ** = $P \leq 0.01$, 1% at wk 8). Sensory deprivation induced earlier remapping into the barrel cortex (wk 4), and behavioral recovery (symmetric limb use) also occurred by wk 4. Arc^{-/-} mice showed no S1fp remapping and limb asymmetry persisted at wks 4 and 8 (31% and 26%; ** = $P \leq 0.01$).

Conclusion: Functional remapping following cortical stroke can be redirected to targeted regions by focal sensory deprivation, resulting in accelerated remapping and recovery. These recovery processes are dependent on Arc, which plays an important role in synaptic



plasticity.

Author Disclosure Block: A.W. Kraft: None. A.Q. Bauer: None. K.P. Smith: None. J.P. Culver: None. J. Lee: None.

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Presentation Number: LB P9

Publishing Title: Stent-Retrievers vs. Medical Therapy vs. Intravenous Thrombolysis in Large Vessel Occlusion Strokes (SMILOS): A Pooled, Patient Level Comparison Study Based on Historical Clinical Trial Data

Author Block: Raul G Nogueira, Emory Univ/Grady Memorial Hosp, Atlanta, GA; Jeffrey Saver, UCLA, Los Angeles, CA; Pooja Khatri, Univ of Cincinnati, Cincinnati, OH; for the SMILOS Investigators

Abstract Body: Background:

The IMS III, SYNTHESIS Expansion, and MR RESCUE trials failed to demonstrate a benefit of endovascular therapy in stroke patients. However, for the most part these trials utilized intra-arterial lytics and/or earlier generations devices and did not evaluate the efficacy of newer devices known to have higher rates of reperfusion.

Methods:

Pooled comparison of historical prospective data accrued in 10 prospective trials. The main inclusion criterion: occlusion involving the intracranial ICA, MCA (M1/M2), or basilar artery confirmed by CTA, MRA, or DSA. Two comparative analyses were performed:

(1) Stent-retrievers + IV Thrombolysis vs. IV Thrombolysis Alone: Combination patients were treated with intravenous tPA within 4.5 hours of symptom onset followed by thrombectomy using a stent-retriever device (Solitarie FR or Trevo) in SWIFT, TREVO-2, STAR, and TREVO-EU. IV thrombolysis patients were treated with intravenous tPA (standard dose of 0.9 mg/kg) alone within 4.5 hours from symptom onset in IMS-III, EPITHET, DEFUSE, MR Rescue, and SYNTHESIS Expansion.

(2) Stent-retrievers Alone vs. Medical Therapy Alone: Retriever alone therapy patients were treated with stent-retriever without IV tPA treatment in SWIFT, TREVO-2, STAR, and TREVO-EU. Medical therapy alone included patients who did not undergo any reperfusion treatment in PROACT-II, EPITHET, and MR Rescue.

Results:

A total of 695 patients across the 10 selected prospective trials (8 randomized controlled and 2 single-arm) qualified for our pooled analysis. The patient distribution along with the median age and baseline NIHSS for the qualifying patients in each trial is provided in the Table. Endpoints: (1) independent functional outcomes (90-day mRS: 0-2; primary), (2) 90-day mortality; (3) symptomatic ICH, (4) mTICI ≥2B (endovascular only), (5) mRS 0-3 vs. 4-6, and (6) mRS shift. The outcome data (analyzed by an independent statistician) will be reported in the meeting.

Stentriever + IV tPA (n=247)	IV tPA Alone (n=166)	Stentriever Alone (n=166)	Medical Treatment Alone (n=116)
SWIFT (n=41) age=63 bNIHSS=18	IMS-III (n=87) age=70 bNIHSS=17	SWIFT (n=48) age=69.5 bNIHSS=18	MR Rescue (n=38) age=74 bNIHSS=16.5
TREVO-2 (n=51) age=70 bNIHSS=19	MR Rescue (n=16) age=70.5 bNIHSS=17.5	TREVO-2 (n=37) age=71 bNIHSS=16	PROACT-II (n=49) age=67 bNIHSS=17
TREVO-EU (n=36) age=65 bNIHSS=16	EPITHET (n=25) age=74 bNIHSS=15	TREVO-EU (n=24) age=67 bNIHSS=20.5	EPITHET (n=29) age=70 bNIHSS=15
STAR (n=119) age=72 bNIHSS=17	DEFUSE (n=4) age=71 bNIHSS=16	STAR (n=57) age=72 bNIHSS=17	
	SYNTHESIS Expansion (n=34) age=73 bNIHSS=14		

Author Disclosure Block: **R.G. Nogueira:** Other; Modest; Stryker Neurovascular (Trepo-2 Trial PI, DAWN Trial PI); Covidien (SWIFT and SWIFT-PRIME Steering Committee); Penumbra (3-D Separator Trial Executive Committee); Coaxia: Clinical T. Other; Significant; Covidien (STAR Trial Core Lab). **J. Saver:** Other; Modest; Dr. Saver is an employee of the University of California. The University of California, Regents receive funding for Dr Saver's services as a scientific consultant regarding trial design and conduct to, The University of California, Regents receive funding for Dr Saver's services as a scientific consultant regarding trial design and conduct to Covidien, Stryker, BrainsGate, Pfizer, and St. Jude Medic, Dr Saver has served as an unpaid site investigator in multicenter trials run by Lundbeck for which the UC Regents received payments on the basis of clinical trial contracts for the number of subjects, Dr. Saver serves as an unpaid consultant to Genentech advising on the design and conduct of the PRISMS trial; neither the University of California nor Dr. Saver received any payments for this voluntar, The University of California has patent rights in retrieval devices for stroke. **P. Khatri:** Other; Modest; Biogen (pays Univ of Cincinnati Physicians for my DSMB role). Other; Significant; Genentech (pays Univ of Cincinnati Physicians for my PRISMS PI role), Penumbra (pays Univ of Cincinnati Physicians for my THERAPY Neuro PI role).

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Presentation Number: LB P11

Publishing Title: Baseline Characteristics and Clinical Outcomes of a Non-valvular Atrial Fibrillation Patient Population Not Treated With an Oral Anticoagulant: a Retrospective Analysis of the Humana Administrative Claims Database

Author Block: Shannon Reynolds, Comprehensive Health Insights, Louisville, KY; Kimberly Siu, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT; Gosia Clore, Rich Scheer, Comprehensive Health Insights, Louisville, KY; Carol Duffy, Janet Schnee, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT; Chad Moretz, Stephen Stemkowski, Comprehensive Health Insights, Louisville, KY; George Andrews, Humana Inc., Louisville, KY

Abstract Body: Objective: Several oral anticoagulants (OACs) are approved to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF). This study examined the characteristics and outcomes of NVAF patients who were not treated with an OAC.

Methods: NVAF patients with medical and pharmacy benefits, aged 18-89 years at index date, defined as 30 days after the first AF diagnosis between 10/1/2010 and 7/31/2012, who had 12-months pre-index continuous enrollment, and no OAC claims prior to the index date, were included and followed until date of first OAC prescription, disenrollment, death, or end of observation period. No acetylsalicylic acid (ASA) use information was available, and patients were included regardless of antiplatelet prescription claims. Primary outcomes were stroke and major bleeding. Secondary outcomes included sub-classifications of stroke and major bleeding, myocardial infarction, venous thromboembolism, and all cause death.

Results: A total of 78,766 OAC-naïve patients met the study criteria. Across the study population, 29.6% had prescription antiplatelet therapy claims. Mean age was 74.4 years, 53.5% male, 82.6% white, and 93.9% were classified as Medicare patients. The most prevalent comorbid conditions included hypertension (87.2%), hyperlipidemia (75.1%), and coronary artery disease (52.5%). The mean CHADS₂ and CHA₂DS₂-VASc scores were 2.1 and 3.7, respectively, with 67% and 92% of members classified as high risk (≥ 2). The mean modified HAS-BLED score was 3.3, with 69.5% scoring ≥ 3 (high risk for major bleeding).

Conclusion: A large proportion of sample NVAF patients who did not receive OACS met criteria to be considered high risk for stroke or for major bleeding. Nearly one third received prescription antiplatelet therapy and the proportion of ASA use was unknown, but the high stroke rate suggests ineffective treatment. Further research is needed to clarify the observed rate of bleeding.

Table 1: Incidence of Primary and Secondary Outcomes in NVAF patients not treated with oral anticoagulants (N=78,766)

PRIMARY OUTCOME		Rate per 1,000 PY (95%CI)	Median days to first event [IQR]
Stroke	4,104 (5.2%)	34.8 (33.7, 35.9)	271 [110-495]
Major Bleeding	4,634 (5.9%)	39.3 (38.2, 40.4)	258 [96-488]
SECONDARY OUTCOME			
Ischemic Stroke	3,995 (5.1%)	33.9 (32.8, 34.9)	272 [110-495]
Hemorrhagic Stroke	258 (0.3%)	2.2 (1.9, 2.5)	268 [116-489]
Major Intracranial Bleeding	961 (1.2%)	8.2 (7.6, 8.7)	275 [116- 522]
Major Extracranial Bleeding	3,802 (4.8%)	32.3 (31.2, 33.3)	255 [94-479]
Major GI Bleeding	2,642 (3.4%)	22.4 (21.6, 23.3)	263 [101-488]
Major Upper GI Bleeding	750 (1.0%)	6.4 (5.9, 6.8)	269 [107-504]
Major lower GI Bleeding	2,497 (3.2%)	21.2 (20.4, 22.0)	262 [102-490]
Major Urogenital Bleeding	678 (0.9%)	5.8 (5.3, 6.2)	269 [88-495]
Major Other Bleeding	1,006 (1.3%)	8.5 (8.0, 9.1)	253 [97-475]
Transient Ischemic Attack	1,476 (1.9%)	12.5 (11.9, 13.2)	290 [119-511]
Myocardial Infarction	2,220 (2.8%)	18.8 (18.0, 19.6)	285 [118-503]
Venous Thromboembolism	2,551 (3.2%)	21.6 (20.8, 22.5)	243 [86-474]
Death	12,629 (16.0%)	107.1 (105.3, 109.0)	239 [75-481]

Author Disclosure Block: **S. Reynolds:** Employment; Significant; Comprehensive Health Insights, Louisville, KY. **K. Siu:** Employment; Significant; Boehringer Ingelheim Pharmaceuticals Inc. **G. Clore:** Employment; Significant; Comprehensive Health Insights. **R. Scheer:** Employment; Significant; Comprehensive Health Insights. **C. Duffy:** Employment; Significant; Boehringer Ingelheim Pharmaceuticals Inc. **J. Schnee:** Employment; Significant; Boehringer Ingelheim Pharmaceuticals Inc. **C. Moretz:** Employment; Significant; Comprehensive Health Insights. **S. Stemkowski:** Employment; Significant; Comprehensive Health Insights. **G. Andrews:** Employment; Significant; Humana, Inc..

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Presentation Number: LB P12

Publishing Title: Risk Associated With The Management Of Unruptured Cerebral Aneurysms In Japan: UCAS Treat Result

Author Block: AKIO MORITA, Nippon Medical Sch, Tokyo, Japan; Shinjiro Tominari, Kyoto Univ, Sch of Public Health, Kyoto, Japan; UCAS Japan Investigators

Abstract Body: Introduction: Management decision of the unruptured cerebral aneurysms (UCA) should be made by balancing rupture risk of the aneurysm, management risk and patient's physical and mental conditions. Rupture risks of UCA have been recently reported, but management risks need to be further clarified. We now report the treatment data of UCAS Japan.

Method: Out of the total cohort of 6,413 patients with UCAs, 2,588 underwent repair (2,274 by open craniotomy and 314 by endovascular treatment) in 212 institutions. Morbidity was defined as decline of modified Rankin scale or became 2 or below if the initial Rankin score was 0 at one month after treatment. Factors with p value less than 0.05 by multivariate cox regression model were considered important risk factors for management. In 107 institutions, case volume for cerebral aneurysms are less than 60 cases in 2year.

Results: Overall morbidity was recorded in 81 cases (3.0%). Important risk factors were as follows; Size (Hazard ratio (HR): 3~4mm; ref., 5~6mm: 0.71, 7~9mm: 1.89, 10~24mm: 2.77, >=25mm: 9.46), Location (MCA: ref., ICA, IC-PCom: 1.00, ACom: 1.43, VA: 1.63, BA: 3.93), Age>=70 (HR: 1.90), Hypertension (HR: 2.27), and Diabetes Mellitus (HR: 2.70). Neither hospital volume nor method of treatment affected treatment morbidity. We created risk prediction model for morbidity from this multivariate analysis.

Conclusions: UCAs can be managed relatively safely unless the aneurysm is larger than 10mm, located at basilar top, age >=70, or history of hypertension or diabetes mellitus. Prediction model of treatment risk should support decision making on UCA management.

Author Disclosure Block: A. Morita: None. S. Tominari: None.

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Presentation Number: LB P13

Publishing Title: Bedtime Home Blood Pressure Strongly Predicts The Development Of Post-stroke Cognitive Decline

Author Block: Yasumasa Yamamoto, Yasuhiro Tomii, Kyoto Katsura Hosp, Kyoto, Japan; Yoshinari Nagakane, Kyoto Second Red Cross Hosp, Kyoto, Japan

Abstract Body: Background and purpose: Home blood pressure monitoring (HBP) has been identified to better predict cardiovascular risk than clinic blood pressure (BP) measurement. We explored how HBP predicted post-stroke cognitive decline as well as stroke recurrence. Methods: We studied 250 patients with non-cardio-embolic ischemic stroke who were treated as first-ever stroke in our hospital and then tracked in the outpatient clinic using HBP. Stroke type consisted of single lacunar infarction (sLI), multiple lacunar infarction (mLI) and atherothrombotic infarction (ATB). Kidney function is categorized based on estimated glomerular filtration rate (eGFR) as follows: GF1; eGFR >60 (mL/min/1.73m²), GF2; 30-60, GF3; <30. The patients were divided into 4 groups in terms of their outcome as follows: G1, those who showed favorable outcome; G2, those who developed silent ischemic lesions; G3, those who showed cognitive decline; and G4, those who showed stroke recurrence. All patients recorded HBP measured in the early morning (mHBP) and just before going to bed (bHBP). HBPs were averaged for 7 successive days. HBP values were dichotomized based on the level of systolic BP /diastolic BP: 135/ 85 mm Hg. Compared with G1, risk for each group was calculated using Cox proportional hazard model. Results: After a median follow-up of 4.1±1.3 years, outcomes turned out as follows, G1: 188 patients (75.2%), G2: 16 (6.4%), G3: 33 (13.2%); and G 4: 15 (6%). Higher systolic mHBP (hsmHBP) was independently associated with G2 (OR: 7.5, p=0.0003). After multivariate analysis including hsmHBP, hsmHBP (OR: 3.1, p=0.0015), stroke type (mLI versus sLI) (OR: 6.5, p<0.0001) and kidney dysfunction (GF3 versus GF1) (OR: 4.3, p=0.018) persisted significantly for G3. When hsbHBP was included, hsbHBP (OR: 4.2, p=0.0001), stroke type (OR: 5.7, p<0.0001) and kidney dysfunction (OR: 3.7, p=0.032) persisted significantly for G3. When hsmHBP was included, hsmHBP (OR: 4.5, p=0.0045) and stroke type (OR: 8.2, p=0.0006) persisted significantly for G4. When hsbHBP was included, hsbHBP (OR: 5.5, p=0.0014) and stroke type (OR: 8.6, p=0.0005) persisted significantly for G4. Conclusions: Higher HBP, especially bedtime HBP, strongly predicts subsequent development of post-stroke cognitive decline.

Author Disclosure Block: Y. Yamamoto: None. Y. Tomii: None. Y. Nagakane: None.

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Presentation Number: LB P14

Publishing Title: Predictors of Mortality in Acute Ischemic Stroke Intervention: Analysis of the NASA registry

Author Block: Italo Linfante, Baptist Hosp, Miami, FL; Gail R. Walker, Baptist Health South Florida, Coral Gables, FL; Guilherme Dabus, Baptist Hosp, Miami, FL; Albert J. Yoo, Massachusetts General Hosp, Boston, MA; Gavin W. Britz, Methodist Neurological Inst, Houston, TX; Alex Abou-Chebl, Baptist Health Louisville, Louisville, KY; Franklin A. Marden, Alexian Brothers Medical Ctr, Elk Grove Village, IL; Amy K. Starosciak, Baptist Health South Florida, Coral Gables, FL; Alicia C. Castonguay, Medical Coll of Wisconsin/Froedtert Hosp, Milwaukee, WI; Alexandria Alvarez, Baptist Hosp, Miami, FL; Osama O. Zaidat, Medical Coll of Wisconsin/Froedtert Hosp, Milwaukee, WI; NASA Investigators

Abstract Body: INTRODUCTION: Acute stroke secondary to large vessel occlusion (LVO) is associated with mortality up to 50%. Recanalization predicts good outcome and reduced mortality. We evaluated effects of recanalization and symptomatic ICH (sICH) on 90-day mortality (mRS=6) and factors associated with mortality despite successful recanalization (TICI \geq 2b) using the North American Solitaire Stent Retriever Acute Stroke (NASA) registry.

METHODS: The NASA Registry recruited 354 stroke patients in 24 centers treated \leq 8 hours of symptom onset with Solitaire FRTM from March 2012 to February 2013. Fisher's exact test compared 90-day mortality and recanalization rates. For successfully recanalized patients, logistic regression evaluated factors for association with 90-day mRS=6. A multivariable model was developed based on backwards selection from factors with at least marginal significance ($p\leq 0.10$) on univariate analysis and retention criterion of $p\leq 0.05$. The model was refit to minimize the number of cases excluded due to missing covariate values; the c-statistic measured predictive power.

RESULTS: Out of 354 patients, 256 (72.3%) were recanalized successfully, of which 234 had 90-day mRS recorded; this was the group analyzed. There were 97 (30.8%) deaths among 315 patients with 90-day follow-up. Mortality was significantly lower with successful recanalization: 25.2% (59/234) vs. 46.9% (38/81), $p<0.001$, but there was no statistical difference in sICH occurrence. Mortality was higher in patients who developed sICH, 72% (23/32) vs. 26% (73/281), $p<0.001$. Univariate tests identified increased risk of mortality among recanalized patients for: site other than M1/M2, initial NIHSS \geq 18 (median), use of rescue therapy ($p<0.05$), TICI 2b ($p=0.070$), 3+ passes ($p=0.085$). In multivariable analysis of 228 cases, site other than M1/M2 (OR: 2.1), initial NIHSS \geq 18 (OR: 3.6), and use of rescue therapy (OR: 2.6) were significant independent predictors of mortality. The model had good predictive power with a c-index of 0.72 (95% CI: 0.64-0.79).

CONCLUSIONS: Failed recanalization is associated with higher 90-day mortality, whereas proximal LVO, high NIHSS, and use of rescue therapy are independent predictors of mortality among successfully recanalized cases.

Author Disclosure Block: I. Linfante: Consultant/Advisory Board; Modest; Covidien. G.R. Walker: None. G. Dabus: Consultant/Advisory Board; Modest; Covidien. A.J. Yoo: None. G.W. Britz: None. A. Abou-Chebl: None. F.A. Marden: None. A.K. Starosciak: None. A.C. Castonguay: None. A. Alvarez: None. O.O. Zaidat: Consultant/Advisory Board; Modest; Covidien, Stryker.

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Presentation Number: LB P15

Publishing Title: Cost-effectiveness of Endovascular Therapy vs. IV t-PA Alone at 12 Months: The IMS III Trial Economic Follow-up Results

Author Block: Kit N Simpson, **Annie N Simpson**, Patrick Mauldin, Yuko Palesh, Medical Univ of South Carolina, Charleston, SC; Michael D Hill, Univ of Calgary, Calgary, AB, Canada; Pooja Khatri, Dawn Kleindorfer, Univ of Cincinnati, Cincinnati, OH; Edward Jauch, Sharon Yeatts, Medical Univ of South Carolina, Charleston, SC; Andrew Demchuck, Mayank Goyal, Univ of Calgary, Calgary, AB, Canada; Bernard Yan, Univ of Melbourne, Melbourne, Australia; Rudiger von Kummer, Univ Clinic, Dresden, Germany; Tudor Jovin, Univ of Pittsburg, Pittsburg, PA; Mikael Mazighi, Bichat Univ Hosp, Paris, France; W J Schonewille, St. Antonius Ziekenhuis, Amsterdam, Netherlands; Carlos A Molina, Vall d'Hebron Hosp Barcelona, Barcelona, Spain; Thomas Tomsick, Univ of Cincinnati, Cincinnati, OH; Joseph Broderick, University of Cincinnati, Cincinnati, OH

Abstract Body: The Interventional Management of Stroke (IMS) III Trial, was a Phase III randomized, parallel-arm, open-label clinical trial with concurrent economic data collection. We recently reported that, among severe strokes, a greater proportion of the endovascular group (IVIA) had a mRS ≤ 2 (32.5%) at 12 months compared to the IV t-PA group (IV-Only) 18.6%, with a significant interaction between treatment group and stroke severity in the repeated measures analysis of mRS ≤ 2 outcome ($p=0.039$). No difference was present for moderately-severe strokes (55.6% vs. 57.7%) in this secondary outcome measure.

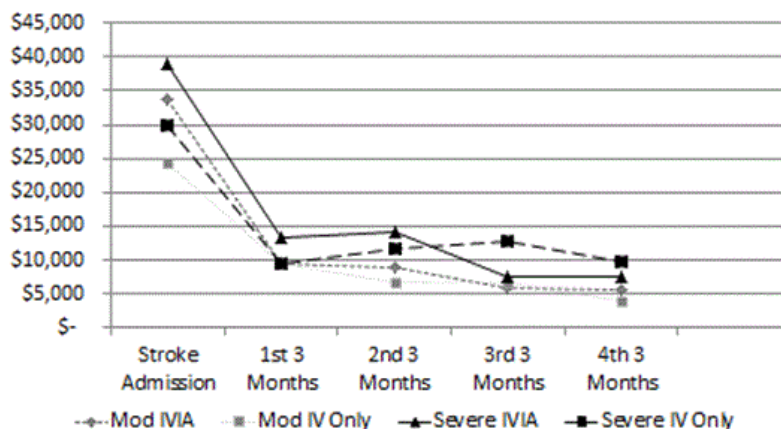
Objective: Compare the cost-effectiveness of IVIA vs. IV-Only at 12 months overall and by stroke severity.

Main Outcome(s): An EQ-5D utility measure was obtained at 5 days and 3, 6, 9, and 12 months for all subjects. Hospital charges for the stroke admission were collected. Resource use after the acute hospitalization was collected from patient or proxy report at 3, 6, 9, and 12 month visits.

Results: In participants with severe stroke, the endovascular group had 35.2 (95% CI: 2.1, 73.3) more quality-adjusted-days (QAD) over 12 months as compared to IV-Only. No difference in QAD 1.5 (-25.5, 19.8) was found for subjects with moderately severe stroke. The incremental cost effectiveness ratio (ICER) for IVIA vs. IV-Only was \$275,608 per quality adjusted life year (QALY). However, the ICER indicating cost effectiveness of endovascular therapy differed greatly by baseline stroke severity; the ICER for moderately severe stroke was \$3,187,805/QALY whereas the ICER for severe stroke was \$97,303/QALY.

Total Cost of Care by Treatment

Severe Stroke and Moderately Severe Stroke Subgroups



Conclusions: Endovascular therapy in severe stroke patients treated with IVIA had an ICER of \$97,303/QALY,

well below the current World Health Organization cost-effectiveness threshold of \$162,000/QALY for the US and therefore may be cost effective in US patients.

Author Disclosure Block: **K.N. Simpson:** Research Grant; Modest; IMS III investigator. **A.N. Simpson:** Research Grant; Modest; IMS III investigator. **P. Mauldin:** Other Research Support; Modest; IMS III investigator. **Y. Palesh:** Research Grant; Modest; IMS III investigator. Other Research Support; Modest; DSMB member Biogen and Braingate trials. **M.D. Hill:** Research Grant; Modest; IMS investigator. Other Research Support; Modest; consulting from Vernalis, rants from Hoffman-La Roche, and Bristol_myers Squibb. Ownership Interest; Modest; Calgary Scientific. Consultant/Advisory Board; Modest; Heart and Stroke Foundation Alberta. Other; Modest; Nunavut and Alberta Innovates-Health Solutions. **P. Khatri:** Research Grant; Modest; Therapy trial, PRISMS trial. Other Research Support; Modest; Penumbra Inc.,. **D. Kleindorfer:** Research Grant; Modest; IMS trial investigator. **E. Jauch:** Research Grant; Modest; Penumbra for THERAPY trial, Stryker for POSITIVE study, Genentech for PRISMS trial. **S. Yeatts:** Research Grant; Modest; Genentech for PRISMS trial. **A. Demchuck:** Research Grant; Modest; Covidien for ESCAPE trial. **M. Goyal:** Honoraria; Modest; Covidian. **B. Yan:** Other Research Support; Modest; Codman. Honoraria; Modest; Stryker, Bio CSL. Other; Modest; Bayer. **R. von Kummer:** Consultant/Advisory Board; Modest; Lundbeck, Penumbra, Covidien, Synarc. **T. Jovin:** Ownership Interest; Modest; Silk Road Medical. **M. Mazighi:** Research Grant; Modest; IMS investigator. **W. Schonewille:** Research Grant; Modest; IMS trial. **C.A. Molina:** Research Grant; Modest; IMS trial. **T. Tomsick:** Research Grant; Modest; IMS investigator. **J. Broderick:** Research Grant; Modest; genentech for PRISM trial. Other Research Support; Modest; study medication from Genentech for IMS trial. Other; Modest; travel support Boehringer Ingelheim.

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Presentation Number: LB P16

Publishing Title: Clinical Trial of Robotic Arm Training in Chronic Stroke: Addition of Transition-to-Task Practice

Author Block: Susan S Conroy, VAMHCS, Baltimore, MD; Min Zhan, VAMHCS, Dept. of Epidemiology & Public Health, Univ. Maryland, Baltimore, MD; Patricia McCarthy, VAMHCS, Baltimore, MD; Hermano I Krebs, Dept. of Mechanical Engineering, MIT, Dept. of Neurology, of Univ. Maryland, Boston / Baltimore, MA; George F Wittenberg, VAMHCS, Dept. of Neurology, PTRS, Univ. of Maryland, Baltimore, MD; Jill Whittall, Dept. of Physical Therapy & Rehab. Sci., Univ. Maryland, Baltimore, MD; Christopher T Bever Jr., VAMHCS, Dept. of Neurology, Univ. of Maryland, Baltimore, MD

Abstract Body: Objective: Investigate the optimal method to employ robotic rehabilitation for functional recovery of the upper extremity (UE) after chronic stroke.

Background: Rehabilitation robots provide high intensity, interactive assist as needed repetitive task practice and have been shown to significantly reduce impairment deficits in the UE segments exercised. This recovery occurs primarily for impairment and generalization to real world functional activities has been questioned.

Methods: Single blind randomized controlled trial consisting of a total of 12 weeks of robot-assisted training on two distinct robots. Training phases included: 4 weeks of wrist robot training, 4 weeks of planar robot training and 4 weeks of alternating sessions between each robot. Subjects with a clinically defined stroke greater than 6 month duration (n=39) were stratified by impairment level and randomized to two groups: 1) Robot therapy (RT) for 60 minutes of robotic training and 2) Transition to Task Training (TTT) for 45 minutes of robotic training followed by 15 minutes of TTT. Primary outcome measures of impairment, function, and participation were the Fugl-Meyer (FM), Wolf Motor Function Test (WMFT), and the Stroke Impact Scale (SIS), respectively.

Results: Interim analysis showed that both groups had modest gains from baseline to final intervention and a significant within group change on the FM. The mean FM change at week 12 for the TTT group (n=20) was 3.9 (± 3.8) and for the RT group (n=19) 3.4 (± 3.2). The week 12 TTT group mean change on the timed tasks of the WMFT was large (-10 sec ± 12) compared to the RT group (-6 sec ± 6) but without significance. Significant within group WMFT changes were seen for both TTT and RT. The TTT group change on the Stroke Impact Scale hand domain was 14 (± 16) with a significant within group change that was not seen in the RT group.

Conclusions: Chronic UE stroke motor deficits are responsive to intensive robot-assistive therapy. The TTT intervention did not show a significant differential effect; however, the TTT group had larger changes at week 12 with a noted expansion of effect on hand use that was unique to this group. Final visits will be in January 2015 and analysis of long-term effects on impairment, function, and participation will be performed at that time.

Author Disclosure Block: S.S. Conroy: None. M. Zhan: None. P. McCarthy: None. H.I. Krebs: Ownership Interest; Significant; Interactive Motion Technologies. G.F. Wittenberg: Research Grant; Significant; NCMRR/NICHHD/NIH. Expert Witness; Modest; Altman, Spence. J. Whittall: None. C.T. Bever: None.

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Presentation Number: LB P17

Publishing Title: Cilostazol Prevents Progression of Atherosclerosis in Ischemic Stroke Patients with Peripheral Arterial Disease: A Randomized, Double-Blind, Placebo-Controlled Trial

Author Block: Jiunn-Tay Lee, Dept of Neurology, Tri-Service General Hosp, Natl Defense Medical Ctr, Taipei, Taiwan

Abstract Body: Background Patients with polyvascular atherosclerotic diseases carry high risks of vascular events and death. Dual antiplatelets by inhibiting atherosclerotic progression could benefit these patients. We aimed to investigate the effect of combination therapy of cilostazol and aspirin on subclinical atherosclerosis progression in patients with ischemic stroke or transient ischemic attack (TIA) who had peripheral arterial disease.

Methods We conducted an investigator-initiated, randomized, double-blind, placebo-controlled trial at 16 centers in Taiwan. Participants with previous ischemic stroke or TIA who had been taking aspirin (100 mg per day), aged 50 years or older with ankle-brachial index (ABI) <1.0 were randomly assigned to receive cilostazol 200 mg per day (n=403) or placebo (n=397) for 1 year. Primary end point was the changes of ABI, and secondary end point was the changes of common carotid artery intima-media thickness. This trial is registered with ClinicalTrials.gov (NCT01188824).

Findings The ankle blood pressure was significantly increased in the cilostazol group than the placebo group (P<0.001), however, with no significant difference in ABI change between the two groups. The regression in mean left, mean right, and maximum left common carotid artery intima-media thickness was significantly greater in the cilostazol group than the placebo group. There was no significant difference in vascular events, death, or major hemorrhagic events between groups.

Interpretation Compared to aspirin alone, combination therapy of aspirin plus cilostazol were more effective in slowing down atherosclerotic progression without increased incidence of hemorrhagic events in this patient population.

Author Disclosure Block: J. Lee: None.

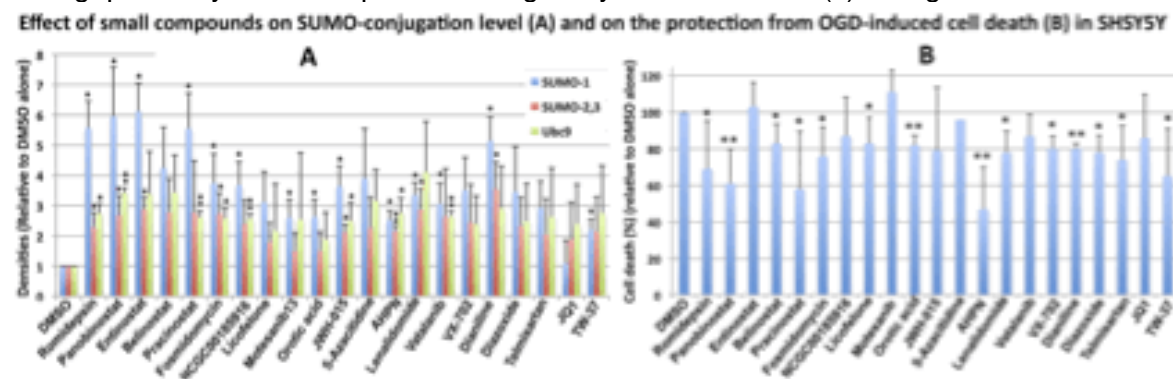
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Presentation Number: LB P18

Publishing Title: A Novel Quantitative High-throughput Screen Identifies Drugs that both Activate SUMO-conjugation via the Inhibition of MicroRNAs 182 and 183 and Facilitate Neuroprotection in a Model of Oxygen and Glucose Deprivation

Author Block: **Joshua D. Bernstock**, NINDS/NIH and Univ of Cambridge, Bethesda, MD; Yang-ja Lee, NINDS/NIH, Bethesda, MD; Noel Southall, NIH/NCATS, Bethesda, MD; Kory Johnson, NINDS/NIH, Bethesda, MD; Jennifer Kouznetsova, NCATS/NIH, Bethesda, MD; Luca Peruzzotti-Jametti, Univ of Cambridge, Cambridge, United Kingdom; Wei Zheng, NCATS/NIH, Bethesda, MD; John M. Hallenbeck, NINDS/NIH, Bethesda, MD

Abstract Body: Background: Hibernation torpor provides an excellent natural model of tolerance to ischemia. We have previously shown that a massive increase in global SUMOylation occurs during hibernation torpor in ground squirrels and that overexpression of Ubc9 and/or SUMO-1 in cell lines, cortical neurons and transgenic mouse brains provides protection against ischemic damage. Recently we demonstrated SUMOylation in the brains of squirrels is controlled in part by microRNAs (miRNA). Herein, we describe the development of a novel quantitative high-throughput screening system (qHTS) designed to identify small molecules capable of increasing SUMOylation via the regulation/inhibition of members of the miRNA-182 family. Methods: Our small molecule screen employs a SHSY5Y human neuroblastoma cell line stably transfected with both a firefly and renilla luciferase reporter system, specific for inhibitors of either miR-182 or miR-183. Results: The assay successfully identifies molecular entities capable of inducing global conjugation of SUMO in both SHSY5Y cells and rat E18 derived primary cortical neurons. Further, protective effects of a number of the identified compounds have been confirmed via an in vitro ischemic model (oxygen/glucose deprivation). Conclusion: Understanding both the burden of disease caused by ischemic stroke and our concurrent lack of therapeutic options we sought to engineer and optimize a novel mechanism to identify molecules capable of inducing global SUMOylation via the inhibition of miRNA. Of note, this assay can be easily repurposed to allow high throughput analyses of the potential drugability of other miRNA(s) with great confidence.



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Presentation Number: LB P19

Publishing Title: Prevalence and Causes of Intracerebral Hemorrhage During Sleep

Author Block: Arne Lauer, Matt T. Bianchi, Hakan Ay, Alison Ayres, Kristin M. Schwab, Anand Viswanathan, Jonathan Rosand, Steven M. Greenberg, M. Edip Gurol, Massachusetts General Hosp, Boston, MA

Abstract Body: Background/Aim: Wake-up ischemic stroke is common (14.3% in a recent large study) and sleep related pathologies are independent risk factors for cerebral infarction. We sought to identify the proportion of intracerebral hemorrhage (ICH) during sleep and compare potential etiologic factors between patients with ICH during sleep and awake.

Methods: Prospectively collected data from patients enrolled after ICH related to small vessel disease (SVD) was analyzed. Activity at symptom onset was recorded (sleep vs awake). The etiology was coded as cerebral amyloid angiopathy (CAA) based on Boston criteria and hypertensive deep ICH (HTN-ICH). The proportion of ICH during sleep and its associations (SVD-type, risk factors, medication use and ICH volume) were analyzed. Results: We identified 1,057 patients (540 related to CAA, 517 HTN-ICH) enrolled between 2005 and 2013. In 282 (27%) patients, ICH during sleep was recorded. This group was older than patients who bled while awake (age: 74.2 vs. 71.7; $p < 0.001$). Frequencies of female sex, vascular risk factors, and antiplatelet use were similar between groups (all $p > 0.2$). Baseline hematoma volumes were not significantly different (39ml for ICH during sleep vs 35ml awake, $p = 0.15$). Patients who suffered ICH during sleep were more likely to use statins (42.4% vs 34%, $p = 0.013$) and selective serotonin re-uptake inhibitors (SSRI; 21.2% vs 11.5%, $p < 0.001$). Cerebral amyloid angiopathy associated ICH occurred more frequently during sleep than HTN-ICH (30% vs. 23%, $p = 0.015$). In a multivariable model including the variables presented above, CAA diagnosis and SSRI use remained as independent predictors of ICH during sleep.

Conclusions: Intracerebral hemorrhage related to SVD is common during sleep, found in 27% of our large cohort. Presence of CAA and SSRI use can interact with sleep pathologies and/or sleep related hemodynamic changes to cause ICH. Prospective studies that use physiologic monitoring during sleep in patients with CAA may clarify such interactions and identify new targets for ICH prevention.

Author Disclosure Block: A. Lauer: None. M.T. Bianchi: None. H. Ay: None. A. Ayres: None. K.M. Schwab: None. A. Viswanathan: None. J. Rosand: None. S.M. Greenberg: None. M. Gurol: None.

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Presentation Number: LB P21

Publishing Title: Impact of Carotid Interventions on Cognition

Author Block: Wei Zhou, Stanford Univ, Stanford, CA; Elizabeth Hitchner, VA Palo Alto Health Care System, Palo Alto, CA; Salil Soman, Stanford Univ, Stanford, CA; Jyoti Bhat, VA Palo Alto Health Care System, Stanford, CA; Allyson Rosen, Stanford Univ, Stanford, CA

Abstract Body: Introduction: Although carotid revascularization procedures have shown to be effective in stroke prevention with minimal neurologic complication, their effects on cognition remain uncertain. This prospective study aims to evaluate the long-term effects of carotid interventions on cognitive function, particularly memory, in patients with severe extracranial carotid occlusive diseases.
Method: A total of 106 patients with severe carotid stenosis who underwent carotid interventions were prospectively evaluated. Carotid stenting (CAS) were offered to patients who were considered high risk for carotid endarterectomy (CEA). Neurocognitive evaluations were performed prior to, and 1 month, 6 months, and one year post-interventions. Memory function was measured using Rey Auditory Verbal Learning Test (RAVLT). Patients also received 3.0 MRI evaluations prior to, within 48 hours, and 6 months post-interventions.
Result: Despite initial decline in delayed memory post-procedure, patients who underwent carotid revascularization procedures experienced improvement in long-term memory. When CEA (n=48) was compared to CAS (n=58), no difference was identified in patient demographics, baseline cognition, or education level between the two cohorts. However, CEA patients experience greater improvement in memory function ($P<0.03$). Within the CAS cohort, those who experienced initial procedure-related memory decline recovered partially long-term, while those who did not suffer procedure-related memory deterioration experienced continuous memory improvement long-term. Segmented brain volume was consistent with cognitive changes.
Conclusion: Our study showed that carotid revascularization procedures improve cognition in patients with severe carotid stenosis and that CEA provides greater benefits in memory function.

Author Disclosure Block: W. Zhou: None. E. Hitchner: None. S. Soman: None. J. Bhat: None. A. Rosen: None.

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Presentation Number: LB P22

Publishing Title: Matrix Metalloproteinase-12 Gene Silencing After Ischemic Stroke Attenuates Blood-Brain Barrier Damage

Author Block: Bharath Chelluboina, Jeffrey D. Klopfenstein, David M. Pinson, David Z. Wang, **Krishna Kumar Veeravalli**, Univ of Illinois Coll of Med at Peoria, Peoria, IL

Abstract Body: Background:

Matrix metalloproteinases (MMPs) are reported to have a central role in compromising the integrity of blood-brain barrier (BBB). Our recent investigations revealed a predominant upregulation of MMP-12 after ischemic stroke and demonstrated the deleterious role played by MMP-12 in ischemic brain damage. The purpose of this study in a rat model of ischemic stroke is to investigate the effect of MMP-12 knockdown by shRNA-mediated gene silencing on the BBB disruption and evaluate the associated underlying molecular mechanisms.

Methods:

Male Sprague-Dawley rats were subjected to transient ischemia by occlusion of the middle cerebral artery. At the end of ischemia, MMP-12shRNA plasmids formulated as nanoparticles were administered either by internal carotid artery or tail vein at a dose of 1 mg/kg body weight. Rats from all groups were sacrificed 24 hours post-ischemia. BBB integrity was assessed by performing various techniques including Evan's blue staining, immunoblot, and immunofluorescence analysis.

Results:

Evan's blue staining demonstrated a significant increase in BBB permeability in untreated ischemia-reperfusion subjected rats. In addition, significant reduction in the protein expression of tight junction proteins such as claudin5, occludin, and zonula occludens (ZO)-1, which is indicative of BBB disruption was noticed. MMP-12 knockdown prior to reperfusion reduced BBB permeability and protected the integrity of BBB by inhibiting the degradation of tight junction proteins. Transcriptional silencing of MMP-12 reduced the endogenous levels of other proteases such as tissue plasminogen activator (tPA) and MMP-9, which are known to be the key players involved in BBB damage.

Conclusions:

MMP-12 knockdown protected the ischemic brain by preserving the BBB integrity and permeability. These results demonstrated the adverse role of MMP-12 in acute damage that occurs after ischemic stroke. The protection offered by MMP-12 knockdown could be a direct effect or mediated through the regulation of other proteases such as tPA and MMP-9.

Author Disclosure Block: **B. Chelluboina:** None. **J.D. Klopfenstein:** None. **D.M. Pinson:** None. **D.Z. Wang:** None. **K.K. Veeravalli:** None.

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Presentation Number: LB P23

Publishing Title: Anti-VEGF Treatment Attenuates Pathological Cerebrovascular Angiogenesis in Diabetes

Author Block: Mohammed Abdelsaid, Georgia Regents Univ, Augusta, GA; Susan Fagan, Univ of Georgia, Augusta, GA; Adviye Ergul, Georgia Regents Univ, Augusta, GA

Abstract Body: Diabetes increases the risk and worsens outcomes of stroke. Our group showed that diabetes increases pathological cerebral neovascularization via augmented VEGF signal. Yet, the effect of anti-VEGF treatment on diabetes-induced cerebral neovascularization is unknown. We hypothesized that SKLB1002, a selective VEGFR-2 antagonist, will prevent/repair pathological cerebral neovascularization in diabetic Goto-Kakizaki (GK) rats via restoration of Robo-4 signaling, a roundabout protein that stabilize vasculature via VEGF inhibition. Methods: Diabetic GK rats were treated with SKLB1002 for 2 weeks starting at the onset of diabetes (10 w) or after established disease (14 w) for prevention and repair arm of the study, respectively. Cerebral neovascularization indices (Vascular volume, surface Area, tortuosity index and vascular Density) were measured using 3D imaging. Robo-4 was measured by immunoblotting. Results: A dose finding study showed that a low dose of 10 mg/kg/day of SKLB1002 significantly inhibited VEGFR2 activation in the brain and this dose was used for the study. SKLB1002 did not alter weights or blood glucose levels of GK rats. SKLB1002 treatment reduced all indices of neovascularization in both 12 and 16 weeks rats compared to vehicle treated GK rats (Table). SKLB1002 increased Robo-4 expression and availability by reduction of Robo-4/ β -3 integrin interaction ($p < 0.05$). Conclusion: Our studies provide evidence that modulation of VEGF signaling prevents/restores diabetes-induced dysfunctional cerebral neovascularization. Our results also suggest that VEGFR-2 and Robo-4 are promising therapeutic targets in treatment of pathological brain neovascularization in diabetes.

		(n=6, *P<0.05 vs vehicle)	% Vascular Volume	% Surface Area	Tortuosity	Vascular Density
12-Week	Cortex	Vehicle	13.7±0.5	13.09±0.6	1.3±0.07	53.8±2.7
		SKLB1002	5.7±0.7*	4.2±0.08*	1.07±0.01*	23±1.14*
	Striatum	Vehicle	5.2±0.03	3±0.6	1.2±0.2	26.9±2.1
		SKLB1002	1.1±0.02*	1.2±.1*	1.1±0.2	18±1.2*
16-Week	Cortex	Vehicle	16.9±2.1	17.8±2.3	1.6±0.09	61.9±4.2
		SKLB1002	6±0.3*	5.5±0.4*	1.1±0.03*	38±2.1*
	Striatum	Vehicle	6.5±0.5	4.5±0.05	1.3±0.1	29.8±0.5
		SKLB1002	2.2±0.51*	1.7±0.14*	1.13±0.08*	20±1.12*

Author Disclosure Block: M. Abdelsaid: None. S. Fagan: None. A. Ergul: None.

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Presentation Number: LB P24

Publishing Title: The Incidence of Intracranial Haemorrhages affecting patients on Antiplatelet and Anticoagulant Agents Referred to a National Neurosurgical Centre

Author Block: Sarah Cuddy, Beaumont Hosp, dublin, Ireland; Elizabeth Ennis, Sajjad Matiullah, Richard Collis, Richard Sheahan, Beaumont Hosp, Dublin, Ireland

Abstract Body: Intracranial Haemorrhage (ICH) is a feared complication of both antiplatelet and anticoagulant medications. A recent report highlighted that newly marketed products, by virtue of their novelty alone, may elicit adverse-event reports at high rates; reporting rates tend to decrease over time. Hence drugs that have been available for over 50 years, such as Warfarin and Aspirin (ASA), would be far less likely to elicit adverse-event reports than would a newer drug with a similar risk. The hypothesis of this study was to examine the frequency of ICH in a consecutive series of patients referred to a National Neurosurgical Centre and the associated use of antiplatelet and anticoagulant agents.

The National Neurosurgical Centre in Beaumont has an estimated referral population of 4 million. All consecutive referrals from July 2013 to January 2014 were reviewed. Data collected included baseline demographics, antiplatelet/anticoagulation usage and indication for same, and CT brain findings of the ICH. There were 978 consecutive patients with an ICH referred in this period. Of these 329(33.6%), with a mean age of 77yrs, female 42.6%, were on an antiplatelet and/or an anticoagulant agent; ASA (n=198, 60.2%), Warfarin (117, 35.6%), Clopidogrel (35, 10.6%), Rivaroxaban (7, 2.1%), Dabigatran (4, 1.2%), ASA/dipyridamole (3, 0.9%). Thirty one (9.4%) patients were on two agents, 19 on ASA & Clopidogrel, 7 on ASA & Warfarin, 2 on Clopidogrel and Warfarin, 2 on Rivaroxaban and ASA, and 1 patient on ASA and Prasugrel. Three patients were on 3 agents, 2 on ASA, Clopidogrel and Warfarin, one on ASA, Clopidogrel and Rivaroxaban. We excluded 22 patients who had an ICH following thrombolysis or recent heparin therapy. The nature of ICH included Intraparenchymal Haemorrhage (n=123), Intraventricular Haemorrhage (28), Contusion (20), Epidural Haematoma (6), Subdural Haematoma (138) and Subarachnoid Haemorrhage (47). This study highlights ASA as the most frequently documented antiplatelet/anticoagulant agent in a real life consecutive series of patients referred to a Neurosurgical Unit with ICH. In discussing the role of anticoagulation with patients, particularly the elderly, the significant risk of bleeding with ASA needs to be highlighted.

Author Disclosure Block: S. Cuddy: None. E. Ennis: None. S. Matiullah: None. R. Collis: None. R. Sheahan: None.

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Presentation Number: LB P25

Publishing Title: Evaluation of Efficacy and Safety of Dalfampridine Extended Release in Patients With Walking Deficits After Ischemic Stroke: A Phase 3 Study Design

Author Block: Seth Finklestein, Stemetix, Inc., Needham, MA; Jenny Qian, Andrew Blight, **Peter Aupperle**, Adrian L Rabinowicz, Enrique Carrazana, Acorda Therapeutics, Inc., Ardsley, NY

Abstract Body: Objective: To evaluate the efficacy, safety, and tolerability of dalfampridine extended release tablets (D-ER) 7.5 mg and 10 mg twice daily administered to patients with stable walking deficits at least 6 months following ischemic stroke.

Background: There is an unmet need for an approved pharmacotherapy to improve chronic sensorimotor deficits such as walking impairments that follow ischemic stroke. An exploratory proof-of-concept study in patients with chronic post-ischemic stroke deficits showed a significant treatment effect for D-ER 10 mg versus placebo in improving walking speed. These data support the continued clinical development of D-ER in patients with chronic poststroke deficits.

Design: This is a multicenter, randomized, double-blind, 3-arm (D-ER 7.5 mg, D-ER 10 mg, and placebo) parallel-group study. The study scheme is: 2-week screening; 2-week placebo run-in, 12-week double-blind treatment period and 4-week follow-up. Patients (≥ 18 years old) with evidence of stable walking deficit due to ischemic stroke ≥ 6 months prior to enrollment, Modified Rankin Score 1–3, and able to complete the 2-Minute Walk Test (2MinWT) and 10-Meter Walk Test (10MWT) are eligible. Those with moderate or severe renal impairment, history of nonfebrile seizures, or prior dalfampridine use will be excluded. Primary efficacy is the proportion of subjects with at least a 20% improvement on the 2MinWT at Week 12; a planned enrollment of 180 patients per group will have 90% power to detect treatment effect in each dose of D-ER versus placebo on primary efficacy. The key secondary efficacy variable is the change from baseline on the Walk-12 scale at Week 12. Other secondary efficacy variables include changes from baseline in 10MWT; projected community ambulation based on changes in 10MWT; Timed Up and Go test; Stroke Impact Scale; and 12-item health survey. Safety and tolerability of D-ER will also be assessed.

Conclusions: This phase 3 study will determine the potential therapeutic effect of D-ER in improving walking deficits in patients with a history of chronic stroke deficits.

Supported by Acorda Therapeutics, Inc.

Disclaimer: D-ER has not been approved in the treatment of stroke deficits

Author Disclosure Block: **S. Finklestein:** Consultant/Advisory Board; Modest; Acorda Therapeutics, Inc. **J. Qian:** Employment; Significant; Acorda Therapeutics, Inc. **A. Blight:** Employment; Significant; Acorda Therapeutics, Inc. **P. Aupperle:** Employment; Significant; Acorda Therapeutics, Inc. **A.L. Rabinowicz:** Employment; Significant; Acorda Therapeutics, Inc. **E. Carrazana:** Employment; Significant; Acorda Therapeutics, Inc..

LATE-BREAKING SCIENCE abstracts/studies presented at the INTERNATIONAL STROKE CONFERENCE 2015:

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Presentation Number: LB P26

Publishing Title: Trevo Registry-Preliminary Data

Author Block: Mandy J Binning, Erol Veznedaroglu, capital institute for neurosciences, pennington, NJ

Abstract Body: Objective

The Trevo Registry is designed to assess real world performance of the Trevo stent retriever which is intended to restore blood flow in the neurovasculature by removing thrombus in subjects experiencing ischemic stroke. The primary endpoint is revascularization status based on TIC1 score at the end of the procedure and secondary endpoints include 90-day mRS, 90-day mortality, neurological deterioration at 24 hours and device/procedure related adverse events.

Methods

The study design is a prospective, open-label, consecutive enrollment, multi-center, international registry of all patients who undergo mechanical thrombectomy for acute stroke using the Trevo stent retriever as the initial device. Enrollment is expected to reach 300 subjects and up to 40 sites.

Results

Interim results show enrollment of 94 patients, 48 men and 46 women, with a mean age of 66 years. The most common medical comorbidities are hypertension (75%), dyslipidemia (47%) and atrial fibrillation (47%). The mean baseline NIHSS is 16.5 and 56% of patients received IV thrombolytics. TIC1 2b or 3 revascularization was achieved in 91% of patients and 25% of procedures required secondary devices in addition to the Trevo device to achieve this result. The mean NIHSS 24 hours post procedure was 9.7 with 32% of patients achieving 10 point or greater improvement in NIHSS at 24 hours. Thirty-five percent of patients were discharged to inpatient rehab and 24% were discharged to home. Ninety-day follow-up data is still pending.

Conclusions

Preliminary data from the Trevo registry reveals TIC1 2b and 3 revascularization rates with real-world usage of the device that are significantly better than those seen in the Trevo trial. There is no significant difference in the need for adjuvant devices for revascularization compared to the Trevo trial. Secondary endpoint data is pending, but short-term outcome data appears promising.

Author Disclosure Block: M.J. Binning: None. E. Veznedaroglu: Research Grant; Modest; stryker. Consultant/Advisory Board; Modest; stryker.

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Presentation Number: LB P27

Publishing Title: Identification of Criteria to Avoid Unnecessary Intensive Care Unit Admission for patients with Intracerebral Hemorrhage

Author Block: Oladi Benthoo, Ashish Kulhari, Kunal Kumar, Wei Xiong, Univ Hosp Case Medical Ctr, Cleveland Heights, OH

Abstract Body: Background

With the rising cost of health care over the past few years, how to efficiently and effectively deliver health care has been the question that many hospital systems have been asking. Intensive care resources, particularly, neuroscience intensive care resources are limited and costly. In most institutions in the country, all intracerebral hemorrhage (ICH) patients are admitted to the Neuroscience intensive care unit without assessing whether these patients need critical care resources. We sought to identify what criteria will allow us to determine which primary intracerebral hemorrhage patients will not need admission to an intensive care unit (ICU).

Methods

We performed a retrospective chart review of all the patients with primary ICH admitted to our Neuroscience ICU during calendar year 2013. After reviewing multiple admitting characteristics, we tested the following as criteria for avoiding ICU admission: supratentorial ICH, ICH volume <15 cc, no IVH, systolic BP <180 mmHg; no respiratory failure, GCS >12. We then reviewed the hospital course of patients that fit this criteria, specifically looking at the ICU length of stay (LOS), requirement for any neurosurgical procedures, and any complications during the hospital course.

Results

165 patients with primary ICH were admitted to the Neuroscience ICU during the year. 21(12.7%) patients fulfilled the "non-admission" criteria as described above. The average NSU LOS was 2 days. 4 patients had an NSU LOS of 3 days. All patients were discharged to either home or inpatient rehabilitation except 1 patient who expired after being transferred to the neurological floor with hospice. This patient was an elderly patient with existing DNR and comfort care orders who then developed respiratory failure while on the floor. None of the patients who met the above criteria required readmission to the ICU, neurosurgical intervention, or developed any serious complications.

Conclusion

We assert that intracerebral hemorrhage patients that fulfill the above criteria do not have to be admitted to an ICU and can be safely monitored in a step down unit.

Author Disclosure Block: O. Benthoo: None. A. Kulhari: None. K. Kumar: None. W. Xiong: None.

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Presentation Number: LB P28

Publishing Title: Validating Accelerometry as a Measure of Physical Activity and Energy Expenditure in Chronic Stroke Survivors

Author Block: **Monica C Serra**, Elizabeth Balraj, Beth L. DiSanzo, Frederick M. Ivey, Charlene E. Hafer-Macko, Univ of Maryland Sch of Med, Baltimore, MD; Margarita S. Treuth, Univ of Maryland Eastern Shore, Princess Anne, MD; Alice S. Ryan, Univ of Maryland Sch of Med, Baltimore, MD

Abstract Body: Following stroke ~80% of individuals develop hemiparesis and ~50% have persistent motor deficits 6 months after onset. Hemiparetic gait elevates the energy cost of ambulation by 1.5-2 fold, thereby predisposing survivors to a sedentary lifestyle. The Actical accelerometer cut-points currently used to distinguish intensity for varying levels of activity are only standardized for the general population and may underestimate intensity in stroke. Hence, our purpose was to derive activity count thresholds specific to stroke disability. Men (n=18) and women (n=10) with chronic residual stroke deficits (43% Caucasian, 57% African American, ages of 47-83 yrs, BMI 19 - 48 kg/m²) participated in the study. Actical accelerometers were placed on the non-paretic hip to obtain accelerometry counts. A K4b² Cosmed portable metabolic system was used to simultaneously measure the metabolic equivalent (MET) level of tasks, derived from EEkg (energy expended during each activity/kg of body weight) during 8 activities of varying intensity. These measurements were obtained during 10 min. of rest and 5 min. each of the following: watching TV, seated stretching, standing stretching, sweeping, stepping in place, over-ground walking, lower speed treadmill walking (1.0 mph/4% incline), and higher speed treadmill walking (2.0 mph/4% incline). Regression analysis was used to determine activity count thresholds based upon MET guidelines for sedentary (<1.5 METs), light (1.5-3), moderate (3-6), and vigorous (>6) activity. These analyses yielded new stroke-specific Actical cut-points as follows: sedentary: <100, light: 100-568, moderate: 569-2059, and vigorous: >2059 counts/min. Accelerometer counts were associated with EEkg (r=0.60, P<0.01). Our revised cut-points for stroke suggest significantly lower thresholds, indicating that standard thresholds derived from healthy individuals are inappropriate for this unique population. Our new thresholds better reflect activity levels after stroke.

Author Disclosure Block: **M.C. Serra:** None. **E. Balraj:** None. **B.L. DiSanzo:** None. **F.M. Ivey:** None. **C.E. Hafer-Macko:** None. **M.S. Treuth:** None. **A.S. Ryan:** None.

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Presentation Number: LB P29

Publishing Title: Use of Botulinum Toxin as a Plasticity Inducing Agent Post Stroke

Author Block: Preeti Raghavan, Seda Bilaloglu, Viswanath Aluru, Kimberly Noel, Daniel Geller, R. Venkata Krishnan, New York Univ Sch of Med, New York, NY

Abstract Body: Sensory denervation has been shown to stimulate neuroplasticity. Here we used low doses of Botulinum Toxin injections to partially denervate a set of upper limb muscles involved in functional tasks. The objective of the study was to test the hypotheses that grasp coordination and hand motor recovery would be enhanced in subjects that received Botulinum toxin (BTX) versus normal saline (placebo) injections.

Design: Prospective, double blinded, randomized controlled clinical trial.

Setting: Outpatient research laboratory

Participants: Sixteen subjects with chronic post-stroke hemiparesis who could grasp a test object were randomly assigned to either the intervention group consisting of BTX and occupational therapy or to a control group consisting of placebo and identical therapy.

Interventions: Twelve upper limb muscles were injected using electrical stimulation to identify the muscles once. 200 units of BTX diluted with 5 cc of normal saline was injected into the intervention group and the same volume of normal saline was injected into the control group. All subjects received 1 hour of conventional occupational therapy two times a week for 9 weeks.

Grasp coordination was assessed using an instrumented grip device equipped with force sensors. Hand motor recovery was assessed using Fugl-Meyer wrist and hand score, pinch strength and 2-point discrimination.

Results: Grasp coordination, measured by the time taken to stabilize an object between two fingers, showed greater improvement in the intervention group from pre- to post-training. The improvement was greater when the subjects first grasped the object with their unaffected hand and then their affected hand, suggesting that they learned from the unaffected hand. Subjects in the intervention group also used lower grip forces than subjects in the control group, suggesting that they did not need to overgrip. The Fugl-Meyer score for the wrist and hand increased similarly in both groups. However pinch strength was higher and the threshold for 2-point discrimination was lower in the intervention group compared with the control group.

Conclusions: The results suggest that low dose Botulinum toxin injections in conjunction with motor training can enhance plasticity for hand motor recovery post stroke.

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Presentation Number: LB P30

Publishing Title: Is Stroke A Winter Disease? Seasonal Variation In Severity And Outcomes Of Ischemic And Hemorrhagic Strokes: NCVS Stroke Registry

Author Block: Kazunori Toyoda, Kaoru Endo, Jun Fujinami, Tomotaka Tanaka, Eijirou Tanaka, Junpei Kobayashi, Hiroshi Yamagami, Yasuteru Inoue, Kazunari Homma, Kenta Seki, Rieko Suzuki, Kazuo Minematsu, Masatoshi Koga, Kazuyuki Nagatsuka, Natl Cerebral and Cardiovascular Ctr, Suita, Japan

Abstract Body: Background: Although most of systemic vascular diseases have a peak in winter months, seasonal variation in stroke remains unclarified. We aimed to determine seasonal variation in severity and outcomes of stroke in the National Cerebral and Cardiovascular Center (NCVC) Stroke Registry dataset (ClinicalTrials.gov: NCT02251665).

Methods: A total of 1793 ischemic stroke patients (Jan 2011 - Dec 2013) and 1060 intracerebral hemorrhage (ICH) patients (June 2004 - May 2009, Jan 2011 - Dec 2013) who were emergently admitted to our stroke care unit were studied from our ongoing single-center prospective registry.

Results: [Ischemic stroke] Stroke onset did not vary by season (24.8% in winter, 25.4% in spring, 26.5% in summer, 23.3% in fall, $p=0.269$). Cardioembolism tended to be more common in winter (28.7%) and non-cardioembolism in summer (27.3%). Baseline NIH Stroke Scale (NIHSS) score ≥ 10 was more common in winter than in fall for overall (OR 1.74, 95% CI 1.29-2.37), cardioembolic (1.68, 1.07-2.67), and non-cardioembolic stroke patients (1.79, 1.13-2.89) after sex- and age-adjustment. Modified Rankin Scale (mRS) of 4-6 was more common in winter than in fall for overall (OR 1.47, 95% CI 1.06-2.05) and non-cardioembolic stroke patients (1.76, 1.11-2.80) after sex- and age-adjustment, but was no longer more common after further adjustment by admission NIHSS. [ICH] Stroke onset significantly varied by season (30.2% in winter, 26.5% in spring, 19.1% in summer, 24.2% in fall, $p<0.01$). Baseline NIHSS score ≥ 10 was less common in winter than in summer for lobar hemorrhage patients (OR 0.29, 95% CI 0.12-0.67), and more common in fall than in summer for non-lobar hemorrhage patients (1.71, 1.10-2.67) after sex- and age-adjustment. mRS 4-6 was similarly common among seasons for overall, lobar, and non-lobar ICH patients.

Conclusion: In our single-center registry, ischemic stroke occurred similarly common among seasons, and patients in winter had more severe neurological deficits than those in fall. ICH occurred 1.6-fold more common in winter than in summer. Lobar hemorrhage was relatively mild in spring and non-lobar hemorrhage was relatively severe in fall. Stroke is not necessary a winter-dominant disease.

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Presentation Number: LB P32

Publishing Title: The Effects of Mineralocorticoid Receptor Blockade On Cerebral Arteries Post-Stroke

Author Block: Janice M Diaz-Otero, Anne M Dorrance, Michigan State Univ, East Lansing, MI

Abstract Body: Hypertension causes cerebral artery remodeling increasing the risk of stroke and dementia. Mineralocorticoid receptor (MR) antagonism reverses artery remodeling in stroke-prone hypertensive (SHRSP) rats. Cerebral ischemia induced by middle cerebral artery (MCA) occlusion (MCAO) increases the lumen diameter of the occluded artery in normotensive rats. We hypothesized that MR antagonism with canrenoic acid (CAN) would increase the MCA lumen diameter and reduce wall stress, wall thickness and vascular damage after MCAO in SHRSP. Ischemia was induced in 18 week old male SHRSP, after reperfusion rats were treated with CAN (20mg/kg/day I.P.) or placebo for two weeks. The ischemic and non-ischemic MCAs were collected for structure analysis by pressure myography. Results at 100mmHg intraluminal pressure are presented as mean \pm SEM. In placebo treated rats wall strain (0.6 ± 0.1 vs 0.4 ± 0.1 ANOVA, $p < 0.05$) and distensibility (62.7 ± 8.2 vs 38.9 ± 6.3 ANOVA, $p < 0.05$) were increased in the ischemic MCA compared to the non-ischemic; the outer and lumen diameter was unchanged. Wall stress was increased in the ischemic MCA at 120mmHg (610 ± 72 vs 472 ± 38 ANOVA, $p < 0.05$). CAN treatment post-MCAO increased the outer (284 ± 7 vs $251 \pm 4 \mu\text{m}$ ANOVA, $p < 0.05$) and lumen (233 ± 7 vs $200 \pm 4 \mu\text{m}$, ANOVA, $p < 0.05$) diameter in the ischemic MCA compared to the non-ischemic. No significant changes were observed in the MCAs from Sham rats. In the ischemic hemisphere, CAN reduced wall stress compared to Sham and placebo treated rats (255 ± 32 vs 500 ± 43 vs 610 ± 72 ANOVA, $p < 0.05$). CAN reduced the arterial stiffening (3.8 ± 0.6 vs 7.7 ± 0.6 ANOVA $p < 0.05$) that was increased by ischemia (7.7 ± 0.6 vs 5.52 ± 0.7 ANOVA, $p < 0.05$); this may be the result of alterations in extracellular matrix deposition. CAN enhanced cerebral perfusion post-stroke (233 ± 34 vs 341 ± 22 perfusion units t-test, $p < 0.05$). CAN may reduce the post-stroke neurodeficit (2.0 ± 0.3 vs 1.5 ± 0.3 , t-test, $p = 0.1$). Our results suggest that CAN administration post-stroke has beneficial effects on the cerebral arteries that could enhance post-stroke perfusion and reduce the damage caused by ischemia.

Author Disclosure Block: J.M. Diaz-Otero: None. A.M. Dorrance: None.

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Presentation Number: LB P33

Publishing Title: A New Diagnostic Tool For Measuring The Effectiveness Of Intravenous Tissue Plasminogen Activator (rt-PA) In The Treatment Of Acute Ischemic Stroke

Author Block: **Tristan Lawson**, Inga Brown, Dana WESTERKAM, Univ of South Carolina Sch of Med Greenville, Greenville, SC; Dawn Blackhurst, Shannon Sternberg, Rodney Leacock, Greenville Hosp System, Greenville, SC; Thomas I Nathaniel, Univ of South Carolina Sch of Med Greenville, Greenville, SC

Abstract Body: Background. Several clinical trials have highlighted favorable outcomes of intravenous tissue type plasminogen activator (rt-PA) in acute ischemic stroke using different measures. Most of the existing tools do not provide an accurate and robust measure for the effectiveness of rt-PA. In this study, we developed a new diagnostic tool for verifying the global effect of rt-PA effectiveness in acute ischemic stroke patients. Methods. Using computer programming and simulations, we developed a new model for assessing the effectiveness of rt-PA in patients that received rt-PA within 3 to 4.5 window time frame following the onset of acute ischemic stroke. Using a multiple year data set, we analyzed pre and post post-rt-PA treatment data and simulated different functional recovery activities. Our simulations identified the most powerful tool that indicates the effectiveness of rt-PA in the treatment of acute ischemic stroke. Principal component analysis (PCA) confirms that the identified tool has the largest diversity within activities that contribute to the variance in the diversity of functional recovery activities. Results. Among functional recovery activities, our model identified the ambulation status during and post-rt-PA treatment as the most powerful diagnostic tool for assessing the global functional recovery of the patient. PCA confirmed a variation of 93.3% for ambulation as the major contributor to the largest diversity in the general functional recovery in the pre and post-rt-PA treatment. Conclusion. Our results indicate that the ambulatory status of an ischemic stroke patient can be used as a new tool to assess the effectiveness of rt-PA the post-rt-PA treatment.

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Presentation Number: LB P34

Publishing Title: Prevalence of Intracranial Atherosclerotic Stenosis in U.S. Elderly Using High Resolution Magnetic Resonance Angiography

Author Block: **M. Fareed K Suri**, Univ of Minnesota, Minneapolis, MN; Ye Qiao, Johns Hopkins Sch of Med, Baltimore, MD; Haitao Chu, Univ of Minnesota, Minneapolis, MN; Eliseo Guallar, Johns Hopkins Sch of Med, Maryland, MD; Yiyi Zhang, Johns Hopkins Sch of Med, Baltimore, MD; Li Liu, Johns Hopkins Sch of Med, Maryland, MD; Xiaoye Ma, Adnan I Qureshi, Alvaro Alfonso, Aaron Folsom, Univ of Minnesota, Minneapolis, MN; Bruce Wasserman, Johns Hopkins Sch of Med, Baltimore, MD

Abstract Body: Background. Intracranial atherosclerotic stenosis (ICAS) is a common cause of stroke, but little is known about its epidemiology. We studied the prevalence of ICAS and its association with vascular risk factors using high resolution magnetic resonance imaging (MRA) in a U.S. cardiovascular cohort. Methods. Atherosclerosis Risk in Communities (ARIC) study recruited participants from four U.S. communities from 1987-1989. We selected 1959 subjects from visit-5 participants (2011-2013), using stratified sampling, for high resolution 3T-MRA. All subjects underwent detailed visit-5 interview and examinations. All images were analyzed in a centralized lab and ICAS was graded as _ no stenosis, <50% stenosis, 50-69% stenosis, 70-99% stenosis and complete occlusion. We report per-vessel and per-person weighted (for n=6,538 visit-5 participants) prevalence of ICAS, and also estimated the U.S. prevalence using age and gender adjustment. We used backward stepwise logistic regression to identify variables associated with ICAS. Results. Subjects who had an adequate MRA (n=1765), were aged 67-90 years, 41% were men, 70% were white and 29% were African-American. Prevalence of any-ICAS was 31% and of ICAS \geq 50% was 9%. Using backward stepwise logistic regression, variables associated with increased odds of ICAS were age, African-American (compared to white), history of diabetes, history of hypertension, systolic blood pressure and low density lipoprotein (LDL); and factors associated with lower odds of ICAS were high density lipoprotein (HDL) and use of cholesterol lowering medication. We found no association of body-mass-index and smoking with ICAS. Conclusion. In U.S. elderly population, estimated prevalence of ICAS is 27% in white and 37% in African-American population. Hypertension, diabetes and elevated LDL are associated with increased odds of ICAS. Smoking status was not associated with ICAS.

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Presentation Number: LB P35

Publishing Title: Neutrophil Activation as a Marker for Systemic Inflammation and Cerebral Disease Burden in a Novel Model of Post-cardiac Arrest Syndrome

Author Block: Nguyen Mai, Landa Prifti, Marc Halterman, Univ of Rochester, Rochester, NY

Abstract Body: Brain injury is the primary cause of mortality in patients with return of spontaneous circulation after cardiac arrest, and central and peripheral inflammation are important therapeutic targets. Here we investigate the dynamics of neutrophil (PMN) activation in a novel model of post-cardiac arrest syndrome (PCAS) and correlate these with CNS injury following reperfusion. Our results argue that early changes in CD11b expression on PMNs could complement established serum markers to predict disease severity. Cerebral ischemia was induced in C57/B6 mice using 3-vessel occlusion (3VO) involving basilar artery cauterization and 15-minute bilateral common carotid occlusion. During reperfusion, mice received a low-dose (50 µg/kg) LPS injection to mimic endotoxemia observed in PCAS. Blood was collected 2, 4, and 6 hours after reperfusion to measure PMN activation by fluorescence activated cell sorting (FACS). Immunohistochemistry was performed after 3 days to correlate CNS injury with PMN migration as determined by loss of microtubule-associated protein 2 (MAP2) staining and expression of the granulocyte marker Ly-6B, respectively. FACS analysis for the activation marker CD11b in Ly-6G(hi) PMNs at 2 hours revealed modest activation in sham mice with systemic LPS (Sham/LPS; MFI = 19736) relative to saline controls (Sham/SAL; MFI = 16684). While 3VO induced marked PMN activation (3VO/SAL; MFI = 25826), the combination of ischemia with LPS produced the greatest activation (3VO/LPS; MFI = 60945). CD11b expression remained elevated at 4 and 6 hours in groups with systemic inflammation. Histological analyses for MAP2 indicated that 3VO/LPS exposure enhanced cortical damage (39.95% ± 10.87) compared to either 3VO/SAL (24.31% ± 4.39, p = 0.003) or sham (4.36% ± 0.61, p < 0.001). We also observed a trend of cerebral PMN influx in 3VO/SAL mice (7.93 ± 4.23 PMN/mm²; p = 0.080), which was significant in 3VO/LPS (9.44 ± 4.89 PMN/mm²; p = 0.049) compared to sham (1.10 ± 0.73 PMN/mm²). 3VO/LPS treatment was also associated with enhanced co-localization of PMNs and areas of injured cortex ($\chi^2 = 8.89$, df = 2, p = 0.012). These data indicate that while CNS ischemia is sufficient to recruit PMNs, peripheral inflammation, indicated by early CD11b upregulation, primes them for injury.

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Presentation Number: LB P36

Publishing Title: Arterial Spin Labeling MRI Identifies Ischemic Stroke Patients with Good Outcome at Hospital Discharge

Author Block: Adam de Havenon, Univ of Utah, Salt Lake City, UT; David Tirschwell, Ali Sultan-Qurraie, Wendy Cohen, Jalal Andre, Univ of Washington, Seattle, WA

Abstract Body: Background: In ischemic stroke patients, the presence of robust collateral blood vessels is correlated with superior functional outcome. On arterial spin labeling (ASL) MRI the presence of collaterals can be inferred by serpiginous areas of hyperintensity along the border of a perfusion abnormality, but it has not been used for this purpose after ischemic stroke.

Methods: We retrospectively identified ischemic stroke patients admitted to our hospital between 2012 and 2104 who had ASL. This yielded 38 patients who were graded for the presence of collaterals by a blinded neuroradiologist. Chart review was also performed and results were analyzed using descriptive and non-parametric statistics.

Results: Mean age was 61.4 (SD 20.5) and 19/38 were male. 32/38 patients had anterior circulation stroke, 12/38 had a large artery occlusion, and 17/38 had >50% stenosis of the stroke parent artery. Mean time from stroke to MRI was 2.2 days (SD 3.2) and 25/38 had collaterals on ASL. Mean NIH stroke scale (NIHSS) on admission was 10.3 (SD 9.8). In the group with collaterals the mean mRS at discharge was 2.2 (SD 1.7) and in the group without collaterals it was 3.6 (SD 1.3). Collaterals were significantly correlated with lower mRS at discharge ($p=0.012$), but not admission NIHSS ($p=0.167$). There was no statistically significant association between discharge mRS and gender, age, blood pressure, respiratory rate, or temperature.

Conclusion: In ischemic stroke patients, the presence of collateral blood vessels on ASL correlates with improved outcome at hospital discharge, independent of admission NIHSS. This novel association could help guide management in patients who are unable to undergo contrast-based radiologic studies and warrants further investigation.

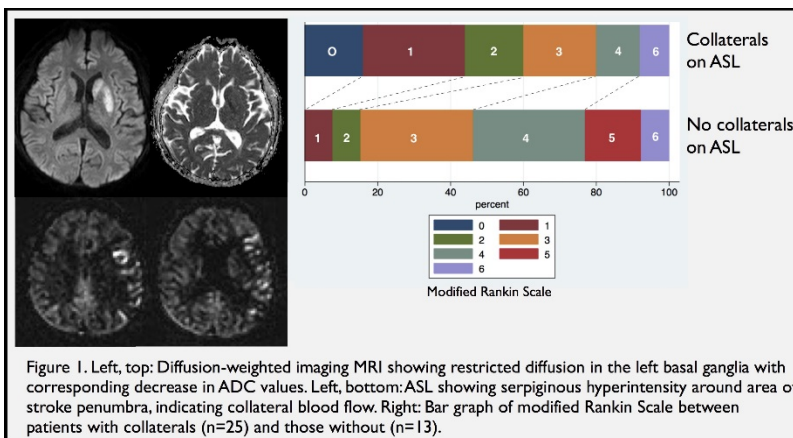


Figure 1. Left, top: Diffusion-weighted imaging MRI showing restricted diffusion in the left basal ganglia with corresponding decrease in ADC values. Left, bottom: ASL showing serpiginous hyperintensity around area of stroke penumbra, indicating collateral blood flow. Right: Bar graph of modified Rankin Scale between patients with collaterals (n=25) and those without (n=13).

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