Presentation Number: LB P1

Publishing Title: A Simple Protocol Dramatically Reduces the Rate of External Ventricular Drain Infections in the ICU

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Abstract Body:

Introduction: External ventricular drains (EVDs) are associated with high rates of infection. EVD infections are an important cause of morbidity and mortality among stroke patients with conditions such as intracerebral hemorrhage and subarachnoid hemorrhage.

Hypothesis: We hypothesized that introduction of an evidence-based EVD Infection Control protocol in the ICU could reduce the rate of EVD infections.

Methods: We analyzed the impact of an EVD Infection Control protocol introduced in a tertiary care Neuro-ICU by comparing the rates of cerebrospinal fluid (CSF) culture positivity and ventriculitis for the three years before and three years after the introduction of an evidence-based EVD Infection Control protocol. A total of 262 EVD placements were analyzed, with a total of 2,499 catheter-days.

Results: The rate of CSF culture positivity decreased from 9.8% (14/143) [11.43 per 1000 catheter-days] at baseline to 0.8% (1/119) [0.79 per 1000 catheter-days] in the EVD Infection Control protocol period (P = 0.001). The rate of ventriculitis decreased from 6.3% (9/143) [7.35 per 1000 catheter-days] to 0.8% (1/119) [0.79 per 1000 catheter-days] (P = 0.02). In multivariable logistic regression, presence in the EVD Infection Control Protocol period and duration of EVD placement were both independent predictors of both CSF culture positivity and ventriculitis.

Conclusion: In conclusion, introduction of a simple, evidence-based EVD Infection Control protocol was associated with a dramatic reduction in the risk of EVD infection.

Background and Purpose: According to the International Study of Unruptured Intracranial Aneurysms (ISUIA), anterior circulation (AC) aneurysms of less than 7mm of diameter have a minimal risk of rupture. However, it is general experience that anterior communicating artery (AcoA) aneurysms are frequent and mostly rupture below the size of 7 mm. The aim of the study is to demonstrate that AcoA aneurysms behave differently from other anterior circulation aneurysms.

Methods: Information about 932 patients newly diagnosed with intracranial aneurysms between November 2006 and April 2012 were collected during the multicenter @neurlST project. The aneurysm status when initially diagnosed, location, size and information about risk factors were analyzed. The risk of rupture associated in each subgroup was estimated by measuring the odds ratio of aneurysms diagnosed as ruptured between groups classified by location or location and size.

Results: The odds ratio for aneurysms to be discovered ruptured was significantly higher for AcoA (OR 2.1; 1.4-3.2 95% CI) and posterior circulation (PC) than for internal carotid artery and middle cerebral artery (OR 0.5; 0.3-0.7 95% CI). AcoA aneurysms less than 7mm were more frequently found ruptured (OR 2.0; 1.3-3.0 95%CI) than anterior circulation aneurysms with a size between 7 and 12mm suggested by ISUIA as a threshold indicating aggressive treatment.

Conclusion: Our observations show that AC aneurysms are not a homogenous group. Aneurysms smaller than 7mm and located in AcoA, distal anterior cerebral artery and PC have a significant risk of rupture. Intervention should be recommended for this high risk lesion group.

Author Disclosure Block: P. Bijlenga: None.
Abstract Body:


Methods: Potentially relevant studies were identified using a review of the 6260 PubMed listed articles with ‘carotid’ in the title published January 1st, 2009 to October 8th, 2012. As before, the main inclusion criteria were prospective study design and >100 patients with procedure-free, baseline 50-99% ACS. Standardised rates were plotted by publication year. Weighted linear regression analysis accommodated differing sample sizes. The Ryan-Holm stepdown Bonferroni procedure corrected for multiple comparisons.

Results: Identified were 3 eligible new studies and 2 otherwise eligible new studies which included some patients (<18%) with remote (>18 months) ipsilateral symptoms. Data referring to 1176 new patients were available for the update (4900 patients in total, mean age 67 years, 63% male, from 16 studies). The new data added to the highly significant falls in average annual event rates seen in the previous meta-analysis (P’<0.00009 in each case, with/without patients with remote symptoms, see Figure for ipsilateral stroke). Between the mid-1980s (when the first eligible studies were published) and 2012, there has been a relative rate fall of 75% for ipsilateral stroke, 80% for ipsilateral stroke/TIA, 90% for any territory stroke and 65% for any territory stroke/TIA. Recently reported average annual stroke rates with medical treatment alone were below those of stented and operated patients in major randomised trials.

Conclusions: Average annual risk of first stroke (+/-TIA) in patients with 50-99% asymptomatic carotid stenosis continues to fall with medical treatment alone, indicating that a procedural approach is unlikely to provide overall benefit.

Figure: Ipsilateral Stroke Rates, Sample Sizes & Statistical Results
Background: Hypothermia is a proven neuroprotectant in patients with ischemia followed by definitive reperfusion as in cardiac arrest. We thus conducted a phase I pilot study to assess the feasibility and safety of performing intravascular hypothermia after intra-arterial reperfusion therapy (IAT).

Methods: ReCCLAIM I was a prospective single arm open label clinical trial conducted at a single center from May-August 2012. Inclusion criterion were patients ages 18-85, NIHSS > 13, ASPECTS 5-7 pre-treatment, occlusion of the M1 or M2 MCA or ICA terminus under 8 hours from last known normal. Intravascular cooling was initiated immediately after definitive reperfusion, and hypothermia maintained at <33.5°C for 12 hours. Post-op hemorrhages and blood-brain-barrier (BBB) breakdown were evaluated on 24 hour CT and 36-72 hour HARM protocol MRIs, respectively. All complications were documented for the entire length of stay.

Results: 73 patients were treated with IAT during the study period, of which 20 met study criteria. The mean age, median NIHSS and median final infarct volume was 59.7±14.6 years, 19 (IQR16-22) and 78 cm³ (IQR 16-107) respectively. The mean time to target temperature was 64±50 mins. Complications were as follows: 5 pneumonias(25%), 1 DVT(5%), and 1 bacteremia(5%). Six patients died due to withdrawal of care. Intracranial hemorrhages were found in 3 patients (15%), of which 1 (5%) was symptomatic. Evidence of BBB breakdown was observed on 3 (21%) out of 14 MRIs. Six patients (30%) achieved mRS of 0-2 and 9 patients (45%) achieved a mRS 0-3 at 90 days. In binary logistic regression modeling comparing ReCCLAIM patients to 68 historical controls at our institution who would have met inclusion criterion prior to the study, hypothermia was protective from any hemorrhage (OR 0.09, 95% CI 0.02-0.56; p<0.01) after controlling for age, NIHSS and final infarct volume.

Conclusion: Hypothermia can be safely performed after definitive IAT in patients with large pre-treatment core infarcts. The current study provides the background to proceed with ReCCLAIM II randomizing patients to hypothermia or normothermia prior to IAT and assess if hypothermia is protective of reperfusion injury.
Presentation Number: LB P5

Publishing Title: North American Solitaire Stent-Retriever Acute Stroke Registry: Post-Marketing Revascularization and Clinical Outcome Results as Compared to the Swift and Trevo-2 Clinical Trials

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Abstract Body:

Background: The recent results of the SWIFT and TREVO-2 trials demonstrated better recanalization and efficacy rates with the SOLITAIRE FR and TREVO devices compared to the MERCI retriever; however, limited post-marketing data exists on use of the SOLITAIRE FR device in clinical practice. The North American SOLITAIRE Acute Stroke (NASA) Registry aimed to assess the real-world performance of the SOLITAIRE FR device in comparison to the results from the SWIFT and TREVO-2 clinical trials.

Method: The investigator-initiated NASA Registry recruited clinical sites within North America to submit demographic, clinical presentation, site-adjudicated angiographic and clinical outcome data on consecutive patients treated with the SOLITAIRE FR. Symptomatic intracranial hemorrhage (sICH) was defined as any parenchymal hematoma, SAH, or IVH associated with a worsening of the NIHSS score by ≥4 within 24 hours. The primary outcome was achieving TIMI ≥2 or TICI ≥2a revascularization. Secondary outcomes were mRS at 3 months, mortality, and sICH.

Results: 287 patients underwent treatment using the SOLITAIRE FR in 21 centers. Baseline demographics were: women 53% (152/287), white 74.5% (210/287), mean age 67.5±14.9 years, median baseline NIHSS of 18 (IQR 14-23), mean time to initial angiogram 374.8±253.3 minutes, and a mean procedure time of 37±29.8 minutes.

The primary outcome showed a TIMI ≥2 rate of 79.8% (229/287) and a TICI ≥ 2a rate of 79.1% (227/287), compared to the operator reported TIMI ≥ 2 rate of 83% in SWIFT and TICI ≥ 2a rate of 85% in TREVO-2. The 90-day mRS outcome was available in 81.5% (234/287) of NASA patients. A good outcome of mRS≤2 was demonstrated in 40.5% (95/234), compared to 37% (SWIFT) and 40% (TREVO-2). The rate of sICH was 8.7% (25/287), compared to 2% (SWIFT) and 4% (TREVO-2). 90-day mortality was 31.2% (73/287) versus 17.2% in SWIFT and 29% in TREVO-2.

Conclusion: The NASA Registry demonstrates that the SOLITAIRE FR stent-retriever recanalization performance in real world clinical practice is comparable to the SWIFT and TREVO-2 clinical trial results.

Neurovascular. G.W. Britz: None. R. Kaushal: None. A. Nanda: None. M. Issa: None. R.G. Nogueira: Consultant/Advisory Board; Modest; Covidien, Stryker, Penumbra, Reverse Medical, and Rapid Medical.
**Abstract Body:**

**Background:** Older adults who reside in disadvantaged communities have higher mortality after stroke. We examined whether the timing of post-stroke outpatient visits contributed to previously observed neighborhood disparities in post-stroke mortality.

**Methods:** We used data from the Cardiovascular Health Study, a population-based, longitudinal study of adults ≥65 years. Center for Medicare and Medicaid Services (CMS) data were used to obtain outpatient visits and pre-stroke comorbidity. Eligible participants had an incident stroke during the study period, survived through the visit interval (7, 14, 21, or 28 days), were matched to CMS records, and had fee-for-service coverage during the follow up period. Neighborhood socioeconomic status (NSES) was a composite of 6 census variables. To examine the associations between time to first post-stroke outpatient visit, NSES, and the dependent variable of mortality at 1 year post-stroke, we constructed multilevel Cox proportional hazard models that also included age, sex, race, stroke type, comorbidity, and an interaction term between time to first visit and NSES. Separate models were constructed for each visit interval.

**Results:** Among the 495 eligible participants (mean follow up 11.5 years), 17.4% had an outpatient visit within 7 days, 27.9% within 14 days, 36.4% within 21 days, and 44.4% within 28 days. In adjusted models, the mortality hazard at one year after stroke was lower among participants without, compared to those with, an outpatient visit within 7 days (HR=0.44; 95% CI=0.24, 0.79), 14 days (HR=0.56; 95% CI=0.36, 0.92), and 21 days (HR=0.57; 95% CI=0.37, 0.94), but not 28 days (HR=0.65; 95% CI=0.41, 1.04). NSES was associated with mortality only for models of outpatient visits within 28 days. The visit x NSES interaction was not significant for any models.

**Conclusions:** Early follow up after stroke, specifically a visit within the first 3 weeks, was associated with lower mortality at 1 year and appeared to mitigate the association between lower NSES and stroke mortality. For those with later follow up, lower NSES remained independently associated with mortality. Early and appropriate clinical care may play an important role in reducing socioeconomic disparities in stroke mortality.
Abstract Body:

Purpose: The Penumbra START Trial was a multicenter, prospective, single-arm trial with the primary aim of testing whether core infarct size on pre-treatment neuroimaging predicts the clinical response to intra-arterial therapy.

Methods: The major inclusion criteria for this study were presence of proximal artery occlusion of the anterior circulation, baseline NIHSS score ≥10, evaluable pre-treatment neuroimaging (noncontrast CT [NCCT], CTA source imaging, CT perfusion or MRI DWI), and treatment with the Penumbra System within 8 hours. Core infarct size was determined by a blinded imaging Core Lab. Infarcts were trichotomized in a prespecified fashion as small (ASPECTS 8-10 [NCCT, CTA-SI] or lesion volume <50 cc [CTP or DWI]), moderate (ASPECTS 5-7 or volume 50-100 cc) or large (ASPECTS 0-4 or volume >100 cc). A total of 144 patients were enrolled at 27 centers. Included in this analysis are 101 patients with Core Lab review and 90 day evaluation. Good clinical outcome was defined as 90-day mRS 0-2.

Results: The mean age was 66. There were 57 females. Strokes involved the left hemisphere in 58 patients. The median NIHSS score was 19. The overall rate of TIMI 2-3 revascularization was 83%. Forty-five patients had a good outcome (44.5%); 28 patients died (27.7%). The number of evaluable scans for each modality is as follows: 32 CTP, 79 CTA-SI, 78 NCCT and 6 DWI. Sixty-nine patients had multiple modalities (1: 32; 2: 44; 3: 25). In aggregate analysis pooling all modalities, there was a statistically significant relationship between core infarct size and good outcome, such that worse outcomes were seen only in the large infarct group. The rate of good outcomes was 54.9% in small, 54.3% in moderate and 16.7% in large infarcts (p=0.0005). This was despite similar rates of recanalization (79% small, 91% moderate, 83% large). Independent predictors of good outcome were age, NIHSS score, time from onset to recanalization, and infarct volume.

Conclusion: Pre-treatment neuroimaging is critical for identifying patients with large infarcts who are unlikely to respond to intra-arterial therapy. These findings support the use of strict imaging criteria in patient selection for future IA trials.
Abstract Body:

<Background>
Carotid artery stenting (CAS) is becoming an alternative Carotid endoarteretomy (CEA). However periprocedural ischemic stroke is one of problem of CAS. It has been reported that statin therapy reduced periprocedual complication in coronary intervention. We aimed to assess whether preoperative stain therapy reduce periprocedural ischemic complication of CAS.

<Material and Methods>
In this prospective study at 11 centers, patients who had carotid stenosis (symptomatic 50>=%, asymptomatic>= 80%) with CEA high risk and without previous statin treatment were divided into 2 groups by LDL cholesterol level (LDL). With LDL >=120mg/dl, Pitavastatin 4mg/day (PS group) were given for 4 weeks, with LDL <120mg/dl, no stain therapy (non- PS group) was for 4 weeks. After 4 weeks, both groups were treated by CAS. New ipsilateral ischemic lesions on MR diffusion weighted image (DWI) within 48 hours after CAS and 30-days major adverse events (MAEs) (transient ischemic attack, stroke, myocardial infarction, death) were assessed.

<Result>
Between July 2010 and September 2012, 80 patients were enrolled. 70 patients (PS group n=36, non- PS group n=34) were treated by CAS. CAS was technically successful in all cases. New ipsilateral ischemic lesions occurred in 25.0% of patients (9 of 36) in PS group and in 52.3% of patients (18 of 34) in non- PS group (P=0.016). MAEs occurred in none of patients in PS group and in 11.8% of patients (4 of 34) in non- PS group (P=0.034).

<Conclusion>
Pretreatment with pitavastatin for 4 weeks significantly reduced periprocedural ischemic complication of CAS.
Abstract Body:

**Background** Stroke is a leading cause of morbidity and mortality however, no specific therapies are available for its treatment thus research in this field is intense. Oxidative stress plays an important role in ischemic stroke. The adaptor protein p66Shc is a key regulator of reactive oxygen species (ROS) production, and a mediator of ischemic tissue damage in ex-vivo hearts. We recently demonstrated that p66Shc knockout mice are protected from ischemia/reperfusion brain injury by a decreased production of NAPDH oxidase-dependent ROS. The herewith described study was designed to investigate the role of p66Shc in stroke in a clinically relevant experimental setup whereby p66Shc knockdown is performed after the ischemic episode.

**Methods** Transient middle cerebral artery occlusion (MCAO) was performed to induce ischemia/reperfusion brain injury in wild type mice. After 45 min of ischemia and directly upon reperfusion, small interfering RNA (siRNA) for p66Shc (sip66Shc) or scrambled siRNA (siScr) were injected intravenously. 48 h post-MCAO, stroke size and neurological deficit were analyzed using magnetic resonance imaging (MRI) and RotaRod test, respectively. To test human relevance, p66Shc silencing was performed on human brain endothelial cells (HBEC) exposed to hypoxia/reoxygenation and, p66Shc gene expression was determined in peripheral blood monocytes (PBM) of patients who suffered an ischemic stroke.

**Results** Post-ischemic in vivo silencing of p66Shc resulted in a 45% reduction in stroke size and an improved neurological function 48 h after MCAO. Additionally, sip66Shc mice displayed a 50% increase in survival 6 days after stroke. sip66Shc HBEC exposed to hypoxia/reoxygenation showed a decreased ROS production compared to control. Lastly, PBM of ischemic stroke patients displayed a strongly increased p66Shc expression as compared to age-matched control subjects.

**Conclusion** The present study, underscores the concrete potential for p66Shc to become a novel target for the treatment of ischemic stroke and set the basis for follow up clinical studies.

Abstract Body:

**Background:** Pseudobulbar affect (PBA) is a disorder of emotional expression, occurring secondary to a variety of neurological conditions and characterized by uncontrollable, inappropriate laughing and/or crying episodes. Although studies suggest PBA is common following stroke, it is thought to be under-recognized. The PBA Registry Series (PRISM) was established to estimate prevalence of PBA symptoms in a clinic sample, including patients with stroke.

**Methods:** Participating sites had IRB approval and were instructed to screen ≥20 consecutive patients with any of 6 conditions associated with PBA, including stroke. Patients were not screened for depression or other psychiatric disorders. Consenting patients (or their caregivers) completed the Center for Neurologic Study-Lability Scale (CNS-LS) and a quality of life (QOL) measure assessing impact of their neurologic condition on QOL on an integer scale (0-10). Demographic characteristics and current use of antidepressants/antipsychotics were also recorded.

**Results:** PRISM enrolled 5290 participants. These results pertain to the 757 (14.3%) patients with stroke as a primary neurological condition. Mean age of patients with stroke was 68.3 years (SD 14.74; median 70), 408 (53.9%) were female, and 286 (37.8%) had symptoms suggestive of PBA as measured by CNS-LS ≥13. Patients with CNS-LS scores ≥13 reported a greater impact of their neurological condition on QOL (mean 6.7 vs 4.5; \(P<0.0001\)), and were more likely to be receiving tricyclic (19.9% vs 7.9%; \(P<0.0001\)) or nontricyclic (38.5% vs 26.5%; \(P=0.0006\)) antidepressants, than patients with CNS-LS scores <13; antipsychotic use was similar in both groups (2.8% vs. 2.1%, respectively).

**Conclusions:** These data highlight the need for greater recognition and awareness of PBA due to the potential burden of these symptoms on patients with stroke and other neurologic conditions. Furthermore, additional research should be conducted to evaluate the extent to which reduction of identified PBA episodes may impact patient outcomes.

**Author Disclosure Block:** J. Fellus: Research Grant; Significant; Avanir Pharmaceuticals, Inc. Speakers’ Bureau; Significant; Avanir Pharmaceuticals, Inc. Ownership Interest; Significant; Avanir Pharmaceuticals, Inc. Consultant/Advisory Board; Significant; Avanir Pharmaceuticals, Inc. D. Crumpacker: Consultant/Advisory Board; Significant; Avanir Pharmaceuticals, Inc. D. Kantor: Consultant/Advisory Board; Significant; Avanir Pharmaceuticals, Inc. B. Brooks: Research Grant; Significant; Biogen Idec, Avanir Pharmaceuticals, Inc. Acorda, Cytokinetics, GlaxoSmithKline Pharmaceuticals, Neuraltus Pharmaceuticals, NINDS Clinical Research Consortium, Synapse. R. Kaye: Employment; Significant; Avanir Pharmaceuticals, Inc. Ownership Interest; Significant; Avanir Pharmaceuticals, Inc.
Background: Axium MicroFx™ Coils (ev3; Plymouth, MN) contain polymer (PGLA) microfilaments designed to significantly impact intra-aneurysmal flow and to encourage aneurysm thrombosis.

Methods: AMERICA is a prospective, multi-center, 100 aneurysm observational study evaluating the safety and efficacy of Axium MicroFX PGLA coils. Enrollment was started in April 2010 and completed in October 2012.

Results: 100 aneurysms were enrolled at 13 centers. Mean patient age was 60.4 years, most were female (72%), and 18% of patients had previously undergone treatment for a separate aneurysm. Twenty-one percent of patients underwent treatment after acute aneurysmal subarachnoid hemorrhage (SAH). Of these patients, all were Hunt and Hess grade 1-3. Pre-procedure modified Rankin score (mRS) was 0-2 in 91% of patients. The majority of aneurysms were anterior circulation (85%), with the most common aneurysm locations being supraclinoid, PCOM, and ACOM (18% each). Mean maximum diameter was 6.5 mm. Fifty-one percent underwent primary coiling and 32% were stent-assisted. The mean number of coils attempted was 5.3 (range 1 to 17) and mean number of coils placed was 4.5 (range 1 to 13). Axium coils could be placed in all but one aneurysm (99%). Any device malfunction related to the coils or catheters used was identified in 11%. Raymond grade at conclusion of coiling was I (complete) in 53%, II (dog ear or residual neck) in 31%, and III (residual aneurysm) in 16%. Discharge mRS was significantly worse in SAH patients (67% mRS 0 to 2) compared to electively treated aneurysms (mRS 0-2 in 92%, p<0.01), though still associated with an excellent good outcome rate versus historical comparators. Any adverse event (AE) occurred in 27% of patients prior to discharge. Fourteen percent of patients experienced an intra-procedural AE. Major events were uncommon (5% thromboembolic events, 3% intra-operative rupture).

Conclusions: This prospective study of Axium MicroFX coils demonstrates excellent aneurysm occlusion rates. While consistent with historical data, the rate of thromboembolic events and intra-procedural rupture is not insignificant and more detailed evaluation of these events is indicated.
Abstract Body:

Purpose: Computed tomography remains the primary method of neuroimaging evaluation for acute ischemic stroke patients who are candidates for intra-arterial therapy but other imaging modalities are often used for patient triage. There remains uncertainty regarding which modality is better for patient selection.

Methods: The Penumbra START Trial was a multicenter, prospective, single-arm trial with the primary aim of testing whether core infarct size on pre-treatment neuroimaging predicts the clinical response to intra-arterial therapy. Major study criteria were presence of proximal artery occlusion of the anterior circulation, baseline NIHSS score ≥10, evaluable pre-treatment neuroimaging (noncontrast CT [NCCT], CTA source imaging, CT perfusion or MRI DWI), and treatment with the Penumbra System within 8 hours. We identified a subset of START patients who underwent both NCCT and CTA-SI. ASPECTS was graded for each modality by a blinded core imaging lab, and trichotomized the infarcts as small (8-10), moderate (5-7) and large (0-4).

Prediction of good outcomes (modified Rankin Scale ≤ 2) by infarct size was compared between the two modalities in ROC analysis.

Results: A total of 58 patients had both pre-treatment NCCT and CTA-SI data. The mean age was 66. There were 32 females (55%). Strokes involved the left hemisphere in 34 patients (59%). The median baseline NIHSS score was 20. The overall rate of TIMI 2-3 revascularization was 88%. Twenty-nine patients (50%) had a good outcome (90-day mRS 0-2); 13 patients (22%) died. The association of infarct size with outcome was statistically significant only for CTA-SI: 78% mRS 0-2 for small, 56% for moderate and 20% for large infarcts (p=0.01). For NCCT, the rate of good outcome was 52% for small, 54% for moderate and 0% for large infarcts (p=0.32). In ROC analysis, CTA-SI ASPECTS had a nominally higher c-statistic for 90-day mRS 0-2 versus NCCT (0.70 vs. 0.54, p=0.07).

Conclusion: CTA source imaging is significantly better than NCCT at predicting the clinical response to IA therapy.
Abstract Body:

SDF1-A has been shown to mobilize Hematopoietic Stem Cells (HSC)/ Hematopoietic Progenitor Cells (HPC) from the bone marrow to the blood and lead to ‘homing’ of the cells to non-CNS areas of injury. Methods: Animals underwent a murine intraluminal filament model of focal cerebral ischemia. Animals were divided into 4 groups (n=5 each): 4hrs sham surgery, 4hrs post reperfusion, 24hrs sham surgery, and 24hrs post reperfusion. Neurological deficit score was recorded and serum SDF1-A was assessed in all groups. HSC/HPC were isolated with LIN negative and SCA1 positive markers. The SDF1-A pathway was blocked using an SDF1-A antibody injected IP before and after surgery. Cell counts and brain SDF1-A levels were evaluated at 24 hours post stroke. Male HSC/HPC were injected IV into female animals both with and without the SDF1-Ab; brain tissue was sectioned and the number of Fluorescence In situ Hybridization (FISH) positive cells counted. Results: Serum SDF1-A levels were elevated at 4hrs and 24 hours compared to sham controls (107±3.8% and 137±11% versus 100±0.04% and 100±0.06%, respectively; 4hrs vs sham: P=NS, 24hrs vs sham: p<0.05). Bone marrow showed an increased production of HSC/HPC at 4 hrs (106±26%) and significantly higher at 24 hrs (272±35%). Mobilization of the HSC/HPC was slightly higher at 4 hrs (167±26%) and significantly higher at 24 hrs (606±91%; P<0.05). Neurological deficit score at 4hrs and 24hrs post reperfusion were 1.846±0.21 and 2.04±0.178, respectively. Following administration of the SDF1-A antibody, HSC/HPC failed to mobilize to the peripheral blood following stroke (bone marrow count: 536±65, blood count 132±3; p<0.05 compared to cell counts without SDF1-A antibody). SDF1-A antibody also led to a significant reduction in SDF1-A levels in the stroked hemisphere (105±3.2 versus 67±17.16; p<0.05). Following stroke, 11±1.3 FISH positive cells were counted in the brain, this number significantly dropped (1±0.4, p<0.05) following administration of the SDF1-A antibody. Conclusions: These data suggests that SDF1-A mobilization of HSC/HPC in response to cerebral ischemia may be a relevant pathway for cerebral injury repair following stroke.

**Presentation Number:** LB P16

**Publishing Title:** 7,8-Dihydroxyflavone Enhances Recovery Following Stroke via Activation of the TrkB Pathway

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**Abstract Body:**

Background: Flavonoids, found in plants and fruit, exert anti-oxidative effects. Recent studies have demonstrated that 7,8 Dihydroxyflavone (DHF) is a potent TrkB agonist mimicking Brain Derived Neurotropic Factor (BDNF), thus making it a powerful potential tool for treating neurological disorders. BDNF binds to its receptor, TrkB, to activate downstream signaling. Methods: Ischemic damage was induced in adult male SD rats (200-250g) with a peri-MCA injection of the vasoconstriction peptide ET-1. DHF or vehicle was injected intra-arterial at reperfusion. Behavior was analyzed using an open field chamber and Ethovision Software. The rats were sacrificed at 48 hours post surgery and their serum analyzed for S100B levels (a protein normally confined to the brain, with increased levels found in serum following disruption of the blood brain barrier) and brain tissue analyzed for BDNF and TrkB RNA levels. Results: The vehicle control group had a significantly higher immobility frequency (137±103) compared to that of the DHF treated group (6±3). In addition, the vehicle control group spent an average of 48 seconds exploring whereas the DHF group spent an average of 103 seconds. S100B levels were significantly lower in the DHF treated group (38±2) compared to stroke alone (63±18) and vehicle control animals (80±5). RNA levels of BDNF in the brain tissue of DHF treated animals were significantly higher (167±17) compared to vehicle control animals (53±10). Levels of TrkB RNA in the brain tissue of DHF treated animals were also significantly higher (163±16) compared to vehicle control animals (73±26). Conclusions: The results suggest that DHF can mimic Brain derived Neurotropic factor and thus may provide a therapeutic tool for treatment of neurological diseases.

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Abstract Body:

**Background:** Lowering blood pressure (BP) and reducing its variation are important for the prevention of stroke and other cardiovascular diseases in hypertensive patients. We aimed to compare BP lowering effect and diurnal BP variation between amlodipine camsylate and losartan potassium in patients with acute stroke.

**Methods:** We studied 77 consecutive hypertensive patients presenting with acute stroke who were enrolled in this randomized, single center, double-blind clinical trial. Patients were all randomly assigned to either amlodipine camsylate or losartan potassium daily for eight weeks. To evaluate whether amlodipine was non-inferior to losartan, we performed ambulatory blood pressure monitoring just before starting the drugs and at the end of the 8th week. We also analyzed BP variables including mean awake, sleep, morning, evening, prewake, nocturnal dipping status, and morning surge.

**Results:** Thirty-nine patients in amlodipine group and 38 patients in losartan group completed the 8-week follow-up. Systolic BP dropped 14.82 ± 11.71 mmHg in amlodipine group and 13.11 ± 12.69 mmHg in losartan. Intention-to-treat analysis showed non-inferiority of amlodipine to losartan (95% CI; -3.83-7.26), however, per-protocol analysis did not reveal it (95% CI; -6.88-4.65) according to the pre-defined non-inferiority margin. As to BP variation, there were no differences between the groups though amlodipine had a more tendency to blunt morning surge than losartan.

**Conclusions:** Both drugs reduced systolic BP in a similar degree and the non-inferiority of amlodipine was confirmed by intention-to-treatment analysis. Furthermore, amlodipine has a favorable effect on a morning surge.

**Author Disclosure Block:** H. Kwon: None. J. Shin: None. J. Lim: None. Y. Hong: None. Y. Lee: None. H. Nam: None.
Objective: To describe the mortality and functional outcome in patients with cerebral venous sinus thrombosis who received intrasinus thrombolysis alone versus mechanical thrombectomy with/without intrasinus thrombolysis.

Background: Small retrospective studies have shown benefit of endovascular treatment with intrasinus thrombolysis alone (IST) or in conjunction with mechanical thrombectomy (ISTMT) in cases of anticoagulation refractory CVST. Our study compares the mortality, functional outcome and peri procedural complications among patients treated with IST versus ISTMT.

Design/Methods: We reviewed clinical and angiographic findings of 63 patients with CVST who received endovascular treatment at three tertiary care centers. Primary outcome variables were discharge mortality and neurological dysfunction, and 3 and 6 month modified rankin score (mRS). mRS≤1 was considered as good recovery. Neurological dysfunction was rated as Neuroscore: 0, normal; 1, mild (ambulatory,communicative); 2,moderate (non-ambulatory,communicative); and 3, severe (nonambulatory,non-communicative/comatose). Statistical analyses were two-tailed and considered significant if p<0.05.

Results: Reasons to pursue MT in CVST patients were anticoagulation failure (84%), venous infarction with midline shift (74%) and extensive involvement of sinuses with delirium or coma (74%). AngioJet was the most commonly used MT device followed by Penumbra and Merci. In patients who received IST, presenting neurological deficits were comparatively minor(p<0.001). When two groups were adjusted for admission Neuroscore, the discharge mortality (7(21%) versus 4(13%),p=0.220) and Neuroscore (p=0.380) were similar in both groups. Rate of peri procedural complications was similar in two groups (14(41%) versus 8(21%),p=0.223). Both groups had similar rates of good recovery at 3 months and 6 months. Conclusions: As compared to IST, ISTMT was performed in more morbid patients with extensive involvement of sinuses.When adjusted for admission neurological dysfunction, both groups had similar mortality and neurological dysfunction at discharge, and functional outcome at 3 and 6 months.

The Haptoglobin (Hp) 2 allele has been previously shown to increase vascular complication risk in both type 1 and type 2 diabetes. Evidence from studies conducted in the general population, however, suggests a lower cerebrovascular disease (CBVD) risk associated with the Hp 2 allele. We, thus, assessed the association between the Hp genotype and CBVD incidence in individuals with childhood onset type 1 diabetes. Participants of the Pittsburgh Epidemiology of Diabetes Complications study without documented CBVD at baseline and data available on Hp genotype were selected for study (n=480). At study initiation (1986-88) mean age was 28 years and diabetes duration, 19 years. Stroke incidence was determined through administration of biennial surveys or physician interviews and, when possible, confirmed with medical or autopsy records. During 22 years of follow-up, 24 (4.97%) had an incident CBVD event. The greatest incidence was observed in Hp 1-1 carriers (5/59, 8.5%), with only 3.7% (8/216) of the Hp 2-1 and 5.2% (11/211) of the Hp 2-2 carriers exhibiting an event. Given the small number of events and the lower incidence in Hp 2 allele carriers compared to Hp 1 homozygotes, further analyses were conducted combining individuals with the Hp 2-1 and Hp 2-2 genotypes. In Cox proportional hazard models allowing for univariately significant risk factors, the Hp 1-1 genotype was associated with a non-significant 69% (95% CI: 0.57-4.99) increased risk of stroke. To diminish potential survival bias, we further restricted analyses to those diagnosed after 1965, wherein mortality was 13% (vs. 40% in those diagnosed before 1965). The Hp 1-1 genotype was associated with over a fourfold significantly increased risk (p=0.03) despite the reduced sample size (n=325, 9 events). The increased CBVD risk associated with the Hp 1-1 genotype in the general population, was also observed in a type 1 diabetes cohort despite the previously reported protective effect against coronary artery disease and decreases in kidney function. This mixed effect of Hp genotype on CVD risk according to outcome studied in diabetes merits further investigation and underscores the need for caution in the universal application of preventive therapies across all Hp genotypes.
OBJECTIVE: To test the efficacy of aggressive anti-platelet treatment for acute penetrating artery (PA) infarcts. 

BACKGROUND: Larger PA infarcts (LPAI) that are predominantly caused by occlusion at the vessel orifices of lager caliber PA by atheromatous plaque frequently show progressive motor deficits (PMD) in acute stage leading to poor functional outcome.

DESIGN/METHODS We have prospectively collected and tried to treat 325 consecutive patients with acute LPAI in the territories of lenticulostriate artery, anteromedial pontine artery and anterior choroidal artery since January 2001 up to September 2012. Between January 1, 2001 and October 30, 2005 (phase 1), the treatment protocol was tailored to the individual patient that was considered optimum on each occasion but generally included drip infusion anti-platelet agents. Between November 1, 2005 and October 30, 2009 (phase 2), we consistently provided combined treatment with cilostazol (200mg per day) and argatroban hydrate. Between November 1, 2009 and September 30, 2012 (phase 3), we consistently added a 300-mg loading dose of clopidogrel on day 1, followed by 75 mg once daily on top of the phase 2 regimen. We compared a functional outcome represented by modified Rankin Scale 3 month after ictus using the Wilcoxon Mann-Whitney test and prevalence of PMD, using phase 1 as reference.

RESULTS: There was no hemorrhagic event during and after the treatment. There was no significant difference in the prevalence of PMD between the 3 phase groups (48%, 49%, 44%, respectively). The phase 2 and the phase 3 had significantly more favorable outcomes than the phase 1 (p= 0.0022 for phase 2 versus phase 1 and p<0.0001 for phase 3 versus phase 1, respectively). The phase 3 showed more favorable outcomes than the phase 2 but did not reach statistically significant. (p=0.0767).

CONCLUSIONS: The more aggressive is the anti-platelet treatment, the better improved the functional outcome in patients with acute LPAI.
Presentation Number: LB P21

Publishing Title: Early Post-admission Intracerebral Hematoma Expansion

Author Block: Christian Ovesen, Louisa Christensen, Anders Christensen, Sverre Rosenbaum, Derk Krieger, Inger Havsteen, Hanne Christensen, Bispebjerg Univ Hosp, Copenhagen, Denmark

Abstract Body:

Background: Reducing early post-admission hematoma expansion (EHE) may represent a treatment target in ICH. The “spot-sign” observed on CT-angiography (CTA) predicts EHE with high sensitivity. We investigated (1): If “the spot sign” predicted global functional outcome, and further (2) explored if the temporal profile of early hematoma expansion would allow a treatment window for heamostatic treatment.

Method: Consecutive patients admitted to our stroke-ward within 4.5 hours of symptom onset were prospectively registered; 118 patients had a final diagnose of spontaneous ICH from 2009 - 2012. To investigate the temporal profile of EHE, consecutive patients from 1st September 2011 underwent serial hematoma volume measurements by transcranial B-mode Ultrasound: every 30 minutes during the first 6 hours, and from 6 - 12 hours every 2 hours. Follow-up CT was performed after 24 hours. Outcome was assessed by modified Rankin Scale (mRS) at 3 months.

Results: 31 patients (26%) had “spot-sign” on admission CTA. Median 3 month mRS in the spot sign positive group was 6 vs. 3 in the spot sign negative group. The spot sign was a significant predictor for miserable outcome (mRS 5-6) (OR, 5.57, P>0.001) and death alone (HR, 3.92, P>0.001).

23 patients completed the ultrasound study until 1st November 2012. 30% of patients expanded within 30 minutes after admission-scan. After 3.5 hours, expansion was observed in only 10%. No expansion was observed 4 hours after admission, figure 1.

Conclusion: The spot-sign represents a good method for selection of patients for haemostatic trials. A treatment window defined by ongoing bleeding exist in the first hours after admission.

Author Disclosure Block: C. Ovesen: Research Grant; Significant; Research grant from The Lundbeck Foundation, Research grant from Eva and Henry Frænkels Memorial Foundation. L. Christensen: None. A. Christensen: None. S. Rosenbaum: None. D. Krieger: None. I. Havsteen: None. H. Christensen: None.
Abstract Body:

Background: Caffeine is a commonly consumed active ingredient worldwide and is a potent antagonist for Adenosine receptor A1 and A2A. Adenosine modulates cellular functions by interacting with specific cell surface G-protein coupled receptors (A1, A2A, A2B and A3). The A1 receptor has been implicated in angiogenesis, the A2A receptor in vasodilation and regulating glutamate and dopamine release in the brain, the A2B receptor in angiogenesis and stimulation of adenylate cyclase in the presence of adenosine and the A3 receptor in inflammation and cell death. In this study we evaluated the protective effects of low levels of caffeine on the brain following stroke. Methods: Twelve SD rats underwent stereotaxic intracortical injection of Endothelin-1 (3ul; 80pmol). Eight of the animals received the Adenosine receptor antagonist caffeine (25mg/ml, IP), 30 minutes prior to Endothelin-1 administration. Neurological deficit score (Bederson/Garcia) was recorded at 24 hours post reperfusion prior to euthanasia. Infarct volumes were confirmed using TTC staining of 2 mm sections of the brain. Brain tissue was harvested for mRNA analysis of the A1, A2A, A2B and A3 receptors; mRNA was reverse transcribed and amplified using gene specific primers for the 4 receptors. Results: Neurological deficit score (Garcia scale) was significantly lower in the stroke+caffeine group (0.5±0.5) compared to stroke alone (1.7±0.5). The neurological score (Bederson scale) was not significant for the stroke alone versus stroke+caffeine groups (14.2±1.3 versus 16.4±1.7, respectively). Mean infarct volume for stroke alone was 50±42 and for stroke+caffeine was 4±5. Animals treated with caffeine had significantly higher RNA expression of Adenosine receptors A1 (Stroke alone: 102±25; stroke+caffeine: 1451±226), A2A (Stroke alone: 141±109; stroke+caffeine: 1043±520) and A2B (Stroke alone: 106±38; Stroke+ caffeine: 218±51) in brain tissue at 24 hours post reperfusion compared to stroke alone. No significant difference was found in Adenosine receptor A3 levels in either group (stroke alone: 119±79; stroke+caffeine 194±79). Conclusions: The results suggest that low levels of caffeine may protect the brain by up regulating expression of adenosine receptors A1, A2A and A2B.

Author Disclosure Block: A. Afzal: None. F. Desland: None. J. Mocco: None.
Presentation Number: LB P23

Publishing Title: Hematopoietic Stem Cell Function is Impaired Following Exposure to tPA, Thus Limiting Recovery following Stroke

Author Block: Aqeela Afzal, Vanderbilt Univ Medical Ctr, Nashville, TN; Saeed Ansari, Univ of Florida, Gainesville, FL; Fiona Desland, Vanderbilt Univ Medical Ctr, Nashville, TN; Edward Scott, Univ of Florida, Gainesville, FL; J Mocco, Vanderbilt Univ Medical Ctr, Nashville, TN

Abstract Body:

Background: Intravenous Tissue Plasminogen Activator (tPA) is the only FDA approved pharmacological recanalization therapy for stroke, however tPA has been associated with deleterious effects on the blood brain barrier in experimental models. A potential contributor to vascular integrity and/or repair following stroke are Hematopoietic Stem Cells (HSCs)/ Hematopoietic Progenitor Cells (HPCs), circulating bone marrow derived mononuclear cells that promote repair in areas of injury. We hypothesized that tPA inhibits HSC/HPC’s function, potentially limiting tPA’s beneficial effects in acute stroke therapy. Methods: Animals were divided into 3 cohorts (n=6 each): sham, stroke alone and stroke+tPA and subjected to a murine intraluminal filament model. Infarction was confirmed using TTC staining of 2 mm sections of the brain. SDF1-A levels in serum were determined using an ELISA. HSC/HPC were harvested from bone marrow and blood using LIN negative and SCA1+ labeled nanoparticles. The harvested cells were counted using a hemacytometer; the HSC/HPC were then migrated towards SDF1-A in a Boyden Chamber. Experiments, and their analysis, were performed in a blinded manner. Results: Infarct volume was significantly reduced in the stroke+tPA animals (stroke alone: 60±15, stroke+tPA: 29±14). Serum SDF1A levels were significantly elevated in stroke alone (136±20) and decreased significantly in stroke+tPA (71±21) compared to sham (100±63). Bone marrow cell counts were significantly elevated in the stroke alone group (279±63) and the tPA+stroke group (229±49) compared to sham (99±24). Mobilization of these cells to the peripheral blood was significantly elevated in the stroke alone group (606±159) and significantly reduced in the tPA+stroke group (3.5±2.3) compared to sham (99±13). Bone marrow from the tPA+stroke group also had a significantly depressed migration towards SDF1-A (0.6±0.8) compared with sham (5±3) and stroke alone (8±4). Conclusion: These results suggest that tPA may reduce the ability of the HSC/HPC to home to ischemic brain following stroke and possibly interferes with repair mechanisms associated with HSC/HPC.

Author Disclosure Block: A. Afzal: None. S. Ansari: None. F. Desland: None. E. Scott: None. J. Mocco: None.
Abstract Body:

Background: Stem cell (SC) therapy has been envisioned as a therapeutic vehicle to promote recovery in resistant neurological diseases. Knowing the logistics and paradigms in recovery processes after Stroke, the disease has pioneered the transplantation therapy. This study presents three year follow up of intravenous mesenchymal stem cells (MSCs) transplantation in patients with chronic stroke.

Methods: We performed an open-label, clinical trial of 12 patients with chronic stroke. Patients were allocated to two groups, those who received intravenous autologous ex vivo cultured MSCs (MSC group) or those who did not (control group), and all were followed for up 3 years from the day of cell transplantation. Clinical and radiological imaging was performed for all patients as outcome measures. MSC was cultured using Stem Pro MSC SFM basal medium (A-10334, Invitrogen) in a T-25 tissue culture flask and incubated at 37°C/5%CO2. Patients were evaluated for safety, i.e. laboratory and radiological tests at repeated intervals till three years. Results and Discussion: The reports have been optimistic regarding safety as we did not find any cell related side effects / mortality till the last follow up (156th week). We observed that modified Barthel Index showed statistical significant improvement at 156th week (95 % CI : -10.27 to 0.07; p =0.041) follow up in the MSC group as compared to controls. The 2nd and 3rd quartile for m BI in MSC group was 89 & 90 respectively suggesting good performance of patients in the stem cell group. The impairment scales i.e., Fugl Meyer, ashworth tone scale, strength of hand muscles (MRC) did not show any significant improvement at 156th week which is similar to our previous published report. This follow up presents behavioural benefits but primarily indicates safety, tolerance and applicability of ex vivo culture expanded mesenchymal stem cells in Stroke which may be used in future clinical trials.

### Table 1: Clinical outcomes in experimental (MSC) and control groups.

<table>
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<th>Months</th>
<th>Area of Lesion</th>
<th>BI Score</th>
<th>1st week</th>
<th>2nd week</th>
<th>3rd week</th>
<th>4th week</th>
<th>8th week</th>
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E: Experimental. C: Control

Author Disclosure Block: A. Bhasin: None. V.P. Srivastava: None. R. Bhatia: None. S. Kumaran: None. S. Mohanty: None.
**Abstract Body:**

**BACKGROUND:**
The incidence of unruptured intracranial aneurysm is increasing due to higher utilization of neuroimaging and aging population. The treatment decisions are based on the estimated risk of rupture of intracranial aneurysms but factors associated with higher risk are not well understood.

**METHODS:**
We conducted a systematic review of clinical studies published in English up to October 2012. A literature search of MEDLINE, PubMed, and Cochrane databases was supplemented by a review of bibliographies of relevant articles and personal files. We included studies reporting original data on aneurysmal rupture in patients with unruptured intracranial aneurysms. Two authors independently extracted data and evaluated study quality.

**RESULTS:**
We identified 10 eligible studies with 15,923 persons with unruptured intracranial aneurysms and average follow-up of 4.8 years. There were 435 primary aneurysmal ruptures with a pooled incidence (per 100 person years) for primary aneurysmal rupture was 0.57 (95% confidence interval [CI] 0.51-0.62). Women (compared with men) had a significantly higher rate of aneurysmal rupture (7 studies, odds ratio [OR] 1.69; 95% CI 1.21-2.37). Intracranial aneurysm size ≥10 mm (6 studies, OR 6.56; 95% CI 3.18-13.52) and posterior circulation location (5 studies, OR 2.79; 95% CI 1.98-3.91) were significantly associated with risk of aneurysmal rupture. Initial presentation with clinical symptoms was also associated with aneurysmal rupture (4 studies, OR 2.94; 95% CI 1.68-5.17). History of previous subarachnoid hemorrhage from another aneurysm (8 studies) and current cigarette smoking (2 studies) were not associated with aneurysmal rupture. Funnel plot statistical test did not identify any significant publication bias (Begg's test >0.05).

**CONCLUSIONS:**
Factors other than size of the intracranial aneurysm including gender, location, and symptomatic status determine the risk of primary aneurysmal rupture in patients with unruptured intracranial aneurysms.

**Author Disclosure Block:**  
S. Majidi: None.  
L.J. Brau: None.  
A.I. Qureshi: None.
**Abstract Body:**

Diabetics are more likely than non-diabetics to suffer a stroke in their lifetime, and their prognosis for recovery is poor. We have previously shown that diabetic mice have chronic behavioral deficits and limited cortical remapping following stroke (Sweetnam et al., *J Neurosci*, 2012). However, the mechanism preventing recovery is unclear. Diabetes is known to have deleterious effects on the vasculature of other organs, but little is known about how diabetes affects the vasculature of the brain. We hypothesized that blood flow dynamics in the diabetic brain are dysfunctional in the acute and/or chronic periods after stroke, and this dysfunction contributes to poor recovery. We used longitudinal *in vivo* two photon imaging through a chronically implanted cranial window to track changes in blood flow dynamics of cortical microvessels before and after photothrombotic stroke (or sham procedures) in diabetic and non-diabetic mice. In the non-diabetic brain, there was an initial increase in blood flow velocity, lumen diameter, and red blood cell flux in peri-infarct cortex. By 7 days post-stroke, all measures of blood flow dynamics returned to baseline levels. In the diabetic brain, the initial post-stroke response was the same. However, the return to baseline was slow or non-existent. Lumen diameter and flux measurements did not normalize until at least 2-4 weeks after stroke. Blood flow velocity remained elevated throughout the chronic post-stroke imaging period (6 weeks). In order to probe for changes in blood-brain barrier integrity after stroke, we performed intravital injections of Evans Blue dye and confocal imaging of brain tissue. Relative to non-diabetics, vessel “leakiness” increased significantly in the diabetic brain acutely (3 days) post-stroke, but normalized by 7 days. Preliminary data from sham operates suggests that long-term uncontrolled diabetes, even in the absence of ischemia, may be a risk factor for vascular dysfunction and “mini-strokes”. These data provide evidence that diabetes alters the brain's vascular response to ischemic stroke. It is conceivable that these dysfunctional vessels could impair stroke recovery by further damaging or impeding the rewiring of surviving neural circuits.

**Author Disclosure Block:**  K.A. Tennant: None. P. Reeson: None. C.E. Brown: None.
Abstract Body:

Background and Purpose: Hematoma expansion is a major factor of poor neurological outcome in patients with intracerebral hemorrhage (ICH). Contrast medium extravasation (CE) is a marker of ongoing bleeding and a predictor of hematoma expansion. In an experimental model of anticoagulation-associated ICH, we compared CE between saline-, dabigatran- and warfarin-treated animals.

Methods: CD1-mice were fed with saline, dabigatran or warfarin. ICH was induced by a stereotactic injection of collagenase type VII into the right striatum. 3 h after ICH induction, 350 µl of contrast agent (Isovue 370 mg/ml) was injected intravenously over 5 minutes. Thirty minutes later, CE was evaluated by quantifying the iodine content in the hematoma using dual-energy computed tomography (DECT). Hemorrhage volume was determined by a photometric hemoglobin assay.

Results: In saline-treated animals, INR was 0.9±0.0, and PTT was 24.3±1.1 sec. Warfarin pre-treatment increased INR values (5.4±2.3), whereas dabigatran mice had elevated PTT values (71.4±4.8 sec). Regarding CE after ICH induction, no significant difference appeared between saline and dabigatran mice (6.1±1.0 µg vs 6.2±1.1 µg). In contrast, CE was significantly increased in the warfarin group (15.7±0.8 µg). Warfarin mice showed a significant 1.5 fold higher hemorrhage volume compared to saline-treated animals (18.9±2.6 µl vs. 12.1±1.6 µl). No difference was found between dabigatran mice and saline controls.

Conclusion: We refined a recently developed model of anticoagulation-associated ICH and used DECT to quantify CE. Whereas warfarin anticoagulation was clearly associated with increased CE compared to saline controls, no difference was found between dabigatran mice and controls. ICH occurring during dabigatran anticoagulation seems to expand less critically than bleedings under warfarin anticoagulation. This constitutes a potential safety advantage of the new oral anticoagulants over vitamin K antagonists.

Presentation Number: LB P28

Publishing Title: Mechanical Thrombectomy for Cerebral Venous Sinus Thrombosis: A Multi-center Experience

Author Block: Chirantan Banerjee, Fazeel Siddiqui, UT Southwestern Medical Ctr, Dallas, TX; Yvonne Zuurbier, Univ of Amsterdam, Amsterdam, Netherlands; Qing Hao, UCLA Medical Ctr, Los Angeles, CA; Chul Ahn, Glenn Pride, UT Southwestern Medical Ctr, Dallas, TX; David Liebeskind, UCLA Medical Ctr, Los Angeles, CA; Mark Johnson, UT Southwestern Medical Ctr, Dallas, TX; Jan Stam, Univ of Amsterdam, Amsterdam, Netherlands

Abstract Body:

Objective: To describe indications, methods, associated complications, mortality, angiographic and functional outcome of Mechanical thrombectomy (MT) with concomitant systemic anticoagulation with/without intra-sinus thrombolysis (IST) in patients with cerebral venous sinus thrombosis (CVST).

Background: CVST is rare but potentially devastating. Systemic anticoagulation remains initial treatment of choice, but IST with or without MT is increasingly used in refractory cases, and in cases with venous infarction. MT has evolved with time, and studies have established feasibility. We present a series of 34 patients treated with MT and systemic heparin, with/without IST.

Design/Methods: Retrospective review of clinical and angiographic findings in 34 patients who underwent MT with heparin with/without IST for CVST at three tertiary care centers from 1995-2012 was carried out. Discharge mortality, recanalization rates, peri-procedural complications, and 3 and 6 month modified Rankin score are reported. Good functional outcome was defined as mRS≤1.

Results: MT was generally reserved for patients who deteriorated despite anticoagulation (84%), had associated venous infarction with midline shift (74%), or had extensive involvement of sinuses with delirium or coma (74%). AngioJet was used in 28 patients, Penumbra system in 3 patients and MERCI device in 1 patient. Plain angioplasty was attempted in 2 patients. Technical difficulties were encountered in 3 AngioJet and 1 angioplasty cases. Post-procedure re-canalization was recorded in 32 patients. 16 (50%) patients had near to complete re-canalization, 13 (41%) had partial re-canalization, and 3 (9%) patients did not re-canalize. Penumbra and MERCI devices achieved 100% complete re-canalization. IST was used in 27 (79%) patients. 23 patients received urokinase and 4 received tPA. Peri-procedural complications occurred in 14 (41%) patients, including 7 deaths. 17/32 (53%) patients had a good functional outcome at 3 months and 16/29 (55%) at 6 months. 1 patient had recurrence of CVST.

Conclusions: MT achieves good recanalization, and is a viable option in treatment refractory CVST. Selection bias in retrospective studies restricts comparison of outcomes with IST or heparin.

Abstract Body:

Introduction. Despite the growing evidence for the effects of robotic stroke rehabilitation on motor function, little is known about who may most likely to benefit from the therapy. This research examined factors predictive of clinically important change in motor function outcome in stroke patients receiving robot-assisted rehabilitation.

Methods. This study involved 33 patients with chronic stroke who received robot-assisted therapy based on the bilateral training approach for a period of 4 weeks. Motor function was evaluated using the Fugl-Meyer Assessment (FMA) before and immediately after the treatment. Potential predictors included age, time post onset of stroke, treatment intensity, manual dexterity measured by the Box and Block Test (BBT), and distal motor impairment of the affected upper limb measured by the FMA. We used logistic regression analyses to study relative importance of these factors for predicting meaningful change in motor function outcomes. Level of clinically important change in motor function was determined based on the threshold values of minimal detectable change of the FMA.

Results and Conclusions. Manual dexterity and higher intensity of therapy were identified as significant predictors of clinically important change on the FMA after the therapy ($P < 0.05$). The findings suggest the importance of dexterous function for achieving meaningful improvement in motor function after robot-assisted stroke rehabilitation. The BBT may be used to facilitate patient selection for optimizing this rehabilitative therapy. Further research based on a larger sample with varying characteristics is needed to validate the findings. In addition, further research may include additional predictors such as bimanual arm use.

Author Disclosure Block: K. Lin: Research Grant; Modest; National Science Council and National Health Research Institute in Taiwan. Y. Hsieh: None. C. Wu: Research Grant; Modest; National Science Council and National Health Research Institute in Taiwan.
Abstract Body:

**Background** Low socioeconomic status may be associated with the mortality in the patients with acute myocardiac infarction (AMI) and stroke in many studies; however, the mechanism behind this association and the influence with insurance plan are uncertain. Our study aimed to determine whether the patients with very low income were associated with higher mortality rates after AMI and stroke.

**Methods** All the hospitalizations for AMI and stroke in one million beneficiaries data during April 2005 to March 2008 were identified from the national insurance database. Our data contains patient-level sociodemographic, diagnostic, procedural and treatment information. Patients were than assigned to three groups based on the mean income of the nation ($13529 in 2004 and $15276 in 2009) and categorized as the very poor, lower income (lower than the mean income) or higher income (higher than the mean income). The very poor patients were recognized by the special codes issued by our social welfare system that have zero copayment for hospital admission. Multivariable analyses were performed to compare the in-hospital mortality rates for the AMI and stroke patients in these three groups.

**Results** Overall, 1285 AMI, 862 hemorrhagic stroke and 2133 ischemic stroke patients were included in the analysis. There was no significant difference in mortality rates in the three groups. Compared with the higher income group, the odds ratios of in-hospital mortality for the very poor patients in AMI was 1.51 (OR = 1.51, 95% C.I = 0.28-8.26). The odds ratios of in-hospital mortality for the very poor patients in hemorrhagic stroke was 1.92 (OR = 1.92, 95% C.I = 0.18-21.38). And the odds ratios of in-hospital mortality for the very poor patients in ischemic stroke was 1.45 (OR = 1.45, 95% C.I = 0.15- 14.13).

**Conclusions** Compared with the other patients, the mortality rates in the very poor patients presenting with AMI and stroke have insignificant higher mortality rates under our insurance plan. Understanding the pathways through which socioeconomic status affects health care may lead to the strategies for the quality improvement.

**Author Disclosure Block:**  D. Harnod: None. R. Chang: None. C. Chang: None.
**Presentation Number:** LB P31

**Publishing Title:** Perlecan Domain V Is A Neuroprotective and Neuroregenerative Experimental Stroke Therapy

**Author Block:** Michael Kahle, Texas A&M Coll of Med, College Station, TX; Stephen Grupke, Jill Roberts, Univ of Kentucky, Lexington, KY; Emma Gowing, Andrew Clarkson, Univ of Otago, Dunedin, New Zealand; **Gregory Bix**, Univ of Kentucky, Lexington, KY

**Abstract Body:**

We need new stroke therapies! Besides the marginal success of the clot-buster t-PA, attempts to protect neurons and further improve stroke patient outcomes have failed. To that end, we have identified perlecan domain V (DV) as a potential novel stroke therapy that is both neuroprotective and a promoter of neurorepair, specifically enhancing post-stroke angiogenesis, neurogenesis, neuronal migration and repopulation of stroked brain tissue. Importantly, DV is an extracellular matrix fragment that is produced rapidly and persistently in situ in both rodents and in human stroke patients, hinting at its translational potential. In two different experimental transient middle cerebral artery occlusion stroke models, DV reduced infarct volume and rapidly restored sensorimotor function to pre-stroke levels. We now report on the efficacy of DV in a 3rd stroke model, photothrombotic permanent middle cerebral artery occlusion in both young adult and aged mice (an important distinction as stroke is more common in the aged population but understudied due to increased post-stroke mortality). When initiated within 3 to 12 hours after photothrombosis, intraperitoneal DV treatment reduced infarct volume measured at post-stroke day 7 and significantly improved sensorimotor function in both age groups. Importantly, DV also increased neurogenesis and the number of immature neurons both emerging from the subventricular zone and migrating into the peri-infarct area (as measured by doublecortin immunohistochemistry). Furthermore, many new neurons were found in the infarct region of DV treated animals (but not in vehicle treated controls) 14 days after injury. In vitro analysis using mouse neural stem cells cultured as neurospheres demonstrated that DV treatment increased neural stem cell proliferation, migration, and preferentially promoted their differentiation into neurons versus other potential cell fates (astrocyte, etc.). Collectively, these results suggest that perlecan DV is a novel neuroprotective and neuroregenerative ischemic stroke therapy worthy of further study.

**Author Disclosure Block:** M. Kahle, None; S. Grupke, None; J. Roberts, None; E. Gowing, None; A. Clarkson, None; G. Bix, None.
Presentation Number: LB P32

Publishing Title: A Fast Track Protocol for Symptomatic Carotid Surgery

Author Block: Michel van Jagt, Michiel Warle, J. Adam van Vliet, Frank van Hoek, Univ Medical Ctr St Radboud, Nijmegen, Netherlands

Abstract Body:

Introduction: Timing of surgery for symptomatic high grade carotid stenosis is essential to prevent additional neurological damage. The preferred timing is within two weeks after the first onset of neurologic symptoms according to the literature. In our practice we did not fulfill those criteria and therefore we implemented a fast track carotid protocol in 2011. Aim of this study is to show the clinical relevance of the implementation of such a protocol.

Methods: A retrospective study to evaluate the clinical relevance of a fast track carotid protocol (Fast), compared to a historic cohort (Standard) in the same hospital in the period 2006-2007. The protocol is a simple flowchart that is initiated after a referral and directed by a nurse practitioner. Visits to the outpatient clinics for the vascular surgeon, anesthetist and the vascular laboratory are combined on one day by reserving slots. Standard operation time slots are weekly reserved for these group of patients.

Results: There were 44 patients in the Standard group and 51 patients in the Fast group. The time between the first neurologic event and surgery was 74±62 days in the Standard group and 24±18 days in the Fast group (p<0.001). Surgical treatment within the preferred 14 days succeeded in 7% (Standard) and increased with the protocol to 25% (Fast). Using standard operation time slots decreased the waiting period for surgery from 16±16 days (Standard) to 10±8 days (Fast)(n=0.03). The percentage of patients with a second neurologic event during the waiting period for surgery diminished from 46% (Standard) to 12% (Fast) with a mean waiting time for surgery of 103±71 days (Standard) and 17±7 days (Fast). These second neurologic events occurred after a mean period of 57±53 days (Standard) and 8±7 days (Fast). If in these patients surgery was performed in the preferred period of 14 days after the first neurologic event a second event could have been prevented in 20 patients in the Standard group and 1 in the Fast group.

Conclusion: This retrospective study emphasizes the clinical need of a good fast track carotid protocol in order to reduce additional neurological deficits in the waiting time for carotid surgery.

**Abstract Body:**

Background: Surgical management of acute stroke patients is an area of interest and study. We investigated the risk of subsequent stroke in all patients who underwent surgical treatment in all public hospitals in England. The risk of stroke was calculated based on person-years of observation. A retrospective cohort was constructed of all people who had a record of hospital admission for an ischaemic stroke and surgical treatment. A comparison cohort comprised people admitted for a wide range of minor medical and surgical conditions (intended by us to be representative of the general population). The rate of subsequent stroke in the ‘surgical’ cohort was compared with the rate of stroke in the comparison cohort; and expressed as a rate ratio (RR) with 95% confidence intervals (CI). The comparison between the cohorts was stratified by age, sex, admission year, area of residence and socio-economic status, such that the cohorts were equivalent in these respects in the final summary comparisons.

Results: The RR of subsequent ischaemic stroke was significantly and substantially high in people who underwent surgery, but its level differed depending on the type of surgery. After carotid artery reconstruction it was 4.6 (4.4 - 4.7, based on 3759 observed cases of subsequent stroke); after graft replacement of carotid artery 8.2 (5.62 - 11.6, based on 32 subsequent strokes); after carotid bypass 8.0 (5.7 - 10.9, based on 40 cases); carotid endarterectomy 4.5 (4.4 - 4.7, based on 3667 cases); open and transluminal intervention on carotid artery 6.9 (6.1 - 7.72) and 7.2 (6.9 - 7.6), respectively; embolectomy of carotid artery 23.1 (17.9 - 29.3 based on 67 cases); open and transluminal operations on cerebral arteries 8.2 (6.2 - 10.6, based on 57 cases), and 10.3 (9.9 - 10.7, based on 3229 cases), respectively; after percutaneous transluminal embolisation of cerebral artery 10.2 (9.4 - 11.1, based on 547 cases).

Conclusion: Findings of a substantially increased risk of subsequent ischaemic stroke in patients who were admitted to hospital with stroke and underwent surgery emphasise the importance of improving secondary prevention of stroke in the survivors of first stroke.

**Author Disclosure Block:** O. Seminog: None. M.J. Goldacre: None.
Recent data demonstrated that angiotensin-(1-7) [Ang-(1-7)] or the angiotensin type 2 receptor (AT2R) agonist Compound 21 (C21) exert significant cerebroprotective actions against ischemic stroke. Based on these findings, and recent evidence of dimerization between AT2R and the Ang-(1-7) receptor Mas, we tested whether the Mas antagonist A-779 can alter the cerebroprotective actions of C21 against ischemic stroke produced by endothelin-1 (ET-1) induced middle cerebral artery occlusion (MCAO). Adult male Sprague Dawley (SD) rats were pre-treated with A-779 (0.0075ug/h) or artificial cerebrospinal fluid (aCSF) via intracerebroventricular (ICV) infusion for 7 days prior to ET-1 induced MCAO. IP administration of C21 (0.03 mg/kg) at 4 and 12 hours post-MCAO significantly reduced the cerebral infarct size to 19.48±2.0% of ipsilateral gray matter, and attenuated the associated neurological deficits (Bederson Exam Score [BES]) of 0.75±0.14 and Garcia Exam Score [GES] of 17.25±0.27, when compared with rats that had received IP 0.9% saline at the same time points (42.76±4.2% infarct, 1.54±0.18 BES, 15.38±0.36 GES; P<0.0001, n=9-13). ICV infusion of A-779 abolished the treatment effect of C21 on infarct size (35.00±2.8%) and neurological deficits (BES of 1.50±0.18 (p=0.0006) and GES of 15.56±0.36 (p=0.0004), measured 72 h after MCAO induction (n=13-16). ICV infusion of A-779 alone had no significant effects on infarct size or behavioral scores. These data support the idea that the cerebroprotective action of C21 either involves activation of Mas or that due to AT2R-Mas-heterodimerization, blockade of the receptor Mas also prevents signaling of the AT2R.
**Presentation Number:** LB P35

**Publishing Title:** Global SUMOylation is an Underlying Molecular Mechanism In Hypothermia-Induced Ischemic Tolerance

**Author Block:** Yang-ja Lee, Yongshan Mou, Dace Klimanis, John M Hallenbeck, The Natl Inst of Neurological Disorders and Stroke, Bethesda, MD

**Abstract Body:**

Background: Despite reproducible demonstrations of hypothermic neuroprotection and active pursuit of clinical trials of hypothermic therapy in stroke patients, the cellular and molecular mechanisms underlying hypothermic neuroprotection are not fully understood. Here we examined global SUMOylation, a form of post-translational modification with the Small Ubiquitin-like MOdifier, as a possible multimodal molecular mechanism for hypothermia-induced ischemic tolerance.

Methods: By means of a human neuroblastoma cell line (SHSY5Y), primary rat cortical neuronal cultures, and mice (wild type and Ubc9 transgenic), the effects of hypothermia treatment on SUMO-conjugation levels and degree of ischemic tolerance were examined. We particularly focused on whether Ubc9 transgenic mice, which overexpress the sole SUMO conjugating enzyme and have increased levels of global SUMOylation even in normothermic conditions, would show as large a hypothermia-induced increase in brain cytoprotection against pMCAO as wild-type animals.

Results: Hypothermia treatments during OGD (oxygen-glucose-deprivation) and/or ROG (recovery from oxygen/glucose deprivation) increased SUMO conjugation levels and protected cells (SHSY5Y, rat cortical neurons) from OGD- and/or ROG-induced cell death. Hypothermia exposure either before (A) or after (B) pMCAO surgery in wild type mice increased brain SUMO global conjugation levels and protected these animals from pMCAO-induced brain damage; hypothermia exposure did not further increase brain protection from pMCAO-induced brain damage in Ubc9 transgenic mice.

Conclusion: An increase in global SUMOylation is sufficient for an exposure to hypothermia to increase cellular tolerance to brain ischemia and OGD. It is likely that global SUMOylation modulates, perhaps in concert with other components of the biological network, the multimodal changes in network dynamics that result in tolerance to the stresses of ischemia and OGD.

**Author Disclosure Block:** Y. Lee: None. Y. Mou: None. D. Klimanis: None. J.M. Hallenbeck: None.
**Abstract Body:**

Background and Purpose: Recent studies have elucidated that the bone marrow stromal cells (BMSC) transplantation have the therapeutic potential against stroke. This study aimed to clarify their neuroprotective effects in vitro and in vivo by secreting some neurotrophins.

Methods: The mice neurons exposed to glutamate were cocultured with mice BMSC. The neutralizing antibodies of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF), or K252a were added to the coculture system, and the cell viability was assayed. The cultured BMSC were processed for fluorescence in situ hybridization (FISH) for BDNF or NGF. In the study in vivo, the Balb/c mice were subjected to permanent focal ischemia and 2×10^5 BMSC derived from green fluorescence protein (GFP)-mouse or vehicle were stereotactically injected into the ipsilateral striatum at 7 days after ischemia (n=10 in each group). They were sacrificed 2 or 4 weeks after the transplantation. The immunostaining against NeuN or MAP-2 was performed to the brain sections. The sections were also processed for FISH and immunostaining against GFP.

Results: The BMSC ameliorated glutamate-induced neuronal death in vitro (P<0.01), and anti-BDNF antibody reduced the protective effect (P<0.05). Also, the treatment with anti-NGF antibody or K252a had a tendency to decrease the cell viability. FISH analysis showed that most BMSC expressed mRNA of BDNF (89.1 ± 2.9%) and NGF (82.6 ± 7.3%) in vitro. When BMSC were transplanted into the ischemic brain, the density of NeuN-positive cells was higher in peri-infarct area (BMSC: 92.4 ± 9.7%, vehicle: 73.2 ± 9.2% vs the contralateral side, P<0.05). FISH analysis showed that half of BMSC expressed mRNA of BDNF (55.9 ± 12.7%) and NGF (56.6 ± 14.3%) 2 weeks after transplantation, but the percentages were decreased in 4 weeks (BDNF: 35.0 ± 13.9%, NGF: 34.1 ± 9.7%; P<0.05, respectively). About the neural transdifferentiation in vivo, the numbers of MAP-2-coexpressing BMSC were increased with the passage of time (2 weeks: 26.2 ± 9.2%, 4 weeks: 73.9 ± 7.2%, P<0.01).

Conclusions: This study clarified that BMSC have the neuroprotective effects in vitro and in vivo by secreting neurotrophins. BMSC have a biphasic therapeutic effect, and ‘nursing effects’ might play a key role in early stage.
Abstract Body:

Purpose
The LUNA Aneurysm Embolization System (AES) is a newly designed self-expandable, round-ovoid implant made from a double layer of 72 Nitinol 25μ wires for the endovascular treatment of intracranial aneurysms. A prospective international multicenter study (aiming at including a total of 63 patients) has been designed to evaluate the safety, performance and efficacy of this novel device based on the concept of intra-aneurysmal flow diversion while maintaining patency of the parent artery.

Methods
Immediate post-implantation angiographic occlusion and parent vessel compromise were evaluated. Patients underwent neurological testing with the Modified Rankin Scale and the National Institute of Health Stroke Scale (NIHSS) at baseline and time of discharge. Follow-up included clinical assessment at one month and 3 months, clinical and angiographic follow-up at 6 and 12 months.

Results
Thirty-five patients (30 women, 5 men) with 35 unruptured and one ruptured saccular aneurysms (16 ICA, 9 MCA, 8 AcoA, 2 basilar tip, 1 PCA, sizes from 5.0 to 8.7 mm) were enrolled to date in the study. One AES was deployed per aneurysm. In 4 cases, the AES embolization was carried out with balloon microcatheter assistance. In one case, the AES embolization was carried out with a stent. In 1 case, AES placement led to aneurysm perforation that was controlled by temporary balloon occlusion and heparin reversion. In 1 case, thrombo-embolic complication was treated with i.a. injection of Abciximab. Immediate complete occlusion was obtained in 11 cases, near complete occlusion was obtained in 12 cases, no occlusion in 13 cases. Clinical follow up was uneventful. To date, 12 patients with 13 aneurysms had follow-up with angiography at 6 months, showing complete occlusion in 6 cases, neck remnants in 4 cases, incomplete occlusion in 3 cases. Four patients with 4 aneurysms had follow-up angiography at 12 months, showing complete occlusion in 3 cases, neck remnant in 1 case. There was no recanalization of previously occluded aneurysm.

Conclusion
Preliminary results demonstrate good safety profile. The first short and mid-term angiographic follow-up are promising.

Objectives: Serving one of the largest retired populations in the United States, we conducted a single center analysis on stroke victims age 90 and beyond. We intended to capture baseline characteristics, outcomes and complications, in order to guide decisions for clinical management and for future clinical trial planning.

Methods: Patients aged 90 and above who underwent evaluation for stroke at Holy Cross Hospital between July 2009 and June 2012, were entered in our database.

Results: Out of 101 patients 13 received intravenous Alteplase infusion, of these 2 patients also underwent mechanical thrombectomy. Four additional patients had catheter intervention only, without prior intravenous Alteplase administration. Average NIHSS at admission was 13.9 in the whole group, 17.5 in the intravenous Alteplase group and 23.8 in the catheter intervention group. The same values measured 24 hours later were 11.7, 14 and 23.6, respectively. Because of the retrospective nature of our study we were unable to gather Rankin data, therefore we decided to measure outcome by discharge placement. Our categories were discharge to home, intensive rehabilitation, skilled nursing facility, hospice and expired. Of the 101 patients 40 (40%) were discharged to home or intensive rehabilitation that were considered satisfactory outcome. Of the intravenous Alteplase group and the catheter intervention group 5/11 (45%) and 1/6 (17%) were satisfactory outcomes, respectively. Complications not directly related to the stroke were frequent in all three groups.

Conclusion: While intravenous Alteplase treatment in this very high age population seems to have benefits, mechanical thrombectomy results are poor. We recommend not to include this patient age group in clinical trials for thrombectomy, and also to share this information about poor expected outcome of catheter intervention with family members at the time of discussing management options.
Abstract Body:

Glial Growth Factor 2 (GGF2) is a neuregulin protein in clinical development for heart failure. Previous studies showed GGF2 treatment improved neurological recovery in a permanent middle cerebral artery occlusion (pMCAO) rat stroke model when treatment was initiated up to 7 days after ischemia. The studies presented here continue the translation of GGF2 towards clinical development for stroke with nonclinical dose-ranging and dose-frequency studies. Mechanisms of enhanced recovery were also explored using histological markers for neuronal growth and synapse formation. In both studies treatment was initiated at 24 hours after pMCAO. Specific tests of the rats ability to place limbs in response to visual, tactile and proprioceptive cues generated fore- and hind limb placing scores that were used to compare treatment groups (n= 12/group). Body swing symmetry was evaluated and infarct volume analysis compared lesion size. The dose ranging study evaluated GGF2 with daily intravenous administration for 2 weeks followed by a week without treatment. Doses were selected that were higher and lower than those previously shown to improve limb placing in rats. The optimal dose from this study was then employed in the dose frequency study which compared once a week, twice a week or daily dosing for 3 weeks, followed by 1 week without treatment. Results demonstrated dose- and frequency-dependent improvements with GGF2 following pMCAO. Improvements in sensorimotor function were not associated with reduced lesion volume, but GGF2 treatment significantly increased expression of growth associated protein 43 (GAP43) in perilesional areas as well as contralateral sensory and motor cortices. These data combined with previous studies demonstrate that GGF2 can enhance recovery of sensorimotor function after stroke without significant acute neuroprotection and with a clinically realistic treatment window. GGF2 is currently in phase 1 human safety studies for another indication and represents a near-term opportunity for clinical development for the treatment of stroke.

Author Disclosure Block:  J.F. Iaci: Employment; Significant; Acorda is developing GGF2 for clinical use. Employees of Acorda may have an equity interest in the company.  T.J. Parry: Employment; Significant; Acorda is developing GGF2 for clinical use. Employees of Acorda may have an equity interest in the company.  Z. Huang: Employment; Significant; Acorda is developing GGF2 for clinical use. Employees of Acorda may have an equity interest in the company.  S.P. Finklestein: Consultant/Advisory Board; Modest; Acting consultant.  J. Ren: None.  A. Ganguly: Employment; Significant; Acorda is developing GGF2 for clinical use. Employees of Acorda may have an equity interest in the company.  A.O. Caggiano: Employment; Significant; Acorda is developing GGF2 for clinical use. Employees of Acorda may have an equity interest in the company.
Abstract Body:

Background and Purpose: Recent studies have elucidated that the bone marrow stromal cells (BMSC) have the potential to improve neurological deficit after stroke. However, it is obscure if BMSC transplantation could be effective against lacunar infarction, because the most basic researches adopted focal ischemia models. This study was aimed to clarify the neuroprotective effects of BMSC with rat lacunar infarct model.

Methods: The BMSC were harvested from green fluorescence protein (GFP)-rat and cultured. They were labeled with superparamagnetic iron oxide (SPIO). Ouabain (2.5mM, Na/K ATPase pump inhibitor) was infused into the striatum of Wister rat (male, 240-260g, n=15). In 7 days after the insult, 5×10^5 cells (or vehicle) were stereotactically transplanted into the contralateral striatum (BMSC group: n=7, vehicle group: n=8). Behavior analysis using rotarod test and 7T-MRI were performed. The animals were sacrificed 6 weeks after the transplantation and histological analysis was performed.

Results: All the animals suffered from hemiparesis after the insult and the rotarod test indicated the significant motor deficit (pre-insult: 150.3±17.6 sec, 1 day after the insult: 44.3±23.0 sec; mean±SD). In MRI study, T2 weighted images showed that the lesion was located the striatum to internal capsule and BMSC were indicated as the signal extinctions. MRI also showed that they migrated toward the lesion via corpus callosum with the passage of time. From 4 to 6 weeks after the transplantation, the motor deficit in BMSC-transplanted animals was ameliorated than vehicle-transplanted ones, significantly (BMSC: 91.7±32.7 sec, vehicle: 45.4±21.8 sec in 6 weeks, P<0.01). In histological analysis, the necrotic change was seen in the center part of the lesion and the neuronal death and gliosis in peri-infarct area in both groups. In the transplanted animals, some BMSC were seen around the lesion, in the corpus callosum and subventricular zone of lateral ventricles. Part of them expressed neural markers such as MAP-2 or GFAP.

Conclusions: This is the first report to show that BMSC transplantation ameliorated motor deficit in rat lacunar infarct model. It suggested the potential of the clinical cell transplantation against lacunar infarct.
Background: Assessment of Carotid stenosis using conventional Doppler ultrasound is operator dependent and time consuming. Recently a new free-hand 3D imaging method, using volumetric transducer became available. This method provides absolute values of plaque volume and carotid stenosis. To our knowledge, there are no clinical studies using this technique so far. Therefore we designed this pilot study to assess the reproducibility in internal carotid artery (ICA) stenosis and plaque volume measurements and to compare it with established spectral Doppler.

Methods: We analysed 47 consecutive patients with history of Stroke or TIA, clinically indicated for carotid ultrasound and having a measurable plaque. 3D ultrasound was performed using a Philips iU 22 ultrasound system equipped with the new single sweep volumetric transducer vL 13-5. The analysis was performed offline with software provided by the manufacturer. The total time taken to calculate both plaque and segmental arterial volumes was less than 10 minutes. Two independent observers measured volumes of plaques and arteries. The ICA stenosis degree by volume reduction method was calculated using following equation: Stenosis=PV/AV *100, where PV is Plaque Volume, AV is the plaque occupied artery volume. The results were classified into 3 groups: 1-49%, 50-69%, >70% stenosis.

Results: The reproducibility between two observers in plaque volume measurement was assessed in 37 cases by Bland Altman agreement analysis showing very narrow limits of agreement (Graphic 1). Table 1 shows the comparison between conventional Doppler and volumetric methods of stenosis measurement, Kappa value=0.525.

Conclusions: In this pilot study good reproducibility of plaque volume measurement was found using a new ultra-fast 3D method. The good agreement between conventional and new 3D volumetric methods of carotid artery stenosis measurement warrants further larger studies.
Abstract Body:

Recent studies have successfully shown the role of Angiotensin (1-7) in decreasing the size of cerebral infarct following ischemic stroke in a rat model. However, a major drawback to the study was that the Ang (1-7) had to be delivered directly into the site of injury via cannulation, therefore potentially limiting human application. This study examines the potential of overexpressing Ang(1-7) in Hematopoietic Stem Cells (HSC) using a lentivirus and intravenously delivering the infected cells so that they may then home to the ischemic hemisphere.

Methods Animals were divided into 4 groups (n=5): control, stroke, stroke+HSC, Stroke+ (Ang1-7) infected HSC. Bone marrow from three additional animals was harvested and used for injection of the HSC and infection with Ang (1-7) lentivirus. Following infection, HSC were cultured in vitro to ensure overexpression of secreted Ang (1-7). Animal behavior was assessed at 72 hours post-surgery using the Garcia scale. Blood and brain samples were analyzed for levels of SDF1-A and bone marrow HSC were counted. Bone marrow cells were also migrated towards an SDF1-A and VEGF gradient in a transwell chamber. Results Ang (1-7) infected HSC secreted the peptide up to 72 hours post infection. Stroked animals injected with the Ang (1-7) infected cells showed rescued behavior on the Garcia scale: stroke only: 11±2, stroke+HSC: 12±2, Stroke+infected HSC: 16±1. Bone marrow significantly increased production of HSC following stroke and injection of infected HSC: stroke only: 96.40±3.5, stroke+HSC: 152.3±17, stroke+infected HSC 222±14.5 (p<0.05). SDF1-A levels in the blood increased significantly following administration of the infected HSC (Control: 1028±25, stroke: 1709±138, stroke+HSC 1965±16, stroke+infected HSC: 2220±176). Ang (1-7) infected bone marrow cells had a significantly higher migration percentage towards SDF1-A compared to uninfected cells (453±31 versus 653±92). Migration towards VEGF was not significant in either group (458±68, 439±98).

Conclusion These data suggest that overexpression of Ang (1-7) in the brain appears to improve post-stroke outcomes, and that infected HSC respond to an SDF1-A gradient rather than VEGF.

Introduction
The Japanese Guideline for the Management of Stroke 2009 recommends various treatment options for prevention of secondary stroke, but many patients still experience stroke recurrence. This study analyzed the clinical features of repeated recurrence of stroke.

Patients and Methods
Participants in this survey consisted of 8,754 patients with stroke recurrence identified from among 66,495 patients registered in the AKITA stroke register from November 1983 through December 2009. Subjects were analyzed for the incidence of cerebral infarction (CI), disease type, mean age at recurrence and incidence.

Results
In the case of recurrent stroke patients who experienced further recurrence, when the previous attack was CI, CI was seen in 896 patients (81.3%), hemorrhage in 185 patients (16.8%) and SAH in 21 patients (1.9%). When the previous attack was hemorrhage, hemorrhage was seen in 181 patients (61.4%), SAH in 7 patients (2.4%) and CI in 107 patients (36.3%). When the previous attack was SAH, SAH was seen in 7 patients (28.0%), hemorrhage in 6 patients (24.0%) and CI in 12 patients (48.0%).

Regardless of whether patients presented with initial stroke, recurrent cases or multiple-recurrent cases, the percentage of cases with CI was high. Breakdown for initial, recurrent and multiple-recurrent infarction cases were: lacunar infarction, 16,304 cases (mean age, 71.0 years), 2,155 cases (72.4) and 351 cases (73.4); atherosclerotic infarction, 13,227 cases (72.0), 1,811 cases (74.4), and 288 cases (74.0); co-morbid atrial fibrillation (AF), 6,773 cases (75.8), 1,302 cases (76.9), and 210 cases (77.4); and unknown etiology, 4,672 cases (71.3), 918 cases (72.3), and 168 cases (72.8), respectively.

Discussion
Patients with stroke recurrence often experience CI. Among the various types of CI, patients with a complication of AF were older. Those patients with co-morbid AF showed a higher incidence of CI recurrence compared with other types of CI.

Conclusion
Aggressive, careful prevention of recurrence in patients with a history of CI and complications of AF, in consideration of their age, appears likely to reduce the number of patients with recurrence.

Author Disclosure Block: M. Sasaki: None. T. Nakase: None. S. Yoshioka: None. A. Suzuki: None.
Background: Due to availability of new technology has resulted in very few aneurysms that cannot be treated with endovascular treatment. Some centers have started offering only endovascular treatment to patients with intracranial aneurysms (endovascular treatment only center [ETOC]).

Objective: To identify the proportion and outcome of patients treated at ETOCs in United States.

Methods: We determined the proportion of endovascular treatment only centers in United States using Nationwide Inpatient Survey (NIS) data files from 2010. We compared various in-hospital outcomes between ETOCs and non-ETOCs. The outcomes studied were favorable outcome (discharge destination to home/self care), in-hospital mortality, length of stay, and hospital charges.

Results: Out of 85 hospitals performing endovascular treatment of un-ruptured aneurysms, 13 (15%) were categorized as ETOCs. Out of the 10447 patients with un-ruptured aneurysms, 1245 (12%) were treated at ETOCs. There were no differences in mean age, gender, and race/ethnicity between patients treated at ETOCs and non-ETOCs. ETOCs were more likely to be non-teaching hospitals (55% versus 8%, p=0.02). The rate of in-hospital mortality (1.2% versus 1.8%) and favorable outcome (88% versus 84%) was similar in patients treated at ETOCs and non ETOC hospitals. The mean hospitalization charges ($125,563±121,515 versus $129,721±123,265) were similar but length of stay (4±7 versus 6±10 days, p<0.0001) was significantly shorter among patients treated at ETOCs.

Conclusions: The recent emergence of ETOCs and provision of treatment with comparable outcomes and shorter length of stay at these hospitals may change the pattern of intracranial aneurysm management in United States.

Abstract Body:

Background
Antiphospholipid syndrome (APS) is a common autoimmune prothrombotic condition characterized by arterial and venous thrombosis and pregnancy morbidity, associated with persistently positive anticardiolipin antibodies and/or lupus anticoagulant. Concerning therapy, satisfactory results have not yet been obtained in therapy for secondary prevention in ischemic stroke patients with APS. We therefore compared single antiplatelet therapy and a combination of antiplatelet and anticoagulation therapy for secondary prevention in ischemic stroke patients with APS.

Subjects and Methods
The subjects were 21 ischemic stroke patients with antiphospholipid antibody, 14 with primary antiphospholipid syndrome and 7 with SLE-related antiphospholipid syndrome. Eligible patients were randomly assigned to either single antiplatelet therapy (aspirin) or a combination of antiplatelet and anticoagulation therapy (target INR: 2.0-3.0; mean 2.4±0.3) for the secondary prevention of stroke according to a double-blind protocol.

Results
There was no significant difference between the two groups in age, gender, NIH Stroke Scale on admission, mRS at discharge, or rate of hypertension, diabetes mellitus, hyperlipidemia, or cardiac disease. We obtained Kaplan-Meier survival curves for each treatment. The primary outcome was the occurrence of stroke. The mean follow-up time was 3.9±2.0 years. The cumulative incidence of stroke in patients with single antiplatelet treatment was statistically significantly higher than that in patients receiving the combination of antiplatelet and anticoagulation therapy (log-rank test, p-value=0.026).

Conclusion
The recent APASS study did not show any difference in effectiveness for secondary prevention between single antiplatelet and single anticoagulant therapy. Our results indicate that combination therapy may be more effective in APS-related ischemic stroke.

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Abstract Body:

**Purpose:** Aneurysm growth was noted in elastase-induced aneurysm after creation. Traditionally, researchers believe the aneurysm will keep growing until 3 weeks after creation. This study was performed to further analyzing the trend of aneurysm growth at more detailed time point after aneurysm creation.

**Materials and Methods:** Forty elastase-induced aneurysms in rabbits were retrospectively analyzed. Follow-up intravenous subtraction angiography was performed immediately, 1, 2, 3, 8, 12, 24 and 36 weeks after creation. Aneurysm sizes (neck, width, height) were measured by comparing with external sizing devices. Aneurysm volume was calculated using the formula as $3.14^*$(aneurysm width/2)$^2*$aneurysm height. Comparison of aneurysm sizes and volumes were at different time points were performed using the Student’s t test.

**Results:** Aneurysm neck size immediately after creation was smaller than that of 1, 2, 3 weeks after creation ($p = .047$, $p = .005$, $p = .02$, respectively). Aneurysm width became bigger at 1, 2, 3 weeks time point comparing that immediately after creation ($p = .0007$, $p = .03$, $p = .001$ respectively). Aneurysm height is larger at 1, 2, 3 weeks time point than immediately after creation ($p = .001$, $p = .009$, $p = .0004$ respectively). Aneurysm volume is bigger at 1, 2, 3 weeks than immediately after creation ($p = .001$, $p = .037$, $p = .03$ respectively). There is no significant difference of aneurysm size (neck, width and height) and volume between 1 week and 3 weeks time point ($p = .7$, $p = .26$, $p = .88$, $p = .32$ respectively). Differences of aneurysm sizes and volume between 3 weeks and later time points (8, 12, 24, 36 weeks) were not significant ($p > .05$ in all the related situations). Mean aneurysm neck, width, height, and volume immediately after creation were $1.64 \pm .45$ mm, $2.02 \pm .20$ mm, $5.66 \pm .91$ mm, $18.11 \pm .02$ mm$^3$, respectively. The mean aneurysm neck, width, height, and volume 1 week and later (2, 3, 8, 12, 24, and 36 weeks) after creation were $3.89 \pm 1.69$ mm, $4.23 \pm 1.25$ mm, $10.72 \pm 2.55$ mm, $150.32 \pm .140.41$ mm$^3$, respectively (Figure A, B).

**Conclusion:** The elastase-induced aneurysm grows significantly within 1 week after creation.

**Abstract Body:**

**Purpose:** The Woven Endobridge (WEB) device (Sequent Medical, Inc., Aliso Viejo, CA) is an intrasaccular, ellipsoid, braided-wire embolization device designed to provide flow disruption along the aneurysm neck. The purpose of this study was to evaluate in an in vivo aneurysm model the acute and chronic performance of the newest generation of WEB device regarding immediacy, degree, and durability of aneurysm occlusion.

**Methods:** The WEB device was implanted in 16 elastase-induced aneurysms in the New Zealand white rabbits and followed for 1 and 3 months. Degree of intraaneurysmal flow disruption was graded on a 4-point scale based on digital subtraction angiography (DSA) within 5 minutes following device implantation. Chronic aneurysm occlusion was rated using a 3-point scale. All aneurysms were harvested for histologic analysis.

**Results:** Immediate post implant Grade 1 (complete flow cessation) was noted in 1 (6%) of 16 cases. Grade 2 (near complete flow cessation) was noted in 3 (19%) cases, 9 cases (56%) showed as Grade 3 (incomplete occlusion). Grade 4 (aneurysm opening) was present in 3 (19%) cases. At 1 month follow up, complete occlusion was noted in 2 (17%) cases. Near-complete aneurysm occlusion was noted in 7 (58%) cases, while incomplete occlusion was noted in 3 (25%) cases. Stable aneurysm occlusion was present in 3 (25%) cases, 9 cases showed progressive occlusion in 9 (75%), and there was no recanalization. At 3 month time point, 1 aneurysm showed complete occlusion, 2 aneurysms were near completely occluded, one aneurysm remained incompletely occluded. Thus 3 (75%) aneurysms indicated progressive occlusion. Histologic findings included aneurysm cavities filled with both unorganized and organized thrombus in 10 of the 12 aneurysms at 1 month time point, aneurysm lumen were filled with unorganized thrombus only in the 2 remaining aneurysms (Figure A-D). Three aneurysms indicated completely organized thrombus within aneurysm cavity 3 months after treatment, only one aneurysm indicated mixture of unorganized and organized thrombus within the aneurysm.

**Conclusion:** The WEB device in experimental aneurysms demonstrated high rates of progressive aneurysm healing.

Figure A-C. DSA images, showing aneurysm before treatment (A), immediately (B) and 1 month (C) after treatment. Figure D, showing unorganized thrombus within aneurysm cavity.