Acute stroke: emergency management, stroke units and complications

AMBULANCE NURSES' PREDICTION OF ACUTE COMPUTED TOMOGRAPHY IN PATIENTS WITH STROKE/TIA-SYMPTOMS AND/OR ALTERED LEVEL OF CONSCIOUSNESS
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Background: When treating patients suffering acute ischemic stroke, the outcome of thrombolytic therapy is time dependent. In-hospital delay may account for 16% of total time lost between stroke onset and computed tomography (CT). The aim of the study was to determine whether ambulance nurses and emergency department doctors had agreement regarding: (1) if a patient should be admitted for an acute CT (CT decision), and (2) if a patient is stable enough to go to the radiology department without a prior medical intervention made by a doctor (stability decision).

Methods: Eligible for our prospective questionnaire survey were patients with symptoms of stroke and/or a Glasgow Coma Scale score <15 arriving with ambulance to the emergency department during a period of October-December 2008. Patients below the age of 18 and patients suffering trauma or cardiac arrests were excluded. For each patient, the ambulance nurse and the emergency department doctor on call completed a questionnaire about CT decision and stability decision (blinded for each other). Cohen’s kappa was used to determine the agreement.

Results: Of 67 patients included, 32 suffered only stroke/TIA-symptoms, 21 only altered level of consciousness and 14 both. The median time (min-max) between rating by ambulance nurses and emergency department doctors was 30 (0-413) minutes. The outcome of the CT decision is presented in table 1 (kappa coefficient 0.32) and the outcome of the stability decision is viewed in table 2 (kappa coefficient 0.19).

Conclusion: There is a fair agreement between ambulance nurses and emergency department doctors regarding patients’ need of an acute CT and a slight agreement when it comes to whether patients were considered stable enough to go to the radiology department without a prior medical intervention made by a doctor. Predefined criteria and additional training are required for ambulance nurses to be able to make decisions about acute CT without first consulting a doctor.

Acute stroke: emergency management, stroke units and complications

LESSONS LEARNED FROM TWO YEARS EXPERIENCE IN INTRAVENOUS THROMBOLYSIS FOR ACUTE STROKE IN THE TEL AVIV MEDICAL CENTER
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Background: Intravenous thrombolytic therapy (ITT) is widely recommended as standard treatment for acute (≤3 hours) ischemic stroke in most clinical practice guidelines. The Israeli experience with ITT is still limited. We describe our 2-year experience (2006-2007) with intravenous tissue plasminogen activator (IV TPA) in the management of 58 patients with acute ischemic stroke. Internal carotid artery (ICA) occlusion has been recently associated with poor clinical outcome in patients with acute ischemic stroke treated with IV TPA. The impact of severe ICA stenosis (70-99%) on thrombolysis response is undetermined. We compared early clinical outcome after IV TPA of 31 patients with stroke in the middle cerebral artery with and without severe ICA stenosis.

Methods: We present demographic data, the most important timing details (from symptom onset to emergency room [ER], ER to CT scan, ER to IV TPA, symptom onset to IV TPA), stroke severity, hemorrhagic complications, mortality, and early outcome. Carotid Doppler and/or CT angiography were performed in 31 patients. National Institute of Health Stroke Scale (NIHSS) scores were recorded before and 7 days after thrombolysis: a decrease ≥4 points indicated neurological improvement.

Results: Our data demonstrate fairly similar parameters of IV TPA treatment compared to other centers based on the Safe Implementation of Thrombolysis in Stroke Monitoring Study (SITS-MOST) registry, and suggest that patients with severe ICA stenosis might be less likely to benefit from IV TPA.

Conclusions: This information may be useful in: (1) the optimization of ITT in patients with acute ischemic stroke, and (2) the planning of ITT in other Israeli hospitals. We propose that an extracranial carotid evaluation should be performed in patients with acute ischemic stroke before deciding on interventions such as thrombolysis (intravenous, intra-arterial) or thrombectomy.

Acute stroke: emergency management, stroke units and complications

MULTIMODAL THERAPEUTIC APPROACH IN ACUTE ISCHEMIC STROKE WITH REAL-TIME NEUROVASCULAR MONITORING
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Background: Intravenous TPA is the only approved drug for ischemic stroke (IS) within 3 hours of symptom-onset. However, recanalization rates remain low & various adjuvant therapies are often employed.

Methods: We report temporal sequence of events in a case with severe IS in whom IV-TPA was coupled with multimodal monitoring & therapeutic approach.

Results: A 63-years old Chinese man, with known hypertension, presented 40 minutes after sudden left-sided weakness. On arrival, he was conscious, had slurred speech and disoriented in time & place. Flaccid weakness was noted on left-side after sudden left-sided weakness. On arrival, he was conscious, had slurred speech and disoriented in time & place. Flaccid weakness was noted on left-side (NIHSS 19). He had atrial fibrillation with pulse 68/minute and BP 136/60mmHg. Emergent brain CT showed hypodense right middle cerebral artery (MCA), CT angiogram of brain revealed occluded right proximal MCA. IV-TPA was started at 85minutes from symptom-onset, with continuous transcranial Doppler (TCD) monitoring. Pre-TPA bolus TCD showed TIBI (Thrombolysis in brain ischemia) grade-1 flows in MCA. A shower of microembolic signals (MES) was followed by complete recanalization (TIBI grade-5) at 22minutes, associated with clinical improvement (NIHSS 9). Frequent MES were noted during the rest...
of TPA infusion & NIHSS at end of TPA infusion was 7points. Cervical duplex sonography performed due to MES showed a large “fresh” mobile thrombus in proximal right internal carotid artery (ICA). This and some deterioration(NIHSS 11) prompted activation of Interventionalist. Thrombectomy occluding the right proximal ICA and carotid-T were extracted by MERCI® retrieval system, resulting in recanalization of ICA, MCA and distal branches. He was kept on mechanical ventilation overnight and the only abnormality detected next day was mild left facial asymmetry (NIHSS 1point). Repeat brain CT showed only a small right striato-capsular infarction. Anticoagulation was started for stroke prevention and he returned to normal activities within a week.

Conclusion: Early recanalization in acute IS results in a good outcome. Fast-track neurovascular assessment, continuous monitoring of the arterial flow parameters may help in optimal treatment decision-making and improve outcome.

Intracerebral/subarachnoid haemorrhage and venous diseases

1 Intracerebral/subarachnoid haemorrhage and venous diseases

DIAGNOSTIC VALUE OF D-DIMER MEASUREMENT IN PATIENTS SUSPECTED TO HAVE CEREBRAL VENOUS SINUS THROMBOSIS

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Background: Cerebral venous sinus thrombosis (CVST) can be presented with headache, seizures, and focal neurological deficit. Brain CT scan may be normal in up to 30% of cases, and MRI may not be available. D-dimer (DD) which is increased in other thrombembolic situations could be a useful test in CVST as well.

Methods: We conducted a prospective study of 104 consecutive patients with headache or unusual ischemic stroke (infection in brain CT, but not compatible with any branch of cerebral arteries), suggesting CVST. DD-dimer test determined for all patients in the emergency ward within the first 24 hours. Titters above 500ng/ml were regarded as positive test. MRI and MRV were performed as a diagnostic gold standard for CVST.

Results: From a total 104 patients, 21 cases (20.2%) were confirmed (by MRI and/or MRV) to have CVST, 20 of whom had positive DD test. so sensitivity of the test was 95.2% (CI 95%: 74.1-99.8). In the remainder 83 (without CVST) it was increased in only 14(16.8). Specificity, negative and positive predictive values of DD test were 83.1 (CI 95%: 73-90.1), 96.6 (CI 95%: 91.2-99.9) and 58.8% (CI 95%: 40.8-74.9) respectively. CVST was associated with oral contraceptives use, seizures, deep vein thrombosis and critical hypertension.

Conclusion: Application of D-dimer test would be useful when CVST is considered a differential diagnosis.

2 Intracerebral/subarachnoid haemorrhage and venous diseases

QUANTOMO: VALIDATION OF A COMPUTER-ASSISTED METHOD FOR VOLUMETRIC ANALYSIS OF HEMATOMA IN INTRACEREBRAL AND INTRAVENTRICULAR HEMORRHAGE

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Background: The ABC/2 method is commonly used to quantify intracerebral hemorrhage (ICH) but is not appropriate for intraventricular hemorrhage (IVH) volume. Computer-assisted techniques may provide more reliable volume measurements; they do not depend on hematomas matching an assumed shape (e.g., ellipsoid). We validated a computer-assisted method for ICH and IVH volume measurement called Quantomo (for quantitative tomography).

Methods: Quantomo was developed using threshold-based region growing algorithms. Raters measure ICH and IVH volumes using Quantomo by (1) selecting a hematoma with a cursor (2) adjusting an intensity threshold (in Hounsfield Units) and (3) manually adding or removing regions to the computer-selected region at their discretion. Four raters measured ICH volumes from 29 randomly selected CT scans 4 times, presented in random order over 4 reading sessions separated by at least 5 days. Quantomo was used for the first two readings and ABC/2 for the latter two. IVH and Total (IVH+ICH) volumes from 20 randomly selected CT scans were subsequently measured twice by 3 raters. Raters were blinded to the results of their measurements and clinical presentations. Estimates of inter- and intra-rater reliability were calculated using a two-way random-effects ANOVA.

Results: The mean and standard deviation of ICH volume measurements across all raters and sessions was 33.0±26.5 ml and 47.6±42.3 ml for Quantomo and ABC/2, respectively. ANOVA analysis revealed that Quantomo is capable of reliably detecting smaller changes in ICH volume compared to ABC/2 (Table 1). IVH volume measurement was more variable than ICH (Table 2).

Conclusion: Quantomo reliably measures ICH volumes and detects more subtle changes in ICH volume compared to the traditional ABC/2 method, and is therefore more appropriate for ICH growth definition in clinical trials. IVH measurement is more variable due to signal intensity variation, making it difficult to separate from ICH.

3 Intracerebral/subarachnoid haemorrhage and venous diseases

GENDER DIFFERENCES IN OUTCOME AFTER INTRACEREBRAL HEMORRHAGE

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Introduction: Recent studies on prognosis after primary intracerebral haemorrhage (PICH) have reported wide differences in case fatality rates at 1 month (from 24 to 51%), as well as in the prognostic impact of gender. We evaluated short term (28 days) and long term (3 years) mortality rate in relation to demographic and clinical factors.

Methods: We analysed consecutive cases of first-ever PICH from 1993 to 2000 in a prospective stroke register covering the Malmö region, Sweden (population ∼250,000). Multivariate logistic regression analysis and Cox’s proportional model was used to explore 28-days and 3 years mortality rate, respectively.

Results: A total of 477 cases were identified (46% women). Women were significantly older than men (77±11 vs 69±12 yrs; p<0.001). There were otherwise no differences in baseline characteristics between genders. In patients <75 yrs, 19% of the women and 22% of the men died within 28 days (p=0.01). In patients >75 yrs, 25% of the women and 41% of the men died within 28 days (p<0.01).

Male gender was an independent predictor for 28 days mortality (Odds Ratio=1.9 95% confidence interval 1.1-3.5). Other independent predictors were volume (30-60 ml, OR=2.2, CI: 0.9-5.2) 60 ml OR=6.4, CI: 3.0-14.6 versus <30 ml (ref), intraventricular haemorrhage (OR=2.0, CI: 1.1-3.3), midline shift (OR=2.0, CI: 1.2-3.3), low conscious level (OR=2.1, CI: 1.1-4.2) for RLS 2-3 resp. OR=12.3, CI: 5.9-25.6 for RLS grade 4-8 versus RLS grade 1(ref) central or brainstem location (OR=4.2, CI: 1.2-8.6) versus lobar (ref); anticoagulation treatment (OR=2.5, CI: 1.2-6.0) and age >75 yrs (OR=2.6, CI: 1.2-5.7). Except for midline shift and anticoagulation treatment, the same factors were independent predictors for 3 years mortality.

Conclusion: Women had better survival than men after PICH. The difference is largely explained by a higher short term mortality in male patients >75 yrs. However, the underlying reasons are yet to be explored.
4 Intracerebral/subarachnoid haemorrhage and venous diseases

DIFFERENCES IN CLINICAL PRESENTATION AND RISK FACTORS BETWEEN POSTERIOR LOBAR AND NON-LOBAR INTRA-CEREBRAL HAEMORRHAGE

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Introduction: Current understanding of the pathophysiology and risk factors for primary intra-cerebral haemorrhage (ICH) is incomplete. Cerebral amyloid angiopathy (CAA) is associated with lobar ICH while hypertension, the most important risk factor for ICH in general, is probably more important in the aetiology of deep non-lobar ICH. The purpose of the study is to examine differences in risk factors and clinical presentation between lobar and non-lobar ICH.

Methods: We used a hospital based Stroke Register to identify patients with primary ICH confirmed by axial imaging on admission between Jan 2003 to June 2004. Images were reviewed by a neuroradiologist to classify into lobar and non-lobar distributions of ICH.

Results: N=116 (male = 68, 50%). Patients’ ages ranged from 33-95 years (mean = 77 years). There were 53 lobar ICH (39%). There were no significant differences between mean age (p = 0.57), sex (p = 0.59), previous history of hypertension (p = 0.54), previous antplatelet use (p = 0.80 for aspirin, p = 0.98 for dipyridamole, p = 0.18 for clopidogrel), previous anticoagulant use (p = 0.69), previous TIA (p = 0.20), or previous stroke (p = 0.06), previous dementia (p = 0.33), and inpatient mortality (p = 0.31) between two groups. There were significant differences in confusion at presentation (p = <0.0001, 51% of lobar Vs. 13% of non-lobar), systolic blood pressure (SBP) on admission (p = 0.001, mean SBP = 162 mmHg for lobar vs. 179 mmHg for non-lobar) and multiple haemorrhages (p = 0.006, lobar =15.1% Vs. non-lobar = 1.2%).

Conclusion: Our study confirmed that patients with non-lobar ICH had higher acutely raised SBP. More patients with lobar ICH had confusion at presentation and a multi-lobar distribution suggestive of CAA. However, previous history of hypertension, TIA, stroke, dementia, and current use of antplatelets or anticoagulants were not predictive for the location of ICH.

5 Intracerebral/subarachnoid haemorrhage and venous diseases

SAFETY OF ANTICOAGULATION IN CEREBRAL VENOUS THROMBOSIS (CVT) WITH POSTERIOR FOSSA LESIONS

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IV or SC anticoagulation (AC) is recommended in the acute phase of CVT. Current evidence also indicates that AC is safe, even in patients with brain hemorrhagic lesions (ICH).

However, in patients harbouring posterior fossa brain lesions, hemorrhagic transformation or additional bleeding related to AC, might cause acute death by brain stem compression or hydrocephalus.

Method: We used the ISCVT database (624 CVT patients) to assess the safety of AC in patients with posterior fossa lesions. Acute death, death or dependency (mRS>2 at last follow up), new hematomas (symptomatic or not) or on repeated CT/MR were compared between patients with posterior fossa lesions who were/were not anticoagulated. Frequency of new ICH and venous infarcts (VINF) (symptomatic or not) on repeated CT/MR was also compared between patients with posterior fossa lesions who were on AC and the remaining subjects of the ISCVT cohort.

Results: 26 patients had posterior fossa lesions (7 ICH, 16 VINF and 3 both), 12 with accompanying supratentorial lesions. Only 2 patients with VINF were not fully anticoagulated. 14 patients (13 on AC) had repeated CT/MR. New ICH developed in 4 patients (3 on AC: 27.3%) and new VINF in 2 (1 on AC: 9.1%) (AC vs. non AC, p=0.71 and 0.35 respectively). In the remaining ISCVT cohort the frequency of new ICH among AC patients was 30/223 (13.5%) (p=0.40) (OR=0.21, 95% CI=0.61-9.60). Two AC patients needed a shunt and 3 (2 on AC) had decompressive surgery. 3/24 AC patients (12.5%) died within 30 days from onset compared with 1 out of 2 (50%) non AC patients (p=0.70). 7/24 AC patients (29.2%) had mRS>2 at final f up, compared with 2 out 2 non AC patients (100%) (p=0.21).

Conclusion: Despite the limitations of the study (small number of patients with posterior fossa lesions, non random allocation to treatment, non blind reading of imaging) this case series suggests that anticoagulation in acute CVT associated with posterior fossa lesions is safe, even in patients with ICH.

6 Intracerebral/subarachnoid haemorrhage and venous diseases

INFLUENCE OF PRE-EXISTING COGNITIVE DECLINE ON FUNCTIONAL PROGNOSIS ONE YEAR AFTER A SPONTANEOUS INTRACEREBRAL HAEMORRHAGE

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Background: Identifying prognostic factors of functional status may help to improve the outcome of patients suffering from a spontaneous intracerebral haemorrhage (sICH).

Aim: identifying prognostic factors for functional dependency or death one year after a sICH.

Methods: PITCH (Prognosis of InTra-Cerebral Haemorrhage) is an ongoing prospective study including all consecutive adults admitted in the Lille University Hospital with a sICH (since November 2004). Patients are regularly followed-up as outpatients and were considered dependent if the modified Rankin score was > 2. Cognitive decline was evaluated with the short version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). Prognostic factors at one year were identified by multivariate analysis in two models: clinical and radiological.

Results: among 350 patients, 41% died before discharge. Our study focused on 197 patients discharged alive (median age 68, interquartile range 53-78; 53% male). Among them, 113 (58%) were dependent at one year. Multivariate analyses identified the following clinical prognostic factors for death or dependency: cognitive decline (OR=1.09 per 1 point increase; 95CI 1.02-1.16), arterial hypertension (OR=5.6; 95%CI 2.0-15.9), and the discharge NIHSS score (OR=1.4 per 1 point increase; 95%CI 1.2-1.5). The radiological predictive factors were: deep location (OR=5.2; 95%CI 2.3-11.6), the haemorrhage volume (OR=1.05 per 1 ml increase; 95%CI 1.02-1.08), cerebral atrophy (OR=1.9; 95%CI 1.2-2.9) and leukoaraiosis (OR=1.9; 95%CI 1.3-2.7).

Conclusion: One year after a sICH, half of the patients were dependent or dead. Patients’ past history (cognitive decline, hypertension) and the severity of the neurological deficit were predictive of a poor functional status. This highlights the importance of developing efficient preventive as well as acute care strategies to improve functional prognosis after a sICH.

7 Intracerebral/subarachnoid haemorrhage and venous diseases

ASSOCIATION BETWEEN GENETIC VARIATION ON CHROMOSOME 9 AND ANEURYSMAL SUBARACHNOID HEMORRHAGE

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Background: Family studies have suggested a role for genetic factors in susceptibility to aneurysmal subarachnoid hemorrhage (aSAH), but little is known about which genes that are involved. A region on chromosome 9 has been reported to be associated to aneurysmal subarachnoid hemorrhage (aSAH). A region on chromosome 9 and aSAH.

Methods: The study comprises 183 patients presenting with aSAH at the neurointensive care unit at the Sahlgrenska University Hospital and 366 healthy age and sex matched controls. Outcome was assessed after one year according to the extended Glasgow Outcome Scale. The region of interest on chromosome 9 was investigated using 5 tag single nucleotide polymorphisms (SNPs). Genotyping was performed with TaqMan assays.

Results: The mean age was 55 years and 74% of the participants were females. Two SNPs showed a significant association with aSAH; rs10757278 (OR for the uncommon allele 1.40, 95% CI 1.09-1.80, p=0.01) and r1333045 (OR 0.76, 95% CI 0.59-0.98, p=0.04). After adjustments for smoking and hypertension the association remained significant for rs10757278 (OR 1.42, 95% CI 1.08-1.87, p=0.01). Seven haplotypes, including all 5 tag SNPs, with an estimated frequency >1% were detected. One common haplotype, with estimated frequency of 30%, showed association with aSAH in an univariate model. However, this association did not remain after adjustment for smoking and hypertension. Neither any SNP nor any haplotype showed association with outcome after aSAH.

Conclusion: In this study a significant association between genetic variations on...
chromosome 9 and aSAH was found. Together with earlier data this strongly suggests that this is a candidate region for aSAH.

8 Intracerebral/subarachnoid haemorrhage and venous diseases

**QUANTITATIVE CT DENSITOMETRY IN PREDICTION OF ACUTE INTRACEREBRAL HEMORRHAGE GROWTH**

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**Background:** Intracerebral hemorrhage (ICH) growth independently predicts disability and death. Therefore, it is a need to identify better predictors of ICH expansion. Qualitative dense heterogeneity analysis independently predicts ICH growth, by various growth definitions. We hypothesized that quantitative CT densitometry of ICH on non-contrast CT brain (NCCT) would improve prediction of ICH growth, beyond known predictors (baseline volume and time to scan).

**Methods:** Using the placebo arm of a phase IIIB trial of recombinant Factor VIIa in ICH, 81/96 baseline CT scans, obtained <3 hrs after stroke onset, were analysed. The other 15 scans could not be analysed for technical reasons, such as image digitization. However, baseline characteristics were similar. Dense histograms describing the distribution of Hounsfield units (HU) of each patient’s ICH were generated. Skewness (measure of distribution asymmetry) and kurtosis (measure of distribution peakedness vs flatness) of each histogram were calculated. A multiple linear regression model, incorporating skewness, kurtosis and known growth predictors was generated.

**Results:** Means ± SDs are presented. Baseline volume was 23±-22 mL (range 1.97-102.5 mL). Time to scan was 108±-33 mins (range 11-187 mins). ICH growth at 24 hrs was 9.2±-1.7 mL (range 0.93-6.6 mL). Skewness was 0.98±-0.31 (range 0.33-1.91). Kurtosis was 0.40±-0.69 (range 1.62-2.9). Multiple linear regression revealed superiority of a model incorporating CT densitometry (adjusted R-squared=0.175, P=0.001) over known predictors (adjusted R-squared=0.11, P=0.003.)

**Conclusion:** Quantitative density profiles of ICH improved a predictive model of ICH growth. Positively skewed and negatively kurtotic HU distributions are signatures of heterogeneous density and actively bleeding ICH. These have more low density liquid blood mixed with organized, higher density clot. A novel, easily-calculated, NCCT-derived predictive model of ICH growth has been created and awaits validation.

9 Intracerebral/subarachnoid haemorrhage and venous diseases

**COMPARISON OF TELEPHONE AND FACE-TO-FACE ASSESSMENT OF THE MODIFIED RANKIN SCALE IN PATIENTS WITH A SUBARACHNOID HAEMORRHAGE**

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**Background:** The modified Rankin Scale (mRS) is a commonly used scale to measure functional outcome after stroke in clinical trials. A structured interview improves the reliability of the mRS, when used face-to-face. A telephone interview is a fast and convenient way to assess the mRS, but its validity is unknown. In patients who had recovered from an aneurysmal subarachnoid haemorrhage (aSAH), we assessed the validity of telephone assessment of the mRS by comparing it with face-to-face assessment.

**Methods:** Eighty-three SAH patients were interviewed twice, once face-to-face and once by telephone, by two of five observers who used a structured interview to assess the mRS grade. Patients staying in a nursing home or rehabilitation centre were excluded. Intermodality agreement was measured using weighted kappa statistics. To check the systematic differences between face-to-face and telephone assessment, the Wilcoxon test for matched pairs was used.

**Results:** Perfect agreement between telephone and face-to-face assessment was 57%. A difference of one level occurred in 31 (37%) patients and this was almost equally distributed over the grades of the mRS. Weighted kappa was 0.71 (95% CI 0.59-0.82). Telephone assessment did not result in a consistently more or less favourable grade than face-to-face assessment (Wilcoxon test for matched pairs, P = 0.33).

**Conclusion:** Telephone assessment of the mRS with a structured interview has a good agreement with face-to-face assessment and can thus be used reliably in the setting of a clinical trial.

10 Intracerebral/subarachnoid haemorrhage and venous diseases

**FAVORABLE OUTCOME AFTER PRIMARY INTRACEREBRAL HEMORRHAGE IN PATIENTS WITH UNTREATED HYPERTENSION DESPITE OF HIGH ADMISSION BLOOD PRESSURE**

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**Background:** Hypertension is the most important modifiable risk factor for primary intracerebral hemorrhage (ICH), but little is known of the effect of elevated blood pressure on outcome. Because a high mean admission blood pressure (MABP) is an independent predictor of early death in patients with ICH we explored its role for outcome separately in normotensive subjects and those with treated and untreated hypertension.

**Materials and methods:** We assessed clinical data and the 3-month outcome of patients with spontaneous ICH (n=455) who were admitted to the stroke unit of Oulu University Hospital within a period of 11 years (1993-2004).

**Results:** Overall mortality within 3 months was 28%. Mortality of patients with untreated hypertension (6%), with treated hypertension (36%) and of patients without hypertension (25%) were significantly different (p<0.05). Patients with untreated hypertension were younger and less frequently had cardiac disease, diabetes and warfarin or aspirin medication, but they showed the highest blood pressures at admission. A high MABP significantly associated with early death in normotensive subjects (p=0.013) and in those who were on medication for hypertension (p=0.007) but not in those with untreated hypertension. All those with a MABP>127 mmHg received medication to reach a lower (<120 mmHg) MABP. In those who had untreated hypertension, we did not observe any significant association of a high MABP with hematoma growth. The high MABPs may result from rapid increases in intracranial pressure.

**Conclusion:** Despite of higher blood pressures at admission, subjects with untreated hypertension showed a better outcome than normotensives and those with treated hypertension. Those with treated hypertension showed the highest death rate and were frequently using warfarin or aspirin while being stricken by hemorrhage.

11 Intracerebral/subarachnoid haemorrhage and venous diseases

**A CLINICALLY RELEVANT DEFINITION FOR HEMATOMA GROWTH FOLLOWING INTRACEREBRAL HEMORRHAGE**

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**Background:** Hematoma expansion following intracerebral hemorrhage (ICH) is a promising therapeutic target. Prior studies have used various definitions of expansion, including absolute growth of either 6ml or 12.5ml, or relative growth of 33% or 40%. To date, no published reports have systematically correlated the degree of hematoma expansion with clinical outcomes. We sought to determine an optimal definition for hematoma growth based on its correlation with poor clinical outcome.

**Methods:** Factor VII-naive ICH patient data was obtained from the Virtual International Stroke Trials Archive. Poor clinical outcome was defined as modified Rankin score of 5 or 6. Receiver operating characteristic (ROC) curves were used to identify the degree of hematoma expansion that best predicted poor clinical outcome.

**Results:** The cohort consisted of 354 patients with ICH. 24% had a poor clinical outcome. The area under the ROC curve for absolute growth definitions was larger than that for relative growth definitions (p=0.03). The optimal definition of absolute growth was 10 ml, predicting poor outcome with 34% sensitivity, 88% specificity, positive predictive value (PPV) 48%, negative predictive value (NPV) 81%, and 75% accuracy. By contrast the 33% expansion definition yielded 41% sensitivity, 86% specificity, PPV 28%, NPV 99%, and accuracy 84%. Patients with >10 ml hematoma growth had a 2.9-fold higher odds of poor outcome (95% CI 1.3-6.4, p=0.001) and 6.9-fold higher odds of ENW (95% CI 3.1-15.8, p<0.001), controlling for other predictors by logistic regression.

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Conclusion: Using a data-driven approach, we found that absolute hematoma growth of 10 ml is a clinically relevant definition for hematoma expansion and provides a slightly better correlation with outcome than 33% hematoma growth.

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EXPERT OPINIONS ON HYPERACUTE BLOOD PRESSURE LOWERING IN PATIENTS WITH INTRACEREBRAL HEMORRHAGE

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Background: Acute hypertension is a major determinant of hematoma enlargement and poor clinical outcome in patients with intracerebral hemorrhage (ICH). It remains unknown, however, how to control blood pressure (BP) during the acute phase of ICH. We conducted a nationwide web questionnaire survey to reveal expert opinions on this issue in Japan.

Methods: We sent the questionnaires to neurosurgeons, neurologists and others responsible for ICH management in 1424 hospitals authorized by the Japan Stroke Society, Japan Neurosurgical Society, and Societas Neurologica Japonica in July, 2009.

Results: Of 600 respondents, 92% belonged to hospital where they managed acute ICH patients. Of them, 99.6% agreed with starting antihypertensive treatment within 24 hours after ICH onset, and 85% started it at an emergency room or CT/MRI room immediately after the diagnosis of ICH was made. Most of them answered that the threshold of SBP for the initiation of antihypertensive treatment was at 180 mmHg (36%) or 160 mmHg (31%), being significantly different between South and North Japan. The goal of SBP lowering was also biphasic, ≤ 160 mmHg (29%) and ≤ 140 mmHg (30%), being also different between neurosurgeons (median ≤ 150 mmHg) and neurologists/othertes (≤ 160 mmHg, p<0.001). The use of nicardipine was the first choice intravenous drug for 57% and the second choice for 27% of the responders. Twenty six percent answered, however, that nicardipine use is inappropriate mainly because of the Japanese official label contraindicating the use of nicardipine for hypertensive ICH patients while active intracranial bleeding continues.

Conclusions: Japanese expert opinions especially by neurosurgeons recommended more aggressive BP lowering than indicated by the EUSI and AHA/ASA recommendations for acute ICH patients. Nicardipine was the most frequently used antihypertensive agent, but this was in conflict with the Japanese official label.

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INR NORMALIZATION IN PATIENTS WITH COUMADIN RELATED INTRACRANIAL HEMORRHAGES – THE INCH TRIAL: A RANDOMIZED CONTROLLED TRIAL TO COMPARE SAFETY AND PRELIMINARY EFFICACY OF FRESH FROZEN PLASMA VERSUS PROTHROMBIN COMPLEX

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Background: coumadin related intracranial hemorrhages (C-ICH) occur in about 10% of patients with CICH. The prognosis of CICH is even worse compared to spontaneous ICH (S-ICH). C-ICH has a mortality rate of about 50 to 60%. The higher mortality and rebleeding rate may in part be due to the higher rate of rebleeding over a longer period after symptom onset. Current recommendations for the treatment of C-ICH include fresh frozen plasma (FFP) and prothrombin complex (PCC). It is known that these drugs lower the INR, and thus it is assumed that normalization of coagulopathy may lead to haemostasis and reduction of rebleeding. However, safety and efficacy of these treatments have never been studied in a prospective trial. Our questions are: how potent are the two drugs in normalization of the INR? What is the safety profile of each of these drugs?

Method: We designed a prospective multicenter trial to compare safety and efficacy of FFP and PCC and C-ICH. Patients will be included if a CT scan shows intraparenchymal or subdural haematoma with and 12 hours after onset of symptoms, if the patient is on treatment with vitamin K antagonist, and the INR is above or equal to 2. Our primary endpoint is the normalization of the INR (≤ 1.2) within 3 hours after the start of infusion. Main exclusion criteria are secondary ICH, known other coagopathies, and known acute ischemic events.

Results: The study will start at the beginning of February 2009. We will present and discuss the design of the study on the background of the current available data.

Conclusion: several points are of interest: this relates to the time window, the choice of the endpoint, the doses for FFP and PCC, the registration and analysis of safety issues, and rescue treatment, etc. We discuss the rational for our design on the basis of the current recommendations.

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SUPERFICIAL SIDEROSES OF THE CENTRAL NERVOUS SYSTEM: A RETROSPECTIVE STUDY OF 17 CASES

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Background: Superficial siderosis of the central nervous system (SS-CNS) is an uncommon disease characterized by progressive sensorineural hearing impairment, ataxia, and dementia, associated with diffuse haemosiderin deposition on the surface of the brain (predominant in the posterior fossa) and/or the spinal cord. There is only one series in the literature describing 30 patients.

Objectives: To study clinical and neuroradiological phenotypes and to determine natural history of SS-CNS.

Methods: Retrospective study including 5 Academic Hospitals. Inclusion criteria: Patients with persistent hemosiderosis (2 brain MRI’s at 6-months interval), without identified bleeding cause.

Results: 17 patients were included, 10 men and 7 women, (mean age of symptom onset: 59.8 years; range 29-81). Deafness or ataxia was the initial symptoms in 9 patients (53%). The remaining 8 patients (47%) had atypical initial neurological symptoms: 59.8 years; range 29-81). Deafness or ataxia was the initial symptoms in 9 patients (53%). The remaining 8 patients (47%) had atypical initial neurological symptoms: 59.8 years; range 29-81). The 3 remaining (28%) were stable during follow-up.

Conclusions: Patients with persistant hemosiderosis (2 brain MRI’s at 6-months interval), without identified bleeding cause.

Poster Session Blue

Intracerebral/subarachnoid haemorrhage and venous diseases
ICVT in Asian patients is associated with good clinical and radiological findings.[4] Conclusion: The diagnosis for SAH patients after admission to a nursing home is not gloomy. The type of rehabilitation that offers best chances to these patients needs to be investigated.

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**ISOLATED CORTICAL VEIN THROMBOSIS – CLINICAL AND NEUROIMAGING RECOVERY**

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**Background:** Compared to dural venous sinus thrombosis, isolated cortical vein thrombosis (ICVT) is an uncommon condition & often difficult to diagnose. Clinical presentations are non-specific & detection of thrombosed cortical vein (“cord sign”) on neuroimaging is rare. MRI enables direct visualization of the thrombus in affected superficial cortical vein as well as the secondary cerebral parenchymal changes. We report clinical & radiological findings in our series of Asian patients diagnosed with ICVT.

**Methods:** We included our Asian patients with ICVT from 2004 to 2008. Clinical data were collected from chart reviews. MRI, MRA and MR Venography were performed in all cases and an independent neuroradiologist reviewed the images. Extensive laboratory investigations were performed to evaluate hypercoagulable states. All patients were followed up and underwent repeat neuroimaging studies.

**Results:** 5 Asian patients (4 males, 3 Chinese and 2 Indians, mean age 41 years) were included. All patients had seizures (3 generalized and 2 simple partial) before presentation; headache of “new type” was seen in 4 cases. Only 1 case was in postpartum period. Abnormal neurological findings were noted in only 1 patient as right hemi-sensory neglect, due to ICVT in left parietal area. While all patients showed significant T2 and FLAIR signal MRI abnormalities, “cord sign” was seen in only 2 cases. An interesting feature was the absence of any EEG abnormality despite extensive cortical changes on MRI. Thrombophilia screening revealed protein-S deficiency in 3 patients. Treatment consisted of oral anticoagulation therapy for 6 months (3 cases), clopidogrel (1 case). One patient was not treated with anti-thrombotic agent due to an incidental AVM. Repeat neuroimaging demonstrated complete resolution of cerebral parenchymal abnormalities. All patients received anti-epileptic medications and remained seizure free during their outpatient follow up.

**Conclusions:** ICVT in Asian patients is associated with good clinical and radiological recovery. A high index of clinical suspicion is required for the diagnosis, especially in patients presenting with headache and seizures of new-onset.

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**ISOLATED CORTICAL VEIN THROMBOSIS – CLINICAL AND IMAGING FINDINGS**

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**Background:** Cortical vein thrombosis not associated with venous sinus thrombosis is rarely diagnosed and may not be recognized in many occasions. Imaging findings may be divided in direct thrombosis evidence (“cord sign” – hyperdense cortical vein in CT scan and equivalent in MRI) or indirect signs as cortical infarct that doesn’t respect an arterial territory, with hemorrhagic component or a cortical hemorrhage.

**Case reports:** We present three patients admitted with the diagnosis of isolated cortical vein thrombosis. Two of them had pro-thrombotic conditions (puerperium and Crohn disease). All shared, as initial manifestation, epileptic seizure (2 partial motor seizure, 1 generalized) followed by focal neurological deficit (transient in two of them). None of the patients presented signs or symptoms of intracranial hypertension. Brain MRI was performed, and two patients evidenced frontal lesions, with hypodensity in T1 and hypersignal in T2, predominantly cortical, associated with a thombosed vascular structure (cortical vein thrombosis and cortical infarct). The third patient presented a lesion hypointense in T2 and FLAIR, with annular contrast enhancement, raising the suspicion of a tumoral lesion or an abscess. A new exam performed three weeks later showed marked reduction of the hypersignal associated with hemorrhagic component, a tubular hypointense structure in long TR sequences and hypointense in T2*, corresponding to a venous infarct with hemorrhagic transformation and thombosed cortical vein. In none of the patients there was evidence of thrombosis in other cerebral venous structures. All patients had a favourable clinical outcome.

**Conclusions:** Focal or generalized epileptic seizures followed by focal neurological deficit, in the absence of signs of raised intracranial pressure should raise the suspicion of isolated cortical vein thrombosis. Diagnosis is usually confirmed by neuroimaging (MRI) although, as described, findings may mimic other pathologies.

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**PREVALENCE AND PROGNOSTIC RELEVANCE OF MICROALBUMINURIA IN PATIENTS WITH INTRACEREBRAL HAEMORRHAGE: A PROSPECTIVE STUDY**

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**Introduction:** Over the past decade, the role of microalbuminuria (MA) as a risk factor for chronic diseases has become apparent. The concept of MA was originally introduced, about 25 years ago, to clinical practice as a useful marker of nephropathy. Since then various studies reported an association of MA with the increased risk of cardiovascular events and all cause of mortality in subjects with or without diabetes. Aim of this study was to investigate the prevalence of MA in intracerebral haemorrhage (ICH) and the predictive value of MA for neurological outcome and its correlation with the volume of haemorrhage.

**Methods:** Patients admitted to our ward for haemorrhagic stroke were prospectively studied. Clinical history, neurological examination and CT scan were performed. Severity of stroke was assessed by NIHSS and outcome by the modified Ranking Scale. The urinary albumin excretion was measured in 24h collection of urine. The volume of the lesion was calculated by using the abe2i index.

**Results:** Of the 68 patients (44M/24F; mean age 63yrs), 12 died; 53 had a medical history of hypertension and 16 of diabetes; the median NIHSS at discharge was 22; the median mRS at discharge was 5. MA was found in about 57% of patients. Patients with MA had sever neurologic condition (p=0.002) and outcome (p<0.001) compared to those without MA. Those patients tend to aggravate during hospitalization. The volume of the bleeding correlated with a bad outcome and death but not with the presence of MA.

**Conclusion:** In our study we found a high prevalence of MA in patients with intracerebral haemorrhage. The presence of MA is associated with a bad outcome at discharge but apparently it is not associated with the volume of the lesion that is well known to influence the outcome. MA was also found to be the only factor associated with a clinical deterioration. This suggests that MA could be a prognostic factor for the outcome and a predictor of intracerebral haemorrhage.

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**OUTWARD HYPERTERTHIC REMODELING AND INCREASED ARTERIAL STIFFNESS IN PATIENTS WITH RUPTURED INTRACRANIAL ANEURYSMS**

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**Background:** Because an underlying arteriopathy might contribute to the development and rupture of intracranial aneurysms (IA), we assessed the elastic properties of proximal conduit arteries in aneurysm patients.

**Methods:** In 27 patients with unruptured IA and 27 control subjects, we determined arterial pressures, internal diameter, intima-media thickness (IMT), circumferential wall stress and elastic modulus (wall stiffness) in the common carotid arteries using applanation tonometry and echotrack. Moreover, carotid augmentation index (AIx, arterial wave reflections) and carotid-to-femoral pulse wave velocity (PWV, aortic stiffness) were assessed.

**Results:** Compared with controls, patients with IA exhibited higher carotid systolic and diastolic pressures (108.4±2 vs. 122.3±3 mmHg), diastolic (73.1±1 vs. 81.5±1 mmHg) and pulse pressures (35.1±1 vs. 41.2±2 mmHg), an increased IMT (546±12 vs. 642±13 μm, all P<0.01) with no difference in diameter. IMT was correlated with pulse pressure in controls (r=0.539, P=0.001) but not in patients (r=0.152, P=NS) suggesting a pressure-independent process. Moreover, patients display an increased elastic modulus (211±2 vs. 368±35 kPa, P<0.001) despite a similar circumferential wall stress between groups. Furthermore, patients with IA have higher PWV (7.8±0.2 vs. 8.3±0.2 m.s-1, P<0.05) which contributes to the increase in arterial wave reflections (AIx: 15.8±2.1 vs. 21.1±1.6%, P<0.05) and thus in systolic and pulse pressures.
Conclusion: This study demonstrates that patients with IA display a particular carotid artery phenotype with an outward hypertrophic remodeling and altered elastic properties which might contribute together with the fatigue effect of increased pulsatile stress on the arterial wall to the pathogenesis of IA.

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INTERVENE INTERLEUKIN-1 RECEPTOR ANTAGONIST ACHIEVES EXPERIMENTALLY NEUROPROTECTIVE CEREBROSPINAL FLUID CONCENTRATIONS WITHIN A THERAPEUTIC TIME WINDOW

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Background: The cytokine interleukin-1 (IL-1) has been heavily implicated in experimental ischaemic brain injury. Its naturally occurring antagonist (IL-1RA) is highly neuroprotective. In humans, it shows few adverse effects and inhibits aspects of the systemic acute phase response to stroke. A pilot study showed penetration into cerebrospinal fluid (CSF) at experimentally-therapeutic concentrations, but this was achieved rather slowly. The optimal protocol for rapid delivery of IL-1RA in acute cerebrovascular disease remains unknown and is essential prior to testing biological efficacy in patients.

Methods: 25 patients with subarachnoid haemorrhage (SAH) and external venous drains inserted for clinical reasons received intravenous (IV) IL-1RA as a bolus followed by a 4 hour infusion. Pharmacometric analysis (simulation) of pilot study data identified the administration regime that could potentially achieve experimentally-therapeutic CSF IL-1RA levels within 30 min (fig 1). For safety reasons, patients were sequentially allocated to five administration regimes. Each regime reflected a stepwise increase in peak plasma concentration of IL-1RA. Plasma and CSF sampling was performed at specified intervals as informed by a D-optimal design.

Results: Plasma and CSF concentrations of IL-1RA in all five regimes fell within predicted intervals (fig 2). The regime leading to experimentally-therapeutic CSF concentrations of IL-1RA within 30 minutes in SAH patients was confirmed as a 500mg bolus followed by an IV infusion at 10 mg/kg/h. No significant adverse events were noted.

Conclusion: It is possible to achieve experimentally neuroprotective CSF concentrations in patients with SAH within a reasonable therapeutic time window (30 minutes). Pharmacometric analysis suggests that IL-1RA transport across the blood-CSF barrier in SAH is passive. Identification of this delivery regime allows further studies of efficacy of IL-1RA in acute cerebrovascular disease.

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LONG-TERM OUTCOME IN PATIENTS WITH INTRACEREBRAL HAEMORRHAGE: THE PROGNOSTIC RELEVANCE OF MICROALBUMINURIA

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Introduction: Stroke is potentially preventable through risk factor reduction. In recent years, the role of microalbuminuria (MA) as a risk factor for chronic diseases has become apparent. MA is independently associated with cardiovascular morbidity and mortality. MA has proposed as a possible risk factor for cerebrovascular disease and has a predictive relevance. Aim of this study was to investigate the predictive value of MA for neurological outcome in patients with intracerebral haemorrhage after 1 year follow-up.

Methods: Patients admitted to our ward for haemorrhagic stroke were prospectively studied. Clinical history, neurological examination and CT scan were performed. Severity of stroke was assessed by NIHSS and outcome by the modified Rankin Scale (mRS). The urinary albumin excretion was measured in 24-h collection of urine. Follow-up was performed after 1 year by a telephonic interview where clinical data and mRS were collected.

Results: Out of 42 patients (26M/16F; mean age 62yrs) after 1 year from the acute event, 8 drop out. Of the remaining 34 patients, 10 had a worsening, 7 of them died, and 9 were unchanged. The median mRS after 1 year was 4. MA was found in about 62% of patients. At the univariate analysis MA was significantly associated with a bad outcome at discharge. Patients with MA had also a more severe outcome after 1 year (p=0.013) compared to those without MA.

Conclusion: In our study we found a high prevalence of MA in patients with intracerebral haemorrhage. The presence of MA is associated with a bad outcome at discharge and also after 1 year follow-up. This suggests that MA could be a prognostic factor for the outcome and a predictor of intracerebral haemorrhage.

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DIPYRONE EFFECT ON PLATELET AGGREGATION OF PATIENTS WITH SUBARACHNOID HEMORRHAGE

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Background: Dipyrone (INN: metamizol) is an analgesic commonly used for treatment of subarachnoid haemorrhage (SAH) headaches in many countries. Some studies suggest dipyrone reduces platelet aggregation and may have hemorraghic potential. We evaluated the effect of its administration on platelet function of patients with SAH.

Method and results: ex-vivo studies of platelet aggregation induced by arachidonic acid (AA) where performed on blood samples of SAH patients one day after the bleeding. 36 patients were included (44% males, mean age 53 years). The 33 patients that have been administered dipyrone at usual dose (1000 mg QID) all showed complete inhibition of platelet aggregation. The platelet function of the 3 patients not given the drug remained within normal range. A second sample was taken one week after the bleeding in 22 patients. 100% of the patients that had stopped taking dipyrone during this time (7 cases) normalised their AA-induced aggregation, while it remained inhibited in the 87% of those still taking the drug. There were no differences in morphimobility in both groups.

Conclusions: Dipyrone inhibits arachidonic acid-induced platelet aggregation, but further research is needed in order to establish its effect on complications such as vasospasm or rebleeding, and the overall clinical outcome of SAH patients.

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INTRACEREBRAL HEMORRHAGE CAUSED BY THROMBOSIS OF DEVELOPMENTAL VENOUS ANOMALY: ENTIRE RECOVERY FOLLOWING ANTICOAGULATION

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Background: Developmental venous anomalies (DVA), previously known as venous angomas, are congenital anatomical variant of normal venous drainage of the brain. Once thought to be a rare lesion with a high propensity for haemorrhage, DVAs are now recognized as the most frequent cerebral vascular anomaly and are rarely symptomatic. At present, there are some controversies about the risk of spontaneous intracerebral haemorrhage (ICH) in patients presenting with a DVA, the classical aetiology being cerebral cavernomas present in association with DVAs in third to half cases.

Method and results: We describe a 44 year-old woman who presented with headaches and seizures due to ICH resulting from venous infarction caused by thrombosis of a developmental venous anomaly (DVA) where performed on blood samples of SAH patients one day after the bleeding. 36 patients were included (44% males, mean age 53 years). The 33 patients that have been administered dipyrone at usual dose (1000 mg QID) all showed complete inhibition of platelet aggregation. The platelet function of the 3 patients not given the drug remained within normal range. A second sample was taken one week after the bleeding in 22 patients. 100% of the patients that had stopped taking dipyrone during this time (7 cases) normalised their AA-induced aggregation, while it remained inhibited in the 87% of those still taking the drug. There were no differences in morphimobility in both groups.

Conclusions: Dipyrone inhibits arachidonic acid-induced platelet aggregation, but further research is needed in order to establish its effect on complications such as vasospasm or rebleeding, and the overall clinical outcome of SAH patients.

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APOE-4 AS PROGNOSTIC FACTOR IN MEXICAN PATIENTS WITH INTRACEREbral HEMORRHAGE

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Background: Intracerebral hemorrhage (ICH) produces more than 35% of all stroke cases in Mexico. The role of genetic factors influencing outcome after acute stroke has been relatively little studied in humans.

Methods: Consecutive patients with imaging evidence of acute spontaneous ICH in a 12 month period were analyzed regarding APOE genotype and final outcome measured by means Rankin scale, NIHSS, volume of ICH.

Results: 76 patients were included and compared with 152 control health people for age and sex. Demographic features, family history, risk factors, volume of ICH, and final outcome were analyzed. There were 39 men (51%). Frequency of genotypes between patients and control has no differences. The frequency of APOE genotypes among patients were: APOE 2, 3 cases (3.9%), APOE 3 (80.2%) and APOE 4, 12 cases (15.7%). Distribution by age disclosed that 20 patients were younger than 40 years (70% of them with APOE-3 and 20% with APOE-4), 48 patients with age between 40 and 70 (83% of them with APOE 3, and 12% with APOE-4) and 18 patients older than 70 years (77% with APOE-3, and 33% with APOE APOE-4). Factors associated with ICH and allele APOE-4 include mainly age higher than 58 years (O.R 5.35, C.I. 1.16-33, p<0.01), as well ICH volume higher than 30 cm3 (O.R 1.28-444, p= 0.009) as well Rankin scale of 5 O.R 3.29, C.I. 0.6-18.3, p= 0.1). Mortality rate related with allele APOE-2 was 21.5%, 0% with APOE-2 and 8% with allele APOE-4.

Conclusions: Allele APOE-4 is present in 15% of Mexican patients with ICH, mainly in older than 40 years and was related to higher volume of ICH not related with higher mortality. Role of APOE4 in predicting early growing of ICH in order to use new therapies (i.e.recombination factor VII) should be investigated.

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MOYAMOYA SYNDROME AND CHRONIC LYMPHOCYTIC LEUKAEMIA: ANY LINK?

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Background: Moyamoya phenomenon is characterized by progressive stenosis of terminal portions of internal carotid arteries and its main branches and can have several aetiologies. Association with treatment for acute leukaemia in childhood could be a first manifestation of Moyamoya syndrome.

Case report: 44-year-old Brazilian male, normal psychomotor development until age of 5 years. At this age he had a probable stroke with cognitive impairment and left hemiparesis as sequelae. He is a smoker and alcohol abuser. No significant head trauma or familial history of vascular disease. He was admitted for acute coma and lymphocytosis. Brain CT: left frontal hematoma and extensive subarachnoid hemorrhage, plus probable old ischaemic lesions of anterior circulation. Angio-CT: poverty of intracranial circulation, possibly by vasospasm. Cervical and transcranial Doppler sonography: no evidence of atherosclerosis, low flow velocities in internal carotids and in small visible segments of middle and anterior cerebral arteries, suggestive of vasculopathy. Conventional angiography: severe Moyamoya pattern. Blood smear and immunophenotyping: chronic lymphocytic leukemia. Negative investigations: erythrocyte sedimentation rate, routine blood chemistry, thyroid function, immunologic study, homocysteine, prothrombotic study, lactate/pyruvate, muscle biopsy. Patient recovered and was discharged scoring I in modified Rankin scale.

Discussion: The event in childhood could be a first manifestation of Moyamoya disease, which then progressed silently. Even knowing that in adulthood Moyamoya phenomenon is characterized by progressive stenosis of carotids and in small visible segments of middle and anterior cerebral arteries, it must be accompanied by raising awareness of its natural history, management and potential complications, as without timely, appropriate therapy, its effects, and those of ICH can be devastating.

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DECOMPENsATED IDIOPATIC INTRACRANIAL HYPERTENSION DUE TO LIGATION OF DOMINANT JUGuLAR VEIN

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Case: A 46 year old man presented with headache, papilloedema, and visual obscurations. Raised CSF opening pressure and normal CT venography at presentation confirmed idiopathic intracranial hypertension (IIH), which improved after treatment with acetazolamide. He subsequently developed a left cholesteatoma, requiring surgical drainage. At work-up, left transverse sinus thrombosis, adjacent to the cholesteatoma, was detected on CT scanning, and during surgical drainage his left jugular vein was ligated, to prevent dispersion/propagation of thrombus. Headache and visual obscurations returned soon afterwards. He re-presented with deteriorating visual field and gross papillodema. MR imaging revealed a surgically occluded left jugular bulb, which was on his dominant venous drainage side, stenosis of the right transverse sinus, a pressure related phenomenon, without evidence of residual thrombosis. Raised intracranial pressure (ICP) was confirmed again by lumbar puncture, and he was treated with steroids, diuretics, frequent lumbar puncture, optic nerve sheath fenestration, and ultimately CSF shunt insertion. Despite these measures which normalised ICP, his vision deteriorated to hand movement detection in both eyes, which is unchanged at follow up over six months later.

Discussion: We believe that ligation of the jugular vein, particularly as it was on the dominant drainage side, caused a dramatic decompenensation in someone at increased risk of raised ICP due to previous confirmed diagnosis of IIH. Detection rates for venous sinus thrombosis are widely accepted to be increasing, with improved access to and sensitivity of different imaging modalities. This increased detection must be accompanied by raising awareness of its natural history, management and potential complications, as without timely, appropriate therapy, its effects, and those of ICH can be devastating.

Vascular biology

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LIPROTEIN-ASSOCIATED PHOSPHOLIPASE A2 ACTIVITY, FERRITIN LEVELS, METABOLIC SYNDROME AND 10-YEAR CARDIOVASCULAR DISEASE:

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Background: To identify factors that influence plasma levels and assess the prognostic value of lipoprotein-associated phospholipase A2 (Lp-PLA2) activity in coronary artery disease and metabolic syndrome.

Methods and results: The Bruneck study is a prospective population-based survey initiated in 1990. Lp-PLA2 activity and baseline variables for the current analysis were measured in 765 subjects aged 45-84 years in 1995. Incident CVD (cardiovascular death, myocardial infarction, stroke and transient ischemic attack) and rates of non-CVD mortality were assessed between 1995-2005. Incident CVD (cardiovascular death, myocardial infarction, stroke and transient ischemic attack) and rates of non-CVD mortality were assessed between 1995-2005. Subjects with incident CVD had higher levels of Lp-PLA2 activity (884 ± 196 μmol/mmol/L versus 771 ± 192, P < 0.001). Increased Lp-PLA2 activity was significantly related to incident CVD (age and sex-adjusted hazard ratio [95%CI] 2.9 [1.6-5.5]; third versus first tertile group; P < 0.001). Increased Lp-PLA2 activity was significantly related to incident CVD (age and sex-adjusted hazard ratio [95%CI] 2.9 [1.6-5.5]; third versus first tertile group; P < 0.001) and with vascular mortality but not with non-CVD mortality. Lp-PLA2 activity was enhanced in subjects with the metabolic syndrome and showed highly significant positive associations with LDL-C, apoB-100, ferritin and HOME-IR, and inverse associations with HDL-C and anti-oxidant levels.

Conclusions: Increased Lp-PLA2 activity is associated with metabolic syndrome and incident fatal and non-fatal CVD but not with non-CVD mortality. Furthermore, Lp-PLA2 activity is strongly influenced by ferritin levels, LDL-C and apoB-100 supporting its integral role in lipid peroxidation. Clinical utility of Lp-PLA2 activity for prediction of cardiovascular risk has to be explored in future studies.
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ENHANCED EX VIVO INHIBITION OF PLATELET FUNCTION AFTER ADDITION OF DIPYRIDAMOLE TO ASPIRIN FOLLOWING ISCHEMIC STROKE – INTERIM RESULTS FROM THE TRINITY ANTIPLATELET RESPONSIVENESS (TRAP) STUDY


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Background: Recurrent vascular events following stroke may, in part, reflect “non-responsiveness” to antiplatelet agents. Longitudinal monitoring of platelet function after addition of dipyridamole to aspirin is not routinely performed in ischaemic cerebrovascular disease (CVD).

Methods: TIA or ischaemic stroke patients, within 4 weeks of symptom onset, were recruited to our ongoing longitudinal “Trinity AntiPlatelet responsiveness study” if changed from aspirin (ASA) to aspirin and dipyridamole combination therapy (ASA & DP). Patients were assessed at baseline on ASA, and then at 14 days (>14d) and >90 days (90d) after the addition of dipyridamole MR 200mg BD to ASA. Inhibition of platelet function in whole blood was assessed with the PFA-100®, a cartridge based-analysener that exposes platelets to high shear stress and biochemical stimulation with either collagen and ADP (C-ADP) or collagen and epinephrine (C-EPI). Ex vivo “dipyridamole responsiveness” was defined as prolongation of PFA-100 closure time (expressed in seconds) during follow-up, compared with the baseline on aspirin, by more than twice the coefficient of variation of the assay (prolongation of C-ADP by >14% or C-EPI by >15%).

Results: To date, 39 CVD patients (mean age 61 years) have been followed up at 14d, and 27 at 90d. Median C-ADP increased from 88s on ASA alone, to 106s at 14d (p=0.01) and 95s at 90d (p=0.025) on ASA & DP. 23/39 patients (59%) at 14d, and 12/27 (44%) at 90d were “dipyridamole non-responders”. Median C-EPI was not prolonged by dipyridamole (p≤0.3). Mean platelet count and platelet distribution width decreased during follow up on ASA & DP compared with ASA mono-therapy (p<0.037).

Conclusions: The addition of dipyridamole to aspirin following TIA or stroke may enhance the inhibition of C-ADP-induced platelet aggregation/aggregation. Further studies are needed to determine whether “dipyridamole non-responders” are at higher risk of recurrent vascular events than “dipyridamole responders”.

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MONOCYTE SUBTYPES PREDICT CLINICAL COURSE AND PROGNOSIS IN HUMAN STROKE

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Background: The number of circulating monocytes increases after stroke, but monocytes are a heterogeneous population and monocyte subtypes have not been studied before in human stroke.

Methods: In 46 consecutive patients and 13 age-matched controls we used flow cytometry in order to measure the proportion and phenotype of monocyte subsets as well as their interaction with platelets at admission and at predetermined time points of follow-up. We studied whether changes in monocyte subsets related to clinical course.

Results: The proportion of the most abundant classical CD14highCD16- monocytes did not change, whereas CD14highCD16+ monocytes increased and CD14dimCD16+ monocytes decreased after stroke. Monocyte subtypes showed clear-cut phenotypical differences. In particular, CD14highCD16+ monocytes had the highest expression of TL2, HLA-DR and the angiogenic marker Tie-2 and CD14dimCD16+ monocytes had the highest expression of the costimulatory CD86 and the adhesion molecule CD49d. Platelet-monocyte interactions were highest in CD14highCD16- and lowest in CD14dimCD16+ monocytes. In adjusted models, poor outcome, increased mortality, and early clinical worsening after stroke were associated to increased proportion of classical CD14highCD16- monocytes at baseline. Contrarily, mortality and infarction size were inversely related to CD14highCD16+ or CD14dimCD16+ monocytes, respectively. Patients with stroke associated infection did not differ at baseline, but later had a greater increase of CD14highCD16+ monocytes.

Conclusion: After stroke each monocyte subtype has a different time course and is associated to a distinct clinical pattern. Therefore, monitoring of monocyte subtypes could help to identify the risk of complications early after stroke onset.

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Some of the vessels demonstrated a circular or elongated appearance whilst others were more irregular, multilobular and often collapsed and non-functional. The presence of neovascularisation was independent from subjects cardiovascular risk factors or concurrent treatments.

Conclusions: Angiogenesis may play an important role in the development of carotid early lesions, with special attention to the neovessels phenotype which can influence in the stability and plaque progression.

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ELEVATION OF CIRCULATING INFLAMMATORY BIOMARKERS IN PATIENTS WITH SYMPTOMATIC LACUNAR INFARCTION

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Background: Although evidences, chronic inflammation contribute to initiate and accelerate atherosclerotic processes, have been accumulated in large artery disease, however, it has not been fully understood yet whether small vessel disease is attributed to chronic inflammatory processes. This study aimed to assess the plasma level of inflammatory markers in patients having history of cerebral small vessel occlusive disease (SVD).

Methods: One hundred and six patients, selected as a SVD group, have previous history of lacunar infarction without any evidence of large artery diseases. There was no evidence of infectious or inflammatory disease after stroke in SVD group. Controls were 119 subjects similar for age, sex, and lipid profiles but without history or evidence of stroke. Plasma levels of matrix metalloproteinase-9 (MMP-9), macrophage inhibitor factor (MIF), tissue inhibitor of metalloproteinase-1 (TIMP-1), and high-sensitive C-reactive protein (hs-CRP) were measured.

Results: MMP-9, MIF, and hs-CRP levels were significantly elevated in SVD group compared with controls (p<0.001, p=0.013, and p=0.008, respectively). There was no significant difference in TIMP-1 between two groups (p>0.724).

Conclusions: Our study presents that chronic inflammation acts a key role on cerebral small vessel occlusion. We suggest MMP-9 and MIF as well as hs-CRP as novel biomarkers for cerebral SVD.

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MODIFIED C-REACTIVE PROTEIN IS EXPRESSED BY STROKE NEOVESSELS AND IS A POTENT ACTIVATOR OF ANGIGENESIS IN VITRO AND IN VIVO

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Background: Native C-reactive protein (mCRP) is a pentameric oligo-protein and an acute phase reactant whose serum expression is increased in patients with inflammatory disease, and which can be irreversibly dissociated to form free subunits or monomeric, mCRP. mCRP can aggregate into matrix-like lattices in tissues, in particular, blood vessel walls and therefore could potentially induce activation of signalling pathways within cells.

Methods: Here, we have used immunohistochemistry, Western blotting and in vitro and in vivo angiogenesis assays to characterise the role of mCRP in modulation of angiogenesis after stroke.

Results: Immunohistochemistry identified expression of mCRP associated with angiogenic microvessels in peri-infarcted regions of patients with acute ischaemic stroke. mCRP was not observed in tissue from either stroke-affected or contralateral regions of the brain. mCRP co-localized with CD105, a marker of angiogenesis in regions of recanalisation. In vitro investigations demonstrated that mCRP was expressed in human brain microvascular endothelial cells following oxygen-glucose deprivation and associated with the endothelial cell surface, and was highly angiogenic to vascular endothelial cells, stimulating migration and tube formation in matrigel, as well as in vivo matrigel mouse-implant vascularization, with a greater potency than fibroblast growth factor-2. The mechanism of signal transduction did not appear to be through the CD16 receptor. Western blotting showed that mCRP stimulated phosphorylation of several mitogenic signalling proteins including ERK1/2. Pharmacological inhibition of ERK1/2 phosphorylation was sufficient to block the angiogenic effects of mCRP.

Conclusions: We propose that mCRP may contribute to the neovascularization process and because of its abundant presence, be a key modulator of angiogenesis in both acute stroke and later during neuro-recovery.

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THE ROLE OF RHOA AND ITS EFFECTOR PROTEIN RHO KINASE IN ISCHAEMIA-MEDIATED BLOOD-BRAIN BARRIER BREAKDOWN

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Background: Brain oedema develops as a result of blood-brain barrier (BBB) breakdown and constitutes one of the leading causes of mortality following an ischaemic stroke. The mechanisms that account for this are unknown and this study investigates the role of RhoA-binding protein RhoA and Rho kinase in this process.

Methods: The levels of protein expression were determined in human brain microvascular endothelial cells (HBMEC) exposed to ischaemia and ischaemia/ reperfusion by Western blotting. The integrity of the BBB was assessed by transendothelial electrical resistance (TEER) and the flux of tracer markers sodium fluorescein (NaF) and Evan’s blue albumin (EBA) across in vitro co-culture models of HBMEC and human astrocytes mimicking the BBB. Changes in HBMEC actin cytoskeleton were assessed via immunocytochemistry.

Results: Ischaemia time dependently induced RhoA and Rho kinase protein expressions while diminishing that of eNOS levels. Reoxygenation attenuated increases in RhoA and Rho kinase protein levels and comparably increased eNOS protein levels following treatment (p<0.05). BBB experiments demonstrated that ischaemia compromised the BBB with elevations in NaF and EBA flux and concomitant reductions in TEER values (p<0.05). These changes were attenuated with reperfusion and co-incubation with a Rho kinase inhibitor Y-27632. These findings are supported by preliminary transfection experiments with constitutively active RhoA showing excessive increases in flux markers and reduced TEER values post treatment. Ischaemia evoked changes in actin localisation and formation accompanied by stress fibre development. Reperfusion and co-incubation of ischaemic cells with Y-27632 attenuated barrier breakdown without exerting prominent changes on actin structure.

Conclusions: Increased expression and activity of RhoA and Rho kinase coupled with concurrent alterations in actin architecture may partly account for ischaemia-induced BBB breakdown in cerebrovascular disease.

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MECHANISMS OF DETRIMENTAL T CELL EFFECTS IN EXPERIMENTAL CEREBRAL ISCHEMIA: THE ROLE OF ANTIGEN RECOGNITION

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Ischemic stroke induces local and systemic inflammatory reactions. T cells critically contribute to brain ischemia/reperfusion (I/R) injury, but the underlying molecular mechanisms are unknown.

In the present study we used transgenic mice with clonal T cell receptors (TCR) and mutations in co-stimulatory molecules to define the minimal immunological requirements for T cell mediated ischemic brain damage. Focal cerebral ischemia was induced in recombination activating gene 1 deficient (RAG1-/-) mice devoid of T and B cells, TCR transgenic mice bearing single CD8+ (2C/RAG1, OTI/RAG1) or CD4+ (OTII/RAG1, 2D2/RAG1 mice) TCR, and mice lacking essential accessory molecules of TCR stimulation (PD1-/-, B71-/- mice) by transient middle cerebral artery occlusion (tMCAO). Infarct volumes and neurological deficits were assessed at day 1. RAG1-/- mice developed significantly smaller brain infarctions (18.6±12.5 mm³ versus 67.9±16.7 mm³; p<0.01) compared to wild-type controls. In contrast to RAG1-/- mice, TCR transgenic mice or mice lacking co-stimulatory TCR signals were fully susceptible to tMCAO (p<0.05). Platelet adhesion and thrombus formation after FeC33-induced vessel injury was not impaired in RAG1-/- mice.

Our data confirm that T cells critically contribute to focal cerebral ischemia, but their detrimental effect does neither depend on antigen recognition nor TCR co-stimulation. Since T cells are also dispensable for thrombus formation, other mechanisms such as T cell mediated activation of the cerebral endothelium must be functional in stroke.

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**PEROXISYNTRITRE, A MEDIATOR OF LESION ENLARGEMENT AFTER STROKE**

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**Introduction:** There is evidence that inflammatory and excitotoxic mechanisms mediate neurologic deterioration (ND) after cerebral stroke. Reactive oxygen species are important mediators of ischemic tissue injury. In this study investigated rejection of Reactive oxygen species with outcome and volume the diffusion weighted image (DWI) lesion after acute cerebrovascular stroke.

**Methods:** MRI was performed on admission (T0) and at 3 days (T1) in 189 patients with acute cerebrovascular infarction of <12 hours' duration. DWI lesion enlargement was calculated as the absolute difference between volumes on T0 and T1 of evolution. NIH Stroke Scale was scored at the same intervals. ND was defined as an increase >4 points within the 72 hours. Nitric oxide (NO) and Peroxisynitrin (ONOO−) levels (as Reactive oxygen species) were analyzed in blood samples obtained on admission.

**Results:** DWI lesion growth was found in 136 (71%) patients (median increase 37 [65.8; 83.4] cm² (2.9)) and ND occurred in 50 (26.4%) patients. Baseline NO (n=0.34), ONOO− (n=0.70), showed a significant correlation with the DWI lesion growth (all p<0.001). After adjustment for potential confounders, ONOO− level was associated with DWI lesion enlargement at 3 days (β=0.20; SD=0.06; p=0.003). **Conclusions:** Production of reactive oxygen species after cerebrovascular stroke may play a role as mediators of lesion enlargement in cerebral ischemia. Plasma ONOO− concentration is one of the independent predictor factor of lesion enlargement in the acute phase of cerebrovascular stroke.

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**ELEVATED OXIDATIVE DAMAGE STATUS CONTRIBUTES TO BREAKDOWN OF THE BLOOD-BRAIN BARRIER UNDER ISCHAEMIC CONDITIONS**

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**Introduction:** Ischaemia stroke occurs due to interference of blood circulation to the central nervous system and is associated with the development of brain oedema. The aim of this study was to investigate the alterations in the expression and activities of parameters that degrade oxidative stress and also examine their relevance to ischaemia/reperfusion injury-mediated brain barrier (BBB) disruption.

**Methods:** Human brain microvascular endothelial cells (HBMEC) and astrocytes were co-cultured to generate an in vitro model of human BBB under normoxic, ischaemic and ischaemia/reperfusion conditions. The mRNA and protein expression of pro-oxidant and anti-oxidant enzymes were measured by RT-PCR and Western blotting, respectively. Enzyme activities were detected through specific spectrophotometric assays. The integrity of the BBB was assessed by transeoside I-1 electrical resistance (TEER) and flux of permeability markers, namely Evan’s blue albumin (EBA) and sodium fluorescein (NaF) using co-culture models.

**Results:** Ischaemia increased expression and activity as well as mRNA and protein levels of antioxidant enzyme CuZn-containing superoxide dismutase (CuZn-SOD) without affecting those of catalase, endothelial nitric oxide synthase (eNOS) and p22-phox, a pivotal subunit for the stability and activity of the most potent pro-oxidant enzyme; NADPH oxidase. Reperfusion following ischaemia led to significant decreases in antioxidant CuZn-SOD and catalase protein expressions and activities while increasing those of p22-phox and eNOS thereby confirming the presence of an elevated oxidative status during ischaemia/reperfusion injury. These findings were substantiated by a prominent decrease in TEER values and concomitant increases in the flux of EBA and NaF across the BBB.

**Conclusions:** Ischaemia alone and followed by reperfusion compromise the integrity of the BBB through, in part, enhancing oxidative stress.

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**INHIBITION OF P38 MAPK ABOLISHES THE PROTECTIVE EFFECT OF THE ANTIOXIDANT PDTC ON BRAIN ENDOTHELIAL CELLS**

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**Background:** Blood-brain barrier disruption plays an important role in edema formation and lesion development in cerebral ischemia and reperfusion. The endothelial cells of the brain microvasculature are exposed to metabolic and acute inflammatory challenges in stroke. The mitogen-activated protein kinase p38 (p38 MAPK) is activated in response to many cell stressors and generally promotes cell death and formation of inflammatory mediators. Its pharmacological inhibition has been shown to be protective in the murine model of middle cerebral artery occlusion (MCAO).

**Methods:** Cell death was induced in bEnd.3 cells by exposure to tumour necrosis factor alpha (TNFα, 50 ng/ml) and cycloheximide (CHX, 20 μg/ml), an inhibitor of translation that was not cytotoxic when administered alone at this concentration. We measured LDH release for general cell death assessment and caspase-3 cleavage by Western blotting to determine apoptotic cell death. p38 MAPK activation was induced by the antioxidant pyrroline dihiiocarbonate (PDTC, 100 μM) and two p38 MAPK inhibitors were used to assess the significance of p38 MAPK for endothelial cell survival.

**Results:** Exposure of the bEnd.3 cells to TNFα + CHX leads to a significant induction of cell death after 6 h (LDH in the supernatant 17% of LDH after complete cell lysis, p < 0.001). Western blotting for caspase-3 activation shows a strong induction of apoptosis which is attenuated by PDTC. A time dependent phosphorylation and hence activation of p38 MAPK is induced by PDTC and pretreatment with inhibitors of p38 MAPK abolished the protective effect of PDTC.

**Conclusions:** Even though inhibition of p38 MAPK via intracerebroventricular injection in animal studies has been shown to reduce lesion size in experimental stroke, our cell culture data point out that inhibition of p38 MAPK, especially via a systemic route, may cause damage to the blood-brain barrier by promoting cell death of the microvascular endothelium.

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**DISTRIBUTION OF DIPYRIDAMOLE IN BLOOD COMPONENTS AMONG POST-STROKE PATIENTS TREATED WITH EXTENDED RELEASE FORMULATION**

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**Background and purpose:** Extended release dipyridamole (ERD) is widely used in patients after ischemic stroke; however, the ability of this antiplatelet agent to be stored in different blood cells has never been explored in post-stroke patients. We hypothesized that since ERD is known to be highly lipophilic, the drug may be present not only in plasma, but also accumulated in platelets, leukocytes, and erythrocytes.

**Methods:** Fifteen patients after documented ischemic stroke were treated with Aggrenox (ERD and low dose aspirin combination) BID for 30 days, and 12 of them completed the study. ERD concentrations in blood cells and platelet poor plasma were measured by spectrofluorometry at Baseline, Day 14, and Day 30 after the initiation of therapy.

**Results:** The background level of spectrofluorometry readings differs slightly among the blood components (132-211 ng/mL) due to the differences in the preparation of samples and cell isolation techniques. As expected, 2 weeks of ERD therapy produced steady state plasma concentration of dipyridamole already at Day 14 (160±81.542mg/mL), followed by a slight non significant decrease at one month (161±408). Two weeks of therapy was sufficient to achieve a consistent dipyridamole accumulation in erythrocytes (361±43), but not in platelets (244±78), or leukocytes (275±49). In fact, while blood cells continued dipyridamole intake beyond 14 days period, and this increase (398±66) was significant (p=0.02) at thirty days.

**Conclusion:** Treatment with ERD in post-stroke patients resulted not only in the achieving of therapeutic plasma dipyridamole concentrations, but also deposition of the drug in erythrocytes and leukocytes, but not in platelets. If confirmed, these data will affect our better understanding of dipyridamole pleiotropy, and may expand future clinical indications of ERD formulation.

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**TLR4 EXPRESSION IN MONOCYTES IS AN INDEPENDENT PROGNOSTIC FACTOR IN HUMAN STROKE**

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**Background:** Toll-like receptors are pattern recognition receptors. They are expressed in many immune cells, most notably in antigen presenting cells. TLR4

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is involved in the brain damage in experimental ischemia. In humans, monocyte numbers increase after stroke. However, the prognostic significance of various monocyte antigens in stroke patients remains unsettled.

Methods: We used flow cytometry in 45 consecutive strokes and 13 age-matched controls to assess the phenotype of monocytes, including their expression of TLR4, TLR2, the antigen presenting HLA-DR, the adhesion molecule VLA-4, and the production of cytokines after stimulation. Cortisol, TNF-α, IFN-γ, and IL-10 were measured in serum. The effects of these parameters on the risk of SAI and poor outcome were tested in multivariate analyses adjusted for confounders (NIHSS score and age).

Results: Compared to controls, stroke patients had reduced expression of HLA-DR, increased expression of TLR2, and impaired production of TNF-α in monocytes. Distinct immune mechanisms were related with functional outcome and the risk of SAI. In multivariate analyses, poor outcome was associated to high expression of TLR4 (quartiles, OR 9.61, 95% CI 1.27-72.47;p=0.02) whereas a rise of cortisol and IL-10 in serum and reduced production of TNF-α in monocytes were independent predictors of SAI.

Conclusions: In human stroke, poor outcome is associated to innate responses mediated by TLR4 in monocytes, whereas the occurrence of SAI reflects the immunosuppressive and anti-inflammatory effects of corticoids, IL-10, and deactivated monocytes. This suggests that agents specifically targeting the innate immune response elicited by TLR4 may be promising for the treatment of stroke in humans.

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ERYTHROCYTE AGGREGATION AS AN EARLY PREDICTOR FOR 1 YEAR SURVIVAL FOLLOWING ACUTE ISCHEMIC STROKE

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Introduction: Inflammation and acute phase response might have deleterious effects in patients with acute ischemic stroke. Several studies have highlighted the role of inflammatory biomarkers as an early signal for acute ischemic stroke progression. This study examines the potential advantage of employing the erythrocyte aggregation (EA) as a possible biomarker at the early stages of acute stroke for identifying patients at high risk for one year mortality.

Methods: Venous blood was obtained from ischemic stroke patients within 24 hours of hospital admission in order to characterize an inflammatory and hemorheological profile (including EA). Neurological state was assessed by the National Institutes of Health Stroke Scale (NIHSS). Differences between one year survivors and non-survivors were assessed and potential risk factors for post-stroke death were evaluated using stepwise logistic regression analysis and Cox predictive models.

Results: A total of 219 acute ischemic stroke patients were included. Cumulative rates of mortality were 7.3% at 1 year. Significant correlation was noted between the degree of EA and the inflammatory biomarkers detected: C-reactive protein, fibrinogen, erythrocyte sedimentation rate and interleukin-6 (r=0.37, r=0.38, r=0.42, r=0.33, respectively; p<0.001). Age, severity of stroke (by NIHSS) and EA were positively associated with death at 1 year after stroke (p=0.05, 0.008 and p=0.04, respectively).

Conclusions: Age, severity of stroke and the degree of EA have merged as the most important determinants of long term mortality after stroke. Although dominated by fibrinogen, EA is probably enhanced by other proteins and can obtain a "summation effect" for the aggregation potential of the inflammatory proteins and thus the intensity of the inflammatory response. This study demonstrates the clinical potential of employing EA as an early stage predictor for acute ischemic stroke survival.

Brain imaging

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ACCUacy OF 3T VS. 1.5T DIFFUSION-WEIGHTED MR IMAGING IN ISCHEMIC STROKE

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Background: To compare sensitivity and specificity of 1.5- and 3-T Diffusion-weighted (DW) magnetic resonance (MR) imaging for acute stroke diagnosis.

Methods: We retrospectively reviewed the DW MR imaging of 108 patients at 1.5-T and 61 at 3-T performed in the six first hours of a carotid ischemic stroke onset. Baseline characteristics were similar at 1.5-T and 3-T: delay to MRI acquisition (median (IQR): 132 min (114-210) vs 152 (114-197), p=0.47) and baseline NIHSS: 15 (8-20) vs. 15 (8-22), p=0.82. Four readers (two neuroradiologists and two stroke neurologists) blinded to clinical data and magnetic field-strength recorded the presence of ischemic lesions on DWI and ADC maps. Sensitivity, specificity and accuracy rate were computed for each reader. The final diagnosis of stroke was based on clinical data and MRI obtained within 24 hours after stroke onset.

Results: We found no difference for the interpretation of DWI and ADC maps by the stroke neurologists or the neuroradiologists (p=0.89 and p=0.94). Sensitivity for DWI in stroke diagnosis decreased from 99.1% at 1.5-T to 92.5% at 3-T (p=0.06) and specificity from 97.8% to 84.1% (p=0.002). Accuracy for DWI alone was superior at 1.5-T (98.8%) than at 3-T (90.9%, p=0.03). When ADC map is employed, modified diagnoses were more frequent at 3-T than at 1.5-T (28.6% vs. 12.9%, p=0.02). Specificity remained lower at 3-T after ADC map lecture (98.9% vs. 1.5-T vs. 90.7 at 3-T, p=0.02).

Conclusions: 3-T DW MR imaging appears to be less accurate than 1.5-T for early diagnosis (<6 hours) of carotid acute ischemic stroke. The major concern is related to the increased number of false negative at 3-T, which rises from less than one percent at 1.5-T to more than one out of 16 patients at 3-T.

2 Brain imaging

ALBERTA STROKE PROGRAM EARLY CT SCORE ON DIFFUSION-WEIGHTED IMAGING IN PATIENTS WITH ACUTE ISCHEMIC STROKE: COMPARISON WITH NON-CONTRAST CT FOR PREDICTING PATIENT OUTCOME AFTER THROMBOLYTIC THERAPY

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Background: The Alberta Stroke Program Early CT Score (ASPECTS) has been applied to diffusion-weighted imaging (DWI) as a semiquantitative criterion for guiding thrombolytic therapy. However, the clinical significance of ASPECTS in DWI has not been fully established. We therefore attempted to determine whether ASPECTS on DWI can predict patient outcome more accurately as compared with that in non-contrast CT (NCCT).

Methods: We examined 58 patients with acute ischemic stroke who were enrolled in the Japan Alteplase Clinical Trial II (JACT-II). NCCT and DWI using standardized protocols were performed in all patients before intravenous administration of alteplase at 0.6 mg/kg within 3 hours after onset. The two reviewers of a reading panel, one neuroradiologist and one neurologist, independently assessed the ASPECTS in NCCT and in DWI, and determined the scores by consensus when the rating differed between the raters. They were blinded to all clinical information besides the affected sides. The modified Rankin Scale (mRS) at 3 months after onset was evaluated in all patients and was employed as an outcome measure. We analyzed the correlation between the dichotomized ASPECTS in baseline NCCT and DWI and a favorable outcome as defined as an mRS of 0-1.

Results: The ASPECTS in NCCT and that in DWI were well correlated (r=0.76), and determined the scores by consensus when the rating differed between the raters. They were blinded to all clinical information besides the affected sides. The modified Rankin Scale (mRS) at 3 months after onset was evaluated in all patients and was employed as an outcome measure. We analyzed the correlation between the dichotomized ASPECTS in baseline NCCT and DWI and a favorable outcome as defined as an mRS of 0-1.

The above values did not differ significantly between NCCT and DWI.

Conclusions: ASPECTS in DWI can predict patient outcome as accurately as that in
NCCT and can potentially be used as one of the criteria for indicating thrombolytic therapy, although the threshold in DWI should be set one point lower than that in NCCT.

3 Brain imaging

**CHOICE OF ECHO TIME ON GRE T2*-WEIGHTED MRI INFLUENCES THE NUMBER OF BRAIN MICROBLEEDS DETECTED**

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**Introduction:** Microbleeds are a topic of increasing interest, but the optimum MRI sequence to detect them is not established. Theoretically, the signal loss on Gradient-recalled Echo (GRE) T2*-Weighted MRI sequences for paramagnetic materials (including microbleeds) could be increased by lengthening the echo time (TE), improving microbleed detection. We used two different TE values to determine whether a longer TE detected more microbleeds.

**Methods:** 22 stroke patients (N=10 with microbleeds, N=12 controls) were imaged on GE Medical Genesis Sigma system using two TE values of T2*-Weighted sequence (TE=40ms and TE=60ms). Two trained observers blinded to clinical details studied 44 sets of images. The presence and number of microbleeds at TE=60ms and TE=40ms were reported using a validated microbleed anatomical rating scale with good intra- and inter-rater reliability (kappa 0.69).

**Results:** A different number of microbleeds was found in 7 (70%) patients with microbleeds on TE=60ms compared to TE=40ms images. Of these, 4 (40%) had more microbleeds at TE=60ms (3 with 2 additional microbleeds and 1 with 7 additional microbleeds) and 3 (30%) had less microbleeds. The remaining 3 (30%) patients with microbleeds had an equal number of microbleeds identified on both sequences. There was no significant difference between the two sequences in the mean number of microbleeds detected (p=0.262). None of the controls were reclassified as having microbleeds on TE=60 compared to TE=40 images.

**Conclusions:** We have demonstrated that the choice of TE influences the number of microbleeds detected, which could alter the results and conclusions of studies on brain microbleeds. However, the effect of lengthening the echo time was not consistent. Further investigation is required to determine how microbleed detection is influenced by MRI sequence parameters and to establish guidelines on the optimal methodology for microbleed detection.

4 Brain imaging

**BASELINE EARLY ISCHEMIC CT CHANGES AND REPERFUSION STATUS: BOTH MAY INFLUENCE FINAL INFARCT SIZE**

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**Background:** In the NINDS tPA Study, increased early ischemic changes on CT scan, as measured by lower baseline Alberta Stroke Program Early CT Score (bASPECTS), were associated with larger 24-hour infarct volumes, but were not influenced by treatment assignment; reperfusion status was not available in this study. We tested whether reperfusion status may independently affect the relationship between bASPECTS and final infarct volume in the pooled Interventional Management of Stroke (IMS) II trials. We also explored whether higher bASPECTS are associated with higher recanalization rates.

**Methods:** The IMS trials treated severe ischemic strokes (NIHSS >10) within 3 hours of onset with combined IV/IA thrombolysis. In IMS II, ultrasound via EKOS Microlysis® Catheter was also used. ASPECTS were determined retrospectively by consensus readings of baseline CT scans blind to outcome. This analysis included only ICA-T and M1 occlusions to limit variability. Successful reperfusion was defined as Thrombolysis in Cerebral Infarction (TICI) 2-3. Digital CT infarct volumes were determined using Cheshire 4.4.8 Image analysis software.

**Results:** In this subcohort of ICA-T and M1 cases (n=60), the median 24-hr infarct volume was 82 cc (mean 98, range 6-333) and the reperfusion rate was 63%. No association was seen between reperfusion rates and bASPECTS dichotomized at both >4 (p=0.10) or ≥7 (p=0.61). Among reperfusion cases (upper thick line), every one-unit decrease in bASPECTS score was associated with a 14 cc increase in 24-hours infarct volume (p=0.0007). Nonreperfusion cases (lower thick line) were associated with a 36 cc increase in 24-hour infarct volume at a given ASPECTS score (p=0.08). See Fig. 1.

**Conclusions:** Our findings suggest that reperfusion may reduce final infarct volume regardless of bASPECTS score. We also confirm that bASPECTS predicts final infarct volume. These findings require further study in larger cohorts using clinical outcomes.

5 Brain imaging

**PATIENT SELECTION FOR STROKE THROMBOLYSIS BASED ON CT ANGIOGRAPHY AND/or CT PERFUSION: “SINGLE” OR “DUAL” TARGET CT IMAGING**

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**Background:** CT angiography (CTA) can identify cerebral vascular occlusion and CT perfusion (CTP) can detect areas of cerebral ischemia with greater sensitivity than non-contrast CT (NCCT) in acute ischemic stroke. The combination of NCCT, CT “single or dual target” imaging using CTA and/ or CTP may afford better selection of patients for stroke thrombolysis.

**Method:** Retrospective review of anterior circulation stroke patients who received intravenous tissue plasminogen activator and had pre-thrombolysis NCCT, CTA and CTP. Patients with internal carotid artery occlusion and posterior circulation strokes were therefore categorized as either CTA+CTP+, CTA-CTP+ or CTA-CTP-. Clinical outcomes of modified Rankin scale (mRS), mortality at three months, and 15. Overall, outcome at 3 months was favorable (mRS 0-2) in 45%. mortality at 3 months was 13%, and sICH 2%. In contrast, the outcomes for CTA- patients (ie. CTA+CTP+ and CTA-CTP-) were similar i.e. the presence of a perfusion deficit did not appear to influence clinical outcome.

**Conclusions:** CTA+CTP+ patients had more severe strokes, but have a greater potential for benefit from thrombolysis. Single target imaging with CTA alone may be adequate, but the addition of CTP aids diagnostic confirmation and stroke localization.

7 Brain imaging

**PRETREATMENT DIFFUSION BUT NOT PERFUSION LESION VOLUME PREDICTS FAVORABLE OUTCOME AFTER IV-THROMBOLYSIS ≤ 6H IN MRI SELECTED PATIENTS**

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1Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany; 2Universitätsklinikum Erlangen, Erlangen, Germany; 3Universitätsklinik Köln, Köln, Germany; 4Klinikum Minden, Minden, Germany

**Background:** We aimed to determine imaging and clinical predictors of favorable outcome in MRI selected patients with acute stroke after IV-thrombolysis with tPA (IV-tPA).

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Brain imaging

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Methods: We analyzed data of acute ischemic stroke patients from a prospective multicenter observational study of MRI based IV-PA treatment within 6 hours from symptom onset. All patients were studied by stroke MRI including perfusion and diffusion weighted imaging (PI and DWI) and treated with IV-PA (<6 hours). Clinical outcome was assessed after 90 days using the modified Rankin Scale (mRS). Favorable outcome was defined as a mRS of 0 to 1. Patients with favorable and unfavorable outcome were compared regarding age, gender, side of ischemic lesion, neurological deficit on admission assessed by the National Institutes of Health Stroke Scale (NIHSS), onset to treatment time (OTT) and PI and DWI lesions volumes.

Results: N=83 (48%) of 174 patients showed a favorable outcome. These patients were younger, showed a lower NIHSS on admission and had smaller DWI lesions as compared to patients with an unfavorable outcome, while perfusion lesion volumes were comparable. Multiple regression analysis identified age (p=0.017), NIHSS on admission (p<0.001) and DWI lesion volume (p=0.047) as independent predictors of a favorable outcome. Odds Ratios (95% CI) for a favorable outcome were - age (per 10 years): 0.68 (0.50-0.93); NIHSS on admission (per 5 points): 0.47 (0.31-0.72); DWI lesion volume (per 10ml): 0.86 (0.73-0.99).

Conclusion: A lower age, lower NIHSS on admission and smaller DWI lesion volume are known to be associated with a favorable outcome in acute stroke patient independent from treatment with IV-PA. In our study these parameters were also predictors of favorable outcome in patients treated with IV-PA. Of note, the volume of pretreatment perfusion lesion was not related to outcome which is most likely due to reperfusion in cases of successful thrombolysis.

8 Brain imaging

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Background: Previously, we showed that in acute ischaemic stroke, brain temperature elevation in the ischaemic lesion is not associated with stroke severity or functional outcome in contrast to pyrexia. To evaluate this further, we investigated the relationship between temperature elevation in “tissue at risk” and the likelihood of ischaemic conversion to infarction (lesion expansion).

Methods: We superimposed multi-voxel magnetic resonance spectroscopic temperature imaging onto DWI on admission (≤24 hours of first symptoms) and compared this hybrid with 3 to 5 day follow-up DWI data in patients with acute ischaemic stroke. We compared tissue temperatures between 1. “healthy-looking brain” voxels that converted to infarction on the follow-up DWI (“infarct expansion voxels”); n=63) with 2. “healthy-looking brain” peri-infarct voxels, which did not convert to ischaemic tissue (“non-expansion voxels”; n=63) on the follow-up DWI.

Results: In 16 patients, mean temperature in voxels where lesion did not appear on the follow-up DWI was on average over 1°C higher than in voxels where the DWI “healthy-looking tissue” on admission converted to infarction (38.14 vs. 37.01°C respectively), but the difference was not statistically significant (p>0.05) due to wide standard deviations.

Discussion: The potential association between elevated peri-infarct tissue temperature and absence of ischaemic lesion expansion suggests the human equivalent of the up-regulation of uncoupling protein 2 (UCP-2), a neuroprotective mechanism seen in experimental ischaemic stroke which simultaneously leads to dissipation of cellular energy into heat (we have previously shown that blood flow is not the explanation). Further studies of UCP-2 expression and regional brain temperature changes in acute ischaemic stroke patients are needed.

9 Brain imaging

FACTORS PREDICTING THE PRESENCE OF ACUTE ISCHEMIC LESIONS ON DIFFUSION WEIGHTED IMAGING IN THE STANFORD TIA STUDY J.-M. Olivot1, C. Wolford2, M. Mlynash3, J. Castle4, N. Schwartz2, S. Kemp4, M.G. Lansberg5, G.W. Albers4
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Background: Transient ischemic attack can be associated with the presence of acute ischemic lesions on diffusion weighted imaging. Several factors may influence the occurrence of acute ischemic lesions with restricted diffusion among TIA patients including ABCD2 scale, time from symptom onset to MRI and TIA etiology. We investigated these relationships in our TIA database.

Methods: Patients with a clinical diagnosis of TIA who underwent MRI were consecutively included from March 2007 to December 2008 were reviewed. We investigated the relation between DWI occurrence and vascular risk factors, the history of atrial fibrillation, ABCD2 score below and above 4 and an imaging delay before and after 24 hours using binary logistic regression.

Results: One hundred and eight cases meet the inclusion criteria; the median ABCD2 score was 4 (IQR: 3-4). Sixteen cases (15%) had a DWI positive lesion(s). Median time to MRI was 50 hours (IQR: 26-100). Median ABCD2 score was 4 (IQR: 3-4). Recurrent vascular events (stroke, MI, vascular death) occurred in only 2 patients (1 stroke and 1 MI) during the first week after symptom onset. Twenty one patients had an MRI within 24 hours. Twenty three had an ABCD2 score≥4. After adjustment for risk factors, clinical score and stroke etiology, 2 factors were associated with the occurrence of an acute DWI lesion:an ABCD2 score≥4: odds ratio (OR) 16.7 95% CI:3.9-71.4; p<0.001 and atrial fibrillation: OR 4.8, 95% CI 1.7-19.8; p=0.029. Patients with MRI performed within the first 24 hours after symptom onset were also more likely to be DWI positive: OR: 4.17; 95% CI: 0.91-19; p=0.066.

Conclusion: Among a cohort of TIA cases with relatively low ABCD2 scores, ABCD2 score and atrial fibrillation remained strong predictors of the occurrence of acute ischemic lesions on DWI.

10 Brain imaging

DIFFUSION TENSOR IMAGING OF CERVICAL SPINAL CORD IN STROKE PATIENTS SHOWS WALLERIAN DEGENERATION IN LATERAL TRACTS P.G. Lindberg1, D. Bensmail2, B. Bussel2, M. Maier1, A. Feydy3
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Background and purpose: After stroke, diffusion tensor imaging (DTI) allows for the detection of Wallerian degeneration in the corticospinal tract at the level of the internal capsule or the brainstem. We studied whether diffusion tensor imaging at 1.5 T could detect Wallerian degeneration of lateral motor tracts in the cervical spinal cord.

Methods: DTI at 1.5 T of the cervical spinal cord was performed in 5 hemiparetic stroke patients with lesions including the corticospinal tract and in 12 healthy controls. Regions of interest were drawn for (i) half and (ii) lateral spinal cord on both sides extending from C2 to C7. Fractional Anisotropy (FA) and Apparent Diffusion Coefficient (ADC) values were obtained.

Results: FA was reduced in stroke patients in the lateral spinal cord on the affected side (compared to the unaffected side, p = 0.007). Groups did not differ in ADC values. FA was lowest in patients with severe upper limb hemiparesis, as indicated by the Action Research Arm Test.

Conclusions: This study supports that DTI at 1.5 T can be used for identification and quantification of Wallerian degeneration in the lateral motor tracts at the cervical level in stroke patients. This may prove useful in future studies of prediction of outcome after stroke.

11 Brain imaging

HICCUPS IN PURE LATERAL MEDULLARY INFARCTION S.B. Kwon, S.H. Hwang, S. Jung, S.Y. Kang
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Background: Hiccups are not a frequent but disabling condition of lateral medullary infarction (LMI). Hiccups can be overlooked, though they may cause
aspiration pneumonia, respiratory depression, and esophagitis. Unlike other symptoms and signs of LMI, the anatomical lesions of hiccups are not well known. Although there were studies about clinical-radiological correlation studies using MRI, few studies have evaluated the relation between the lesional location of LMI and hiccups. We therefore performed this study to correlate hiccups and MRI based lesional location in pure LMI and to identify the difference of clinical disability between patients with and without hiccups.

**Methods:** Between 1997 and July 2007, we identified 15 patients with pure LMI (LMI without concomitant pontine or cerebellar infarction) who presented with hiccups in addition to typical lateral medullary syndrome. Thirty one pure LMI patients without hiccups were included as a control group. Clinical and radiologic findings were compared between two groups. MRI-identified lesions were classified rostrrocaudally as rostral, middle, and caudal, and horizontally as typical, ventral, large, lateral, and dorsal.

**Results:** The pure LMI patients with hiccups had more frequent aspiration pneumonia ($P < 0.05$) and longer hospital stay ($P < 0.05$) significantly. The patients with hiccups significantly more often had dorsolateral rather than ventral lesions at horizontal levels ($P = 0.03$, likelihood ratio test for trend). On the contrary, there were no rostro-caudal differences at vertical levels.

**Conclusion:** We suggest that pure LMI associated with hiccups often locates in horizontal levels ($P = 0.03$, likelihood ratio test for trend). On the contrary, there were no rostro-caudal differences at vertical levels.

**12 Brain imaging**

**PERFUSION ABNORMALITIES CAN PREDICT PROGRESSION TO HEMIMEDULLARY INFARCTION FROM MEDIAL OR LATERAL MEULLARY INFARCTION**

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**Background:** To date, few hemimedullary infarction (HMI) have been reported, and the incidence and predictors of lesion progression in HMI from lateral medullary infarction (LMI) and medial medullary infarction (MMI) remain to be settled.

**Methods:** We studied 37 patients (28 men, 9 women; mean age, 56 ± 11.8 years; range 33–77 years) who had DWI lesions mainly involving the medulla. Time-to-peak (TTP) maps were performed in 30 patients and Tmax deconvoluted TTP were calculated in 25 patients.

**Results:** Twenty-five patients (17 males) presented with hiccups (LMI without concomitant pontine or cerebellar infarction) who presented with hiccups in addition to typical lateral medullary syndrome. Thirty one pure LMI patients without hiccups were included as a control group. Clinical and radiologic findings were compared between two groups. MRI-identified lesions were classified rostrrocaudally as rostral, middle, and caudal, and horizontally as typical, ventral, large, lateral, and dorsal.

**Conclusion:** The progression of the medullary infarct (mainly in HMI) was common in this series; considering total of 7 HMIs initially manifested as LMI or MMO. Our data illustrate that HMI often accompany with PMC territory perfusion delay, which is more severe than those with LMI and MMI. These findings suggest PWI may predict progression of LMI or MMf to HMI. Likewise anterior circulation infarction, PWI may guide treatment approach, especially in medullary infarction.

**13 Brain imaging**

**DIGITAL ATLAS REVEALS HETEROGENEITY IN INFARCT PATTERNS FOLLOWING ICA OCCLUSION**

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**Background and purpose:** Knowledge of infarct patterns has implications for patient management and design of thrombotic trials. We hypothesized that the extent of infarction after ICA occlusion depends upon the additional occlusion of the MCA.

**Methods:** Sequential patients with ICA and MCA occlusion on MR were recruited. Forty five patients with ICA occlusion were separated into those with MCA occlusion (ICA-1) and those without MCA occlusion (ICA-2). Infarct patterns were compared between groups and with that of patients with MCA occlusion alone (MCA) using the method of statistical parametric mapping at a voxel based level.

**Results:** There were 25 patients (17 males) in the ICA-1 group, with a median age of 64 years (range: 26–84 years), 20 patients (13 males) in the ICA-2 group with a median age of 73 years (range: 25–87 years). The mean and standard deviation of the infarct volumes were as follows: ICA-1 group, 112.5 ml ± 113.4 ml; ICA-2 group, 21.1 ml ± 24.1 ml; and MCA group, 68.0 ml ± 66.1 ml. Infarct pattern was similar between the ICA-1 group and the MCA group. Compared with either MCA or ICA-1 groups, infarction was less likely to involve the insula (p < 0.0001) and superior temporal lobe (p = 0.0001) in the ICA-2 group.

**Conclusion:** The pattern of infarction following ICA occlusion depends on whether there is coexistent MCA occlusion. In the absence of MCA occlusion, infarcts resulting from ICA and MCA occlusion have different topography.

**Abstract 12 – Fig. 1. Typical examples of DWI and Tmax map of lateral medullary infarction (LMI) with progression to hemimedullary infarction (HMI) (A–D) and without progression (E–G). DWI of LMI with progression showed acute lateral medullary infarction in the right upper medulla (A, solid arrow) followed by additional medullary medulla infarction (B, open arrow). Tmax map demonstrated severe perfusion delay of the PICA territory (C, D). DWI of LMI without progression revealed acute lateral medullary infarction in the left middle medulla (arrow head) and small scattered lesions in the PICA territory (E). Tmax map of this patient showed mild perfusion delay in the PICA territory (F, G).**
Brain imaging

CEREBRAL MAGNETIC RESONANCE IMAGING (CMRI) FINDINGS IN PATIENTS WITH POSTSTROKE EPILEPSY: RESULTS AFTER 1.5 YEARS OF FOLLOW UP

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Background: Cerebral lesions due to cerebrovascular diseases are the main cause of symptomatic epilepsy in elderly patients. One aim of this study was to detect specific patterns in cerebral magnetic resonance imaging (cMRI) which might predict the occurrence of late epileptic seizures (LES), taking place > 2 weeks after stroke.

Methods: Besides other parameters we analysed cerebral computed tomography (cCT) at day 1 and cMRI (“AVANTO” by Siemens; 1.5 tesla) at day 8-10 poststroke in 173 patients with first-time stroke (aged 65.5 years). For standardized evaluation of the cerebral imaging we analysed T1-, fluid attenuated inversion recovery (FLAIR)- and Diffusion-weighted (DW) images, using the Alberta stroke Programme Early CT Scoring (ASPECTS) score, looked for hemorrhagic transformation and enhancement of contrast agent (gadolinium). During a recruiting period of one year we included 173 patients of which 153 could be followed up for 1.5 years.

Results: After 1.5 years 12 out of the 153 patients suffered from LES. In those we could find no correlations to lesion side or volume of infarction in cMRI. Yet patients with hemorrhagic transformation showed higher risk of developing LES (5 out of 12) as well as those with combination of micro-and macroangiopathic character of the ischemic lesions (5/12). But the most astonishing finding was, that patients with an initial mismatch in the DWI also seem to have a higher risk of developing LES (4/12), which could not be shown in our patients with early epileptic seizures, taking place within the first 2 weeks of stroke-onset.

Conclusion: The accumulation of patients with LES and DWI mismatch in the first 1.5 years after stroke provided predictive value in the Emergency Department (ED) setting as a marker for stroke with potential epileptogenic effects. Further examinations with a greater number of patients are necessary to explore these coherences.

Brain imaging

CORTICAL CORRELATES OF SPASTICITY IN THE FLEXOR MUSCLES OF THE HAND AFTER STROKE

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Background and purpose: Previous studies have shown that (i) in healthy subjects, there is a cortical involvement in the long-latency electromyographical (EMG) response to stretch in activated hand muscles and (ii) in stroke patients, a reduction in spasticity can result after electrical nerve stimulation distant to the site of spasticity (i.e., centrally mediated effect). These findings may suggest the possibility of cortical involvement in spasticity. We thus hypothesised that there are cortical activation correlates to spasticity in stroke patients with increased muscle tone of the wrist flexors.

Methods: Stroke patients and controls were scanned using event-related fMRI during slow and fast passive movements of the hand with simultaneous recording of Passive Movement Resistance (PMR).

Results: Control subjects had velocity-dependent activity (i.e., activity greater in slow than fast) of two types: (i) in areas that were also more active in passive movement than rest and (ii) in areas that were also more active in rest than passive movement. In the patient group, with large inter-individual variation of spasticity, we thus hypothesised that there are cortical activation correlates to spasticity in stroke patients with increased muscle tone of the wrist flexors.

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CT brains performed in the ED over a 4.5 month period. All scans were assessed independently by a Neurologist, Neuroradiologist, trainee Neurologist and a first year doctor, all of whom were unaware of the clinical presentation. Reviewers were instructed to give a subjective opinion on the presence of conjugate eye deviation, and to avoid any assessment of brain parenchyma.

In cases identified with eye deviation, the medical record was obtained and clinical details recorded.

**Results:** 530 CT Brains were reviewed and 14 cases excluded as the eyes were not visible. 93 cases of eye deviation were identified by at least one observer, though agreement between observers was variable.

Medical records were obtained for 91 patients, 2 were unavailable, 60 (65.9%) had a significant neurological diagnosis identified. The majority of these were stroke (44/60; 73%) or seizure (11/60; 18%).

A review of the CT Brain report was undertaken for those patients with eye deviation. The formal radiology report did not comment on eye deviation in any case. In 44 patients with a final diagnosis of stroke, only 18 (40.9%) had an acute parenchymal abnormality and 3 (6.8%) cases demonstrated a dense middle cerebral artery sign.

**Conclusion:** In our study, we found the presence of eye deviation on CT brain showed a trend towards a stroke diagnosis. The presence of eye deviation may be an aid to the diagnosis of stroke, particularly when the scan is otherwise normal. The presence of conjugate eye deviation was easily assessed for by doctors with different levels of expertise, although there was some interpreter variation.

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**SIGNIFICANCE OF PERFUSION COMPUTERIZED TOMOGRAPHY SCAN (PCT) IN ACUTE ISCHEMIC STROKE MANAGEMENT**

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**Introduction:** Ischemic stroke is a medical emergency that is still associated with high morbidity and mortality. Intravenous or intraarterial thrombolysis is an effective treatment to improve stroke outcomes when applied within 4.5 to 6 hours after symptom onset. Before thrombolysis an intracerebral hemorrhage has to be ruled out by computed tomography (CT) or magnetic resonance imaging (MRI). CT angiography (CTA) and perfusion CT (PCT) are additional CT-based methods, that are readily available and allow for a direct demonstration of acute ischemia.

**Aim:** The aim of this retrospective study was to evaluating the predictive value of PCT for infarct volume, initial stroke-related deficit, and early improvement and mid-term outcomes after stroke in patients receiving thrombolysis and those that did not.

**Methods:** 92 subjects (47 received thrombolysis) with ischemic stroke who underwent non-enhanced CT and PCT on admission and a non-enhanced CT after 24 hours were included. PCT parameters were measured and their predictive value for stroke volume, initial deficit, early improvement, and outcome were evaluated.

**Results:** The larger the perfusion deficit and the older the patient, the graver stroke volume. Initial deficit, early improvement, and outcome were evaluated. Results: The larger the perfusion deficit and the older the patient, the graver stroke volume. Initial deficit, early improvement, and outcome were evaluated.

**Conclusion:** PCT imaging provides parameters that are correlated with the acute deficit and predict final lesion size and functional outcome. PCT represents a useful exam that should be added to the diagnostic CT work-up for acute ischemic stroke, because it provides direct evidence of ischemia that can be used for the determination of prognosis. This study does not allow for conclusions about MRI in the acute setting, which may still be the superior method when compared with CT.

**Key words:** ischemic stroke, perfusion CT, TTP, CBV, Penumbra, final infarct size, functional outcome

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**MULTIRESOLUTION FUZZY CLUSTER ANALYSIS OF DYNAMIC CONTRAST ENHANCED MR-DATA**

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**Background:** This study demonstrates the technique of multiresolution fuzzy...
classification as a tool for segmenting contrast enhanced brain tissue. The classification is based upon the dynamic signal behavior in dependence of the portion of contrast agent within a voxel. It is examined if certain classified regions within an ischämically affected brain are a predictor for the success of the outcome of treatment.

Methods: The advantages of a multiresolution fuzzy clustering algorithm (MFCA) in the context of the classification of DCE data are discussed. The MFCA is as much as a factor of 1.5 to 3 faster than the FCA and in a region of SNR of 1-6dB the MFCA is more robust than the FCA and takes significantly less iterations to converge. Especially the FCA converges frequently to unwanted local minima whereas the MFCA behaves better in this respect. Additionally to the standard perfusion parameters (TTP,CBF,CBV,PBP), the representative dynamic signal characteristics for each class provide further parameters that are necessary to describe the dynamics: the velocity of the in- and outflowing contrast agents, the time, it will rest within certain brain tissue compartments, and the time of aerial.

Results: Nine patients with a hemispheric stroke were examined with a first pass bolus tracking single shot EPI (N=40 acqu., S=12 slices). The ischemic core and the penumbra could be classified without need for diffusion weighted imaging maps (ADC).

Conclusion: Multiresolution fuzzy clustering enables the segmentation of MR perfusion maps into irreversible affected brain regions and the penumbra.

References:

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CT ENHANCEMENT IMMEDIATELY PRECEDING HEMORRHAGIC TRANSFORMATION INDICATING RAPID BLOOD-BRAIN BARRIER BREAKDOWN IN TOP-OF-THE- BASILAR EMBOLISM

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Introduction: Parenchymal contrast enhancement, either seen with CT or T1-weighted MRI is an indicator of blood-brain-barrier (BBB) disruption. In acute cerebral ischemia it can be used to assess the risk for hemorrhagic transformation and thus is especially useful in patients to undergo thrombolysis. In the literature such an enhancement is reported to typically occur within the first 5 days.

Case: A 83-year-old female patient was admitted to our emergency room in a comatose state after she had developed acute right-sided hemiplegia. A non-enhanced CT (NECT) 5 hours after symptom onset revealed signs of generalized cerebral microangiopathy as well as chronic ischemia in the anterior left insular region but no signs of acute infarction or hemorrhage. In the CT angiography the left posterior cerebral artery (PCA) was occluded proximally. All other major arterial vessels were found to be patent. A CECT immediately afterwards showed an enhancement in the anterior left-sided thalamus. Six hours after clinical onset we performed an MRI (3 Tesla) with regard to the existence of a perfusion-diffusion-mismatch including susceptibility-weighted imaging (SWI) to check, whether the patient was eligible to a systemic thrombolytic treatment.

Discussion: In the present case we found an contrast enhancement that was very early with regard to the clinical onset as well as to the contrast agent administration. The CECT findings, supported by SWI-MRI thereby averted a potential harmful treatment.

Conclusion: Perfusion imaging to demonstrate even mild hyperperfusion, we sought to analyze non-invasive information on cerebral perfusion. Given the high sensitivity of ASL tests.

Methods: We analyzed data of 99 consecutive patients with stroke symptoms indicating a hemispheric stroke in whom we performed multimodal CT. Patients received standardized clinical examination (NIHSS, Barthel) and laboratory tests (c-reactive protein, blood count, INR, fibrinogen, electrolytes, creatinine and liver enzymes). The mismatch between CBV and MTT was automatically determined and correlated with definite infarct size, clinical parameters and laboratory tests.

Results: 60 patients (61%) received thrombolytic treatment with r-PA within 3 hours after stroke onset. Patients had a NIHSS of 11.2 (±4.35), the patients treated with thrombolysis had a NIHSS of 11.2 (±3.66), the medium level of c-reactive protein in for all patients was 1.033 mg/dl (±1.411), in patients treated with thrombolysis 0.98 mg/dl (±1.022). Results of mismatch calculation and correlations with clinical parameters and laboratory tests will be presented.

Conclusion: Multimodal CT appears to be useful in identification of patients suitable for thrombolysis. Further studies are needed to determine whether CBV/MTT mismatch on perfusion CT can be used to predict infarct size and outcome in patients treated with rPA after acute stroke.

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VISUALLY EVOLED CHANGES OF CEREBRAL BLOOD FLOW DEMONSTRATED BY ARTERIAL SPIN LABELLING MR PERFUSION IMAGING


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Background: Visual stimulation is known to activate the visual areas of the occipital cortex which is associated with a mild local increase of cerebral blood flow (CBF), as it may be demonstrated e.g. by functional MRI and transcranial Doppler. Arterial spin labeling (ASL) is a new MRI technique that provides non-invasive information on cerebral perfusion. Given the high sensitivity of ASL perfusion imaging to demonstrate even mild hyperperfusion, we sought to analyze whether this method allows assessment of visually evoked CBF changes in healthy volunteers.

Methods: A 1.5T scanner (Magnetom Sonata, Siemens, Erlangen, Germany) was used. ASL perfusion maps were obtained using a single-shot 3D-GRASE read-out module by using time series which allow determining the dynamics of blood inflow to the cerebral microcirculation. For time series, multiple inflow times (TI) ranging as much as a factor of 1.5 to 3 faster than the FCA and in a region of SNR ± 0.0085. Moreover symptomaticity also significantly correlates with fatty plaques (p=0.0085). Moreover symptomaticity also significantly correlates with fatty plaques (p=0.0085).

Conclusion: MDCTA allows to adequately evaluate the type of plaque other than stenosis degree. We observe a strong, statistical confirmed, correlation between cerebral lesion, symptomatic and fatty plaque in the carotid artery. Stenosis degree also correlates with cerebral lesion and symptomaticity, but the statistical results show a weaker link. It may be useful, to include, between primary parameters in the evaluation of patients class risk, the type of carotid plaque.

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MULTIMODAL CT IN ACUTE STROKE: CORRELATIONS WITH CLINICAL PARAMETERS AND SIGNS OF INFECTION AT ADMISSION

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Background: Multimodal computed tomography (CT) consists of native CT, CT perfusion and CT-angiography. Every patient arriving within 3 hours after stroke onset receive multimodal CT in our clinic. Results may help to identify patients best suitable for systemic thrombolysis. Aim of the present study was to correlate results of multimodal CT, especially mismatch in cerebral blood volume and mean transit time with the size of infarction in repeated native CT and to correlate mismatch volumina with clinical severity of the stroke (NIHSS) and signs of early infection (c-reactive protein at admission).

Methods: We analyzed data of 99 consecutive patients with stroke symptoms indicating a hemispheric stroke in whom we performed multimodal CT. Patients received standardized clinical examination (NIHSS, Barthel) and laboratory tests (c-reactive protein, blood count, INR, fibrinogen, electrolytes, creatinine and liver enzymes). The mismatch between CBV and MTT was automatically determined and correlated with definite infarct size, clinical parameters and laboratory tests.

Results: 60 patients (61%) received thrombolytic treatment with r-PA within 3 hours after stroke onset. Patients had a NIHSS of 11.2 (±4.35), the patients treated with thrombolysis had a NIHSS of 11.2 (±3.66), the medium level of c-reactive protein in for all patients was 1.033 mg/dl (±1.411), in patients treated with thrombolysis 0.98 mg/dl (±1.022). Results of mismatch calculation and correlations with clinical parameters and laboratory tests will be presented.

Conclusion: Multimodal CT appears to be useful in identification of patients suitable for thrombolysis. Further studies are needed to determine whether CBV/MTT mismatch on perfusion CT can be used to predict infarct size and outcome in patients treated with rPA after acute stroke.

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from 250 ms to 2500 ms were measured in 10 time steps (TR 3000 ms). Following a measurement with closed eyes, visual stimulation during ASL MRI was performed using an on-off block design with a checkerboard as stimulus: 1Hz, 2Hz and 4Hz flashing checkerboard, 20sec ON/ONOFF intervals. Microvascular perfusion (CBF) and bolus arrival time (BAT) were extracted from time series using nonlinear least-square optimization.

Results: ASL perfusion maps were obtained of 8 healthy volunteers during visual stimulation. A significant local CBF increase of >15% located in the visual areas of the occipital cortex could be identified. ASL perfusion maps show a marked signal increase in both occipital lobes under visual stimulation (white arrows, bottom) compared to the control without visual stimulus (top) (see figure).

Discussion: Visually evoked transient hyperperfusion in the occipital cortex may be demonstrated using ASL perfusion techniques. This new approach offers the opportunity to analyze the neurovascular response to exogenous stimuli under various physiological and pathophysiological conditions.

Small vessel and white matter disease

1 Small vessel and white matter disease

ASSOCIATION BETWEEN DECREASED RENAL FUNCTION AND CEREBRAL SMALL VESSEL DISEASE SEVERITY IN PATIENTS WITH FIRST-EVER LACUNAR INFARCTION
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Background and objectives: Silent brain infarcts and white matter lesions are associated with an increased risk of subsequent stroke and cognitive decline in minor stroke patients. Renal vascularization shares physiological characteristics with brain microcirculation. The prevalence of subclinical renal disease and silent cerebral small vessel disease is very high among elderly subjects. The purpose of this study was to assess whether subclinical renal dysfunction is related to the severity of cerebral small vessel disease in first-ever lacunar infarct (LI) patients.

Methods: We measured creatinine clearance (CCl) and estimated glomerular filtration rate (eGFR) using the Cockcroft-Gault equation and the Modification of Diet in Renal Disease formula in consecutive patients with symptomatic LI. Renal vascularization shares physiological characteristics between Hp phenotype and silent signs of hypertensive cSVD (asymptomatic cerebral small vessel disease), whereas the Hp1 allele has been associated with cerebral atherosclerotic disease, whereas the Hp2 allele has been associated with extracerebral atherosclerotic disease, whereas the Hp1 allele has been associated with symptomatic cerebral small vessel disease (cSVD). We examined the relationship between Hp phenotype and silent signs of hypertensive cSVD (asymptomatic cerebral small vessel disease (LACs) and white matter lesions (WMLs)) on MRI in hypertensive patients.

Methods: Hp phenotype was determined using starch gel electrophoresis in 154 hypertensive patients without symptomatic vascular disease. On MRI we quantified the volume of deep and periventricular WMLs. Because of skewed distribution of Hp phenotypes, we used least-square optimization.

Results: A total 185 patients with first-ever LI were included. In univariate analysis, moderate to severe white matter disease was associated with older age (p<0.001), higher serum homocysteine level (p<0.001), increased brachial-ankle pulse wave velocity (p=0.004), lower CCl (p<0.001) and eGFR (p=0.002). After adjustment for age, sex, hypertension and diabetes, lower CCl (OR, 3.02;95% CI, 1.12-8.14, p=0.028) and eGFR (OR, 4.14;95% CI, 1.31-13.2, p=0.016) were independently related to moderate to severe white matter disease. Persons with lower CCl had a higher prevalence of multiple lacunar infarcts but this association was not statistically significant in multivariate analysis.

Conclusions: Our findings indicate that subclinical renal dysfunction is associated with a greater burden of cerebral white matter disease, suggesting that it reflect ischemic brain damage caused by generalized microvascular damage. Therefore, early identification of mild renal dysfunction could be needed to reduce the risk of cerebral small vessel disease.

2 Small vessel and white matter disease

RISK FACTORS OF CEREBRAL WHITE MATTER LESIONS IN COMMUNITY-DWELLING HEALTHY ADULTS
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Background: Cerebral white matter lesions (WMLs) are common radiologic findings in elderly people. These are associated with increased risk of stroke and dementia, cognitive dysfunction in non-demented elderly, and geriatric syndromes such as falls, depression, urinary incontinence. Therefore, it is very important for prevention of stroke and dementia to know risk factors of these lesions in general population.

Objectives: To measure prevalence and to study of risk factors of WMLs in population-based sample of healthy middle-aged and elderly people

Methods: The Prevention of Stroke and Dementia (PRESENeT) Project is a regional government-funded ongoing community project in Ansan, Korea for prevention of stroke and dementia by education, public relations, early medical check-up to healthy adults older than 50 years recruited by systemic random sampling. We assessed vascular risk factors and physical examination by in-person interview and performed brain CT scan in 480 stroke- and dementia-free participants (235 Men, 245 women). Associations between presence of WMLs and risk factors were analyzed by logistic regression.

Results: We found in our population-based study a prevalence of cerebral white matter lesions that abruptly increased with age from 2.4% in 50- to 59-year-old participants, 9.0% in 60-69 years to 32% in the oldest (70 years of age and older). Among conventional risk factors, older age and hypertension (adjusted OR, 3.0; 95% CI, 1.2-7.24) were the most important risk factors of WMLs but DM and dyslipidemia were not after adjustment. The adjusted OR of WMLs for higher than 50 percentile of serum homocysteine, compared with lower than 50 percentile was 5.2 (95% CI, 2.2-12.1). The highest quartile of serum CRP has adjusted OR of 2.2 when compared with the lowest quartile. Abdominal obesity based on waist circumference also increase risk of WMLs (adjusted OR, 2.3; 95% CI, 1.06-4.97).

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HAPTOGLOBIN PHENOTYPE CORRELATES WITH DEEP WHITE MATTER LESIONS IN HYPERTENSIVE PATIENTS
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Background: Haptoglobin (Hp) 2-2 phenotype has been associated with extracerebral atherosclerotic disease, whereas the Hp1 allele has been associated with symptomatic cerebral small vessel disease (cSVD). We examined the relationship between Hp phenotype and silent signs of hypertensive cSVD (asymptomatic cerebral small vessel disease (LACs) and white matter lesions (WMLs)) on MRI in hypertensive patients.

Methods: Hp phenotype was determined using starch gel electrophoresis in 154 hypertensive patients without symptomatic vascular disease. On MRI we quantified the volume of deep and periventricular WMLs. Because of skewed distribution of Hp phenotypes, we used least-square optimization.

Results: A total 185 patients with first-ever LI were included. In univariate analysis, moderate to severe white matter disease was associated with older age (p<0.001), higher serum homocysteine level (p<0.001), increased brachial-ankle pulse wave velocity (p=0.004), lower CCl (p<0.001) and eGFR (p=0.002). After adjustment for age, sex, hypertension and diabetes, lower CCl (OR, 3.02;95% CI, 1.12-8.14, p=0.028) and eGFR (OR, 4.14;95% CI, 1.31-13.2, p=0.016) were independently related to moderate to severe white matter disease. Persons with lower CCl had a higher prevalence of multiple lacunar infarcts but this association was not statistically significant in multivariate analysis.

Conclusions: Our findings indicate that subclinical renal dysfunction is associated with a greater burden of cerebral white matter disease, suggesting that it reflect ischemic brain damage caused by generalized microvascular damage. Therefore, early identification of mild renal dysfunction could be needed to reduce the risk of cerebral small vessel disease.

4 Small vessel and white matter disease

OBJECTIVES: To measure prevalence and to study of risk factors of WMLs in population-based sample of healthy middle-aged and elderly people

Methods: The Prevention of Stroke and Dementia (PRESENeT) Project is a regional government-funded ongoing community project in Ansan, Korea for prevention of stroke and dementia by education, public relations, early medical check-up to healthy adults older than 50 years recruited by systemic random sampling. We assessed vascular risk factors and physical examination by in-person interview and performed brain CT scan in 480 stroke- and dementia-free participants (235 Men, 245 women). Associations between presence of WMLs and risk factors were analyzed by logistic regression.

Results: We found in our population-based study a prevalence of cerebral white matter lesions that abruptly increased with age from 2.4% in 50- to 59-year-old participants, 9.0% in 60-69 years to 32% in the oldest (70 years of age and older). Among conventional risk factors, older age and hypertension (adjusted OR, 3.0; 95% CI, 1.2-7.24) were the most important risk factors of WMLs but DM and dyslipidemia were not after adjustment. The adjusted OR of WMLs for higher than 50 percentile of serum homocysteine, compared with lower than 50 percentile was 5.2 (95% CI, 2.2-12.1). The highest quartile of serum CRP has adjusted OR of 2.2 when compared with the lowest quartile. Abdominal obesity based on waist circumference also increase risk of WMLs (adjusted OR, 2.3; 95% CI, 1.06-4.97).

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WML volumes while adjusted for age, gender, 24-hour mean arterial pressure, duration of hypertension and previous antihypertensive treatment (ordinal regression, p≤0.034). No association is found between Hp phenotype and periventricular WML volumes (ordinal regression), or between Hp phenotype and the presence of LACs (logistic regression).

Discussion: Hpl-1 phenotype is known to relate to less vascular regenerating power against endothelial injury. Therefore, the association between Hpl-1 phenotype and the extent of hypertensive deep white matter damage we found, may relate to this functional property of Hp phenotype. As we found no association with the other signs of cSVD, such effect of Hp polymorphism may be vasculature-specific, even within the domain of cSVD.

4 Small vessel and white matter disease

C-REACTIVE PROTEIN IN HEALTHY INDIVIDUALS IS ASSOCIATED WITH EXECUTIVE DYSFUNCTION AND WHITE MATTER ALTERATIONS

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Background: High-sensitivity C-Reactive Protein (hs-CRP) is a sensitive marker of low-grade inflammation. CRP levels have been associated with systemic vascular disease as well as cerebral small vessel disease. There is also growing evidence of a correlation of CRP with cognitive function.

Objective: Under the assumption of an association between structural and functional pathology we tested whether hs-CRP is correlated with cognitive performance and white matter integrity.

Methods: We investigated 273 stroke-free individuals from the population-based SEARCH Health Study, aged 35-82 years (mean 63y, 134 female). Subjects underwent extensive neuropsychological test battery, covering the domains of verbal learning and memory, attention and executive function, working memory and visuospatial skills. MRI was performed at 3.0 Tesla, including FLAIR images for assessment of white matter hyperintensities and Diffusion Tensor Imaging (DTI) for calculation of global and regional fractional anisotropy (FA). DTI is highly sensitive to alterations in white matter architecture. Serum hs-CRP concentration was measured by a high sensitivity assay.

Results: Hs-CRP was negatively associated with executive function, even after adjustment for age, gender, education and cardiovascular risk factors in multiple linear regression models (β = -0.201, p≤0.008). We also observed a positive correlation between hs-CRP and the extent of white matter hyperintensities (p≤0.035). Moreover, even after adjustment there was an inverse relationship between hscrP and global FA (β = -0.211, p = 0.007) as well as regional FA values of the frontal lobes (β = -0.255, p = 0.001) and the genu of the corpus callosum (β = -0.280, p = 0.001).

Conclusion: Our findings support the hypothesis of an inverse relationship between hs-CRP levels and cognitive performance. This association might be mediated by alterations of the white matter interrupting pathways of executive function.

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THE ROLE OF VITAMIN B12 STATUS IN THE IMPAIRED VITALITY OF ENDOTHELIAL PROGENITOR CELLS IN LACUNAR STROKE PATIENTS


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Background: Earlier, we reported that endothelial progenitor cells (EPC), which are important for the maintenance of endothelial integrity, were less vital in lacunar stroke patients (200 pmol/l) as a cut-off point between normal and low Vit B12 status.

In 32 prospectively included first-ever lacunar stroke patients, EPC vitality was assessed using cultures (median counts of EPC clusters per well with interquartile range: c/w; IQR) and numbers were counted with flow cytometry. Vit B12 played a role in EPC function. We hypothesize that in lacunar stroke patients, Vit B12 status is known to relate to less vascular regenerating power against endothelial injury. Therefore, the association between Hpl-1 phenotype and the extent of hypertensive deep white matter damage we found, may relate to this functional property of Hp phenotype. As we found no association with the other signs of cSVD, such effect of Hp polymorphism may be vasculature-specific, even within the domain of cSVD.

Discussion: Lower folate level. We hypothesize that in lacunar stroke patients, Vit B12 status relates to a lower EPC number and vitality in lacunar stroke. Though mechanisms have yet to be determined, these findings could open new strategies for the treatment of patients with lacunar stroke and its consequences.

6 Small vessel and white matter disease

MULTIPLE LACUNAR INFARCTS WITH AND WITHOUT WHITE MATTER LESIONS: DIFFERENCES IN CLINICAL PRESENTATION AND RISK FACTOR PROFILE

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Background: Patients with multiple lacunar infarcts (MLI) with and without white matter lesions (WML) have a wide range of symptoms and signs. The objective of this study was to determine clinical features of MLI in patients with WML in comparison with characteristics of MLI occurring in patients with WML. Risk factor profiles were also compared between these two groups of patients.

Methods: We evaluated 124 patients with MLI. Patients were divided in two groups according to the absence (n=68) and presence (n=56) of WML. Standard protocol included: medical history, neurological and cerebral examination, MRI scan and laboratory tests.

Results: There was no significant difference in sex ratios between observed groups. Majority of patients in both groups had two or more different clinical symptoms (65.3%), but associated symptoms were significantly more often in patients with WML (p<0.01). The most frequent clinical features in both groups were pyramidal (63.7%), followed by vascular cognitive disorder – VCD (vascular cognitive impairment and vascular dementia) (30.6%), extrapyramidal (29.0%) and cerebellar signs (27.4%), depression (26.6%), epilepsy (13.1%), falls (9.7%), urinary dysfunction (6.5%). Patients with MLI and WML showed significantly higher frequency of VCD (p<0.01), depression (p<0.05) and falls (p<0.05). The vast majority of patients with MLI (with or without WML) had cerebrovascular risk factors (93.5%), and amongst them, 73.4% had two or more associated factors. Hypertension was the leading risk factor (71.0%), and then, according to the frequency, came: dyslipidemia (37.1%), cardiovascular diseases (30.6%), diabetes mellitus (29.0%) and smoking (13.1%). Patients with WML were significantly older (p<0.01). There were no other differences in risk factor profile between these two groups.

Conclusion: Presence of WML in patients with MLI is significantly correlated with VCD, depression, falls and older age.

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NONINVASIVE PERIPHERAL BLOOD VISCOSITY MEASURING METHOD FOR DETECTION OF ASYMPTOMATIC BRAIN DISEASE

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Background: The asymptomatic cerebral white matter lesions (CWMH) such as periventricular hyperintensity (PVH) and deep, subcortical white matter hyperintensity (DSWMH) are known to be important risk factors for subclinical clinical cerebrovascular disease. We developed a noninvasive peripheral blood viscosity measuring method which can measure hemorheology. In this study, we investigated the relationship between the change in peripheral blood viscosity and grades of CWMH detected by brain magnetic resonance imaging (MRI) in the subjects who received “Brain Dock” (detection of asymptomatic brain disease).

Methods: We investigated 273 stroke-free individuals from the population-based SEARCH Health Study, aged 35-82 years (mean 63y, 134 female). Subjects underwent an extensive neuropsychological test battery, covering the domains of verbal learning and memory, attention and executive function, working memory and visuospatial skills. MRI was performed at 3.0 Tesla, including FLAIR images for assessment of white matter hyperintensities and Diffusion Tensor Imaging (DTI) for calculation of global and regional fractional anisotropy (FA). DTI is highly sensitive to alterations in white matter architecture. Serum hs-CRP concentration was measured by a high sensitivity assay.

Results: Hs-CRP was negatively associated with executive function, even after adjustment for age, gender, education and cardiovascular risk factors in multiple linear regression models (β = -0.201, p≤0.008). We also observed a positive correlation between hs-CRP and the extent of white matter hyperintensities (p≤0.035). Moreover, even after adjustment there was an inverse relationship between hs-CRP and global FA (β = -0.211, p = 0.007) as well as regional FA values of the frontal lobes (β = -0.255, p = 0.001) and the genu of the corpus callosum (β = -0.280, p = 0.001).

Conclusion: Our findings support the hypothesis of an inverse relationship between hs-CRP levels and cognitive performance. This association might be mediated by alterations of the white matter interrupting pathways of executive function.

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CWML by MRI in each subject, the grade of CWML and the change in peripheral blood viscosity were compared.

**Results:** ACI and/or CWML were found in 17 subjects (40%). In the comparison of the studied subjects with normal parameters (such as age, body mass index and blood pressure and so on) between the groups, only the blood viscosity was lower in the ACI and/or CWML group than the normal group (p=0.0297). There was no relationship between changes in blood viscosity and grades of PVH. However, peripheral blood viscosity was lower in the DSWMH progressed group (grade equal or more than 2) (p=0.0362).

**Conclusion:** It is reported that high blood pressure is one of the strongest risk factors for ACI and/or CWML (specifically in CWML). In conclusion, our method could be useful to measure risk for cerebrovascular diseases related to high blood pressure such as CWML.

8 Small vessel and white matter disease

**ASSOCIATION BETWEEN WHITE MATTER LESIONS IN MRI, CAROTID ATHEROSCLEROSIS AND CENTRAL SYSTOLIC BLOOD PRESSURE**

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**Objectives:** White matter hyperintensities (WMHs) observed on magnetic resonance images (MRIs) are associated with age and hypertension; suggesting a vascular mechanism in pathogenesis. Central systolic blood pressure (cSBP) parameter of arterial blood pressure correlates more closely with the measures of cardiovascular disease (CVD) risk than brachial pressure. We sought to determine whether the cSBP correlates with WMHs and whether cSBP can serve as a better predictor of CVD.

**Methods:** In an unselected consecutive subject who underwent B-mode ultrasound of the common carotid arteries for the far wall intima-media thickness (CCA-IMT); radial anplation tonometric measurement for cSBP and augmentation index (AI) was carried out. WMHs were assessed retrospectively in FLAIR-MRIs as periventricular hyperintensities (PVH) and deep white matter hyperintensities (DWMH) and rated using Fazekas scale.

**Results:** 179 patients, 95 (52%) males with mean age 66±13 years were included. 17, 74, 67, and 21 patients had PVH grades 0, 1, 2, and 3 respectively. 48, 69, 49, and 13 had DWMH grades 0, 1, 2, and 3 respectively. PVH correlated with age, brachial SBP, cSBP and AI (r=0.49, 0.28, 0.23, p<0.002 and 0.13, p<0.05). DWMH also correlated with age, brachial SBP and cSBP (r=0.41, 0.302, 0.22 p < 0.003) but not with AI. Mean CCA-IMT was 0.68±1.33mm. CCA-IMT correlated with PVH/DWMH and increased with PVH/DWMH grades. Patients with grades 0-1 and 2-3 stratified into two-groups; CCA-IMT more-than and less-than median (0.8mm) showed significantly high cSBP in > median group.

**Conclusions:** cSBP, measure of arterial stiffness correlated with PVH and DWMH in FLAIR-MRIs and also with the CCA-IMT. cSBP might serve as the better predictor of cerebral WMHs and systemic atherosclerosis.

9 Small vessel and white matter disease

**SYMPTOMATIC AND SILENT LACUNAR INFARCTS ARE LOCATED IN DIFFERENT SMALL VESSEL TERRITORIES**

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**Background:** Most reports on lacunar infarcts have focused on anatomical structures instead of vascular territories. One earlier CT-study found different vascular territories for silent and symptomatic lacunar infarcts. Such difference may hypothetically point at different vascular pathologies. As CT is quite insensitive for the detection of lacunar infarcts, we now repeated the study with MRI.

**Methods:** To detect lacunar infarcts, we now repeated the study with MRI.

**Results:** 179 patients, 95 (52%) males with mean age 66±13 years were included. 17, 74, 67, and 21 patients had PVH grades 0, 1, 2, and 3 respectively. 48, 69, 49, and 13 had DWMH grades 0, 1, 2, and 3 respectively. PVH correlated with age, brachial SBP, cSBP and AI (r=0.49, 0.28, 0.23, p<0.002 and 0.13, p<0.05). DWMH also correlated with age, brachial SBP and cSBP (r=0.41, 0.302, 0.22 p < 0.003) but not with AI. Mean CCA-IMT was 0.68±1.33mm. CCA-IMT correlated with PVH/DWMH and increased with PVH/DWMH grades. Patients with grades 0-1 and 2-3 stratified into two-groups; CCA-IMT more-than and less-than median (0.8mm) showed significantly high cSBP in > median group.

**Conclusions:** cSBP, measure of arterial stiffness correlated with PVH and DWMH in FLAIR-MRIs and also with the CCA-IMT. cSBP might serve as the better predictor of cerebral WMHs and systemic atherosclerosis.

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**ARTERIOLES IN CAA AND VASCULAR DEMENTIA**

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**Background:** Small cerebrovascular lesion was one of the most important factors in CAA and VDs. We analyzed the difference of arterial pathology between CAA and VDs.

**Methods:** Ten deceased CAA patients and twelve deceased Vascular Dementia patients without CAA were available for this study. Five deceased patients without known cerebrovascular diseases served as controls. All transversely cut arterioles in the gray matter and white matter with external diameter equal or larger than 30μm and with maximum of 300μm were examined. The internal and external diameters of arterioles were measured.

**Results:** The external diameter of GM in the CAs was significantly greater than Controls. In GM arterioles, the diameter of lumen in VDs is markedly smaller than those in CAs, whereas there are no difference between CAs and Controls. CAs and VDs may cause remarkable thickening of the artiurial walls, Both in WM and GM. The SI of arterioles in VDs was significantly greater than CAs and Controls.

**Conclusions:** Fibrotic thickening and stenosis of the walls of arterioles occur both in CAs and VDs, but the tendency is more significant in VDs. Arterioles of CAs also display the expanding in GM, which may be related with lobar haemorrhage.

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**NOCTURNAL LIMB MOVEMENTS ARE CORRELATED WITH CEREBRAL WHITE MATTER DISEASE BURDEN**

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**Background:** Obstructive sleep apnea is an independent risk factor for cerebrovascular disease and is associated with white matter hyperintensities (WMH). Recently, periodic limb movements (LM) have been associated with significant increases in blood pressure in sleep as well as cardiovascular and cerebrovascular disease. We hypothesized that LM and other intrinsic sleep abnormalities might be associated with WMH.

**Methods:** Patients assessed for cognitive complaints in a tertiary memory clinic were referred for polysomnography for various sleep concerns. Polysomnography, which occurred within one year of neuromaging, was scored according to the American Academy of Sleep Medicine criteria. WMH were rated using Age Related White Matter Changes Score (ARWMC) from FLAIR and microbleeds were counted on gradient echo MRI. Polysomnographic results (transformed where necessary) were correlated with ARWMC using Pearson correlations.

**Results:** Participants (N=22; 64% male) were 66.3±11 years, with hypertension (27%), dyslipidemia (32%), diabetes (5%), prior stroke (14%) and had mildly affected cognition with mean MMSE score of 26.4±4.1. Four patients were diagnosed with neurodegenerative disease including Lewy Body (n=2), Alzheimer (n=1) and early Huntington’s (n=1). LM per hour of sleep was highly correlated with WMH, r=0.55 p=0.004 as was sleep efficiency (time asleep/time in bed) r=-0.65, p<0.001. One patient with microbleeds (lobar) had severe restless legs and significant oxygen desaturation to 68% while the other (1 deep, 1 lobar) had very poor sleep efficiency (53%).

**Discussion:** LM were significantly correlated with WMH, consistent with emerging evidence implicating their association with cardiovascular and cerebrovascular disease. Sleep efficiency was also highly correlated with WMH. These findings suggest that LM associated with poor quality sleep may lead to a hypertensive stress which contributes to white matter disease.

Poster Session Blue

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FREQUENCY OF NOTCH 3 GENE MUTATIONS IN PATIENTS SUSPECTED CADASIL: RETROSPECTIVE ANALYSIS IN JEJU ISLAND, KOREA

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Background: Several characteristic clinical features and cranial magnetic resonance imaging (MRI) findings have been reported in patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopa-thy (CADASIL). However, the frequency of Notch 3 gene mutations in patients showing such characteristics has not been evaluated thoroughly as yet. The purpose of this study is to determine the frequency of Notch 3 gene mutation in patients who had MRI indicative of CADASIL or clinically suspected as CADASIL.

Methods: We retrospectively reviewed clinical, cranial MRI findings of the patients who underwent analysis of the mutations of Notch 3 gene between September 2004 and August 2008 at the department of Neurology, Jeju National University Hospital. From September 2004 to December 2006, we had screened exon 3, 4, 11, 18 and then we extended analysis to exon 2–11, 18 for the rest of the study period. The patients showed at least one of the following lesions on MRI: leukoaraisis with an involvement of external capsule or anterior temporal lobe, or presence of lacunar infarctions. We also included the patients who were clinically suspected as CADASIL.

Results: During study period, the mutations of Notch 3 gene was screened in 165 symptomatic patients from 164 families. The mean age of the patients was 65.5±12.2 years (range from 34 to 98) and 50.3% were men. Among them, we found the Notch 3 gene mutations in 57 patients (34.5%) including new unconfirmed mutations. All patients except eight patients had made a same mutation in exon 11 (R544C).

Conclusions: The mutations of Notch 3 gene are frequently found in patients who had MRI indicative of CADASIL or were clinically suspected as CADASIL in our population. The presence of a predominant mutation suggests a possible founder effect in an island population.

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DIFFUSION TENSOR IMAGING DEMONSTRATING FIBER IMPAIRMENT IN SEVEN PATIENTS WITH SUSAC’S SYNDROME

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Background: Susac’s syndrome is a rare disease that is thought to occur mainly in young women. It is characterized by the triad of hearing loss, branch retinal artery occlusions, and encephalopathy with predominantly cognitive and psychiatric symptoms. Treatment consists of immunosuppressive therapy. Focal ischemic lesions in the corpus callosum detectable by conventional MRI are a typical feature of Susac’s syndrome. The appearance of these lesions is not, however, correlated with the type and severity of the neuropsychological deficits.

Methods: We compared the pattern of lesions and impaired fiber integrity and tested the hypothesis of whether widespread tissue damage of the otherwise normal-appearing white matter (NAWM) could be detected in three men and four women with Susac’s syndrome using diffusion tensor imaging (DTI); a noninvasive technique for detection of macro- and microstructural impairment of fiber integrity on the basis of normal values for the fractional anisotropy (FA), compared to a group of 63 healthy controls.

Results: Impairment of fiber integrity in every patient was found. Compared to the controls, every patient showed disruption of fiber integrity in the genu of the corpus callosum.

Conclusion: We hypothesized that the neuropsychological symptoms in patients with Susac’s syndrome are correlated well with the FA alterations detected with DTI. The fiber impairment in the genu seems to be specific for patients with Susac’s syndrome.

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PATHOGENETIC DIFFERENCE BETWEEN DEEP WHITE MATTER HYPERINTENSITY AND PERIVENTRICULAR HYPERINTENSITY OF MRI IN PATIENTS WITH CEREBRAL INFARCTION

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Background: Small ischemic lesions of the cerebral white matter are classified as deep white matter hyperintensity(DWMH)or periventricular hyperintensity(PVH), and scored respectively. These lesions contain asymptomatic small cerebral infarctions, and predict development of symptomatic cerebral infarction in the future. We investigated the difference of clinical significance between DWMH and PVH in patients with cerebral infarction.

Methods: Subjects were 1264 consecutively admitted inpatients(796 men;468 women;mean age: 72 years)from 2005 to 2007 with a diagnosis of acute cerebral infarction. DWMH and PVH were scored respectively(Fazekas et al, 1993)in each patient using head MRI FLAIR image, there scores were evaluated comparatively with clinical data(e.g. previous histories, the types of cerebral infarction, etc).

Results: Positive correlation was seen in past symptomatic cerebral infarctions, high blood pressure, and the age in both DWMH and PVH score. They showed negative correlation to smoking. On the other hand, high plasma homocysteine value and existence of lacunar infarction indicated strong positive correlation only to the DWMH score. Positive correlations were also observed against diabetes and kidney dysfunction. Hypertension and existence of atherosclerosis correlated positively only to the PVH score.

Conclusion: Both DWMH and PVH are related to age and hypertension that are strong risk factors of cerebral infarction. DWMH is more likely to be related to small vessel disease. There may be pathogenetic difference between DWMH and PVH.

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AUTOANTIBODIES AGAINST OXIDIZED LIPOPROTEINS RELATE TO SILENT ISCHEMIC LESIONS IN LACUNAR STROKE PATIENTS

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Introduction: Auto-antibodies against oxidized low density lipoprotein (oxLDL) and heat shock protein 60 (HSP60) as well as higher levels of C-reactive protein (CRP) relate to atherosclerosis and its consequent vascular events. Both atheroscle-rosis and arteriolarosclerosis can lead to cerebral small vessel disease (cSVD). Of these two entities, arteriolarosclerosis most likely causes silent ischemic lesions (SIL). These entities however differ in their pathology, which in part may relate to a difference in the involvement of auto-antibodies.

Methods: In 178 consecutive lacunar stroke patients and 43 healthy controls we investigated the difference of clinical significance between DWMH and PVH in patients with cerebral infarction.

Results: hsCRP concentrations were lower in healthy controls than in patients (3,13±2,56 vs 5,56±12,90 mg/L; p=0,02). Furthermore, the IgM anti-MDA-oxLDL ratio was higher in healthy controls than in lacunar stroke patients with SIL (5,53±3,06 vs 4,63±2,25; p=0,03) but not higher in patients without SIL (5,03±2,45). Furthermore, in lacunar stroke patients without SIL, IgG anti-hypochlorite-oxLDL levels were lower than in those with SIL (OD 0,48±0,11 vs 0,34±0,19; p=0,02).

Discussion: Firstly, higher levels of hsCRP in lacunar stroke patients point at inflammatory activation in cSVD in general. Secondly, results of IgM anti-MDA-oxLDL suggest a possible protective role of this antibody in healthy controls as well in lacunar stroke patients without SIL, in which the titre is higher. Finally, higher IgG anti-hypochlorite-oxLDL levels in patients with silent lesions indicate an autoimmune reaction in arteriolarosclerosis. However, whether this reaction is causal to WML requires further investigation.
Primary angitis of the central nervous system of childhood (cPACNS) is a recently recognized disorder causing acute ischemic strokes and other neurological deficits in this age group. cPACNS can be divided into large-, medium, and small-vessel vasculitis.

We report the clinical course combined with the development of CSF- and brain MRI-findings in a now 15 year old female patient. First symptoms appeared at age 9 with headaches and right-sided hemiparesis. A slightly elevated CSF-protein and multiple left-hemispheric hyper intense lesions on T2 weighted MR-images led to the diagnosis of acute disseminated encephalomyelitis (ADEM). Within the following 12 months two more relapses with almost complete remission occurred. Later she developed a progressive disease course with an aggravating hemiparesis, dysarthria, and impaired cognitive functions. The additional finding of oligoclonal bands in CSF and the progression of MRI changes made the diagnosis of multiple sclerosis (MS) highly possible. Following a considerable clinical deterioration accompanied by increasing MRI lesions a brain biopsy established the diagnosis of a small-vessel vasculitis. This new diagnosis has important therapeutic implications for the patient.

Heart & brain

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SUBDIAPHRAGMATIC VISCERAL INFARCTION PREVALENCE IN PATIENTS WITH CARDIO-EMBOLIC STROKE

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Background: The prevalence of subdiaphragmatic visceral infarction (SDVI) in autopsied patients with brain infarction is 22% with a significant association between SDVI and cardio-embolic strokes (Multiple Atherosclerosis Site in Stroke study)

Objective: To evaluate the prevalence of SDVI in patients with definite cardio-embolic stroke or TIA using Diffusion-Weighted Imaging abdominal MRI

Results: A total of 27 consecutive patients with stroke or TIA and a history of non rheumatic valvular atrial fibrillation were included in the study. 26 patients had brain infarction and 1 patient had definite TIA. The mean age of all patients was 81 years; 40,7% were male; high blood pressure was present in 27%, diabete mellitus in 27%, cigarette smoking in 26% and hypercholesterolemia in 27%. SDVI were considered if hyperintensity signals were found in Diffusion Weighted Imaging (DWI) abdominal MRI (positive in B0 and B600 sequences). 3 renal and 2 splenic infarctions were found in 4 patients (14,8%). We found no hepatic infarction. There was no significant association in atrial fibrillation characteristics or transphotoac and transesophageal echocardiography findings between patients with or without SDVI.

Conclusion: Using abdominal MRI DWI, prevalence of SDVI is 14.8%. This prevalence was higher in the MASS study probably because it is derived from an autopsied database. Signification of abdominal MRI DWI findings has to be correlated with a further study combining abdominal CT and DWI MRI findings.

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INTENSIVE CARDIAC MONITORING AFTER TRANSIENT ISCHAEMIC ATTACK IDENTIFIES A SIGNIFICANT NUMBER OF PREVIOUSLY UNKNOWN PAROXYSMAL ATRIAL FIBRILLATION

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Background: Atrial fibrillation (AF) and paroxysmal AF (PAF) are significant risk factors for stroke. Strategies to improve detection will help reduce stroke recurrence. In previous studies, cardiac telemetry detected new AF in 2.5%; 24 hour monitoring 3.8-6.7%; event loop recorders 5.7-15%; and auto-triggered loop recorders 36%. We aimed to evaluate the incidence of new diagnoses of AF and PAF in a TIA population using a combination of inpatient telemetry and outpatient 72 hour cardiac monitoring.

Methods: From 1st January 2008 to 30th July 2008, all TIA patients at Southend University Hospital with no prior diagnosis of AF or PAF underwent evaluation of cardiac rhythm. High risk TIA’s were admitted for 24-72 hours cardiac telemetry and further outpatient 72 hour cardiac monitoring if required. All low risk TIA’s received 72 hour outpatient monitoring. Primary end point was detection of AF and PAF. Medical notes, ECGs and cardiac monitor reports of all TIA patients were analyzed retrospectively.

Results: There were 115 diagnoses of TIA. The average age was 73.6 years. 20 (17.4%) had pre-existing AF or PAF. Of the remaining 95 patients, 4 (4/95 = 4.2% yield) had AF on initial 12 lead ECG. 62 high risk TIA’s underwent inpatient telemetry. This identified a further 4 patients (4/62=6.5% yield). Of the remaining un-diagnosed 87 patients, 72 underwent outpatient 72 hour cardiac monitoring. This detected another 17 (17/72=23.6% yield) cases of PAF. Of these 17, 8 had previously normal inpatient telemetry. In total there were 25 new diagnoses of AF or PAF (25/95=26.3%).

Conclusions: An intensive cardiac rhythm monitoring strategy after TIA identifies a significant proportion of patients with previously unknown AF or PAF in our population. This is at a higher level than previous reports, and comparable with longer and more expensive methods. We recommend 72 hour monitoring rather than 24 hour monitoring as a standard in patients without known AF or PAF following TIA.

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PREVALENCE OF HIGH INTENSITY TRANSIENT SIGNALS IN PATIENTS WITH ACUTE CORONARY SYNDROMES

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Background: High intensity transient signals (HITS) are frequent in patients with atherothrombosis and are correlated to the risk of cerebrovascular events. Only one study examined the prevalence of HITS in patients with ACS, almost 10 years ago and found a 17% prevalence, their presence was associated to stroke risk. Since then, ACS treatment has changed and the incidence of stroke has diminished. We aimed at evaluating the incidence of HITS in ACS, and at exploring their predictive value for stroke events.

Methods: From December 2004 to October 2006, 209 consecutive patients with ACS were studied within 72 hours of symptom onset. ACS were categorized into unstable angina, non-STE MI, STE-MI. Patients with prosthetic heart valves or previous stroke were excluded. HITS monitoring was performed on both middle cerebral arteries by transcranial Doppler (DWL type Multipod device) during 30 minutes. Data were analysed on-line and off-line by two neurologists.

Results: All patients were treated according to current ESC guidelines. Specifically, heparin(s) were prescribed in 99% of the patients, aspirin in 100%, clopidogrel in 83%, intravenous glycoprotein IIb/IIIa inhibitor in 60%, fibrinolysis in 8% and angioplasty in 77%. TCD monitoring was performed at a median delay of 32 hours after symptom onset (inter-quartile range, 20 to 46 hours). HITS were only detected in 7 patients (incidence rate 3.4%; 95%CI 4.6-8.8). Except a significant higher incidence of HITS in patients with unstable angina compared to other ACS (8.5% vs. 1.9%, p<0.047), none of the factors among baseline characteristics, clinical features, and cardiac findings were associated with the presence of HITS. During hospitalization, one stroke and two TIA’s occurred, all in patients without HITS.

Conclusion: The prevalence of HITS among ACS patients was very low and did not appear to correlate with the risk of in-hospital stroke/TIA. This may be related to the current high rates of use of combination antithrombotics.
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CAROTID ARTERY DISEASE AND STROKE IN CARDIAC SURGERY. A SINGLE-CENTER EXPERIENCE ASSESSING THE UTILITY OF A PREOPERATIVE CEREBROVASCULAR CONSULTATION

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Background: Carotid disease has been implicated in the aetiology of perioperative stroke after cardiac surgical procedures. The aim of this study was to assess the risk of stroke/TIA in patients undergoing cardiac surgery and the value of a guide designed and applied by the Stroke Unit for an appropriate treatment of the stenosis carotid.

Methods: We prospectively collected consecutive patients admitted to the Department of Cardiovascular Surgery between May 2005 and November 2008. All patients underwent a routine ultrasonic screening before surgical procedure. Patients with carotid stenosis were referred to the Stroke Unit for a cerebrovascular consultation (neurological examination, Transcranial Doppler and MRI angiography). Patients were considered for carotid intervention if they had a pre-operative lesion (>80%), a symptomatic carotid >70% or a contralateral occlusion and significant stenosis >70%. We analysed the influence of carotid stenosis on stroke/TIA within 60 days after surgical intervention.

Results: We recruited 250 patients, (213 men and 47 women, mean age 70.5±6.9) admitted for isolated coronary-artery bypass grafting (CABG) (n=189), combined CABG and valve surgery (n=39), and isolated valve surgery (n=32). The rate of postoperative stroke was 6.5%. In the group of patients with carotid stenosis >70% the rate of stroke was 16.7% (6/30, p=0.018). The incidence of stroke was significantly greater in the group with combined CABG valve surgery (9/30; p<0.001). 5 staged carotid stenting procedures and 1 simultaneous carotid endarterectomy/CABG were performed.

Conclusions: We found a relationship between carotid stenosis and perioperative stroke after CABG surgery. The results indicate that the management of these patients needs new studies to evaluate the stratification of risk and to establish new treatment strategies.

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VAScULAR MORPHOLOGICAL AND FUNCTIONAL IMPAIRMENTS IN SYMPToM-FREE, NON-TREATED HYPERTENSION PATIENTS

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Background: Chronic hypertension (HT) results in morphological and functional changes in the vessels. Our aim was to verify these initial subclinical alterations in early stage hypertension.

Methods: The diagnosis of HT was based on ambulatory blood pressure monitoring. Diabetic patients were excluded and all HT patients had normal CT. 78 HT patients (mean age: 44.8±10.1 years, male/female: 0.85) were compared with 85 age-matched controls (mean age: 43.5±9.3 years, male/female: 1). In both groups blood tests, immuno-media thickness (IMT) and vascular stiffness parameters were measured. Attention and memory, anxiety and depression state were also determined by twelve neuropsychological tests. Continuous, non-invasive and simultaneous monitoring of cerebral (MCA velocity) and cardiac haemodynamical parameters were analyzed during head-up tilt table testing (HUTT).

Results: No significant differences were observed between the blood values of the two groups. The IMT was significantly thicker in the HT patients compared to the control group (0.62±0.11 mm vs. 0.54±0.08 mm, p<0.0001). Significant differences were also found in stiffness parameters: brachial augmentation index (AIx-br) was -7.69±29.63% in the HT group and -21.23±26.28% in the control group (p=0.0031), aortic pulse wave velocity (PWV) was 10.06±6.23/ in the HT group and 8.64±1.96/ in the control group (p=0.0001). Alterations of neuropsychological performances of HT patients were also observed in some tests (WAIS Digit Span Test-forward recall p<0.0001, WAIS Digit Symbol Test p<0.0054). Anxiety was significantly more often present in the HT patients. The results of the parameters obtained by HUTT are under evaluation.

Conclusion: Early morphological and functional impairments of the CNS could be detected in the symptom-free non-treated hypertensive patients.

Heart & brain

MAXIMIZING THE HEMODYNAMIC BENEFIT OF EXTERNAL COUNTERPULSATION (ECP); EFFECT OF ECP ON MIDDLE CEREBRAL ARTERY MEAN FLOW VELOCITY IN STROKE PATIENTS UNDER DIFFERENT CUFF INFLATION PRESSURE

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Background: External counterpulsation (ECP) uses ECG-triggered pressure during diastole applied by air-filled cuffs around the lower extremities. The diastolic augmentation and systolic unloading increase blood flow to the heart and brain. An optimal cuff inflation pressure for maximizing the hemodynamic effect of ECP is unknown. We evaluate ECPs effect on blood pressure (BP), cardiac parameters and middle cerebral artery (MCA) cerebral blood flow velocity (CBFV) under various cuff inflation pressures.

Methods: Eight patients (67.6±9.9 years) with acute MCA territory infarct were studied. CBFV of bilateral MCAs were measured by transcranial Doppler. Hemodynamic parameters were measured with a simultaneous radial arterial pressure measurement to validate the results of bilateral measurements. CBFV was measured before, during and after ECP.

Results: ECP induced a significant increase in HR, BP, CO and mean CBFV. Mean BP increased with increasing cuff inflation pressure and reached its maximum at 262.5 mmHg. A maximum increase in ECP of EDC was detected in the symptom-free non-treated hypertensive patients. The incidence of stroke was significantly greater in the group with combined CABG/valve surgery (>70%) compared to the group with isolated CABG (6.7%). The changes in MCA CBFV were not significantly different between the groups. The IMT was significantly thicker in the HT patients compared to the control group (0.62±0.11 mm vs. 0.54±0.08 mm, p<0.0001). Significant differences were also found in stiffness parameters: brachial augmentation index (AIx-br) was -7.69±29.63% in the HT group and -21.23±26.28% in the control group (p=0.0031), aortic pulse wave velocity (PWV) was 10.06±6.23/ in the HT group and 8.64±1.96/ in the control group (p=0.0001). Alterations of ECPs effect on blood pressure (BP), cardiac parameters and middle cerebral artery (MCA) cerebral blood flow velocity (CBFV) under various cuff inflation pressures.

Conclusion: Early morphological and functional impairments of the CNS could be detected in the symptom-free non-treated hypertensive patients.
Conclusion: ECP induced a maximum increase in cardiac output as well as mean CBFV in bilateral MCAs under an inflation pressure of 225 mmHg.

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BRUGADA SYNDROME REVEALED BY VERTIGO DUE TO CEREBELLAR INFARCTION
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Background: Brugada syndrome (BrS; OMIM 601144) is an electrical cardiac disorder characterized electrographically by a typical ECG pattern of ST segment elevation in precordial leads and right bundle branch block, associated with susceptibility to ventricular tachyarrhythmia, leading to syncope or sudden death. BrS occurs both as a sporadic or a familial autosomal dominant condition. BrS patients present a large variability in clinical presentation, including seizure-like episodes due to recurrent convulsive synapses. More recently, atrial fibrillation and vulnerability has been shown to be enhanced in BrS.

Method and results: A 36-year-old man with no history of vascular disease was admitted for isolated vertigo, nausea and vomiting. Neurological examination disclosed imbalance with bi-directional gaze evoked nystagmus. Brain MRI showed recent cerebellar infarction. Repeated ECG identified transient atrial fibrillation, associated with ST elevation in the precordial leads and incomplete right bundle branch block. Electrophysiological study including ajmaline test confirmed Brugada Syndrome. According to recent guidelines, the patient underwent an implantable defibrillator defibrillator, to prevent syncope and sudden death, in association with anticoagulation to avoid new cerebral infarction. Familial screening identified a resistant persistent atrial fibrillation in his father, and sudden death in 2 paternal uncles in their fifth decades.

Conclusion: Cardiogenic stroke as first manifestation expands the spectrum of BrS clinical presentation. Brugada Syndrome diagnosis justifies a specific treatment (defibrillator implantation) which prevent sudden death and cardiac arrest in these patients, and permit prevention in “healthy” At risk family members.

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NT-PROBNP CONCENTRATION IN DIFFERENT STROKE SYNDROMES AND ITS RELATION TO STROKE SEVERITY AND MORTALITY OF ACUTE STROKE
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Background: We have studied the differences in the concentrations of NT-proBNP in stroke syndromes and TOAST classification categories and related these to stroke severity and mortality.

Methods: Acute stroke patients studied for the variables of NT-proBNP, measured within a mean of three days. Stroke severity was measured with Scandinavian Stroke Severity Score (SSS). Outcome was measured as mortality at 120 days.

Results: One hundred fourteen patients, mean age 73±12, 59 females were studied. 13 patients had died at 120 days. Mean concentrations of NT-proBNP in the stroke syndromes were: TACS (19 patients), 594±1085; PACS (49), 153±295 and LACS 184±499. There were significant differences in these concentrations between groups on ANOVA analysis – p=0.04; the most significant difference was between TACS and PACS, p=0.01. NT-proBNP concentrations in the TOAST groups were: atherosclerotic (ATH) 267±769; cardioembolic (CE) 373±558 and lacunar (LAC) 102±252. ANOVA revealed no significant differences between groups, p>0.29 although there were significant differences between CE vs ATH, p<0.04, and CE vs LAC, p=0.01. Stroke severity analysis with SSS revealed significant differences between stroke syndromes (ANOVA for stroke syndromes p=0.04 and for TOAST classification 0.001); the most severe strokes were in TACS (SSS 15±6) and atherosclerotic groups (SSS 14±9). There was a significant negative correlation between NT-proBNP and SSS, r = -0.39, p=0.02. Regression analysis revealed NT-proBNP to be the most significant variable predicting mortality at 120 days,wald 15, p<0.001; followed by stroke severity SSS, wald 4.3, p=0.04. Stroke syndromes and TOAST groups were not significant.

Conclusions: NT-proBNP concentrations differ significantly in clinical stroke syndromes and thus may be determined by stroke severity. NT-proBNP however is the most significant variable to predict mortality when stroke syndromes and stroke severity are entered into the equation.

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CEREBRAL MICROBLEEDS ARE UNCOMMON IN ISCHEMIC STROKE PATIENTS ASSOCIATED WITH NONVALVULAR ATRIAL FIBRILLATION
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Background: Patients with cardiogenic ischemic stroke from nonvalvular atrial fibrillation (NVAF) are candidates for long-term anticoagulation as stroke prevention. With increasing age, the benefit/risk ratio becomes unfavorable because of the higher incidence of intracranial hemorrhages. Cerebral microbleeds (MBs) are often associated with both ischemic and in particular hemorrhagic stroke, but rare (about 5%) in a healthy population. Thus, they may be suggest a higher risk for bleeding complications in patients treated with long-term anticoagulation agents (AA).

Methods: 140 ischemic stroke patients with NVAF admitted to our Stroke Unit and undergone MRI studies with T2* imaging were recruited. NIHSS scores were documented every 6 hours and cerebrovascular risk factors were recorded, according to a standardized Stroke Unit protocol.

Results: Among 140 patients (mean age 74±9; 9 years), only nine had MBs as evidenced from T2* MR images. No statistically significant differences between 131 patients without MBs and 9 with MBs were observed regarding hemorrhagic transformation (45/131, 34.4% versus 4/9, 44.4%), arterial hypertension (105/131, 80.2% vs. 9/9, 100%), small vessel disease (100/131, 80.9% vs. 9/9, 100%), diabetes (31/131, 23.7% vs. 3/9, 33.3%), coronary heart disease (61/131, 46.6% vs. 29, 22.2%) and hyperlipidemia (48/131, 36.6% vs. 5/9, 55.6%). However, significantly more patients with MBs than without MBs had already suffered a stroke prior to admission (21/131, 66.6% vs. 6/9, 16%; p<0.01). MBs seem to be uncommon in patients with cardiogenic acute ischemic stroke associated with nonvalvular atrial fibrillation (only 6%), different from what is known in a general heterogeneous stroke population. They do, however, occur significantly more often in patients with repeat cerebrovascular events of either hemorrhagic or ischemic subtype. Incidental detection of MBs should not distract patients from stroke prevention with AAs.

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CEREBRAL BLOOD FLOW IN PATIENTS WITH REDUCED CARDIAC OUTPUT
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Background and purpose: Cerebral blood flow (CBF) is an important variable in cerebrovascular disorders. A noninvasive measurement of global CBF is approved with color duplex sonography of the extra cranial cerebral arteries. In aim to determine changes of CBF in patients with reduced myocardial function, was performed the study in a group of 60 patients (ejection fraction < 40%), aged 40 to 85 years; mean age, 58 years in either sex.

Methods: The internal carotid arteries and the vertebral arteries were examined with the use of a 7.0-MHz transducer of a computed sonography system. Angle-corrected time-averaged flow velocity and the diameter of the vessel were measured. Intravascular flow volumes were calculated automatically as the product median mean flow velocity and the cross-sectional area of the circular vessel. CBF volume was determined as the sum of flow volumes in both internal carotid and vertebral arteries. Left ventricular ejection fraction (LVEF) is measured by trans thoracic echocardiography.

Results: The mean global CBF was 76±9 cm³/min. Mean LVEF was 28±5%. Relative contributions of the carotid and the vertebral arteries to global CBF volume were 78% versus 22%. CBF correspond significantly with LVEF especially in patients with severe reduction of cardiac output (LVEF < 25%).

Conclusion: Our results of noninvasive sonographic measurement of CBF according to echocardiographicale measured ejection fraction suggest on significantly reduced CBF in severe cardiomyopathy patients.

11 Heart & brain

CARDIOVASCULAR EVENTS AFTER A FIRST ATEHEROTHROMBOTIC STROKE
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Background: Atherosclerosis is the first cause of morbimortality in developed...
HEART & BRAIN

THE IMPACT OF ATRIAL FIBRILLATION AND OTHER RHYTHMIC ABNORMALITIES ON THE ONSET AND OUTCOME OF CEREBRAL STROKE

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Background: Rhythmic and conduction abnormalities can decrease cardiac output below a critical level. Aim: to analyse an impact of AF and other rhythm disturbances on the onset and outcome of cerebral stroke (CI).

Material: 2500 pts with the first-ever CI, data from Medline, Cochrane Library, ICI EMBASE (1995-2008)

Methods: conv. EKG, Holter EKG, TTE, TEE, CT, MRI, PET, NIHSS scale, battery of biochemical, hematological parameters according to special protocol.

Results: Risk of CI increases 4-fold in CHD pts, both with or without congestion. AF prevalence in CI pts was 18%. and increases with age. Among people age 50-59, AF is linked to 6.7%, by ages 80-89%, responsible for 36.2% of all CI. Outcome: AF is independent RF for recurrent CI, important cause of death, 28-day mortality was 21.9% as compared to 10.2% in non-AF group, adjusted mortality risk was 23% higher, clinical picture was significantly more severe, CI size: Cls related to AF are larger and disabling compared to other CI causes. The AF existence, not duration, or absolute embolus size is RF. “Silent infarction” was found in 87% comparing to 22% without AF.

ECG abnormalities: Analysis showed ECG abnormalities in 68.1% in Holter monitoring pts as compared to 21.3% by conv.EKG. In improved CI pts, ectopic activity was found in 18.0% in comparison with 43.0%, in deteriorated pts was found in 33.0% in comparison with 68.0%. Heart and brain: close relationship was found: isolated ventricular arrhythmia: decreased CBF by 8%, isolated AF by 12% and atrial/ventricular tachycardia by 25%.

CI prognosis: Combination of two or three abnormalities: peaked P wave, longer QT, arrhythmia, peaked T wave, ST changes were associated with higher incidence of complications or death.

Conclusions: The important RFs for the onset and outcome of CI is not only AF but also other rhythm and conduction abnormalities. 2. RFs interact multiplicatively rather than by summation. Supported by gov. grants APVV05856, LP00156
Acute stroke: reorganization and recovery

1 Dalhousie University, Halifax, Canada; 2Dalhousie University and Queen Acute stroke: reorganization and recovery

Poster Session Blue

Acute stroke: reorganization and recovery

WITHDRAWN

2 Acute stroke: reorganization and recovery

Background: Stroke poses a significant burden on the health care system as a major source of disability and caregiver dependence. Following acute stroke, it is estimated that 21 to 38% of patients will develop aphasia. Aphasic stroke patients have been shown to have significantly higher mortality rates and decreased rates of recovery than individuals with non-aphasic strokes.

Methods: A database was used to obtain information regarding stroke type, stroke severity and level of independent functioning prior to admission to the Acute Stroke Service at the QEII Health Sciences Centre in Halifax, Nova Scotia. Patients eligible for study inclusion had to be admitted from 2001 to 2002, meet the unit admission requirements of suspected or confirmed disabling stroke or intracranial hemorrhage not requiring surgery, and be deemed independent prior to hospital admission. Follow-up data pertaining to patient place of residence and level of independent functioning was collected at 12 months.

Results: 21.8% (104/476) of the study population had strokes which resulted in aphasia. Analysis of stroke severity scores on admission revealed that significantly more aphasic individuals (68%) had severe strokes compared to non-aphasic individuals (7%)(p<0.0001). A higher percentage of aphasic patients (66%) were dead or dependent at 12 months compared to non-aphasic stroke patients (34%)(p=0.0001). 20% fewer aphasic stroke survivors returned home and 12% more were living in a long term care facility than non-aphasic patients at 12 months.

Conclusions: Our data has demonstrated that aphasic stroke patients are at higher risk of having severe strokes and being dead, dependent or living in a long term care facility at 12 months. It is hoped that the information gained from this evaluation can be utilized by primary care practitioners in the assessment of acute stroke patient outcomes to facilitate evaluation of patient prognosis and adequate planning for optimal patient care.

3 Acute stroke: reorganization and recovery

PREDICTORS OF DISCHARGE DESTINATIONS AFTER ACUTE HOSPITALIZATION FOR STROKE

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Background: Early identification of stroke patients in need of rehabilitation facilities or nursing homes care may promote better use of health care resources and improve outcome. We determined predictors of discharge destinations after acute hospitalization for stroke.

Methods: This study was part of a prospective, nationwide, multicentre, hospital-based, observational study including all the consecutive incident cases of stroke within a 4-month period. Patients were assessed on admission by the National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS).

Results: We included 2,966 patients, 2,529 (85.3%) with an ischaemic and 437 (14.7%) with an haemorrhagic stroke. Among the 2,780 (94.0%) survivors, 1,695 (61.0%) patients were discharged to home, 772 (27.8%) to rehabilitation facilities, and 223 (8.0%) to nursing homes; 90 (3.2%) patients were discharged to other hospital departments for comorbidities, need of surgery or of further evaluation. At the multivariate analysis, including demographic variables and vascular risk factors, older age (odds ratio [OR] 1.01, 95% confidence interval [CI] 1.01-1.02; P=0.019 for each 1-year increase) and higher scores on admission at the NIHSS (OR 1.14, 95% CI 1.11-1.17; P<0.001 for each 1-point increase) and at the mRS (OR 1.68, 95% CI 1.54-1.83; P<0.001 for each 1-point increase) were associated with a higher probability of being discharged to rehabilitation facilities or nursing homes with respect to home. Patients with an NIHSS score >7 had a 65.9% probability of being discharged to rehabilitation facilities or nursing homes (estimated sensitivity=0.820; estimated specificity=0.592); this probability increased up to 69.1% in patients with an NIHSS score >7 and a mRS score >3.

Conclusions: After an acute stroke, more than one third of the patients needed rehabilitation facilities or nursing homes. Severity of the event on admission was the most important predictor of discharge destination.

4 Acute stroke: reorganization and recovery

SUBJECTIVELY REPORTED MEASURES OF SLEEP QUALITY ARE NOT ASSOCIATED WITH FATIGUE FOLLOWING STROKE AND TIA

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Introduction: Fatigue affects up to 70% of people following stroke. Sleep disordered breathing (sleep apnoea and hypopnoea) also affects up to 70%. 30% of older people suffer symptoms of insomnia and stroke is associated with significant disruption of sleep structure. We determined the relation between self reported sleep difficulties and fatigue/sleepiness in patients following stroke.

Methods: Subjects were recruited from neurovascular and secondary prevention clinics, interviewed and completed questionnaires as to their sleep habits. They also completed Fatigue Severity Scores (FSS) with a score <4 regarded as indicative of significant fatigue. The Epworth Sleepiness Scores (ESS) with a score >10 indicate significant daytime somnolence. 5 point likert scales (“never”, “rarely”, “sometimes”, “often” or “always”) were completed as to frequency of sleep disorders. Reports of “often” or “always” were recorded as significant.

Results: 92 subjects were interviewed with complete data available on 89. Median age was 70 years, 46% were male. Mean FSS was 3.9, mean ESS was 6.6 (>10 is significant). Reported sleep associated problems were as follows: n Proportion I often feel sleepy during the day. 28 (31%) Any of the above 73 (82%) There is significant). Reported sleep associated problems were as follows: n Proportion I have problems falling asleep. 25 (28%) I wake frequently at night. 32 (36%) I wake early in the morning. 40 (45%) I have problems rising in the morning. 18 (20%) I often feel sleepy during the day. 28 (31%) Any of the above 73 (82%) There was no significant correlation between ESS and FSS (r=0.067, P=0.55 Pearson’s Rho) or with any Likert scale, but “I have problems rising in the morning” and “I feel sleepy during the day” correlated with FSS (r=0.267, P=0.16 and r=0.300, P=0.086).

Conclusion: Self reported features consistent with impaired initiation and maintenance of sleep are very common in this population but they correlate poorly with measures of daytime sleepiness and fatigue scores.
6 Acute stroke: reorganisation and recovery

**EFFECT OF STROKE GUIDELINES ON STROKE MORTALITY DURING ADMISSION AND THE SUBSEQUENT 3 YEARS**

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**Introduction:** We present here the effect of stroke guidelines on mortality during admission and for the three years after discharge from hospital.

**Methods:** Data on all patients aged 18 years and over were collected for the years 1998, 2003 and 2005. The hospital has a 30 bedded stroke unit and stroke guidelines were first implemented in 1999. There is an integrated stroke care pathway for all patients admitted with stroke.

**Results:** Total number of stroke patients admitted were 369 (1998), 349 (2003) and 331 (2005). The rate of brain imaging was 66% in 1998 and 95% in 2005 (p<0.005). The number of patients who died during their admission with stroke was 40% (146/369) in 1998 and 29% (97/331) in 2005 (p<0.05). The mortality rates for the years 1, 2 and 3 following discharge were 17% (39/223), 8% (14/170) and 9% (14/170), 12% (22/176) and 9% (14/170) for the year 1998 and 16% (38/234), 12% (22/176) and 9% (14/170) for the year 2005 respectively.

**Conclusions:** Our data show that rigorous implementation of stroke guidelines can result in a significant improvement in overall stroke care and reduce inpatient stroke mortality. However, the reduction in mortality is not sustained for the subsequent 3 years after discharge.

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**Abstract 6 – Table 1. Yearly mortality figures following discharge in acute stroke patients**

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Discharged in 1998 (n=number)</th>
<th>Yearly mortality following discharge (proportional)</th>
<th>Alive in 2008 (n=number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 yrs</td>
<td>47</td>
<td>6% (34/6)</td>
<td>2% (1/41)</td>
</tr>
<tr>
<td>66-75 yrs</td>
<td>68</td>
<td>15% (10/6)</td>
<td>3% (1/30)</td>
</tr>
<tr>
<td>76-85 yrs</td>
<td>80</td>
<td>24% (19/80)</td>
<td>4% (1/25)</td>
</tr>
<tr>
<td>86-95 yrs</td>
<td>25</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td>223</td>
<td>17% (38/223)</td>
<td>9% (14/156)</td>
</tr>
</tbody>
</table>

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7 Acute stroke: reorganization and recovery

**MORPHOLOGIC CHANGES OCCUR IN THE SUBVENTRICULAR ZONE AFTER AN ISCHEMIC STROKE IN HUMANS**


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**Background:** Studies in animal models have shown enhancement of cell proliferation in the subventricular zone (SVZ) after an ischemic stroke. We analyzed the morphologic changes that occurred in the SVZ in patients after an ischemic stroke.

**Methods:** We evaluated the ipsilateral (iSVZ) and the contralateral (cSVZ) SVZ in brain slices from patients with a cerebral non-lacunar infarction. We detected cell proliferation using immunocytochemistry with Ki-67 and PCNA. We used Tuj-1 for immature neurons and PSA-NCAM for migrating cells. We studied changes in the cyto-architecture in the ependymal, gap (hypocellular) and ribbon SVZ layers.

**Results:** The study included 7 patients with a mean age of 82±5 years, who died after a mean of 10±5 days after the ischemic stroke. In comparison with the cSVZ, the following changes were observed in the iSVZ: a prominent gap (mean thickness 78.2±23.3 vs 48.9±13 μm, p<0.001) and ribbon (113.69±22 vs 64.65±13.7 μm, p<0.0001) layers; an increase in cell density of the ribbon layer (1703.07±585.44 vs 1107.87±598.26 nuclei per mm², p<0.0001); an increase of Ki-67-positive cells (17.05±13.15 vs 7.74±11.07 cells per mm², p=0.028). In the iSVZ, mitoses and cells that stained for either Tuj-1 or PSA-NCAM markers were observed more frequently than in the cSVZ, and we also found an enlargement of the cytoplasmic volume of astrocytes.

**Conclusion:** We found unequivocal evidence of activation of the ipsilateral subventricular zone following an ischemic stroke in our patients.
Acute stroke: reorganization and recovery

COMPUTERIZED DYNAMIC POSTUROGRAPHY FOR THE REHABILITATION AFTER STROKE
G.H. Lee
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Background: Balance disturbances are common in individuals after stroke. One way to define these deficits is to provide the individual with a force platform while balance activities are performed. To determine if visual platform feedback improves the platform standing balance outcomes in clients with stroke.

Methods: Thirty patients with hemiplegia after a single-hemisphere stroke that occurred at least 12 months before the study were randomly assigned to one of 2 balance rehabilitation programs-with and without visual cue deprivation. Each lasted for 1 hour and was implemented 5 days a week for 4 weeks. Mean outcome measures Balance under 6 sensory conditions was assessed by computerized dynamic posturography (EquiTest), gait velocity, timed stair climbing, and self-assessment of ease of gait before and after program completion.

Results: Force platform feedback did not improve clinical measures of balance when moving or walking. Significant improvements in laboratory force platform indicators of stance symmetry were found for regimens using visual feedback. There were no significant effects on laboratory postural sway indicators at follow-up assessment.

Conclusions: Balance improved more after rehabilitation with visual deprivation. Posturography improved the measuring methods of assessing stance symmetry, clinical balance outcomes or measures of independence.

Acute stroke: reorganization and recovery

ISCHEMIC STROKE IN CHILDHOOD: FOLLOW-UP WITH DIFFUSION Q-BALL IMAGING
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Introduction: The maturing brain has a remarkable flexibility to recover after paediatric stroke. There has been a longstanding discussion as to what extent injuries in specific areas may impact on other brain regions. Moreover, the time lapse of structural changes in childhood is largely unknown. The aim of this study is to obtain objective records of individual cerebral reorganisation processes after ischemic strokes in childhood.

Subjects and methods: Three affected children/adolescents underwent Diffusion Q-Ball imaging examination within 4 weeks after the acute event, on follow up at 3 and 12 month. We applied a twice-refocused balanced echo planar sequence with house-internal modifications. Furthermore, generalized fractional anisotropy and apparent diffusion coefficient maps were calculated in order to detect neuronal degeneration and in order to investigate potential structural changes in other brain areas between the three scanning sessions.

Results: The comparisons of intra-individual Diffusion Q-Ball imaging data of the different scanning sessions gave us an insight into the individual axonal changes over time. As assumed variances in the distribution of the axonal fibres have been detected near the initial lesions, in homotopic areas of the injured tissue as well as in functionally connected areas. In addition, the analysis points out the additional benefit anisotropy images provide in comparison to conventional structural scans.

Conclusion: Therefore, we conclude that Diffusion Q-Ball imaging provides a unique insight into the dimensions of neuroplasticity after ischemic stroke in childhood. Its non-invasive character allows individual analysis of the extent of structural changes over time. This method may thus be an excellent instrument to assess the severity of ischemic brain insult. In the future it may also help evaluate therapeutic interventions and may provide another benchmark for the effectiveness of rehabilitation after stroke.

Acute stroke: reorganization and recovery

PREDICTORS OF TOLERANCE OF EARLY REHABILITATION USING TILT-TABLE IN ACUTE STROKE PATIENTS
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Background: The aim of this study was to assess the predictors of tolerance of early rehabilitation using tilt-table in acute stroke patients.

Methods: We prospectively included 25 patients (64% males; mean age 59.1 ± 11.2 years) with stroke (84% were ischemic; 16% hemorrhagic) within 24 hours of stroke onset. Patients with arhythmias, severe internal diseases and damages of peripheral nervous system were excluded. All patients were treated using the standard medical and physiotherapy. Eleven patients (main group) were vertigolesed using tilt table under blood pressure (BP), heart rate and SpO2 control. Fourteen patients (control group) changed their position with functional hospital bed. The analysis of heart rate variability (HRV) using short-term recordings (5 minutes) was performed. Total power (TP; m2), standard deviation of the NN intervals (SDNN; ms), low frequency component (VLF; m2), low frequency component (LF; m2), high frequency component (HF; m2) and SDNN were calculated.

Results: Eight (72.7%) patients in main group were successfully tilted using tilt-table on the first day, mean NIHSS score and Glasgow Coma Scale (GCS) at admission were 7.5 ± 1.6 and 15.0 ± 1.5 respectively. The analysis of HRV revealed TP 1050.8 ± 1009.1 m2, SDNN 35.8 ± 11.29 ms. Three patients (27.3%) presented significant decreasing of BP during session on the first day. These patients presented more severe deficit at admission (NIHSS 17.0 ± 3.0, GCS 12.6 ± 2.3, p < 0.05) and lower TP (478.7 ± 72.7 m2) and SDNN (19.6 ± 1.5 ms) (p < 0.05) before session in comparison with patients with good tolerance of tilt table verticalization. All patients in control group presented an adequate reaction.

Conclusion: Severe stroke may lead to disturbances in autonomic nervous system that can limit pathways of rehabilitation. The decreasing of indices of HRV is an indication of such disorders. It is possible that severe stroke and low TP, SDNN are predictors of inadequate respond to early rehabilitation using tilt table.