

# **ABSTRACT BOOK**

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## ORAL PRESENTATIONS

### Wednesday, 21 August 2013

#### STROKE AWARENESS: AN IMPORTANT FACTOR INFLUENCING PREHOSPITAL DELAY AT STROKE ONSET

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Early arrival at the hospital is essential for a good outcome of stroke. However, several studies have shown that only about a third of ischemic stroke patients arrive at the hospital within 3 h of stroke onset. The reasons for late arrival may be associated with different factors, such as the awareness of stroke symptoms, knowledge of stroke treatment possibilities, availability of ambulance service and local medical services. The overall awareness of stroke in Estonia is good. In contrast, several other studies have shown low public awareness of stroke warning signs and stroke risk factors which contribute to late arrival and limited use of intravenous thrombolysis. It has been shown that there is a discrepancy between theoretical stroke knowledge and the reaction in an acute situation which could mostly depend on the severity of initial symptoms. We have interviewed a total of 195 consecutive stroke patients admitted to the Tartu University Hospital about stroke symptoms, actions on stroke onset and family history. The main finding in our study was the strong association between early hospital arrival and the first call being made to the emergency number. The most common reasons for delaying were the hope for spontaneous subsidence of symptoms and perception of the time elapsed from symptom onset as insignificant. Therefore, the necessity to call the emergency number immediately at stroke onset should be stressed during stroke awareness campaigns.

#### PREHOSPITAL STROKE DIAGNOSIS – WHAT IS POSSIBLE?

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A short time to diagnosis and treatment of acute stroke is ultimately linked to lower morbidity and mortality. Neurologists so far focused (and still need) to improve the door-to-needle time in ischemic stroke, but most patients fail to qualify for IV thrombolysis due to long pre-hospital delays from symptom onset. In general, three obstacles need to be addressed that significantly delay arrival the stroke patients in dedicated stroke centers: a.) Decision delay: less than a quarter of stroke patients recognize stroke symptoms themselves, and relatives often are troubled to immediately call the dispatch center; b.) The time after notifying the dispatch center up to arrival in the clinic; c.) The emergency doctors and/or paramedics should be able to identify stroke patients and direct the patients to the next stroke units, perhaps with neurosurgical and interventional expertise, according to the local/regional conditions. Efforts to improve prehospital decision times are programs to increase public stroke awareness (a) and improvement of emergency medicine infrastructure (b). The ultimate goal in prehospital stroke diagnosis is to, first, separate stroke mimics from stroke and, secondly, differenti-

ate ischemic stroke from hemorrhagic stroke. Several tools have been developed from prehospital stroke assessment scales, to blood serum markers, portable color-Duplex systems for assessment of the intracranial circle of Willis, and telemedical support systems. Currently mobile computed tomography scanners in a dedicated ambulance care include point of care laboratory equipment and telemedical support from stroke experts in the clinic – enabling pre-hospital stroke treatment with significantly reduced time to treatment. This talk summarizes current strategies depending on differences in rural and urban areas and availability of resources.

#### TIME IS BRAIN, TIA AS AN EMERGENCY

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Transient Ischemic Attack (TIA) should be considered as an emergency and work-up has to be done within 24 hours like acute unstable angina pectoris. It is known that about 23% of stroke are preceded by TIA. Several studies have shown that the risk of subsequent stroke in the first 2 weeks after a TIA is about 1% per day. In 2 published well conducted studies, EXPRESS (P. Rothwell) and SOS\_TIA (P. Amarenco) it was shown that very early management in a TIA clinic will reduce the risk of subsequent stroke by 80% at 3 months. Therefore, work-up evaluation has to be performed within 24 hours in a dedicated organized structure.

Several stroke registries reported that carotid stenosis is the cause of embolic stroke in about 25–30% of all ischemic strokes. Current guidelines recommend immediate intervention either by carotid endarterectomy (CEA) or stenting (CAS) in patients with symptomatic carotid stenosis greater than 50%.

Carotid duplex is a reliable, non-invasive, accessible tool for evaluation of carotid stenosis with very high level of accuracy. Therefore, carotid duplex should be the first line tool for rapid evaluation of every patient with TIA in order to detect a potential treatable carotid stenosis for stroke prevention. It is recommended to establish an 'Acute TIA clinic' equipped with immediate accessible Duplex device to enable rapid evaluation of the carotid system in order to detect potential treatable carotid stenosis.

#### TIME DELAYS IN PRE-HOSPITAL CARE IN ACUTE STROKE IN TALLINN, ESTONIA

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**Background.** Guidelines for pre-hospital stroke management were introduced in Tallinn Emergency Medical services (EMS) in 2008.

**The aim** of the study was to analyse time delays in acute stroke management and adherence to treatment guidelines in pre-hospital stroke care.

**Methods.** The data of all visits to stroke patients by EMS was analysed from January 1st 2010 to December 31st 2012. Recorded procedures were compared to current treatment guidelines. Pre-hospital data of all consecutive stroke patients who received intravenous thrombolytic therapy (stroke-T) were recorded prospectively at a single Tallinn Stroke Centre.

**Results.** EMS received 3287 stroke calls during the study period. Emergency Rescue Centre (112) gave high priority (D/C) to 66% of stroke patients. The average response time was 7.5 minutes and time on mission 51 minutes. 96.4% of stroke patients were transferred to emergency departments (EM). Blood glucose was documented in 29.8% of cases. ECG was performed in 38.5%.

T-stroke patients were given either C/D priority in 71% (127/178). Mean time from notification of EMS to EM was 43 minutes with T-stroke patients, in 10% it exceeded 59 minutes. Blood glucose was documented in 55%, ECG was in performed in 31%, ECG without blood glucose was documented in 12.5. No significant occurred from 2010 to 2012.

**Conclusions.** T-stroke patients elicit on average 10 minutes quicker response time from EMS. Adherence to treatment guidelines is better for T-stroke. Still, blood glucose is unsatisfactory documented, additional time delays are caused by performing ECG in 44% of T-stroke and 38.5% all stroke patients.

## THROMBOLYSIS THROUGH FINNISH TELESTROKE

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**Background.** At 2007, it was estimated that about half of the population of Finland could not be served with 24/7 thrombolysis service for ischemic stroke by hospitals in their own region. This led to Finnish Telestroke network, a physician-driven publicly funded non-profit initiative, between five community hospitals (the Spokes) and the Department of Neurology at HUCH (the Hub). Funding for the pilot project was provided by the State Provincial Office of Southern Finland and the participating community hospitals. To date, we have used telemedicine for over five years via bidirectional video-conferencing equipment to facilitate thrombolysis delivery to patients in hospitals with an own stroke unit but without 24/7 neurologist service available.

**Methods.** Thrombolysis patients were treated in community hospitals served by HUCH in a telestroke network starting from year 2007.

**Results.** The present service covers 9 community hospitals. About 100 teleconsultations are registered at HUCH yearly. The telestroke consultations have led to thrombolysis treatment in over half of the patients. The safety and benefit of thrombolysis based on teleconsultation was equal to thrombolysis treatment given on site at HUCH after two years of pilot service as published before.

**Conclusions.** A special feature of the Finnish pilot is the high percentage of consultations leading to thrombolytic treatment with features and results very similar to on-site thrombolysis. Given that we enlarge our network to cover whole Finland and all teleneurology, we certainly will need a dedicated on call specialist 24/7 and we estimated that we can run this national system with approximately 700 000–800 000 euros annually including all costs.

Sairanen T, Soinila S, Nikkanen M, ym. for the Finnish Telestroke Task Force. Two years of Finnish Telestroke. Thrombolysis at spokes equal to that at the hub. *Neurology* 2011; 76: 1145–52.

## WRITING SCIENTIFIC PAPERS AND REVIEWING FOR JOURNALS

*Marc Fisher*

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Writing good scientific papers is an important aspect of academic productivity and necessary for the dissemination of research results. I will discuss how to organize papers to best achieve the goals of writing papers that are likely to be accepted. I will also discuss when to write, what to write and how to present your results succinctly and in a focused manner. Authors should carefully adhere to the requirements of the journal they are submitting to. Reviewing papers is also an important aspect of academic life. I will discuss how to approach the review of paper when you are asked to do so.

## Thursday, 22 August 2013

### ATRIAL FIBRILLATION AND STROKE

*David Russell*

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Atrial fibrillation (AF) is the commonest sustained arrhythmia in clinical practice with higher prevalence in the elderly. The life-time risk of developing AF is high; one in four for both men and women after the age of 40 years. AF is the strongest risk factor for stroke and the cause of 15–20% of all ischemic strokes. The prevalence of AF is expected to increase by at least 50% within the next 20 years due to the growing elderly population.

The most important risk factors for AF are: advancing age, congestive heart failure, valvular heart disease, myocardial infarction, diabetes and hypertension. It is quite evident that abnormal left atrial remodeling precipitates and perpetuates AF. Hypertension is the most common condition associated with AF.

The commonest symptoms in patients with AF are palpitations, shortness of breath, chest pain, dizziness and fatigability. It is not uncommon to note incidental AF in patients with embolic stroke. Furthermore, in a significant proportion of AF patients (around 12–15%) the arrhythmia is discovered by chance, having given rise to no symptoms whatsoever. AF should be considered when assessing cryptogenic strokes as it is possible that 25–50% of cryptogenic strokes may be due to undetected AF. Paroxysmal AF (PAF) which constitutes 1/3 of all AF cases carries the same stroke risk as permanent or persistent AF. The recognition of PAF remains clinically problematic because most patients with PAF are asymptomatic.

There is evidence suggesting that patients with AF have more severe strokes than their age-matched counterparts who suffer strokes due to other etiologies. AF often results in the formation of large emboli which commonly result in the sudden occlusion of a large cerebral artery. As a result, there may also be insufficient time to allow for the development of a collateral blood supply, compared with patients with arterial stenosis.

The underlying mechanisms for thrombogenicity in AF are complex and only partly understood. AF fulfils all the components of Virchow's triad, that is, abnormal changes in vessel wall, blood flow and blood constituents, leading to a prothrombotic or hypercoagulable state. In AF, abnormal vessel

wall is recognized as structural changes that appear to be manifest at both macroscopic and microscopic levels, thereby promoting thrombogenesis. Abnormal blood flow is manifest as stasis within the left atrium, partly related to the loss of atrial systole. Abnormal blood constituents include abnormal platelet and fibrinolytic function, as well as coagulation indices, which have all been demonstrated in AF patients, contributing to thrombogenesis.

## DISTRIBUTION, RISK PROFILE AND POPULATION SCREENING FOR ATRIAL FIBRILLATION

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**Background.** Atrial fibrillation (AF) is a frequent source of cardiac emboli in patients with ischemic stroke. AF may be asymptomatic and therefore undiagnosed. As oral anticoagulation (OAC) treatment is effective for stroke prevention, screening for silent AF seems suitable in risk populations. We hypothesize that AF screening in this age group will reduce stroke incidence.

**Methods.** All inhabitants in Stockholm County and Region Halland, Sweden age 75–76 years (n=25 415) are randomized in a 1:1 fashion either to be invited to a screening program for AF or as control group. In the screening group, participants are invited to undergo intermittent ambulatory ECG recordings during two weeks. Participants in whom AF is detected are offered OAC treatment. Screening and control groups will be followed prospectively for 5 years with regard to thromboembolic events, bleeding and mortality.

**Results.** During a 10-month period, 10 503 inhabitants in the screening arm had been invited and 4783 (46%) participated. Previously undiagnosed AF was found in 131 (3%) of participants and another 85 (2%) have been identified with previously known AF but without OAC treatment. The total prevalence of AF in the screening group exceeds 11%. Participation is lower in urban Stockholm (45%) in comparison to rural areas (64%). More than 90% of the patients with undiagnosed AF were started on OAC.

**Conclusion.** Population based AF screening in a 75-year old population identifies 5% of the population as new candidates for OAC treatment. There is considerable local and regional variation in participation in the screening program.

## MONITORING FOR ATRIAL FIBRILLATION FOLLOWING STROKE

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**Background.** The true frequency of atrial fibrillation (AF) in patients with cryptogenic stroke or transient ischaemic attack (TIA) is not well defined. The cryptogenic stroke accounts for up to one third of a general stroke population despite a comprehensive search for causation. Aim was to estimate frequency and burden of AF by long term monitoring and compare with current published data.

**Methods.** In our current study, patients with minor stroke or TIA were included if workup revealed no mechanism for their

stroke. A loop-recorder was implanted subcutaneously allowing monitoring for up to 3 years. Endpoints included episodes of AF, time of AF and burden of AF. Similar devices have initiated studies with similar criteria for pooled analysis of the studies.

**Results.** We found 20.7% paroxysmal atrial fibrillation (PAF) in our cohort of 85 patients with cryptogenic stroke or TIA. The burden was defined by duration of events. PAF patients had events lasting predominantly between 1 and 4 hours, but with a large range. All events were asymptomatic.

**Summary.** PAF occurs frequent in cryptogenic stroke and other current studies are finding similar results using long term monitoring. These new monitoring techniques and studies using them are raising more questions for discussion:

What is the best strategy for monitoring for AF after stroke?

Are there any predicting factors in the cryptogenic stroke cohort, to be screened for?

Should we focus more on finding PAF in our stroke population?

How much AF is dangerous in terms of burden?

## NEW ANTICOAGULANTS FOR STROKE PREVENTION IN PATIENTS WITH ATRIAL FIBRILLATION AND COMBINATION ANTITHROMBOTIC THERAPY

*Marc Fisher*

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The efficacy of warfarin for primary and secondary stroke prevention is well established and the drug is widely used for these purposes. Using warfarin is however associated with a significant risk for side effects, primarily bleeding, and lack of patient compliance. Three new anticoagulants, dabigatran, rivoroxiban and apixiban were developed to overcome these problems associated with warfarin. All 3 of the newer anticoagulants when compared directly to warfarin in atrial fibrillation patients demonstrated a significantly lower risk of intracerebral hemorrhage. Dabigatran had a significantly lower risk of ischemic stroke while both rivoroxiban and apixiban demonstrated non inferiority. These 3 new oral anticoagulants do not require INR monitoring and do not have the dietary restrictions associated with warfarin use.

An increasing problem especially in the United States is the frequent use of warfarin in combination with aspirin or other antiplatelet drugs. This combination is associated with a substantially increased risk for major hemorrhagic side effects but not proven efficacy for greater reduction in cerebral or cardiac ischemic events. The combination should be avoided and monotherapy with warfarin in patients with both atrial fibrillation and coronary artery disease is likely sufficient. The use of the newer anticoagulants is problematic in this situation.

## INTERVENTIONAL CLOSURE OF LEFT ATRIAL APPENDAGE IN ATRIAL FIBRILLATION

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Recurrent stroke risk is high among stroke patients with AF. Although oral anticoagulation (OAC) is effective, the downside of this treatment is severe bleeding complications or OAC may be contraindicated. Neurologists fear iatrogenic intracerebral bleeds, the most devastating side-effect from

OAC treatment and several studies show that in general practice OAC is underused or terminated early after a few years of treatment.

An alternative non-pharmacologic approach is occlusion of left atrial appendage (LAA) as about 90% of embolism origin from LAA. Percutaneous endovascular LAO has been used during the past 10 years. A proof of concept study among 707 patients show LAO to be non-inferior compared to Warfarin and since this study the method has improved further and so the complication rates due to device embolization and pericardial effusion has dropped down to half the numbers in the initial studies (~3%). It seems that the long-term protection from stroke/TIA may even be superior to long-term warfarin treatment.

Guidelines recommend LAO to be considered in AF patients with a high stroke risk where long-term OAC are contraindicated.

## ATRIAL FIBRILLATION AND THE BURDEN OF ANTICOAGULATION: CAN WE DO BETTER?

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**Introduction.** Atrial fibrillation (AF) is a common theoretically avoidable cause of stroke and prevention depends on consistent anticoagulation. How often does failure to achieve this result in a stroke? With new oral anticoagulants available the place of warfarin must be re-evaluated.

**Methods.** A stroke database was retrospectively analysed to provide information on patients who were in AF and admitted with possible TIA/Stroke over a period from 2001–2012.

**Results.** Total of 918 patients with paroxysmal/ sustained AF were identified in a total of 5088 stroke admissions. Only 19% were on warfarin at admission, and only a third of these (6% of the total) were within the therapeutic range. Of those on warfarin at the time of ischaemic stroke 58% were subtherapeutic. Ten were thrombolysed after point-of-care INR testing. Of the 36 who had stopped taking anticoagulation 13 suffered stroke within a month of stopping. Indications included pre-operatively, falls or side effects. A majority of patients with haemorrhagic stroke on warfarin were over the therapeutic range (24/42, 57%). An individual patient had INR testing every 2 weeks for 18 months but spent only 40% time in therapeutic range despite close monitoring and high motivation, exemplifying the problem with warfarin.

**Conclusion.** This study demonstrates the failure to achieve effective anticoagulation in everyday clinical practice, the consequence being both ischaemic and haemorrhagic strokes. It is time to increase the use of newer oral anticoagulants which do not require monitoring and are non-inferior or superior to warfarin.

## MOTOR FUNCTION AFTER STROKE, WHAT CAN WE DO TO ENHANCE IT?

*Katharina Stibrant Sunnerhagen*

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Motor function is commonly impaired after a stroke. In the acute setting, gait is impaired in around 60% (according to Copenhagen stroke study) and upper extremity function is impaired in around 50%.

There have been many different theories for regaining motor control have been developed, but no approach has yet been

proven superior to another. The importance of early, intensive training has been emphasized even more in recent years with increasing knowledge about recovery after an injury of the brain (such as stroke). Today, many use the approach called the Motor Relearning Programme (MRP), which is asked oriented as it emphasizes training of functional tasks in environments meaningful to the patient. Task oriented practice is based on a dynamic model of learning where the therapeutic interventions are specific to the task being trained, which is considered important for improvement. MRP is widely used in stroke rehabilitation today. It is based on movement science theory that took into account neurophysiology, neural plasticity, biomechanics, muscle physiology, neuropsychology and theories for skill acquisition and stressed that the patient must be active in solving his motor problems.

New methods are used, such as use of treadmill training with or without body weight support, computer games, robotics, forced use and mirror therapy.

## REHABILITATION OF MOBILITY AFTER STROKE: BALANCE, CONSTRAINT-INDUCED MOVEMENT THERAPY AND WALKING

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**Background and Objective.** To determine the evidence of effectiveness of 1) active balance training on the balance and walking outcomes 2) Constraint Induced Movement Therapy (CIMT) and modified CIMT on activity and participation 3) walking training on walking and self-care in patients with stroke by reviewing the results of randomized controlled trials).

**Data sources.** A systematic literature search of the Finnish study was conducted in MEDLINE, CINAHL, EMBASE, PEDro, OTSeeker, CENTRAL, and by manual search.

**Review methods.** RCTs for patients over 18 years old with stroke and published in Finnish, Swedish, English or German were included. Studies were collected up to 1) to January 2012 (Balance), 2) to the first week in May 2011 (CIMT), and 3) to the end of August 2012 (Walking). The evidence was high, moderate, low or no evidence according to the quality of RCTs and the results of meta-analyses.

**Data synthesis.** 29 RCTs were included in the balance review. Balance training produced better balance (high evidence), but not walking (high evidence), outcomes compared to no/placebo treatment. Balance training did not improve balance (moderate evidence) or walking outcomes (moderate evidence) when balance training compared to other training or balance outcomes (high evidence) when balance training with conventional physiotherapy was compared to conventional physiotherapy only. 38 RCTs were included in walking review. High evidence: In subacute stage of stroke, specific walking training improved walking speed and distance more than traditional walking training of the same intensity. In the chronic stage, walking training increased walking speed and walking distance compared to no/placebo treatment, and increased walking speed compared to overall physiotherapy. On average, 24 training sessions for 7 weeks were needed.

27 RCTs were included in CIMT review. Original amount of CIMT practice for 60–72 hours during over two weeks produced better mobility, i.e. ability to carry, move and handle objects, with high evidence compared to control treatment. CIMT for 20–56 hours during over two weeks, 30 hours over three weeks and 15–30 hours over 10 weeks improved mobility of the affected upper extremity. However, with self-care as an outcome measure, only 30 hours of CIMT practice over three weeks demonstrated an improvement.

**Conclusions.** Balance training proved to be more effective in improving balance than no treatment or placebo control following stroke. Active training for improving trunk or lower extremities function improved balance and walking as much as specific balance training. Balance training with physiotherapy did not have an extra impact compared to conventional physiotherapy. Further studies are needed to conclude balance training and rehabilitation. CIMT and mCIMT proved to be effective on affected hand mobility and to some extent self-care on the WHO's international classification of functioning, disability and health activity and participation component, but further studies are needed to find out the optimal treatment protocols for CIMT. Walking training improves walking capacity and to some extent self-care in different stage of stroke, but the training frequency should be a fairly large.

## COGNITIVE AND EMOTIONAL CONSEQUENCES OF STROKE

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When stroke survivors are asked, they rate fatigue and depression as the most burdening consequences of stroke. The same question put to their living partners reveal personality change and cognitive impairment as other major burdens post-stroke. Fatigue, cognitive impairment, depression, anxiety, personality change and emotionalism are all common and disabling consequences after stroke. Recognizing and accommodating these "hidden" functional limitations into both acute and post-acute care remains a huge potential to further improve clinical stroke service quality.

## IMAGING STRATEGIES TO ASSESS CLINICAL RECOVERY IN STROKE

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One in six will suffer a stroke during their lifetime and stroke remains the primary cause of new handicap in adult age. The three main approaches to stroke treatment remain improved prevention, acute revascularisation and rehabilitation. Functional MRI has a major potential for improving treatment by documenting pathophysiology of stroke recovery and further document different effects of interventions.

Functional connectivity is based on the neural structure and is dependent on the system integrity. Resting state and task based fMRI combined with clinical tests may therefore visualize the recovery process and the effects of treatment. Task based fMRI requires tailoring of the task to the research question and population. This hold some obvious challenges in a stroke population but a number of approaches have been propose to overcome this. Further, specific considerations must be made in relation to patients with severe stroke or acute stroke, who need close observation and cannot tolerate longer scan-times. Activity and connectivity studies are complementary; and combining the two approaches deepens the understanding. Technical challenges include physiological noise correction, which is feasible and allows the integration of fMRI into clinical workflow. The post-processing may be either model-based or data-driven. fMRI has the same contraindications (including claustrophobia and metal implants) as

structural MRI-scans and MRI has so far no known side effects.

Serial fMRI may improve development of new treatment options in stroke by offering a new and more specific surrogate measure of effect of stroke recovery. This that may prove useful in planning future intervention trials.

## ONE YEAR FOLLOW-UP OF WALKING BALANCE, EXPRESSED AS TIMED UP AND GO, AFTER STROKE: POSTURAL STROKE STUDY IN GOTHENBURG (POSTGOT)

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**Background and purpose.** The aim of the study was to investigate the walking balance, expressed as Timed Up & Go (TUG), in patients during the first year after a first event of stroke. Additional objectives were to establish whether recovery in walking balance differed between age groups.

**Methods.** As a part of the Postural Stroke Study in Gothenburg (POSTGOT), 91 patients were assessed using the TUG with repeated assessments during the first week and at three, six and twelve months after stroke.

**Results.** Between the first week and tree months after stroke, the mean TUG time was reduced from 17.8 to 12.5 seconds ( $p < 0.001$ ). No further improvement in TUG time was seen between three and 12 months after stroke. In a mixed model approach to linear regression, there was a significant age difference, as patients at age 80 and above deteriorated in terms of TUG time between three and 12 months after stroke, while patients aged 65–79 and below 65 years of age did not ( $p = 0.011$  for interaction between age group and time).

**Conclusions.** A significant improvement in TUG time from the first week to three months after stroke was found, but thereafter no improvement could be detected. The recovery in TUG time differed among different age groups, where patients 80 years or older tended to deteriorate in terms of TUG time.

## A PROSPECTIVE MULTICENTER STUDY OF STROKE REHABILITATION IN SIX COUNTRIES: NORWAY, CHINA, USA, RUSSIA, ISRAEL AND PALESTINE

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**Introduction.** Stroke s the the leading cause of serious, long-term disability. Acute stroke rehabilitation can successfully be administered in the general hospital but some individuals are in need of specialized rehabilitation. Few persons with stroke receive this extra service. Priority patients are in these cases the younger stroke patients with more severe outcomes and / or with a need for work related rehabilitation.

**Aim of the study.** To examine the content of specialized stroke rehabilitation in seven different countries. To establish

change of activities in daily life and life quality before and after rehabilitation in persons with stroke in the same clinics and to follow-up psycho-social factors 6 months after the stroke rehabilitation.

**Method.** The design is a prospective, descriptive study of specialized rehabilitation of stroke patients in China, US, Russia, Israel, Palestine and Norway with a total of 9 rehabilitation clinics participating. The characteristics of the specialized rehabilitation units in the different countries, therapies provided and the respective principles for admission and discharge will be described and provide an overview of current practice of specialized stroke rehabilitation in the participating countries. Primary outcome measure for the specialized rehabilitation period and 6 months follow-up will be Functional Independence Measure (FIM), a measurement of activities of daily living, Life Satisfaction Scale (LISAT-11) and a semi-structured interview based on open-ended questions with focus on the social situation 6 months after rehabilitation.

**Results.** A preliminary result is being analyzed and will be presented at the conference.

## POST-STROKE REHABILITATION AT HOME REDUCED DISABILITY AND IMPROVED QUALITY OF LIFE: A RANDOMIZED CONTROLLED TRIAL

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**Introduction.** In Denmark stroke is the most frequent cause of disability among adults, and many patients suffer from permanent physical, cognitive and speech impairments. The cost of treatment and rehabilitation of stroke patients represents 4% of the total health expenditure. Stroke patients often have complex problems requiring a close and coordinated cooperation between hospital and municipality. The present study was designed to evaluate the efficacy of home based compared to standard rehabilitation in stroke patients.

The study was a randomized, controlled intervention study. Included patients were at least 18 years old, hospitalized in our stroke unit for more than three days, diagnosed with focal neurological deficits from acute stroke and in need of rehabilitation. The intervention group received home based rehabilitation for up to 10 weeks, to replace part of usual treatment and rehabilitation services. The control group received treatment and rehabilitation following usual guidelines for the treatment of stroke patients. Three months after inclusion, all participants were retested. The following parameters were used as endpoints: motor rehabilitation, cognitive rehabilitation, quality of life and treatment-associated economy.

**Results.** Sixty-four patients completed the study (31 intervention and 33 control patients). Three months after inclusion, patients in the intervention group experienced improved quality of life ( $P < 0.05$ ) and achieved higher difference in motor rehabilitation scores ( $P = 0.01$ ) compared to controls. Furthermore the amount of home based training proportionally correlated with both Barthel-100 Index scores ( $P < 0.00001$ , Spearman  $R = 0.49$ ), Motor Assessment Scale scores ( $P < 0.001$ , Spearman  $R = 0.62$ ) and quality of life scores

( $P = 0.01$ , Spearman  $R = 0.47$ ). Economically, total savings of both hospitals and municipalities were about 100 for each intervention patient compared to controls.

**Conclusion.** Early home based rehabilitation improved motor rehabilitation and quality of life, and the amount of home based training proportionally correlated with both rehabilitation of functions and quality of life. Economy was improved by home based rehabilitation of stroke.

## THE IMPACT OF NEUROSONOGRAPHY IN ACUTE STROKE PATIENTS

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The most potential treatment of acute ischemic stroke has been implemented without vascular assessment on the basis of an appropriate time window, exclusion of cerebral hemorrhage by computed tomography and stroke severity more than 15 years ago. Since then vascular assessment in this neurovascular disease, deservingly, has gained increasing attention to identify patients in need of additional therapy (i.e. endovascular clot retrieval), with unclear time window (i.e. perfusion/diffusion mismatch) or in stroke surveillance (i.e. recanalization). While ultrasound investigations worldwide exceed that of computed tomography (CT) and magnetic resonance imaging (MRI), its value in acute stroke assessment has seemingly dropped – but only in hospitals with CT-angiography and/or MRI 24/7. However, neurosonography with its Doppler-based and pulse-reflection-based techniques supplemented with ultrasound contrast-agents (UCA) offer a unique and robust impression of the cerebral vasculature in the hands of the experienced sonographer. Occlusion of major arteries of the circle of Willis can be easily identified, using UCAs even in the not-so-experienced hands. The real-time character allows surveillance of recanalization and, if performed continuously, sonothrombolysis. In the fast majority of stroke patients, CT, electrocardiogram and neurosonography will bring the underlying pathology to light, enabling early secondary stroke prevention. If CT-angiography or stroke MRI are available, neurosonography should be seen complementary, not as competition. In any case, neurovascular diagnostics should be performed in any acute stroke patients as soon as possible.

## IMPACT OF BRAIN TISSUE AND VESSEL IMAGING IN ACUTE STROKE PATIENTS

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Proper diagnostic imaging in acute stroke is crucial for the treatment; thus, its impact can hardly be overestimated. The diagnostic impact arises from the primary task is to provide immediate information to on the relevant pathophysiology and the therapeutic impact from the successful identification of patients to enable the right choice of treatment. If imaging is successful in attaining the primary goals, it will eventually have a high-level impact on the stroke-related death and disability through improved efficacy of our stroke treatment and better overall recovery of our patients.

The goal of imaging sets high and challenging demands. One the fundamental challenges is the dynamic and multifactorial nature of the object under study. Furthermore, the scanning method is to be available and feasibly applicable fast and without delay on patients that may be seriously affected by

the condition; it should be sensitive to the pathophysiology and sufficiently accurate in defining the target as well as specific to preclude treatment in stroke mimics. Diagnostic imaging should not pose unnecessary risks, either. Since the groundbreaking trials of thrombolysis in stroke the classical non-contrast CT has been the mainstay of diagnostic imaging which reasonably fulfills the main criteria, with high specificity for ischemic damage. CT has remained the standard with great impact despite the old contention of MRI replacing it.

Multimodal imaging methods (CT/MRI) have dramatically evolved during the last decade, adding to our understanding of the ongoing pathophysiology, and they have entered strongly into the clinical practice, changing the approach to stroke management. The fast-track methods to visualize the occlusion, collateralization, the extent and depth of the ensuing perfusion deficit and ischemic injury, and reasonably distinguish tissue-at-risk from irrecoverable damage may allow tailored stroke treatment, and in principle facilitate our decision-making and improve the overall efficacy of our efforts.

The more complex methodology inevitably poses further questions. Universal definitions for central concepts are lacking, and the wide range of definitions and techniques may produce unacceptable variability. The compatibility of the different methodologies is debated, especially CT perfusion, although it has been successfully used even in some controlled studies for imaging-based inclusion. MR standardization and validation attempts are underway.

The crux in the clinical use of the impact of multimodal imaging is the lack of evidence base. Despite great expectations and promises, several carefully designed trials have failed to prove the impact of penumbral imaging for patient selection in acute stroke. At the same time, stroke centers have widely adopted the methodologies producing local 'in-house' practices to utilize the wealth of information provided by multimodal approach, as an extension of the clinical assessment and a guide to treatment.

Despite the present shortage of evidence, the rising impact of tissue and vessel imaging in acute stroke is envisaged. Steps in increasing understanding of the dynamic pathophysiology with improving, revised hypotheses, better evaluation of the collateralization and risk stratification, will prospectively be evident in terms of clinical effectiveness. Apart from judicious use of imaging, the clinicians are advised to concerted efforts of gathering clinical data, best within well-designed controlled trials when available.

## IMAGING CRITERIA DEFINING ACUTE ISCHEMIC STROKE PATIENTS FOR CLINICAL TRIALS

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Acute stroke treatment decisions are mainly based on clinical information, including time delay since stroke onset. Use of mismatch on acute imaging to select patients with salvageable tissue was suggested 20 years ago, and use of arterial data a decade ago. Since then, thresholds to differentiate ischemic, non-viable tissue ("core"), viable tissue ("penumbra") and non-threatened tissue ("benign oligoemia") have been developed for MR and CT imaging. Semi-automated threshold maps and rapid cervico-cerebral arterial assessment are now available. Through systematic work, several important markers for benefit from acute revascularization treatment have been identified:

- Core volumes below 70–100 ml
- Penumbral volumes below 85–150 ml

- A ratio of total ischemic tissue / core > 1.5–1.8
- Low extent of arterial occlusions (low "clot burden")
- Good flow in collateral arteries

Some of these factors are interrelated so that not all need to be measured before revascularization decisions. The combination on MRI-based imaging of a core <70 ml, a significant hypoperfusion of <100 ml and a mismatch ratio of 1.8 has been labeled "target mismatch" by the DEFUSE group in order to describe the patient with an increased benefit from acute revascularization.

Recent failures of endovascular recanalisation trials highlight other crucial ingredients for success in revascularization treatment:

- Speed between multimodal imaging and revascularisation
- Presence of an occluded and recanalizable vessel at the time of intervention
- Completeness of revascularization of occluded vessels

Given that in the first 2–3 hours after stroke onset, most patients have substantial penumbra and few have large infarcts, intravenous thrombolytics should be given immediately after exclusion of major contraindications. Multimodal imaging may guide further treatment decisions such as:

- Adding mechanical revascularization treatment
- Treating patients arriving late or with unknown stroke onset
- Avoiding exposure of patients with spontaneous good prognosis to side effects
- Avoiding overtreatment that is likely futile or harmful
- Selecting the best treatment modality to achieve rapid reperfusion.

Revascularisation is currently best achieved through thrombolytic and mechanical recanalisation, but still occurs too late or incomplete in many patients. Phase III reperfusion trials using multimodal imaging are now under way, selecting patients based on tissue viability, occlusion patterns, or both. Depending on the results of such trials, "time is brain" could be replaced by "target mismatch is brain" and "rapid revascularisation is brain". Furthermore, better pre- and in-hospital organization, enhancement of thrombolysis by drugs or ultrasound, more effective mechanical clot removal, augmentation of collateral flow and neuroprotection including cooling may enhance the reperfusion benefits in patients selected by advanced imaging.

## OUTCOME ASSESSMENT WITH IMAGING IN CLINICAL TRIALS ON ACUTE ISCHEMIC STROKE TREATMENT

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**Background.** Clinical trials on acute ischemic stroke treatment use disability and death as outcome events. Brain tissue and vessel imaging may help to better understand trial results.

**Methods.** Review of major clinical trials on treatment with IV rt-PA, tenecteplase, desmoteplase, and on endovascular treatment (SWIFT, TREVO, IMS III, SYNTHESIS, MR RESCUE).

**Results.** Absolute reduction of disability and death was 13% (NINDS II) and 7% (ECASS-3) only in the only 2 positive randomized trials on IV rt-PA. It remains unknown, whether this small effect size was due to patients without arterial occlusion at baseline or because arterial recanalization was not achieved. Vessel imaging was not performed. A post-hoc

analysis of DIAS-2 revealed that only patients with major artery occlusions at baseline had a positive treatment response. The tenecteplase-trialists very carefully selected 75 out of 2788 patients with the help of brain tissue, vessel, and perfusion imaging and could show that tenecteplase is superior to alteplase with regard to recanalization, reperfusion, and clinical outcome. Endovascular treatment of acute ischemic stroke inevitably requires vessel imaging, but is associated with poor clinical outcomes in the majority of patients. Trials show that arterial recanalization does not mean tissue reperfusion in all patients. Grading of arterial recanalization and tissue reperfusion will help to improve this treatment approach.

**Conclusions.** Brain tissue and vessel imaging at baseline and follow-up is essential to understand the treatment effects in order to further improve treatment of acute ischemic stroke patients.

## IS THERE FINALLY CLOSURE ON PFO-CLOSURE

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Persistent foramen ovale occur in 25% of the general population. Among patients with cryptogenic stroke PFO is found by transesophageal echocardiography in about 50%. Clinicians therefore may assume that PFO is the cause of stroke, although it may be incidental. The most effective strategy for recurrent stroke in cryptogenic stroke patients with PFO is uncertain. Three randomized trials published recently compare percutaneous endovascular PFO closure to standard medical care. So far none of the trials alone showed benefit of closure over medical treatment in the primary intention to treat analysis. In parallel with inclusion to trials off-label use of PFO closure has been widely used, especially in patients judged to be of high risk for re-stroke (patients with recurrent cryptogenic stroke, septal aneurisms or large PFO's). The trial patients may therefore not be representative for the cryptogenic stroke population. All the trials however, showed a relatively low risk of stroke recurrence in cryptogenic stroke, which make the routine use of closure at this stage unwise without a clearer knowledge of who is likely to benefit.

## THROMBOPHILIAS AND STROKE: WHEN TO TEST AND HOW TO TREAT?

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Patients with ischemic stroke of unclear etiology are often screened for hypercoagulable syndromes or thrombophilias. Thrombophilia has both acquired (antiphospholipid antibody syndrome, APS) and inherited causes (most common are the factor V Leiden, FVL and prothrombin G20210A gene mutation, PGM). Although the prevalence of thrombophilic disorders is low in stroke patients, identification of a thrombophilia may influence selection of therapies to prevent recurrent stroke. But the definitive data as to whom to test and what to do with the results are not available.

There is quite convincing evidence that the APS is associated with an increased risk of ischemic stroke, but it is unclear whether this is also true for positive antiphospholipid antibodies in the absence of other characteristics of APS. While inherited coagulation disorders are recognized risk factors for ve-

nous thrombosis, there is no substantial proof for an association with arterial ischemic stroke (even in young patients and patients with patent foramen ovale), possibly with the exception of the PGM, protein C deficiency and the FVL in children and young adults.

The diagnostic yield of thrombophilia tests in unselected stroke patients is very low, but may improve with careful selection of younger patients who have an otherwise undetermined cause of stroke or a history of venous thrombosis or multiple miscarriages. The results of non genetic tests may be affected by a patient's comorbid medical conditions, medications, and timing from the thrombosis.

Secondary prevention with anticoagulation therapy for patients with ischemic stroke and a coagulation disorder is often initiated, but this strategy is based on consensus or expert opinion rather than good quality evidence.

## CURRENT TREATMENT OF BASILAR ARTERY OCCLUSION

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Basilar artery occlusion (BAO) is associated with high mortality (85–95%) if recanalization does not occur. Evidence of the efficacy of different therapy protocols of intravenous thrombolysis (IVT) or intraarterial thrombolysis (IAT) and/or mechanical endovascular treatment is based on retrospective or prospective patient cohorts, since randomized controlled trials (RCTs) do not exist. Roughly a third of BAO patients reach functional independence by three months following thrombolysis. From those with successful recanalization about half will reach independence. In noninvasive and endovascular protocols, recanalization of BAO is reached in 60–85% of the patients. While invasive endovascular approaches afford greater recanalization rates, they have not been proven superior to IVT in terms of functional outcome. Meaningful survival after BAO requires rapid access to thrombolysis. "Bridging" protocols have been introduced where rescue therapies such as endovascular thrombolysis and on-demand mechanical thrombectomy or angioplasty are used. Multimodal imaging techniques should be used to choose the best therapeutic option individually. BAO still remains a difficult clinical challenge despite improved diagnostic methods and modern therapy forms.

## THROMBOLYSIS OF BASILAR ARTERY OCCLUSION: IMPACT OF BASELINE ISCHEMIA AND TIME

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Treatment strategies of basilar artery occlusion (BAO) remain empirical and differ from RCT-guided protocols in hemispheric stroke. We evaluated the impact of extensive baseline ischemic changes on functional outcome after BAO thrombolysis, and analyzed effect of time to treatment in absence of such findings. We prospectively analyzed 184 consecutive patients with angiography-proven BAO. The majority of patients received iv thrombolysis and concomitant full-dose heparin. Extensive baseline ischemia was defined as pc-ASPECTS < 8. Onset-to-treatment time (OTT) was analyzed both as continuous and categorical variable (0–6h, 6–12h,

12–24h, and 24–48h). Successful recanalization refers to TIMI score of 2–3. Poor 3-month outcome was defined as modified Rankin Scale (mRS) 3–6. Majority (96%) of patients with baseline pc-ASPECTS <8 had poor 3-month outcome, and this was not different (94%) in those with confirmed recanalization (51.5%). In contrast, half of the patients with pc-ASPECTS ≥8 and recanalization (confirmed in 73.2%) achieved good outcome. In these patients, OTT was neither associated with poor outcome as continuous nor as categorical variable. Symptomatic intracranial hemorrhage (sICH; ECASS-2 criteria) occurred in 25% of patients with pc-ASPECTS <8, compared with 11.5% in those with pc-ASPECTS ≥8 ( $p=0.03$ ). In the latter group, higher age, baseline NIHSS, lack of recanalization, history of atrial fibrillation, and sICH were independently associated with poor outcome. In the model including patients with any pc-ASPECTS, pc-ASPECTS <8 was independently associated with poor outcome (OR 5.83; 1.09–31.07). In absence of extensive baseline ischemia, recanalization of BAO up to 48 hours was seldom futile and produced good outcomes in 50% of patients; independently of OTT.

### BIGGER, FASTER? ASSOCIATIONS BETWEEN HOSPITAL THROMBOLYSIS VOLUME AND SPEED OF THROMBOLYSIS ADMINISTRATION IN ACUTE ISCHAEMIC STROKE

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**Background.** There is evidence that concentrating services for some conditions into higher volume hospitals produces better patient outcomes. We aimed to identify if there were any associations between hospital thrombolysis volume and speed of thrombolysis (tPA) administration in patients admitted with acute ischaemic stroke.

**Methods.** Data were drawn from two national clinical audits in England: the Stroke Improvement National Audit Programme (SINAP) and the 2012 Sentinel Stroke Audit. Hospitals were categorised into three groups based on the annualised volume of thrombolysis: 0–24, 25–49 and ≥50 cases per annum. Multilevel logistic models were used to estimate the odds of receiving tPA within 60 minutes, adjusting for patient characteristics.

**Results.** Of 42,024 patients with acute ischaemic stroke admitted to 80 hospitals, 4347 received tPA (10.3%). Patients admitted to hospitals with an annual thrombolysis volume of ≥50 cases per annum had median arrival-tPA times that were 28 and 22 minutes shorter than patients admitted to hospitals with volumes of 0–24 and 25–49 respectively. The fastest times were observed for the highest volume hospitals, with volumes of >100 per annum. In multivariable analysis, patients admitted to hospitals with a volume of ≥50 cases per annum had 4.33 the odds of receiving tPA within <60 minutes of arrival. No differences were observed in 30 day mortality or thrombolysis complication rate.

**Conclusions.** Hospitals with higher volumes of thrombolysis activity achieve statistically and clinically significant shorter delays in administering tPA to patients after arrival in hospital. These findings may have important implications for the configuration of stroke services.

### RENAL DENERVATION TO TREAT HYPERTENSION AFTER STROKE – A NEW CONCEPT?

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**Background.** Hypertension is the major stroke risk factor and hypertension after stroke remains frequently uncontrolled. Renal nerve denervation (RND) presents a new option for patients with resistant hypertension. The aim of this ongoing pilot study is to determine the safety and efficacy of RND in patients with resistant hypertension after stroke.

**Method.** This is an open observational cohort study including 25 patients with prior stroke and resistant hypertension, defined as above 140/90 mmHg with >2 antihypertensive medications. Screening includes office- and 24-hours blood pressure measurements, biochemistry, renography, plasma Chrome-clearance and renal CT-angiography. The endpoints are safety defined by procedural complications and serious adverse events during the study period and relevant reduction (> 15 mmHg systolic) in 24-hour blood pressure readings 1, 3, 6 and 12 months after RND. Inclusion has been ongoing since September 2012.

**Results.** Out of 300 patients 38 had resistant hypertension. Of these, 8 patients exceeded the 24-hour blood pressure of a mean >135 mmHg systolic and 2 patients have so far been ablated with RND. No clinical adverse events are observed. The first patient experienced a temporary renal artery spasm that responded to nitro-glycerine during the procedure. The office blood pressures (1: 126/79 mmHg, 2: 150/75 mmHg) and the 24-hour blood pressure at 1 month (1: 118/70 mmHg) were relevantly reduced.

**Discussion.** Resistant hypertension in stroke patients is rare (number to screen=37.5). Preliminary experience of RND in this patient group showed no safety concerns and relevant blood pressure reductions. We anticipate the study to be finished in late 2014.

### CRUSHING THE CLOT: THE NORWEGIAN SONOTHROMBOLYSIS IN ACUTE STROKE STUDY (NOR-SASS)

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**Background.** Ultrasound augments intravenous thrombolysis (sonothrombolysis). Studies show that 2-MHz pulsed-wave ultrasound can double the chance of recanaliza-

tion without increasing the risk of intracerebral haemorrhage. Contrast enhanced sonothrombolysis (CEST), adding iv gaseous microspheres, may potentiate the effect of ultrasound. Ultrasound in the absence of tPA also accelerates clot break-up through mechanical mechanisms (sonolysis). These mechanisms are enhanced by echo contrast. Contrast enhanced sonolysis (CES) may therefore be clinically more effective than ultrasound alone.

**Methods.** Patients 18 years with acute ischaemic stroke with/without visible arterial occlusion on CTA. CT/CTA on admission. Ultrasound diagnosis (TCCS) and sonothrombolysis (TCD) <4h.

In presumed distal MCA<sub>2</sub>-occlusions (embolic infarct), sample volume is set at 40 mm depth with continuous slight 'fanning' of the beam. In presumed proximal M1-perforator occlusion (lacunar infarct), sample volume is set at 50 mm depth. SonoVue 10 ml (2 vials/80 l microbubbles) is given as an infusion of 0.3 ml/min for ~30 minutes, using an infusion pump. Recanalisation of peripheral arteries is assessed at 60 minutes after start of thrombolysis. MR/MRA after 24 hours.

**Conclusions.** If a positive effect can be proven, contrast enhanced ultrasound treatment would be an option for acute ischemic stroke patients eligible or ineligible for intravenous thrombolysis and for those who do not have the possibility for intra-arterial treatment. More importantly, sonothrombolysis would benefit stroke patients and improve clinical outcome.

## STROKE GENETICS: AN OVERVIEW AND UPDATE

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Stroke genetics encompasses many different topics: (1) analyses of DNA variations indicating risk of monogenic or common stroke syndromes, including common main types of stroke and subtypes of ischemic stroke; (2) hereditary studies on familial aggregation of stroke; (3) genetics of conditions related to stroke e.g. atrial fibrillation and hypertension; (4) genetic impact on expression of different proteins during brain injury; (5) genetic influence on stroke recovery; and (6) pharmacogenetics. Methods used for genetic research include Genome Wide Association Studies (GWAS), family studies; RNA and protein analyses; and advanced computer-aided analytical methods to detect statistically significant associations. Several new methods are evolving e.g.: Exome content analysis; Next generation sequencing; Whole genome sequencing; and Epigenetics. These hold promise for obtaining better understanding of stroke genetics.

During 2012–2013, several Single Nucleotide Polymorphisms (SNPs) have been related to ischemic stroke risk. Certain SNPs have been associated with risk of specific ischemic stroke subtypes such as large vessel disease and cardiac embolism. SNPs have also been associated with particular subtypes of intracerebral hemorrhage (ICH), especially lobar ICH, and with prognosis after ICH. New large international studies on stroke recovery and exome content are ongoing. With advanced mathematical models, efforts are made to understand how several SNPs can act together and e.g. increase stroke risk burden. Several of the above efforts demand availability of large numbers of patients and controls and this is achieved by co-operation in large international consortia such as the International Stroke Genetics Consortium.

This presentation will provide an update on stroke genetics in general and also on different genetic variations that may influ-

ence stroke risk and present some of the latest reports on stroke genetics published in high impact journals. The role of pharmacogenetics and an overview of the current situation from a clinical standpoint as well as future aspects will be discussed.

## GENETICS OF SUBCLINICAL ATHEROSCLEROSIS

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Carotid intima-media thickness (IMT) and subclinical atherosclerotic plaques are widely accepted markers of an increased vascular risk. However, traditional risk factors explain only a rather small proportion of the variability of these markers suggesting that other undiscovered environmental and genetic factors may play a substantial role in the development of atherosclerosis. The purpose of this review is to provide an overview of the literature on the genetic background of subclinical atherosclerosis. Twin and family studies suggested a high degree of heritability, however, the genes involved have not been identified, so far. Studies on candidate genes revealed positive associations with genetic variants related to matrix deposition (MMP-3), intimal proliferation (ACE), inflammation (interleukin 6), and lipid metabolism (APO-E, PON-1). The Human Genome Project identified approximately 2.5 million single nucleotide polymorphisms (SNP) with minor allele frequencies of 5% or greater which indicate genomic loci that determine an individual's genetic variability. Genome-wide association studies (GWAS) revealed new gene loci related to LDL metabolism (APOC1), endothelial dysfunction (EDNRA), platelet function (PIK3CG), and telomerase inhibition (PINX1). Although the effect size of these loci on markers of subclinical atherosclerosis is rather low, they may give insight to new disease pathways as potential targets for therapeutic interventions.

## THE SAHLGRENSKA ACADEMY STUDY ON ISCHEMIC STROKE (SAHLSIS) – FOCUS ON HAEMOSTASIS AND GENETICS IN RELATION TO SUBTYPES OF ISCHEMIC STROKE AND LONG-TERM OUTCOME

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Blood clot formation is a key mechanistic event in ischemic stroke, thus this project focuses the haemostatic pathway. As crosstalk occurs between hemostasis and inflammation, we are also studying the inflammatory pathway. Both genetic and plasma protein analyses are performed.

SAHLSIS is ongoing and consecutively recruits adult patients with ischemic stroke before 70 years of age. One important aim is to study the different etiological subtypes of ischemic stroke, which are classified both according to TOAST and the Causative Classification of Stroke (CCS) system. In brief, we found associations between several prothrombotic factors and all main subtypes including cryptogenic stroke, although there are subtype-specific differences. In contrast, an independent association to the inflammatory marker hsCRP was only detected for the subtype of large vessel disease (LVD). The latter finding is in line with recent genome wide association studies (GWAS) that have identified associations specifically for LVD.

In the first phase of SAHLSIS, we included 600 patients at four stroke units and 600 population-based controls matched for

age, sex, and geographical region. There are few studies on long-term outcome after ischemic stroke, and we are therefore performing a longitudinal study of this cohort. With regard to recurrent vascular events and death, the mean follow-up time is now 8.6 (SD 2.1) years. Together with more established prognostic factors, stroke subtype and living alone prior to index stroke emerged as important independent predictors of recurrent events. In addition, high plasma level of tissue-type plasminogen activator (t-PA) antigen at inclusion was an independent predictor of vascular death. A subgroup of patients participated in a more extensive 7-year follow-up including outcome measures on cognition, depression, fatigue, life satisfaction, activity and participation. Preliminary data show that, in the younger age group (<50 years), high t-PA antigen levels at inclusion correlated with low cognitive performance, especially in the domain of attention.

In conclusion, there is still a need to increase our knowledge on risk factors and biomarkers in the different etiological subtypes of ischemic stroke, which can contribute in delineating pathophysiological pathways. There is also a need to further our knowledge on the consequences of ischemic stroke in the longer perspectives and on the predictors of outcome.

## DYSLIPIDEMIA, STATINS AND STROKE: AN UPDATE

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Lipid abnormalities are a key risk factor for stroke, elevated LDL-cholesterol being the most common abnormality. No clear association has been shown between elevated LDL-cholesterol and stroke incidence, possibly due to the lack of appropriate etiopathophysiological classification of stroke in most studies.

Nevertheless, over the last years, numerous clinical trials and meta-analyses have clearly demonstrated a significant and safe decrease in risk of first or recurrent stroke by HMG-CoA reductase inhibitors (statins) and reduction of LDL cholesterol, despite a significant but small increase in hemorrhagic stroke. Discovery of statins and their implementation into clinical practice are the most important advances in cardiovascular prevention since aspirin and blood pressure-lowering. International guidelines advise an objective assessment of cardiovascular risk to determine the appropriateness of statins for primary prevention and near universal use of statins for secondary prevention after the acute phase of ischemic stroke. However, there is lack of consensus with regard to the choice of agent, timing of initiation, dose and duration of therapy.

Mechanism of statins is not limited by lipid lowering action. Beneficial cholesterol-independent (pleiotropic) effects of statins include vasoprotective mechanisms such as improved vasodilatation, inhibition of inflammatory responses, plaque stability and immunomodulation. Consequently, statins may be beneficial in various disorders associated with acute and chronic endothelial dysfunction. Recent findings showed that, in addition to risk reduction, statin therapy at stroke onset was associated with improved outcome. However, abrupt interruption of statins following acute vascular cerebrovascular event may impede vascular function and increase morbidity and mortality, therefore, abrupt discontinuation of existing statin treatment in patients with acute stroke should be avoided.

Statins could also serve as an adjuvant for enhancing the efficacy of thrombolysis and other neuroprotective compounds, as it additionally exerts profibrinolytic, immunomodulatory, and antioxidant effects. However, so far, there are only limited

clinical data on the effect of statin therapy on stroke outcome. In conclusion, statins are emerging as a new and promising avenue for the prevention and potentially treatment of ischemic stroke, and may be recommended in essentially all non-cardioembolic stroke patients. There is a clear need for further research into identifying deficiencies in long-term management, barriers to optimal secondary prevention and novel interventions to overcome these barriers.

## INTRACRANIAL ATHEROSCLEROSIS (ICAS) VS. EXTRACRANIAL ATHEROSCLEROSIS (ECAS): ARE THEY DIFFERENT?

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ICAS accounts for 30–60% of stroke in East Asia while it accounts for approximately 10% of stroke in Caucasians. According to PROSAC (prospective registry on symptomatic atherosclerosis) study, the ratio of symptomatic ICAS and ECAS is approximately 7:3 in Korea. It has been shown that ECAS is closely related to old age, male gender and coronary heart disease, while ICAS is related to metabolic syndrome and low serum adiponectin level. However, the reason for ethnic differences in the location of cerebral atherosclerosis remains incompletely understood. Genetic and hemodynamic differences may in part explain this difference. Differences between anterior vs. posterior circulation atherosclerosis and difficulties in identifying non-atherosclerotic vascular lesions complicate our understanding on this issue.

Symptomatic ICAS tends to be associated with concomitant asymptomatic ICAS while the opposite is the case for ECAS. While artery to artery embolism (AAE) is the major stroke mechanism in ECAS, the stroke mechanisms of ICAS are diverse and include in-situ atherothrombotic occlusion (IAO) and atheromatous branch occlusion (ABO). Anterior circulation ICAS is more often associated with AAE and less often with ABO than posterior ICAS. In symptomatic ECAS, strong antiplatelet agents (i.e., aspirin + clopidogrel) may be efficacious at least in the acute stage while agents modulating vessel wall damage such as cilostazol may be more effective in preventing progression of ICAS. After stenting, perforator occlusion and dissection are worried in ICAS patients while reperfusion injury and vasomotor instability are troublesome in those with ECAS. Prevention and management strategies should be based on proper understanding of these characteristics.

## INTRACRANIAL STENOSIS AND OCCLUSIONS IN FINNISH POPULATION

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**Introduction.** It's estimated that brain ischemia is caused by intracranial stenosis in 10% of patients in the USA. The frequency of brain ischemia caused by intracranial stenosis is highest in Asian countries where ICAS accounts 28–60% of brain ischemia. Caucasians are not in high risk for ICAS. There are only few studies about the prevalence of intracranial stenosis in European district.

**Methods.** We investigated 703 consecutive patients with brain ischemia. CT angiograph was done to 480 patients (68.2%). Main reasons why CT angiograph was not done were severe stroke, allergy to contrast medium or impaired kidney function.

Our neurointerventionist and neuroradiologist assessed the degree of stenosis for every vessel segment in CT angiograph data. We included to analysis 50% stenosis or occlusions of intracranial ICA, MCA, ACA, PCA and VA.

**Results.** In our study population the most frequently stenosis or occlusions were found in origin of VA (18.3%) in intracranial ICA (16.0%) and in intracranial VA (14.9%). 7.7% of patients had stenosis or occlusion in MCA and 3.5% in BA. Only 1.8% had stenosis or occlusion of PCA and 0.4% in ACA. Further results with influence of age and gender in degree and distribution of stenosed and occluded arteries will be presented in the congress.

**Discussion.** Our study suggests that most of the burden of intracranial stenosis is located in intracranial ICA and VA.

## TIA AND STROKE IN THE YOUNG: THE SIFAP STUDY

### *Bo Norrving*

Lund University, LUND, Sweden  
on behalf of SIFAP investigators

Although stroke in the young often causes life long disabilities, there are few large prospective studies on causes and risk factors. To this end, the Stroke in Young Fabry Patients (SIFAP) study (principal investigator Arndt Rolfs) recruited 5023 patients aged 18 to 55 years with TIA, ischemic stroke (about 2 thirds of all) or intracerebral hemorrhage in 15 European countries and 47 centers between 2007 and 2010. A comprehensive protocol including MRI, vascular imaging, and molecular genetics was used.

Median age in the overall cohort was 46 years. The most common causes of ischemic stroke were large artery atherosclerosis (18.6%) and dissection (9.9%). Despite the extensive protocol, one third of all patients were diagnosed as cryptogenic strokes. Modifiable risk factors (hypertension, diabetes, smoking, dyslipidemia, physical inactivity) were highly prevalent, particularly in men and older patients, and were often multiple. Silent infarcts on magnetic resonance imaging were seen in 20% of patients with a first-ever stroke, and in 11.4% of patients with transient ischemic attack and no history of a previous cerebrovascular event. Cerebral microbleeds were rare. On vascular imaging, proportions of patients with intracranial arterial disease and extracranial atherosclerosis were similar. Definite or probable Fabry disease, and CADASIL, were each diagnosed in <1% of all patients.

The SIFAP study shows that a considerable proportion of all stroke in the young relate to traditional risk factors and should be potentially preventable. Cryptogenic strokes constitute one third, and dissection one tenth, of all cases, whereas monogenic causes of stroke remain rare.

## CAUSES OF CARDIOEMBOLISM IN YOUNG ADULT PATIENTS

### *Jukka Putaala*

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Identified cardiac sources of embolism account for one fifth of ischemic strokes in patients aged below 50 years. This frequency is slightly lower than that reported for general stroke patients. The spectrum of etiology of cardioembolism is markedly different in young as compared with elderly patients. For example, atrial fibrillation (AF) is relatively rare in the young whereas sources with low or uncertain primary risk of stroke are much more common. Based on recent literature, in approximately half of the cases with presumed cardioembolism

the source is related to the latter conditions, namely interatrial echocardiography findings including patent foramen ovale with or without atrial septal aneurysm (ASA). High-risk sources of cardioembolism – including AF, flutter, sick sinus syndrome, cardiomyopathies, valvular abnormalities, congenital cardiac malformations, endocarditis, intracardiac tumors – appear more common in males, whereas low-risk sources are more frequently encountered in female patients. PFO is common in the general population (approx. 25%) and the well-recognized clinical question with PFO is how to demonstrate its causality with the current stroke (or clinically silent strokes). In age-inclusive studies the probability that PFO is incidental is 33% and reduces to approximately 20% in younger (<55 years) patients, but remains 48% in older patients (>55 years). Because of its uncertain causality, PFO-related stroke, with or without ASA, is considered cryptogenic. Since PFO closures are frequently performed despite compelling scientific evidence, there is a clear need for developing better tools to identify conditions where PFO likely is a causal finding. Finally, as up to 60% of all ischemic strokes at young age can be considered cryptogenic, large international consortium is needed to study the underlying reasons, not least to be able to determine the optimal primary and secondary prevention for these patients.

## OUTCOMES AND CONSEQUENCES OF STROKE IN THE YOUNG

### *Annette Fromm*

Bergen Stroke Research Group, Department of Neurology, Haukeland University Hospital, BERGEN, Norway

Thrombolysis with IV alteplase is safe in young ischemic stroke patients and they benefit more compared to older patients. However, despite previous assumptions that young individuals have a favorable overall outcome after stroke, recent publications indicate that this may not be true. Long-term consequences of early cerebrovascular disease are pregnant both for the individual patient and in socio-economic context. Vascular co-morbidity is high, as is recurrency of cerebrovascular events, and mortality is increased compared to healthy age-matched controls. Besides physical disability, high numbers of young stroke patients have to cope with cognitive decline, fatigue and post-stroke depression, resulting in a reduced quality of life. Post-stroke epilepsy is more common than previously thought. There have been identified several potential factors predicting outcome.

## THE INTERNATIONAL STUDY ON PRIMARY ANGIITIS OF THE CENTRAL NERVOUS SYSTEM (INTERSPACE): A CALL TO THE WORLD

*Sylvain Lanthier<sup>1</sup>, Leonard H. Calabrese<sup>2</sup>, José M. Ferro<sup>3</sup>, Jukka Putaala<sup>4</sup>, Daniel Strbian<sup>4</sup>, Miguel Chagnon<sup>1</sup>, Matthew P. Frosch<sup>5</sup>, Aneesh B. Singhal<sup>5</sup>, Laurent Létourneau-Guillon<sup>1</sup>, Jean Raymond<sup>1</sup>, Francois Guilbert<sup>1</sup>, Alexandre Y. Poppe<sup>1</sup>*

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Current knowledge on primary angiitis of the CNS (PACNS) mainly derives from single-centre or small-sized series, implying potential biases. The affected vessel size, appropri-

ate diagnostic process, optimal treatment, markers of treatment response, and prognosis remain controversial. INTERSPACE is an ongoing, international, multi-centre, prospective, cohort study, which was designed to describe clinical manifestations, investigation results, diagnostic process, misdiagnoses, current treatments, and outcomes (treatment failures and recurrences) in 200 PACNS patients. Its primary objective is to identify predictors of death or dependence (modified Rankin Scale: 3–6) following >1 year of clinical follow-up. Eligibility criteria are age >15 years, acquired neurological dysfunction consistent with PACNS, imaging study of CNS vessels or CNS histopathology consistent with PACNS, and exclusion of conditions that may mimic PACNS. Exclusion criteria are immunosuppressive therapy initiated before obtaining MRI of the CNS or >30 days before study enrolment, and study consent not signed. Data on INTERSPACE participants are collected in a web-based database (accessible at [www.youngstrokenetwork.org](http://www.youngstrokenetwork.org)) at baseline and during clinical follow-up. Diagnosis of PACNS and outcome events (treatment failure and recurrence) are adjudicated to maximize validity of INTERSPACE. Multivariate analysis will identify predictors of death or dependence. Since October 2012, 3 study subjects were enrolled from 2 active study sites. In 2013, 5 more sites were activated and 24 are in the process of ethics approval. Fourteen American, European and Asian countries are represented. Assuming recruitment of 0.5 participant/site/year, 69 additional sites must join INTERSPACE to complete enrolment and follow-up of 200 adjudicated PACNS patients in 5 years.

## STROKE IN WOMEN – ORAL CONTRACEPTION AND PREGNANCY

### Kirsi Rantanen

Department of Neurology, Helsinki University Central Hospital, Helsinki, Finland

Women have a higher lifetime risk of stroke than men, which is partly explained by longer life expectancy in female population. Women also account for the majority of stroke deaths. It is known that men have a higher incidence of stroke up until the age of 75, but there is evidence that the incidence might be increasing in the middle-aged women. One recent study indicated that the incidence of stroke in women aged 45–54 years was twice as high as in the men in the same age group. In another study, between the years 1999–2004, women aged 45 to 54 years had twice the odds of having experienced stroke compared with men of the same age, and that the transition from ages 35 to 44 years to 45 to 54 years marked the steepest increase in stroke prevalence over successive midlife decades for women. In a Finnish series of 1008 young stroke patients, there was preponderance of women in patients under 30 years of age.

Women do have unique risk factors such as oral contraception, pregnancy, puerperium and menopausal hormone therapy. Women also have poorer outcomes from stroke than men. WHI trials showed that hormone therapy increases the risk of stroke. It remains unresolved why estrogen, thought to be neuroprotective, actually can turn out to be harmful. In addition to estrogen, there are many gaps of knowledge when it comes to females and stroke.

In this talk the main emphasis is to cover the risk of stroke linked to use of oral contraception and the specific hazards during pregnancy and puerperium. I also try to cover the aspects of antithrombotic medication in the acute phase and in the secondary prevention, especially in pregnant women during the gestation and immediately after giving birth.

## WORLD WIDE EXPANSION OF SITS REGISTRY – NEW STUDIES AND PROTOCOLS

### Nils Wahlgren

Karolinska Institutet, Stockholm, Sweden, Chairman SITS International

SITS (Safe Implementation of Treatments in Stroke) is an academic-driven, non-profit, international collaboration with a base at Karolinska Institutet in Sweden. It is an initiative by the medical profession to certify excellence in acute stroke management and secondary prevention of stroke. The SITS Network includes over 60 countries and 1300 hospitals.

Today SITS includes a general stroke registry, an intravenous thrombolysis registry and a thrombectomy registry. Two further registries are in preparation, an intracerebral haemorrhage registry and registry of patients with atrial fibrillation. These alternative registries are optional for SITS centres. Most centres have used SITS for documentation of iv thrombolysis, but the recently opened thrombectomy registry has raised a great interest. Some countries have the ambition to use SITS for a national stroke registry.

Within thrombolysis, we are currently working with further evaluation of the SITS Symptomatic Intracerebral Haemorrhage (SICH) risk score, recently published in *Stroke*. Another current initiative is the SITS-WATCH study aiming to bring down the door-to-needle time in SITS global centres from 60 minutes to below 40 minutes. This project is ongoing and a success would mean better treatment outcomes and more patients treated.

On the platform of the SITS mechanical thrombectomy platform (SITS-TBY) we are currently launching the SITS Open study, a comparative study in 600 patients between iv thrombolysis + thrombectomy compared to thrombectomy alone in patients with an acute stroke caused by occlusion of terminal carotid artery, proximal middle cerebral artery, or basilar artery.

The registry continues to expand and because of the global structure, three regions have, or are just on their way, decided to set up regional networks: the SIECV-SITS in Latin America, the SITS EAST in Central and Eastern Europe, and recently Middle East and North Africa (MENA). These regional organisations have proven very useful for stimulation of quality improvement and research. The SITS group has now generated more than 30 publications, mostly in high-impact scientific journals.

## LOGISTICS OF THROMBOLYTIC TREATMENT: WHAT WE LEARNT FROM SITS REGISTRY

### Robert Mikulik

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Abstract. Shortening of onset-to-treatment time (OTT) for the thrombolytic treatment of stroke will improve treatment efficacy. Therefore, it is one of the top priorities of stroke management to improve logistics of thrombolytic treatment.

OTT has two components: time from stroke onset to hospital admission (onset-to-door time, ODT) and door-to-needle time (DNT). ODT reflects mostly the awareness about stroke in public because response of stroke patients or witnesses is the most important determinants of ODT. In the lecture, we cover the Czech Republic experience with programs aimed at increased stroke awareness. We will underscore the challenges of media campaigns to increase stroke awareness and suggest alternative ways of public education.

DNT reflects stroke management in hospitals and is therefore easier target for positive change as compared to ODT. We performed 2 analysis of SITS-EAST registry: one related to DNT and the other related to door-to-imaging time (DIT). Both analyses showed very different performance of different centers with respect to DNT and DIT (e.g. the proportion of patients treated with DNT 60 minutes ranged from 18 to 84% [ $p < 0.0001$ ] in different centers). Also our analysis showed that both DNT and DIT depends on ODT: i.e. patients coming later after stroke onset to hospital have shorter time to imaging and to treatment with thrombolysis. Several other important predictors of DIT and DNT were identified and will be presented.

In conclusion, our data showed that logistics can be improved in many centers and in patients arriving to hospital early. Shortening of DNT is achievable and stroke centers should implement strategies to shorten DNT. SITS is conducting SITS-WATCH project to decrease DNT and involvement in this project should lead to shortening of DNT in participating centers.

## TRENDS IN TREATMENT AND OUTCOME OF STROKE PATIENTS IN FINLAND. PERFECT STROKE, A NATIONWIDE REGISTER STUDY

*Atte Meretoja*

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A stroke-specific registry was set up in Finland ten years ago largely using cross-linkage of nationwide administrative databases. The linkage approach was possible due a unique personal identifier used in all the databases, high validity of stroke diagnoses in the discharge registries, and national coverage of all public and private in-patient care. The Performance, Effectiveness and Costs of Treatment episodes in Stroke (PERFECT Stroke) registry is a special national stroke registry in: monitoring the whole chain of recovery, throughout acute care, rehabilitation, and long-term care; covering also the smallest of hospitals; and including itemized patient-level long-term costs for all national stroke patients.

The PERFECT Stroke registry currently includes 125,000 stroke patients, demonstrating an annual 2% reduction in age- and sex-adjusted incidence of stroke over the last decade. Over the same period, ischemic stroke 3-month case-fatality has declined from 16% to 12%, and median survival has increased from 6 years to 8 years. Factors possibly explaining these positive trends include an increasing proportion of patients treated at specialized stroke centres, up from around 50% to 80%, and a higher proportion of patients receiving a triple combination of antithrombotic, blood pressure, and lipid lowering secondary preventive medications, up from around 35% to 65%. The improved level of care and increased survival are reflected in increased overall health-care costs of the stroke patients, up by 10–20% more than healthcare costs in general over the same period.

## THE DANISH STROKE REGISTRY: PRACTICAL EXPERIENCES AND RESEARCH PERSPECTIVES

*Syren Paaske Johnsen*

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The Danish Stroke Registry was established in 2003 as part of a nationwide initiative to monitor and improve the quality of care for specific diseases by monitoring fulfillment of quality of care indicators. The registry is financed and owned by the regions of Denmark and is headed by a multidisciplinary board

with representation of scientific societies and professional organisations. Together with approximately 60 other national clinical registries, the registry receives administrative, clinical epidemiological and biostatistical support from a national infrastructure dedicated to establish and maintain clinical registries.

Reporting to the registry is mandatory for all Danish hospitals treating patients with acute stroke (ischemic stroke and intracerebral hemorrhage). Upon hospital admission, data on care and patient characteristics (including sociodemographic data, Scandinavian Stroke Scale (SSS) score, comorbidity and lifestyle factors) are collected for all patients admitted with stroke. Detailed written instructions are available to ensure the data accuracy. Data are entered into an internet-based database. A structured audit process is carried out every year on a national, regional, and local basis to critically assess the quality of the dataset and the results. The data are subsequently released publicly, including recommendations from the audit groups on how to improve the quality of care further.

More than 100,000 admissions with stroke have been reported to the registry since 2003. The completeness of the patient registration appear high (i.e., >90%). The number of quality of care indicators has grown steadily over years (currently 15 process and 3 outcome indicators). Substantial improvements have been observed for all process indicators since the start of the monitoring.

The perspectives of the registry includes an extension to patients with TIA as well as more extensive use of individual-level record linkage with other health care registries in order to facilitate more efficient data collection. The registry is increasingly used for research including both epidemiological and clinical studies, however, the potential is much larger than reflected by the current level of research activities.

## ETHNICITY AND DOSING ISSUE OF IV tPA – INSIGHTS FROM SITS-NEW STUDY

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Since the NINDS rtPA study, thrombolytic therapy has been the only approved treatment for the acute ischemic stroke for almost 20 years. But many issues of clinical practice are still unresolved yet.

First of all, the proportion of subjects under intravenous (IV) thrombolysis remains still quite low. The main reason is supposed to be too many contraindications for IV tPA, though each one of which lacks scientific background. Now there is growing consensus that some contraindications could be regarded as relative, and the risk and benefit of IV tPA in a given patient should be considered individually.

Age, particularly over 80, is another subject of debate for the IV tPA indication. Also, the definition of minor symptom, which usually excludes the IV tPA use, has no universal criteria and have to be determined more comprehensively and precisely.

Because most pivotal trial for the thrombolysis in acute ischemic stroke has been run in Western countries, some concerns about the ethnic difference in response to thrombolytic therapy has been raised, and reduced dose (0.6 mg/kg) IV tPA is used in some Asian countries and particularly in Japan. But according to a recently published IV tPA registry study in Asian countries (SITS-NEW) which used standard dose (0.9 mg/kg) IV tPA, even though counteracted by slight tendency of more hemorrhagic risk, the overall efficacy was better in adjusted comparison with similar study in Europe (SITS-MOST). A clinical trial (ENCHANTED), which compares the two doses regimen, is recently initiated and the result can answer whether reduced dose would show better safety without loss of efficacy.

## SOCIOECONOMIC INEQUALITIES IN ACCESS TO STROKE THROMBOLYSIS AND THROMBECTOMY – OBSERVATIONS IN THE SWEDISH STROKE REGISTER (RIKS-STROKE)

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**Background.** Previous studies show regional and sex differences in the implementation of thrombolytic therapy for acute ischemic stroke. We used Riks-Stroke, the Swedish Stroke Register, to test the hypothesis that higher socioeconomic position is associated with increased access to thrombolysis and thrombectomy.

**Methods.** This study included 85 885, 18–80 year old ischemic stroke patients, admitted to Swedish hospitals, registered in the national stroke register, Riks-Stroke, 2003–2009. Individual patient information on socioeconomic status (education) was retrieved from Statistics Sweden. Data on reperfusion therapy (thrombolysis and thrombectomy) and patient characteristics was acquired from Riks-Stroke. Multiple logistic regression was used to analyze the association between reperfusion therapy and socioeconomic status, adjusting for potential confounding factors (year, sex, age, level of consciousness, dependence in p-ADL, history of stroke, atrial fibrillation and diabetes).

**Results.** Patients with university education were more likely to receive reperfusion therapy (5.6%) than patients with secondary (4.7%) or primary school education (3.6%,  $p < 0.001$ ). The inequality associated with education was still present after adjustment for other patient characteristics. The odds ratio of receiving reperfusion therapy was 1.16 (95% CI: 1.05–1.28) for university and 1.10 (1.01–1.19) for secondary school compared to primary school education. The absolute difference between the groups with lowest and highest education remained similar between 2003 (0.6% vs. 1.9%) and 2009 (7.9% vs. 10.4%).

**Conclusion.** Patients with higher education have better access to stroke reperfusion therapy, the inequality remains although the relative difference between educational groups have been reduced over time.

## Friday, 23 August 2013

### CHALLENGES AND CURRENT STATUS OF TREATMENT OF SPONTANEOUS ICH

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A spontaneous acute intracerebral hematoma (ICH) volume larger than 30 ml will most likely lead to severe dependency or death. In 75% of the patients with ICH the bleeding continues significantly during the first 24 hours, leaving a therapeutic window for therapy. Early surgical therapy might be effective in smaller and superficial lobar hematomas, the results of the STICH trials will be summarized. In patients treated with antithrombotics, hematomas are often more severe and with prolonged bleeding, and antidotes are recommended to revert the antithrombotic state. Hemostatic treatment may at-

tenuate hematoma growth, thereby improve recovery, reduce growth of the brain damage, reduce functional loss (e.g. paresis and cognition), reduce dependency and mortality. Recombinant activated Factor VII compared to placebo significantly reduced hematoma growth from 26% to 11% of initial ICH volume, but did not improve clinical outcome, which might reflect unfavorable baseline imbalance between treatment and controls. Contrast spots by CT-angiography is a highly sensitive predictor of hematoma growth, and a marker of poor outcome. It is recommended as a clinical tool for prognostication and an entry criterion for future acute ICH treatment trials. Tranexamic acid is routinely used in a number of hemorrhagic conditions in a number of different organ systems, and the risk of ultra-early re-bleed in subarachnoid hemorrhage significantly decreased from 10.8% in the control group to 2.4% by tranexamic acid, but has never before been prospectively tested in the hyperacute phase following ICH, and several clinical trials are planned, and one recruiting (TICH-2). The primary objective is to examine whether tranexamic acid can reduce growth of ICH and is safe with acceptable occurrence of major thromboembolic complications and other severe adverse events including death. Secondary objectives are to examine if tranexamic acid reduce neurological impairment, functional neurological deficit, disability and death, and impairment in quality of life.

### CAUSES OF ICH IN ELDERLY PATIENTS

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In 2013, intracerebral haemorrhage (ICH) remains a devastating disease with a mortality rate of 40% within the first week of ICH onset. Its incidence over the past three decades is reported as stable. These disappointing findings suggest that any reduction in ICH incidence associated with improvements in primary prevention, namely better control of blood pressure, might have been offset by an increase in cases of ICH associated with other factors including the use of anti-thrombotic drugs in the ageing population. Indeed, ICH profiles have changed in the last 20 years suggesting that some bleeding-prone vasculopathies in the elderly are more prone to bleed when antithrombotic drugs are used, as illustrated by the rise in the incidence of lobar ICH in the elderly, with a possible strong implication of cerebral amyloid angiopathy. The aim of this talk is to review data on causes of ICH in the elderly patients and to discuss the impact of the underlying vessel disease on outcome including dementia.

### OPPORTUNITIES FOR IMPROVING OUTCOMES OF BRAIN HEMORRHAGE

*Byung-Woo Yoon*

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Intracerebral hemorrhage (ICH) takes about 15% of all first-ever stroke. ICH has worse outcome than ischemic stroke. While rTPA has been approved to be effective in hyperacute ischemic stroke, we do not have specific treatment for ICH yet.

Globally overall incidence of ICH is 24/100,000, which shows no significant decrease over the decades. The incidence of ICH has ethnic difference. It is notable that the rate in Asians is higher than double. According to a large scale case-control study, population attributable risk (PAR) of identified risk factors for ICH was about 85%, meaning need for identification of more risk factors.

ICH has higher mortality than ischemic stroke, which varies from 31 to 59% according to reports. It is noteworthy that Japanese data showed much lower rate, 17%. It is not clear why they have low mortality. Case fatality of ICH has been decreasing in Korea according to national health insurance claim data.

Old age, initial neurological severity, hematoma location, size and growth, and intraventricular extension have been known to be poor prognostic factors for ICH. It was reported that ICH patients with extensive white matter lesion have worse outcome. Admission blood glucose was suggested to be associated with 30-day mortality. Patients with overweight or obesity showed better survival than those with normal or low weight. Whether aggressive management of high blood pressure can improve outcome is a recent issue of acute management for ICH.

Better understanding of risk factors and prognostic indicators will improve the prevention and outcome of patients with ICH, although we need to seek effective therapy for ICH.

### ICH DUE TO WARFARIN USE IS ASSOCIATED WITH EARLY CLINICAL DETERIORATION, LARGER HEMATOMA AT PRESENTATION, AND INCREASED MORTALITY

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**Background.** Oral anticoagulation (OAC) is a major cause of intracerebral hemorrhage. We compared several aspects of OAC-associated ICH with non-OAC-associated ICH.

**Methods.** We performed a retrospective chart review of consecutive ICH patients treated at the Helsinki University Central Hospital, January 2005 to March 2010 (n=1,013). We considered an ICH as OAC-associated if the patient was on warfarin treatment at the time-point of the ICH. Deterioration was defined as any neurological worsening. Radiological measures as lesion volume estimation, growth of hematoma (>6 ml or 33%) were analyzed.

**Results.** There were 132 (13%) OAC-associated ICH patients with 50.4% in an INR range of 2.0–3.0, 6.9% INR below 2.0, and 42.7% INR values greater than 3.0 on admission. They were older and had more severe symptoms on admission than non OAC-associated ICHs. OAC-associated ICH deteriorated more often and earlier, but did not have more hematoma growth. Deterioration and hematoma growth predicted 3-month mortality.

After adjustment for confounding factors, 3-month mortality was predicted by age, male gender, NIHSS on arrival, ICH volume, intraventricular hemorrhage, low thrombocytes, and INR at baseline (HR 1.06; CI 1.03–1.09 per 0.1). Increased 3-month mortality was found for INR range 2.0–3.0 (HR 4.06; CI 1.73–9.55) and for INR>3.0 (HR 5.51; CI 2.04–14.89).

**Conclusions.** OAC-associated ICH patients deteriorated earlier, showed increased hematoma volume on admission, died earlier, and had higher mortality compared to ICH patients with other etiologies. This patient group needs urgent improvement of care. The INR value at admission is a predictor of mortality.

### TIME COURSE OF ACTIVE POST-ADMISSION INTRACEREBRAL HEMATOMA EXPANSION

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**Background.** The time course of active hematoma expansion after acute hospital admission in patients with intracerebral hematoma (ICH) has remained unknown mainly because techniques capable of serial ICH volume assessments are challenging. We aimed at determining the temporal profile of ICH expansion after hospital admission by using transcranial B-mode ultrasound (TCUS).

**Method.** Consecutive patients presenting with spontaneous ICH within 4.5 hours after symptom onset from September 2011 until December 2012 were assessed. On admission, patients underwent non-contrast CT and CT-angiography (CTA) followed by serial hematoma volume monitoring using TCUS: every 30 minutes during the first 6 hours, and every 2 hours from 6–12 hours after admission. Follow-up CT was performed after 24 hours. The hematoma volume was estimated by CT and TCUS using the validated ABC/2 formula.

**Results.** 25 patients completed all study procedures. Mean (SD) time from onset to CT was 108.6 (45.7) min. When stratified by CTA ‘spot sign’ positive mean hematoma expansion-pace was observed 4 hours after admission. In patients with no spot sign on CTA, no significant hematoma expansion was observed within 12 hours after admission (Friedman test, P=0.476). TCUS and CT volume assessment were correlated with an absolute volume deviation within 7 mL and minimal systematic error (mean derivation 1.3 mL (CI: -0.1; 2.6)).

**Conclusion.** Active hematoma expansion occurs up to 4 hours after acute hospital admission in patients with spot sign. This study suggests a treatment window for haemostatic and antihypertensive treatment in spot sign positive patients.

### PREMORBID STATIN USE AND LIPID LEVELS IN OUTCOME OF INTRACEREBRAL HEMORRHAGE

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**Background and purpose.** We aimed to clarify the controversy on whether pre-morbid statin use affects outcome of intracerebral hemorrhage (ICH), or whether blood lipid profiles are associated with the outcome of ICH.

**Methods.** The Helsinki ICH Study, a single-center observational consecutive registry of ICH patients was used to study the associations between pre-morbid statin use, baseline lipid levels and clinical outcome. The study cohort was divided into three groups; statin users, nonusers with cholesterol levels <4.5 mmol/L (nonusers-low), and nonusers with cholesterol levels >4.5 mmol/L (nonusers-high).

**Results.** We included 521 ICH patients with data on pre-morbid statin use and known lipid levels in this retrospective study. There were 96 statin users (18%), 216 nonusers-low (42%) and 209 nonusers-high (40%). Statin users were significantly older than nonusers (median 74 years;

IQR 64–79; 65; 57–76 and 65; 57–75 respectively,  $P < 0.001$ ), had more comorbidities, prior cardiovascular medication, and lower lipid levels (median 4.0, 3.9 and 5.1 respectively;  $P < 0.001$ ), but equally severe ICHs (median baseline NIHSS 7, 9, 7;  $P > 0.05$ ). In-hospital, 3-month and 12-month mortalities were significantly higher among statin users and nonusers-low compared to nonusers-high in univariate analyses ( $P < 0.05$ ). The lower cholesterol levels did not, however, predict mortality after adjusting for ICH prognostic factors i.e. age, NIHSS, GCS, ICH volume and intraventricular location, at any time points analyzed ( $P > 0.1$ ).

**Conclusions.** Premorbid statin use did not affect the outcome of ICH. Patients having lower cholesterol levels had higher mortality, but the association was not significant after adjusting for ICH prognostic factors.

## CURRENT STATUS AND FUTURE DIRECTIONS OF ACUTE STROKE THERAPY

### *Marc Fisher*

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Tissue plasminogen activator (tPA) is the only approved therapy for acute ischemic stroke and usage is increasing around the world. Despite the results of the ECASS III trial a time window extension beyond 3 hours was not approved in the US. The benefit of i.v. tPA in the 3–4.5 hour time window is marginal based upon the ECASS III results and many unanswered questions remain about which patient and imaging subgroups benefit or do not benefit. Several devices have been evaluated for acute stroke treatment and the data from the recent stent retriever trials are encouraging. Conclusive proof of clinical benefit for such devices remains lacking but new trials are underway to provide such evidence. The use of imaging will likely be helpful in extending the therapeutic time window for acute ischemic stroke. Data from the two DEFUSE studies, EPITHET and MR Rescue will be discussed and the lessons learned from these trials put into context as to how future imaging based trials may succeed.

## AN INTEGER-BASED SCORE TO PREDICT FUNCTIONAL OUTCOME IN ACUTE ISCHEMIC STROKE

### *Patrik Michel*

Centre Cérébrovasculaire, Département des Neurosciences Cliniques, LAUSANNE, Switzerland

Prediction poor functional outcomes and mortality after stroke is needed for patients, their next of kin, and clinicians for guiding treatment decisions, counseling, discharge and rehabilitation planning, and discussions related to end-of-life decisions. Also, it may be used in non-randomized studies to control for case-mix variation and in controlled clinical trials as a selection criterion.

A clinical prognostic model should be easily applicable in the everyday setting, i.e. contain a limited number of covariates that are readily available and do not require sophisticated calculations. Examples of currently used scores in the clinical setting are the CHA<sub>2</sub>DS<sub>2</sub>VASc score to predict the stroke risk in patients with atrial fibrillation or the ABCD score to predict stroke after TIA.

Our aim was to create a simple and reliable score for acute ischemic stroke (AIS) which can be calculated in the emergency room to predict 3 months disability or death.

Using data from 1'645 consecutive non-disabled AIS patients from our center, we derived a score consisting of six param-

eters (AUC of 0.85). It was then validated in 2'312 patients from the Athens and Vienna stroke registries (AUC of 0.90 in the pooled validation cohort). The acronym of the derivation registry (ASTRAL) is also used for the prognostic score (ASTRAL score); each letter now indicates one of the covariates included in the score:

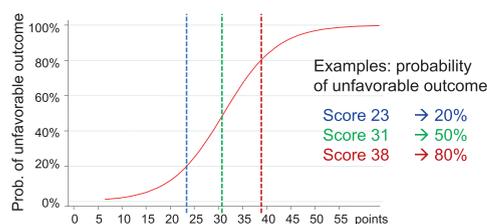
**ASTRAL score** for acute ischemic stroke to predict on admission unfavorable outcome at 3 months

<b>Age</b>	for every 5 years	1
<b>Severity</b>	for every NIHSS point	1
<b>Time</b>	onset to hospital door >3 hours	2
<b>Range</b>	of visual field defect	2
<b>Acute</b>	glucose >7.3 mmol/l or <3.7 mmol/l	1
<b>Level</b>	of consciousness decreased	3

Most of these variables have been identified as markers of prognosis in AIS before. One of the reasons why a longer time delay to arrival was a marker of poorer prognosis might be the lower rate of thrombolysis in such patients. We had decided not to include multimodal imaging and acute revascularization treatments in the score because such interventions may not yet be available everywhere.

As shown in the figure below, a score of 38 in the hyperacute phase indicates a 80% probability of the patient being disabled or dead at 3 months:

Prognosis: ASTRAL-score  
3-months probability of unfavorable outcome



Other prognostic scores for AIS are the model of the **German Stroke Database** using age and initial NIHSS (Weimar C. et al, Stroke 2004; AUC=0.81 in external validation with VISTA). The **Six Simple Variables** model uses age, living alone, independence in activities of daily living before the stroke, the verbal component of the Glasgow Coma Scale, arm power, ability to walk (Counsell C. et al, Stroke 2002; AUC=0.82 in the validation with IST-3). The **iScore** predicts poor functional outcomes at hospital discharge and also 30 day mortality (Saposnik G et al, Stroke 2011; AUC=0.82 in the validation with IST-3). In addition to age and admission NIHSS, the score includes preadmission disability, admission glucose values, stroke type, atrial fibrillation, congestive heart failure, cancer, and renal dialysis. For prediction of poor outcome in basilar artery occlusion, there is the **BASICS prognostic score** (Greving JP et al., Neurology 2012; AUC=0.80 in the derivation cohort). For acute intracerebral haemorrhage, the **FUNC** score was developed (Rost NS. et al., Stroke 2008, AUC=0.82 in the validation cohort).

The advantage of the **ASTRAL score** is not only its high accuracy in different populations (Liu et al, Stroke 2013; AUC=0.82) and up to five years (Papavasileiou V et al., Stroke 2013; AUC=0.89), but also the fact that it was developed and validated for very early use within 24 hours of stroke onset. Its drawbacks are that acute recanalisation treatments were not analysed and that it is only applicable to patients who were independent before the stroke. Further developments of the ASTRAL score may include the use of multimodal imaging, acute revascularization treatments and subacute phase covariates.

## IV THROMBOLYSIS: PREDICTING LONG-TERM OUTCOME BEFORE STARTING OF THE TREATMENT

*Daniel Strbian*

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A reliable scoring tool for prediction of long-term outcome of acute ischemic stroke patients treated with iv alteplase would be useful for early estimation of prognosis and for early identification of patients with very high likelihood for a miserable outcome despite iv thrombolytic treatment. This can lead to rapid arrangements for invasive add-on treatment strategies such as endovascular treatment, which is currently not evidence-based medicine. However, once considered, arrangements should be done quickly. Alternatively, patients with high probability of miserable outcome can be enrolled into future randomized controlled trials testing add-on strategies (not only endovascular) and into trials testing new experimental treatment modalities. Ideally, such prediction scoring tools shall be based on baseline parameters, quick to perform, based on objective criteria, and not costly. The prediction tools shall optimally be combined with scores predicting development of symptomatic intracranial hemorrhage following the stroke thrombolysis. Naturally, prediction scores can only provide estimates, but clinician's knowledge and experience is crucial for the decision-making process.

## FUTURE ADD ON THERAPIES FOR PREVENTING POST tPA HEMORRHAGES

*Wolf Rüdiger Schäditz*

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The main rtPA related complications result from its thrombolytic activity including bleeding events and reperfusion injury. The main cause of reperfusion injury are oxygen-derived free radicals. While monotherapy with antioxidants failed to translate into clinical success, the focus of preclinical research shifted to combination therapies with thrombolysis to prevent post rtPA hemorrhages and minimize rtPA induced reperfusion injury. Candidate antioxidant drugs with a better pharmacokinetic profile or multitarget activity are discussed as well as novel antiplatelet strategies.

## PRINCIPLES AND CURRENT STATUS OF ENDOVASCULAR THERAPY

*Derk W. Krieger*

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Currently, intravenous thrombolysis (iv-tPA) administered within 4.5 hours after stroke onset remains the only proven treatment and continues to be the first-line approach.

Recanalization rates after iv-tPA are lower than those reported for endovascular intervention, in particular with stent retrievers in patients with large vessel occlusions. Stent retrievers are the decisive leap in the evolution of devices to clear the cerebral vasculature.

Experiences from recent endovascular trials taught that other factors than recanalization rates, in particular time to recanalization and quality of leptomeningeal collaterals, are crucial for favorable outcomes.

Stratification of patients for endovascular therapy with penumbra-imaging has not proven helpful so far. Although, this

may be related to methodological issues the imaging selection hypothesis as currently conceived may be flawed. Comprehensive imaging in acute stroke patients adds complexity with little or no additional value for patient selection.

The intricacy of the end organ paired with relentless consequences of time endow the chagrin of those supporting endovascular therapy. In synthesis of the past trials I propose that investigator recruitment bias led to disproportionate study populations and performance bias diminished the effect size of the intervention at test. To overcome drawbacks and to acknowledge the towering costs, future investigators need to recognize that (1) only evidence will drive policy changes and (2) only networks of high volume/quality centers will create a 'culture' of doing trials in this area (250 words).

## ENDOVASCULAR THROMBECTOMY IN ACUTE ISCHEMIC STROKE – THE EFFICACY, SAFETY AND OUTCOME

*Karlis Kupcs, Andrejs Millers, Helmutis Kidikas, Evija Miglane, Janis Savlovskis, Andris Veiss, Maija Radzina, Viktorija Kenina, Raimonds Balodis*  
University Hospital, Radiology, Head, RIGA, Latvia

**Purpose.** Mechanical thrombectomy can be used in acute ischemic stroke patients with large artery occlusion and contraindications for intravenous thrombolysis or known to have suboptimal outcome.

The purpose was to evaluate safety and efficacy of endovascular thrombectomy as a treatment of acute ischemic stroke during large artery occlusion.

**Methods and materials.** 73-patients with acute ischemic stroke, who were hospitalized in Paula Stradins Clinical University hospital from 28.12.2010 till 01.09.2012.

Telephone interviews were performed-3 months after thrombectomy using modified Rankin Scale-(mRS) and National Institute of Health Stroke Scale (NIHSS).

The data were analysed using SPSS-16.0. T-test.

**Results.** There were 40 (54.8%) males and 33 (45.2%) females with in this study. Mean age of the patients was 66,0111,05(SD) years. Mean time from stroke's onset to mechanical thrombectomy was 274110,62(SD) min. in anterior circulation area and 448,67247,26(SD), in posterior circulation area.

NIHSS until thrombectomy was 16,76,8(SD), mean NIHSS after the treatment was 8,87,88(SD) The difference was statistically significant between these groups,  $p < 0.0001$ .

mRS before thrombectomy – mRS-3 got 1 (1,4%) patient who had mild disability, mRS-(4-5) got 72 (96,8%) patients who had severe disability. At-3 months after thrombectomy, 25 (34.2%) patients had good outcome mRS-2 and less, 14 (19.2%) patients had mild disability, 9 (12.5%) patients had severe disability, mRS-(4-5). There are no data about 7 (9.4%) patients after 3 months. Total mortality after-3 months was 18 (24.7%)-mRS-6.

Complications developed in 5 (6.84%) patients – all had intracerebral haemorrhage.

**Conclusion.** Mechanical thrombectomy is an effective and relatively safe treatment for patients with acute occlusion of cerebral arteries.

It can significantly improve neurological outcome in patients with severe ischemic stroke.

## A BRAVE NEW WORLD: REAL-WORLD EXPERIENCE WITH STENTRIEVERS

*Claus Z. Simonsen*

Department of Neurology, Aarhus University Hospital, Aarhus, Denmark

Ischemic stroke is a common cause of death and disability in the western world. Intravenous (iv) recombinant tissue plasminogen activator (t-PA) has proven efficacious as acute treatment. Intraarterial treatment with t-PA and/or instrumentation of the vessel with the attempt to manipulate the clot and remove it (called Intra Arterial Therapy (IAT)) is emerging as a tool for treating patients with contraindications to iv t-PA or for patients with large clot burden, where iv t-PA is often unsuccessful. The concept of treating “big strokes” with catheters, bear resemblance with cardiology, where angioplasty and stenting are now preferred in the treatment of ST-elevation infarcts. If this analogy holds, IAT could be the “next big thing” in acute stroke treatment.

But IAT is not yet an evidence based treatment. It has proved to be successful in case series and recanalization with IAT has proved more efficacious than no recanalization, but in a randomized trial against iv t-PA, it failed to produce better outcomes.

Recanalization and time to recanalization are factors that are directly related to the treatment and are playing a pivotal role in the success of IAT. Therefore, much hope is connected to the new “stent-retrievers” or “stentriever” which have been shown to have higher recanalization rates and good outcomes. These tools were not used in the trials. Stentriever are temporary stents that are placed and removed after a few minutes, often with the clot trapped in the wall of the stent. Furthermore, recanalization is often achieved early at the time of deploying the stent.

But one thing is how stentriever perform in a study, another is how they perform in “real life”. In this talk, the use and performance of stentriever will be discussed and the impact on recanalization and outcome in a single center will be shown.

## THE ART TO CUT DOWN ON TIME: LOCAL ANESTHESIA AND OTHER TIME SAVERS FOR SUCCESSFUL ENDOVASCULAR STROKE THERAPY

*Markus Holtmannspöetter*

Center for Diagnostic Radiology, Dept. of Neuroradiology, Rigshospitalet, University of Copenhagen, COPENHAGEN, Denmark

There is no time window for the individual stroke patient!

The recent triad of studies on endovascular therapy has started an engaged discussion questioning the benefits of endovascular thrombectomy in large vessel occlusive stroke. Among other shortcomings in these studies it turns out that time delays reduce the chances for a good outcome (mRS 0–2) by 14% per 30 minutes. Therefore, recanalization rate of up to 90% with novel stent retrievers will only translate into beneficial outcomes if endovascular treatment can be offered with no time delay. The quality of the collateral supply is probably as important as the time window. Collaterals are individual but can be supported in the acute phase.

To effectively cut down on the time to recanalization the pathway of endovascular patients need to be scrutinized. Time from onset of symptoms to medical care depends on various extrinsic factors, such as urban versus rural location or time of the day. Emergency systems are designed to deliver stroke

patients to primary stroke centers, however, delivery to the comprehensive stroke centers is much more variable.

With the clinical symptoms suggestive of an acute cerebral artery occlusion a native CT-scan preferably including a CT-angiography has to be performed to exclude an intracranial hemorrhage with highest priority and intravenous thrombolysis has to be made available without further delay. Every patient transfer inhouse or from extern takes time, so after start of i.v. thrombolysis the patient should be transferred to endovascular thrombectomy immediately. Depending on spontaneous clinical improvement or through intravenous thrombolysis the indication for thrombectomy has to be reevaluated upon arrival in the angiosuite by the neurointerventional team including a neurologist, neuroradiologist and anesthesiologist. All procedural preparations, such as catheter selection and preparation can be easily performed before the patient arrives. If the patient is cooperative a thrombectomy in local anesthesia with conscious sedation may be preferred. Avoiding general anesthesia saves time and reduces the likelihood of untoward blood pressure effects that may compromise collateral arterial blood flow. The anesthesiologist should always be on stand-by during the interventional procedure because neurological symptoms tend to fluctuate and necessitate general anesthesia over time.

Take home message: There is no time window for the individual patient when considering endovascular therapy. The initial stroke damage is associated with the quality of the collaterals bypassing the acute vascular occlusion. According to recent data every 30 min reduction in time to recanalization reduces the likelihood of favorable outcome by 14%. Endovascular therapy can only benefit appropriately selected patients managed with minimal time delay.

## INTERVENTIONAL STROKE TREATMENT: LESSONS FROM IMS-3

*Pooja Khatri*

University of Cincinnati, Cincinnati, Ohio, USA

Endovascular therapies have been increasingly used after the administration of intravenous tissue plasminogen activator (tPA) for patients with moderate-to-severe acute ischemic stroke. This combined approach was not demonstrated to be more effective than intravenous tPA alone in the Phase III, randomized Interventional Management of Stroke (IMS) trial.

This talk will review the overall results of the IMS III trial, and key secondary post hoc analyses, to consider patient subgroups most likely to benefit from acute endovascular therapies and inform current and future clinical trials.

## RECENT TRENDS OF STROKE EPIDEMIOLOGY IN EUROPE

*Daiva Rastenytė*

Clinic of Neurology, Academy of Medicine, Lithuanian University of Health Sciences, KAUNAS, Lithuania

**Background.** Cerebrovascular stroke is the second leading cause of death worldwide and the leading cause of lost disability-adjusted life years in most regions. It is also the most feared cardiovascular event among healthy subjects and those with cardiovascular diseases. Recent available data demonstrates changes in the epidemiology of stroke globally and in Europe in particular.

**Content.** Based on data available by the WHO, mortality rates from cerebrovascular diseases decreased by more than 50% in the EU during the last 30 years. A clear declining trend is observed in mortality rates in all countries of the Baltic and the

Nordic region except that in Poland and in Lithuania. These divergent trends may be due to sociological, demographic and epidemiological transitions in populations. For instance, still Lithuania ranks a first place according to the prevalence of arterial hypertension and the mean systolic blood pressure among the countries of the EU.

**Conclusion.** Despite a fact that advancement in stroke prevention and management has led to many successes, the large variations and inequalities exist in the management of stroke across the populations. Facing aging of the populations, many challenges remain to design effective interventions at the population and at the individual level in order to decrease risk of stroke in all countries of Europe.

## STROKE STATISTICS IN KOREA: EPIDEMIOLOGY

*Keun-Sik Hong*

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Stroke is the second leading cause of death after cancer and the first leading cause of death due to a single organ disease in Korea. This is to present the data of stroke epidemiology of Korea in the first decade of the 21st century. Every 5 minutes stroke attacks someone (105,000 incidence/year), and every 20 minutes stroke kills someone (26,000 stroke death/year) in Korea. Stroke accounts for 1 of every 10 deaths. The estimated nationwide annual disability-adjusted life years lost to stroke was 344,000. An estimated prevalence of stroke in people with 30 years of age is 795,000. Nationwide total cost for stroke care was estimated to be US\$ 3.3 billion in 2005. The annual stroke death rate substantially decreased by 28.3% during the first decade of the 21st century (74.2 per 100,000 person-years in 2001 and 53.2 per 100,000 person-years in 2010). The proportion of ischemic stroke has steadily increased and accounted for 76% of all strokes in 2009. According to the 2011 OECD report for healthcare indicators, Korea had the lowest in-hospital 30-day case-fatality rate for ischemic stroke and ranked third lowest for hemorrhagic stroke among OECD countries in 2009. Hospital registry studies reported that 90-day mortality rate was 3–7% for ischemic stroke and 17% for intracerebral hemorrhage. For risk factors, one in 3–4 Korean adults has hypertension, one in 10 diabetes mellitus, one in 7 hypercholesterolemia, and one in 3 obesity. Nearly 50% of men are current smokers, whereas less than 10% of women are smokers. Over the last 10 years, the prevalence of hypertension slightly decreased, diabetes and obesity slightly increased, and hypercholesterolemia remained stable. The population in Korea is aging fastest among the Organization for Economic Cooperation and Development (OECD) countries. Therefore, stroke burden must substantially increase in the near future, and healthcare providers as well as health policy makers need to cope with the changes.

## ICD-11 AND STROKE: WHAT'S NEW

*Bo Norrving*

Lund University, LUND, Sweden  
on behalf of the WHO Cerebrovascular Disease ICD-11 working group

ICD-10 was completed in 1990, and represents the longest time without revision in the history of ICD. Revision into ICD-11 is currently ongoing at WHO. The new classification aims to be adopted at the World Health Assembly at WHO in May 2015. A novel feature of ICD-11 is the inclusion of detailed definitions for all main diagnostic entities.

The new classification will reflect the major advances in stroke that has occurred since ICD-10, such as diagnostics, pathophysiological insights, and links between symptomatic and silent cerebrovascular disease. In ICD-11, cerebrovascular diseases will constitute one single block under "Diseases of the nervous system", making stroke a visible entity of its own.

For TIA a tissue based definition will be used. Use of the term "stroke" requires acute neurological dysfunction, and is further subdivided into cerebral ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and stroke not known if ischemic or hemorrhagic. A new section on "Cerebrovascular disease with no acute cerebral symptom" is introduced, and includes silent cerebral infarct, silent cerebral microbleed, and silent white matter abnormalities associated with vascular disease. The section on "Other specified cerebrovascular diseases" has been updated based on current knowledge, and includes revised categories of intracranial vascular malformations and cerebral vasoconstriction syndromes. Use of codes for acute stroke should be restricted to the acute stroke and immediately related hospitalization episodes, and should be separated from "late effects of cerebrovascular disease".

The Cerebrovascular Disease section in ICD-11 has been approved at WHO, and electronic field testing is currently in progress.

## STEPS TO SHORTEN DOOR-TO-NEEDLE TIME IN STROKE THROMBOLYSIS

*Atte Meretoja*

University of Helsinki, Helsinki University Central Hospital, HELSINKI, Finland

The Helsinki model of reducing in-hospital delays in stroke thrombolysis was developed and fine-tuned over a period of more than ten years and described in detail in 2012 when the median door-to-needle time was world fastest at 20 minutes. The main components of the protocol involve ambulance pre-notification with patient details, going with the ambulance stretcher straight to CT instead of an ED cubicle, and delivery of tPA right after the imaging, on the CT table.

Several factors make Helsinki an optimal place for fast-tracking a tPA service: there is only one ambulance dispatch service and only one hospital with tPA for stroke; province-wide electronic patient record and PACS systems make the past medical history and previous imaging readily available; with a centralized service the hospital annually admits 1200 ischemic stroke patients and employs 40 full-time doctors at the department of neurology allowing for 24/7 in-house tPA skilled personnel. Most stroke services around the world would work under less optimal circumstances.

However, the main component of the Helsinki model, going straight to CT on the ambulance stretcher, seems to be the primary driver of faster treatment. This was recently demonstrated in Melbourne, Australia, where the existing 'code stroke' model was restructured during business hours to include key components of the Helsinki model: pre-notification with details, going direct to CT, and delivery of tPA in the CT. In just 4 months the median door-to-needle time was halved from 43 minutes to 25 minutes, demonstrating rapid transferability of an optimized tPA protocol across different healthcare settings. With the cooperation of ambulance, emergency, and stroke teams this succeeded in the absence of a centralized service, a dedicated neurological emergency department, or electronic patient records. In Melbourne, the challenge remains in providing the same service out-of-hours with only half the personnel of Helsinki.

## QUALITY ASSURANCE OF STROKE CARE IN KOREA

*Hee-Joon Bae*

Seoul National University Bundang Hospital, Seongnam-si, Korea

Stroke is a second leading cause of death in Korea and its incidence in 2030 will be more than 3 times compared to that in 2004 mainly due to rapid aging of the population. The efforts to prevent stroke and improve its outcome are crucial for reducing the burden of stroke to our society. And one of those efforts is to assess and improve the quality of stroke care in Korea.

In 2006, the Korea Center for Disease Control and Prevention (KCDC) and the Health Insurance Review & Assessment Service (HIRA) performed a project to construct the national surveillance system for cardiovascular and cerebrovascular diseases. As a part of the project, 10 process indicators were developed to monitor the quality of stroke care in each hospital. And in 2007, the HIRA launched the quality assessment service for in-hospital stroke care in Korea. One-hundred eighty seven institutions to take care of 50 or more stroke patients per year were subjected to the assessment and the results were open to the public. As of April of 2013 the 4th assessment was completed and the 5<sup>th</sup> assessment is ongoing. This lecture will cover the details of the assess results and the impact on stroke care in Korea.

In 2006, the Korean Government started to fund the Clinical Research Center for Stroke (CRCS) with the purpose of improving the quality of stroke care mainly through developing and implementing clinical practice guidelines in Korea. The fifth section of the CRCS project (CRCS-5) is dedicated to epidemiological studies for characterizing the epidemiology of stroke and the status of stroke care in Korea. The lecture will also cover the various activities of CRCS-5 related to monitoring and improving the quality of stroke care in the participating centers that are located nationwide in Korea.

## HYPOTHERMIA IN STROKE PATIENTS TREATED IN THE ICU. THE ØRESUND EXPERIENCE

*Christian Ovesen*

Department of Neurology, Copenhagen University Hospital, Bispebjerg, COPENHAGEN, Denmark

Therapeutic cooling remains one of the most promising treatment options in acute stroke, however, since the dawn of this treatment concept, methodological considerations have been puzzling.

Multiple feasibility and methodological studies have been conducted in both animals and in acute patients with a great span in the cooling environment (intensive care unit (ICU) vs. stroke ward), degree of hypothermia, length of treatment period and in the choice of cooling strategy (surface vs. endovascular).

Treatment in the ICU process many benefits as analgesation and better control of cooling. Studies have, however, indicated major shortcomings as well. Most of these are related to analgesation and life support rather than hypothermia itself and include difficulties in clinical monitoring of patients, respiratory infections and limited capacity of ICU-beds in many institutions.

Further, the cooling strategy varies between studies. Surface and endovascular strategy remains to date the best investigated cooling strategies. Studies indicate that cooling with endovascular catheter may provide the shortest induction period and therefore desirable benefits in terms of fast hypother-

mia. However, placement of endovascular catheters require trained personal in order to ensure quick placement and low complication rate. Surface cooling with cooling sheets may have a longer induction period, but has desirable advantages over endovascular cooling in being quicker to place and requires less training.

In conclusion, the methodology of therapeutic hypothermia is still the subject of discussion and pros and cons should be outweighed in ensuring maximum benefit in terms of hypothermia control and short onset-to-treatment time.

## HYPOTHERMIA IN THROMBOLYZED AWAKE STROKE PATIENTS. THE HELSINKI EXPERIENCE

*Katja Piironen*

Helsinki University Central Hospital, HELSINKI, Finland

In my lecture of "Results of the Helsinki Mild hypothermia in thrombolized stroke patients study" I will report the preliminary results (safety, feasibility and outcome) of our study.

We performed a single-center investigator-initiated randomized controlled open safety and feasibility trial with blinded clinical outcome assessment. The study was registered with ClinicalTrials.gov as NCT00987922.

We included 36 adult patients, who were randomized 1:1 to mild hypothermia (35 °C) or to normal care. Inclusion criteria were: age 18–85 and moderate to severe neurological symptoms (NIHSS 7–20) at one hour after initiation of IV thrombolysis. Exclusion criteria were: severe cardiac failure, recent history of unstable angina pectoris or sepsis, intracranial hemorrhage or tumor on CT scan, pregnancy, hemodynamical instability, severe thrombocytopenia, pre-existing neurological disability with mRS>2, or violation of the in-house guidelines of thrombolytic therapy.

Pre-randomization procedures included medical history and physical examination, non-contrast brain CT, NIHSS, 12-lead ECG, chest X-ray, urinary catheter with intravesical temperature probe, intra-arterial catheter, and routine blood tests. All patients were treated in our acute stroke unit.

Brain CT was repeated within 30 hours to detect hemorrhage and edema.

Patients randomized to the hypothermia group (n=18) were sedated with triple medication: IV dexmedetomidine, buspirone and IV meperidine. For the hypothermia we used 2000 ml of cooled saline within two hours and non-invasive surface cooling device. The core temperature was continuously monitored from the bladder. Active cooling was restrained gradually after 12 hours at <35.5 °C.

The primary outcome of this study was the percentage of patients whose core temperature remained below 36 °C for >80% of the 12-hour cooling period.

Clinical outcome was evaluated at a 3-month outpatient visit including modified Ranking Scale (mRS), Glasgow Outcome Scale (GOS), NIHSS, and Barthel Index (BI). Good outcome was defined as mRS 0–2 and poor outcome as mRS 4–6.

## DEFINING THE OPTIMAL TARGET TEMPERATURE TO PROTECT THE BRAIN AFTER CARDIAC ARREST

*Niklas Nielsen, Hans Friberg*

Lund University, LUND, Sweden

**Introduction.** Experimental studies and clinical trials suggest an improvement in mortality and neurological function with in-

duced hypothermia after out-of-hospital cardiac arrest (OHCA). Previous trials have included highly selected populations and the optimal target temperature is not known.

**Hypothesis.** To evaluate differences in efficacy and safety with target temperature management at 33°C and 36°C for 24 hours after OHCA.

**Methods.** The Target Temperature Management after Cardiac Arrest trial (TTM-trial) is a randomized trial with 1:1 concealed allocation of 950 OHCA patients to temperature control for 24 h at 33°C versus 36°C with blinded outcome assessment. Temperature control is delivered with temperature management equipment at the discretion of the trial sites.

**Inclusion criteria:** age ≥ 18 years, OHCA of presumed cardiac cause, sustained return of spontaneous circulation (ROSC), unconsciousness (Glasgow Coma Score <8).

**Exclusion criteria:** pregnancy, known bleeding diathesis, suspected or confirmed acute intracranial bleeding or stroke, unwitnessed asystole, persistent cardiogenic shock, known limitations in therapy and “do not resuscitate” order, known disease making 180 day survival unlikely, known pre-arrest cerebral performance category 3 or 4.

**Primary outcome:** All-cause mortality at maximal follow-up (at least 180 days).

**Secondary outcomes:** Composite outcome of all-cause mortality and poor neurological function (Cerebral Performance Category (CPC) 3 and 4) at hospital discharge and at 180 days. Cognitive status at 180 days. Bleeding, pneumonia, sepsis, electrolyte disorders, hyperglycemia, hypoglycemia, cardiac arrhythmia, renal replacement therapy.

**Results.** The TTM-trial finished randomization on Jan 10 this year. Thirty-four sites in 10 countries have been involved. The study population has a mean age of 65 (interquartile range 56–73), 81% are male gender. The initial rhythm was VF or non-perfusing VT in 78%. The last follow-up will be performed in July 2013 and the results will be available in the autumn.

**Conclusion.** The TTM-trial is the largest trial to date investigating target temperature management after cardiac arrest. The TTM-trial will broaden the base for a well-founded judgment of the efficacy of temperature management after OHCA and help define the optimal temperature target.

## CURRENT STATUS OF THE EUROHyp-1 TRIAL

*Derk W. Krieger*

Department of Neurology, Bispebjerg Hospital, COPENHAGEN, Denmark

Stroke is a leading cause of death and disability. Stroke incidence rises with age increasing social expenditures for the future. Options for acute ischaemic strokes include presently only reperfusion therapies. Systematic review of stroke models suggest cooling as a promising intervention. In experimental studies, cooling to 35°C reduced infarct size by about 1/3, and to 34°C by almost 1/2. Several observational human studies have shown an association between raised temperature and poor outcome, and low temperature and favorable outcome. Therapeutic cooling of patients with ischaemic stroke to 35°C has been shown feasible and safe. Clinical benefit has not yet been tested in an adequately-sized randomized trial. EUROHyp-1 is an open, randomized, phase III, multicenter, international clinical trial with masked outcome assessment testing the benefits and harms of therapeutic cooling in 1500 awake patients with acute ischaemic stroke. Cooling will be initiated within 6 hours of symptom onset with

an intravenous infusion of 20 ml/kg cooled normal saline (4°C) over 30 to 60 minutes, followed by either surface or endovascular cooling to 34 to 35°C, maintained for 24 hours. Shivering and discomfort will be prevented with anti-shivering drugs. Patients will receive best medical treatment, including intravenous thrombolysis or thrombectomy as indicated. Primary outcome will be the common odds ratio of improvement on the modified Rankin Scale at 90 days by multiple ordinal logistic regression analysis. Secondary outcomes include death and dependency, infarct volume, quality of life, and serious adverse events.

## Saturday, 24 August 2013

### NEW APPROACHES OF NEUROPROTECTION AND NEUROREGENERATION

*Wolf Rüdiger Schäbitz*

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While neuroprotection aims to salvage neuronal tissue from death during ischemic stroke, neuroregeneration induces and supports poststroke regenerative processes such as sprouting and neurogenesis. Both together are thought to improve general stroke treatment and may eventually improve the neurological outcome in patients. Despite successes in experimental stroke studies, treatment studies in humans with protective or regenerative drugs have failed so far. In this presentation, lessons from recent failures of translation are discussed and promising novel candidate drugs in preclinical and early clinical stage are described.

### MICROBLEEDS AND ALZHEIMER'S DISEASE

*Charlotte Cordonnier*

Lille University, LILLE, France  
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Brain microbleeds (BMBs) are radiological construct. They are small dot like lesions appearing as hypointense on gradient echo T2\* MR sequences. In Alzheimer's disease (AD), BMBs are of special interest as they may have a crucial role in the pathophysiology of AD. They may be a missing link between the two most important theories on the neuropathogenesis of AD: the amyloid cascade hypothesis and the vascular hypothesis. Moreover, they may affect clinical course of the disease and may have therapeutic consequences. The aim of this talk is to review available data to understand the meaning of brain microbleeds in clinical terms and underlying pathology in the context of AD.

### CEREBRAL MICROBLEEDS AND ANTITHROMBOTIC TREATMENT

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Antithrombotic medications including antiplatelet agents and warfarin are essential for prevention of primary or secondary ischemic stroke. A meta-analysis demonstrated that treatment with aspirin was associated with a reduction of 39 ischemic strokes per 10,000 persons. However, this treat-

ment was also associated with an increase of 12 hemorrhagic strokes per 10,000 persons as compared with controls. With regard to warfarin medication, the bleeding complication is more frequent and serious than that of antiplatelet medications. Bleeding complications during long-term antithrombotic treatment is the most important and critical in practice. In this context, identification of patients with high risk of bleeding would be much helpful, if possible before the treatment. Cerebral microbleeds is typical findings of small-artery disease which is seen on T2\*-weighted gradient-echo MR sequence as minute signal loss lesions within 5 mm of diameter. They are pathologically tiny extravasations of blood from lipohyalinized cerebral arterioles. Hypertension, old age, low serum cholesterol, cerebral amyloid angiopathy, and glycated hemoglobin have been demonstrated as risk factors for these lesions. It is of potential importance that the lesions are closely associated with spontaneous intracerebral hemorrhage (ICH), and they may predict future occurrence or recurrence of ICH. These lesions are also associated with the severity of ICH. Microbleeds may be indicative of a bleeding-prone state in the brain, and they may be regarded as risk lesions of spontaneous ICH. Prognostic role of microbleeds will be discussed in the symposium.

## HORMONE REPLACEMENT THERAPY AND AGE AT STROKE

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**Background.** Hormone replacement therapy (HRT) in postmenopausal women has been shown to increase their risk of stroke.

**Methods.** We did a cohort study of 1306 patients admitted to Copenhagen Hospitals with stroke or TIA from April 2004 till September 2007. 553 female participants provided data on use of HRT. Information on age at menopause, hypertension, hypercholesterolemia, diabetes, dietary habits, current smoking, use of alcohol, and physical activity were obtained by interview. We did a regression analysis of predictors of age at stroke onset. HRT and variables with a  $p$ -value < 0.2 in the univariate analyses (diabetes, current smoking, alcoholic drinks per week, overuse of alcohol, and physical activity) were entered into the model.

**Results.** 180 (33%) women reported use of HRT. HRT was introduced at a median age of 48 years (IQR 44–50), and continued for a median of 4.5 years (IQR 1–19). We found no difference between treated and untreated women regarding median age at menopause: 49 years in the HRT-group vs 50 years  $p=0.154$ . HRT-treated women were significantly younger on admission with stroke: median age 77 years (IQR 69–83) vs 80 years (IQR 69–87)  $p=0.010$ . Regression analysis showed that age at stroke onset was predicted by current smoking  $p<0.0001$ , number of drinks per week  $p=0.0002$ , and sedentaryness  $p<0.0001$ , age at menopause  $p=0.0037$ , but not by use of HRT.

**Conclusion.** Women on HRT had their stroke at a younger age; however, use of HRT did not predict age at stroke onset in this Copenhagen stroke population.

## CAROTID INTIMA-MEDIA THICKNESS – A POTENTIAL PREDICTOR FOR RUPTURE RISK OF INTRACRANIAL ANEURYSMS

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**Background.** Atherosclerosis is a possible etiological factor for aneurysm development and rupture. Smoking and hypertension increases rupture risk, and patients with atherosclerosis have an increased prevalence of intracranial aneurysms.

Carotid ultrasound with evaluation of intima-media thickness (IMT) is a validated technique for quantification of subclinical atherosclerosis and assessment of cardio- and cerebrovascular risk. The aim of this study was to investigate IMT in patients with unruptured intracranial aneurysms (UIA) and aneurysmal subarachnoid hemorrhage (aSAH), and to assess if IMT might be associated with aneurysm rupture risk.

**Methods.** Patients treated for intracranial aneurysms from February 2011 to August 2012 were included. Standardized ultrasound assessment of carotid arteries was done after aneurysm treatment, and vascular risk factors were recorded. Healthy partners of young patients with ischemic stroke were used as controls.

**Results.** 69 patients treated for UIA ( $n=28$ ) and aSAH ( $n=41$ ) were compared with 80 controls. Mean IMT was higher in patients with aSAH (0.79 mm) than patients with UIA (0.65 mm) and controls (0.63 mm). Multiple multinomial regression analysis comparing aSAH, UIA and control groups demonstrated that IMT was the only variable predicative of aSAH compared to UIA. According to the regression model, the probability of having aSAH compared to non-rupture increased by 62% for each 0.10 mm increment of mean IMT (RRR=1.62,  $p=0.017$ ).

**Conclusion.** There is an association between IMT and intracranial aneurysm rupture status at the time of aneurysm treatment. Carotid IMT may be a predictor of aneurysm rupture, and a helpful tool in risk stratification and patient counseling.

## POST-STROKE USE OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS AND CLINICAL OUTCOME AMONG PATIENTS WITH ISCHEMIC STROKE

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**Background.** Post-stroke depression (PSD) is a common, debilitating condition affecting about 40% of stroke patients within the first year, and about 15% of post-stroke patients suffer from pathological crying. These conditions may be successfully treated with selective serotonin reuptake-inhibitors (SSRIs). However, SSRI treatment is associated with an increased bleeding risk. We aimed to investigate whether its potential antiplatelet effects have important clinical implications.

**Methods.** We did a nation-wide, register based follow-up study among ischemic stroke patients between 2003 and 2009. 5833 SSRI users were propensity-score matched with non-users in a 1:1 ratio. Cox regression analysis was de-

ployed to compute hazard ratios (HRs) of acute myocardial infarction (MI), re-stroke, major bleeding, and death.

**Results.** In total, 10.6% had an MI or recurrent ischemic stroke, 20.2% major bleeding, 1.4% intracranial bleeding, and 34.4% died during follow-up. SSRI users had a lower risk of the combined outcome of MI or recurrent ischemic stroke (adjusted HR 0.77, CI: 0.62–0.96), but also a higher risk of bleeding (adjusted HR=1.33, CI: 1.14–1.55). Mortality was increased in SSRI users (adjusted HR=1.13, CI: 1.00–1.28), and death caused by bleeding was increased (adjusted HR=1.89, CI: 0.97–3.66) compared with death by other causes (adjusted HR=1.11, CI: 0.98–1.26).

**Conclusions.** SSRI use after ischemic stroke was associated with a lower risk of new cardiovascular events, but also with an increased bleeding risk. The increased mortality among SSRI users may reflect a combination of uncontrolled confounding by indication due to the underlying depression and an increased bleeding risk.

## GENDER DIFFERENCES IN HEALTH PERSPECTIVES TEN YEARS AFTER STROKE

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**Aim.** To follow-up survivors ten years after a first-ever stroke from a population-based group of patients in the Lund Stroke Register and to compare if there were any gender differences.

**Method.** Data were collected from a group of 416 stroke-patients registered from March 1, 2001 – February 28, 2002. The survivors were followed up 10 years later by a specialist nurse regarding functional status (Barthel Index), and self-report on their health status measured with EQ5D and a general question from SF-36 regarding view on health and questions regarding dizziness and falls.

**Results.** Among the 145 stroke survivors (age mean 76.3 years, range 27–97) ten years after stroke, 86 (59%) were men, and they graded their general health ( $p=0.05$ ), and ability to perform daily activities ( $p=0.04$ ) to be better than women's estimate. Men also had less pain than women ( $p=0.01$ ). However there were no differences regarding functional status measured with Barthel Index. Women reported more dizziness ( $p=0.04$ ) and falls causing more hip fractures ( $p=0.001$ ) and other fractures than men. However in the total group, 62% estimated their general health to be excellent/very good/good, and 24% fairly good, which was related to possibility to participate in social activities.

**Conclusion.** Survivors ten years after stroke experienced having a good life even though their functional status was not always optimal. However women experienced ADL and mobility to be more disabled than men, and had more pain, dizziness, falls and hip fractures.

## IMPAIRMENTS IN EPISODIC-AUTOBIOGRAPHICAL MEMORY, SOCIAL INFORMATION AND EMOTIONAL PROCESSING IN CADASIL DURING MID-ADULTHOOD

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Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a small-vessel disease of the brain that is genetically transmitted and usu-

ally has its onset in middle adulthood. It can lead to progressive cognitive deterioration, emotional and personality changes. The disorder is often erroneously diagnosed as it may mimic other neurological or neuropsychiatric conditions.

This work's objectives are establishing greater recognition among health care providers of this relatively rare cause of cognitive and emotional changes.

We present a middle-aged patient of a strong intellectual background with genetically confirmed CADASIL. The patient underwent extensive neuropsychological testing. In addition, he underwent comprehensive medical, neurological, neuro-radiological and genetic investigations.

Neuroimaging data showed significant changes in both white and gray matter. Neuropsychological investigations revealed impairments in various executive functions, emotional and social information processing and conscious mnemonic processing (episodic-autobiographical memory).

Impairments in episodic-autobiographical memory, executive functions and social and emotional processing could represent early neuropsychological changes in CADASIL. Identifying both the early neurological and neuropsychological features of this condition, in order to enable early accurate diagnosis, is a crucial task for future research.

## DIFFERENCES IN STROKE CARE QUALITY BETWEEN URBAN AND RURAL AREAS

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**Introduction.** The association between hospital location and the quality of stroke care in Poland has not been already studied, in spite of previous reports showing different emergency procedures in urban and rural stroke units (SUs).

Thus we aimed to compare quality and effectiveness of stroke care between urban and rural SUs in Poland.

**Materials & methods.** We evaluated the medical records of 1592 patients treated in urban and 3132 patients treated in rural SUs consecutively reported to the Pomeranian Stroke Register from January 2011–March 2012.

**Results.** NIHSS score on admission and mean age did not differ between groups of patients from urban and rural SUs (8.0 vs. 7.7 pts,  $p=0.26$  and 70.6 vs. 70.6 yrs,  $p=0.97$ ; respectively). There were no significant differences regarding in-hospital mortality between rural and urban SUs (11.6 vs. 12.9%,  $p=0.06$ ) but proportion of patients independent at discharge was lower in urban than rural SUs (60.5 vs. 66.3%,  $p<0.001$ ). Use of iv-thrombolysis or statins were more common in urban than rural SUs (7.7 vs 5.0%,  $p<0.001$  and 75.6 vs. 67.6,  $p<0.001$ ; respectively). Carotid ultrasound or MRI were more frequently performed in urban than rural SUs (87.3 vs 80.8%,  $p<0.001$  and 14.2 vs. 5.0,  $p<0.001$ ; respectively), unconfirmed stroke aetiology was reported in 10.7% urban and in 15.7% rural SUs ( $p<0.001$ ). Patients from urban SUs were more frequently referred to rehabilitation units (13.8 vs. 7.7%,  $p<0.001$ ).

**Conclusions.** Significant differences concerning stroke care between urban and rural SUs indicate a great necessity of constant development of Polish SUs.

## POSTER PRESENTATIONS

### Topic 1: AWARENESS AND PREVENTION OF STROKE

#### EFFICACY OF NITRIC OXIDE IN STROKE (ENOS) TRIAL – A PROSPECTIVE RANDOMISED CONTROLLED TRIAL IN ACUTE STROKE

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**Rationale.** Acute hypertension is associated with a poor outcome after stroke. No large trials have assessed the effect of altering BP during the acute phase of stroke on outcome. We are testing whether nitric oxide, given as glyceryl trinitrate (GTN), is safe and effective in improving outcome after acute stroke. Approximately half of all patients admitted with acute stroke are taking antihypertensive therapy immediately prior to the stroke. No data exist as to whether it is beneficial or safe to stop or continue this treatment during the acute phase.

**Design.** ENOS is a prospective, international, multicentre, randomised, parallel-group, blinded, controlled trial. 3,500–5,000 ischaemic or haemorrhagic stroke patients with systolic BP 140–220 mmHg, and within 48 hours of onset will be included. Subjects will be randomised to 7 days of single-blind treatment with transdermal GTN or control. Those patients taking prior antihypertensive therapy will also be randomised to continue or temporarily stop this for 7 days. ENOS is conducted over a secure internet site. The primary outcome is modified Rankin Scale at 90 days which is carried out by a blinded assessor. The analysis will be by intention to treat.

**Trial status.** As at 11<sup>th</sup> April, 2013, 3743 patients had been recruited from 169 centres (Australia, Canada, China, Denmark, Egypt, Georgia, Greece, Hong Kong, India, Italy, Malaysia, New Zealand, Norway, Philippines, Poland, Republic of Ireland, Romania, Singapore, Spain, Sri Lanka, Sweden, Turkey and UK).

**Funding:** The Medical Research Council.

#### TRIPLE ANTIPLATELETS FOR REDUCING DEPENDENCY AFTER ISCHAEMIC STROKE (TARDIS). A RANDOMISED CONTROLLED TRIAL

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**Rationale.** The risk of recurrence is greatest immediately after stroke or TIA. Existing prevention strategies (antithrombotic, lipid/blood pressure lowering, endarterectomy) reduce, not abolish, further events. Dual antiplatelet therapy – aspirin & clopidogrel (AC) for ischaemic heart disease, aspirin & dipyridamole (AD) for stroke, is superior to aspirin monotherapy. We hypothesise that triple antiplatelet therapy (ACD) will be superior to current guideline therapy (AD or C) in patients at high-risk of recurrence, providing bleeding does not become excessive.

**Design.** TARDIS is a multicentre, parallel-group, prospective, randomised, open-label, blinded-endpoint, controlled trial. In the start-up (3 years) phase, we assessed the safety, tolerability and feasibility of intensive antiplatelet therapy (ACD) versus guideline therapy given for 1 month in 902 patients with acute stroke/TIA. The main 5 year phase will assess the safety and efficacy of intensive or guideline therapy in up to 4,100 patients. The primary outcome is ordinal stroke severity (fatal/severe non-fatal/mild/TIA/none) at 90 days. Secondary outcomes include death, myocardial infarction (MI), vascular events, function, bleeding, serious adverse events; sub-studies will assess cerebral emboli and platelet function.

**Trial status.** The start-up phase of the trial started in April 2009, and the main phase 1<sup>st</sup> October, 2012. As of 11<sup>th</sup> April, 2013, 1087 patients have been recruited from 59 live centres within the UK Stroke Research Network.

**Funding.** The National Institute of Health Research, Health and Technology Assessment Programme.

#### TICH-2 TRIAL – TRANEXAMIC ACID FOR INTRACEREBRAL HAEMORRHAGE 2

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**Rationale.** To assess in a pragmatic phase III prospective double blind randomised placebo-controlled trial whether tranexamic acid is safe and reduces death or dependency after primary intracerebral haemorrhage (PICH). The results will determine whether tranexamic acid should be used to treat PICH, which currently has no proven therapy.

**Design.** Patients will be randomised (1:1) to receive either tranexamic acid or placebo (0.9% saline) within 8 hours of acute primary intracerebral haemorrhagic stroke.

Randomisation will be computerised and minimised on key prognostics age; sex; time since onset; systolic blood pressure; stroke severity (NIHSS); presence of intraventricular haemorrhage and known history of antiplatelet treatment. Patients randomised to placebo will receive intravenous normal saline. Patients, investigators and outcome assessors will be blind to treatment allocation. The primary outcome is death or dependency (modified Rankin Scale, mRS) and telephone follow-up is at day 90.

**Trial status.** The start-up phase of the trial commenced on 1 March 2013 and will run for 4 years. The recruitment target is 300 participants in the start up phase and 2,000 in the main phase. As at 11<sup>th</sup> April, 2013, 4 patients have been recruited from 3 centres. The objective is to have 80 UK centres and 40 international centres from Australia, Brazil, Chile, China, Denmark, Egypt, Georgia, India, Malaysia, New Zealand, Nigeria, Portugal, Romania, Singapore, Sri Lanka, Sweden, and Ukraine.

**Funding.** The National Institute of Health Research, Health and Technology Assessment Programme

## Topic 2: CEREBRAL SMALL VESSEL DISEASE

### CORRELATIONS BETWEEN ANGIOPATHY AND PERIPHERAL NEUROPATHY IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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**Introduction.** Data about the relationships between complications of type 1 diabetes (DM1) are ambiguous. Especially the impact of diabetic neuropathy on cerebral angiopathy remains unclear.

Thus we aimed to assess the relationships between neuropathic and micro- or macrovascular dysfunction in DM1.

**Material and methods.** We examined 52 patients (22 males, 30 females; mean age 35.4 6.4 years) with DM1 (disease duration 17.6 6.9 years). Neuropathic symptoms were assessed with use of clinimetric scales (Michigan Neuropathy Screening Instrument [MNSI], Neurological Symptoms Score, Neurological Disability Score) and quantitative vibration sensory testing [QVST]. Macroangiopathic injuries were reflected by intima-media complex thickness (IMT) of the common carotid artery and pulse-wave velocity (PWV); cerebral microangiopathy was assessed by vasomotor reactivity reserve (VMR) and pulsatility index (PI) of middle cerebral artery measurements.

**Results.** We found no differences concerning IMT, PWV, VMR and PI between groups of patients distinguished with use of clinimetric scales. Patients with neuropathy confirmed by QVST showed higher IMT [0.57 vs 0.42 mm;  $p=0.02$ ] and PWV [10.5 vs 9.1 m/s;  $p=0.03$ ] than patients without sensory dysfunction, no differences concerning PI and VMR existed. There were correlations between IMT, PWV and vibration perception thresholds [ $r=0.400$ ,  $p=0.003$  and  $r=0.433$ ,  $p=0.004$ , respectively] as well as MNSI [ $r=0.274$ ,  $p=0.04$  and  $r=0.440$ ,  $p=0.003$ , respectively], no correlations concerning PI and VMR existed.

**Conclusions.** Association exists between presence of diabetic neuropathy and macroangiopathic, but no microangiopathic impairment in patients with type 1 diabetes mellitus.

### WHITE MATTER LESIONS PREDICT HOSPITAL ADMISSIONS DUE TO TRAUMA AFTER ISCHEMIC STROKE

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**Background.** Cerebral white matter lesions (WMLs) are a surrogate for small-vessel disease. They have been shown to be associated to decreasing mobility, gait instability, and

falls. The objective of this study was to investigate whether WMLs of the brain are associated with increased incidence of hospital admissions due to trauma in a cohort of stroke patients.

**Methods.** We followed-up for 12 years 383 consecutive patients from the SAM cohort with ischemic stroke admitted to Helsinki University Central Hospital. Hip-fractures, traumatic injuries, survival data, and causes of death were reviewed from national register data. A subanalysis for patients <65 years was performed.

**Results.** There were more hip-fractures in the moderate to severe than in the none to mild WMLs group (13.5% vs 6.5%; log-rank  $p=0.01$ ) during the 12-year follow-up. There were also more hospital admissions due to trauma in the moderate to severe than in the none to mild WMLs group (23.4% vs 7.7%; log-rank  $p=0.02$ ) among patients <65 years.

Only age was a significant independent predictor of hip-fractures (HR 1.06; 95% CI, 1.01–1.11) and for traumatic injuries (HR 1.04; 95% CI, 1.01–1.08) after adjusting for age, gender, and moderate to severe WMLs lesions in the Cox analyses of the whole cohort. Moderate to severe WMLs independently predicted hospital admissions due to traumatic injuries (HR 5.24; 95% CI 1.25–21.9) among patients <65 years.

**Conclusions.** Younger stroke patients with more than mild WMLs are at high risk to suffer serious traumatic injuries requiring hospital treatment.

### POSTSTROKE DEPRESSION AND DEPRESSION-EXECUTIVE DYSFUNCTION SYNDROME PREDICT RECURRENCE OF ISCHEMIC STROKE

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**Background.** The objective of this study was to investigate whether patients with poststroke depression or depression-executive dysfunction syndrome have increased rates of stroke recurrence.

**Methods.** We included 223 consecutive patients with ischemic stroke admitted to Helsinki University Central Hospital with a follow-up of 12 years. National register data was reviewed for all diagnosis codes of ischemic stroke, survival data and causes of death.

A Cox multivariable model with forced entry was used to adjust for stroke risk-factors as age, gender, smoking, atrial fibrillation, hypertension, diabetes, peripheral arterial disease, and hypercholesterolaemia.

**Results.** Compared to other patients, the mean time to first recurrent stroke was shorter for depressed patients (8.15; 95% CI 7.11–9.19 versus 9.63; 8.89–10.38 years) and even shorter for patients with depression-executive dysfunction syndrome (7.15; 5.55–8.75 versus 9.75; 9.09–10.41 years). During 12 years follow up the cumulative risk for recurrent ischemic stroke in was higher in the depression group (Log Rank  $p=0.04$ ) and in the depression-executive dysfunction

syndrome group (Log Rank  $p=0.01$ ) compared to other patients.

Independent predictors of recurrent stroke in the Cox multivariable analyses were increasing age (1.05; 1.01–1.08 / year), the absence of hypercholesterolaemia (0.24; 0.09–0.59), depression (1.68; 1.07–2.63), and depression-executive dysfunction syndrome (1.95; 1.14–3.33).

**Conclusions.** Depression and even more depression-executive dysfunction syndrome predict the recurrence of ischemic stroke. Executive dysfunction without depression is not a predictor of stroke recurrence. Diagnosis and treatment of depressive syndromes should be considered as a part of secondary prevention in patients with ischemic stroke.

### Topic 3: ENDOVASCULAR TREATMENT FOR CEREBROVASCULAR DISEASES

#### INTRA-ARTERIAL MECHANICAL PROCEDURES IN TREATMENT OF ACUTE STROKE

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**Abstract.** Some of the methods of treatment for acute stroke after therapeutic window for intravenous thrombolysis (3–4.5 h) are neuro-interventional procedures: intra-arterial thrombolysis and endovascular potentiating of thrombolytic effect.

**Case report.** Patient (64), admitted at 13 h, because of stroke, with severe right-sided limbs pyramidal deficit, motor dysphasia (NIHSS 14). First symptoms have appeared abruptly at 7 h. Patient underwent digital subtraction angiography (DSA) due to MSCT was malfunction. DSA findings 7 h after onset: occlusion of temporal branch of left MCA. Following DSA, aspiration thrombectomy was performed, using aspiration catheter size 4 Fr, with thromb aspiration with negative pressure using syringe of 60 ml, and procedure is repeated until complete thromb extraction is achieved. Control DSA showed complete recanalisation. Patient showed signs of fast recovery, initially in lower limb, immediately followed by recovery of upper limb, maintaining motor dysphasia (NIHSS 5). MR endocranium on the next day showed hyper density in zone of left MCA,  $1 \times 1.5$  cm.

**Discussion.** Based on experience in MMA in treatment with intra-arterial thrombolysis and aspiration techniques, of 5 treated patients, full recovery has been achieved in 4, while one resulted in death. It is a fact that patients with time expired on the therapeutic window for intravenous fibrinolysis, but immediately treated with intra-arterial fibrinolysis or mechanical thromb extraction as possible therapeutic option, have much better prognosis.

**Conclusion.** Blood vessel recanalisation in presented patient is achieved by effect of mechanical thromb extraction and it does not represent standard therapeutic procedure. Presented data indicate possibility of widening the therapeutic window.

#### INTRACRANIAL ENDOVASCULAR STENT IMPLANTATION OF MIDDLE CEREBRAL ARTERY STENOSES – INITIAL RESULTS OF 39 PATIENTS

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**Introduction.** Intracranial stent-assisted angioplasty is an emerging treatment modality for intracranial atherosclerotic stenosis. There are many reports that stent-assisted angioplasty is useful and safe. However, stent placement in MCA still remains as a challenge due to the risk of vascular dissection, elastic recoil, vasospasm stenosis.

**Purpose.** The purpose of this study is to evaluate the initial success rate of the stent-assisted angioplasty for reducing the risk of second attack stroke in MCA stenosis.

**Materials and methods.** 39 lesions of 35 patients were included in this study from March 2004 to September 2010. All patients had symptoms of acute cerebral infarction with stenoses in MCA (more than 50%). The locations of the stent implantation were all in M1 segment in MCA.

**Results.** The stent implantation was successful in 34 patients (87.1%). We had one case of microselection failure due to the tortuosity of the target vessel. There was one case (2.56%) of MCA rupture during the procedure and the patient expired after 1 week. There was no periprocedural thromboembolism in our study.

**Discussion & conclusion.** In our study, initial success rate of MCA stenoses stent implantation was 87.1%. Stent implantation in MCA stenosis is technically feasible and has relatively low rate of periprocedural complication. Long-term follow up study is necessary.

### Topic 4: EPIDEMIOLOGY OF STROKE AND CEREBROVASCULAR DISEASES

#### STROKE INCIDENCE AND RISK FACTORS OVER 32 YEARS – THE PROSPECTIVE POPULATION STUDY OF WOMEN IN GOTHENBURG

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**Background.** The Population Study of Women in Gothenburg is a unique long-term population based study with few participants lost to follow-up. The aim was to study incidence of first-ever stroke during 32-years and associations to risk factors.

**Methods.** All cases with unspecified stroke diagnoses in the Swedish computerised Hospital Linkage System were scrutinized to obtain specified codes from medical records including reports from rehabilitation personals and CT scans. Fatal stroke defined as death within 28 days without other apparent cause. Among risk factors smoking, BMI, WHR, blood pressure, AF, MI, diabetes, physical inactivity, perceived stress, depression, sleep habits and low education were selected.

**Results.** Of the 1460 women at baseline (1968–69) 184 (12.6%) had a first ever stroke during 32 years. Ischaemic stroke accounted for 138 strokes (9.5%), haemorrhagic stroke 25 (1.7%), non-specified 21 (1.4%). The scrutinizing procedure diminished unspecified diagnoses from 37% to 11%. BMI (OR 1.09 CI 1.03–1.15), smoking (1.58 CI 1.06–2.36), low education (OR 1.17 CI 1.01–1.36) showed association to IS. Total stroke only significant association to BMI and smoking. Smoking was associated to fatal stroke (OR 4.52 CI 1.99–10.30). Kaplan Meyer estimates of survival curves free from stroke were associated with no diabetes and no atrial fibrillation. Hypertension was not associated to any type of stroke possibly explained by early intervention.

**Conclusion.** Quality in this population study could be improved by securing HLS diagnoses to increase specified diagnoses. Smoking and high BMI were associated to higher stroke risk. Low education showed strong association to IS.

### VASCULAR ENDOTHELIAL GROWTH FACTOR – BIOMARKER OF LETHALITY AFTER ISCHEMIC STROKE

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**Purpose.** The purpose of the study is evaluation of the influence of vascular endothelial growth factor (VEGF) expression on survival of patients after acute ischemic stroke (AIS).

**Methods.** A prospective study involved 44 patients with AIS and 12 healthy volunteers. Determination of VEGF concentration was performed by ELISA.

**Results.** Predictors of moderate or severe neurologic deficit development at discharge from hospital (7–42 score of the National Institutes of Health stroke scale) were initial severity of stroke, postinfarction atherosclerosis, congestive heart failure and VEGF level 222 pg/ml. Survival analysis by the method of Kaplan-Meier curves showed that survival at 180 days was 0.750 (95% CI {0.582; 0.966}) for patients with VEGF levels < 222 pg/ml, and 1.0 – for patients with the content of VEGF > 222 pg/ml;  $p=0.001$ . The VEGF level in blood of patients with a lethal outcome was lower than one of surviving patients: 143 {127; 152} and 242 {173; 241} pg/ml, respectively,  $p=0.009$ . VEGF content at the first 48 h of stroke 222 pg/ml increased the probability of death within 180 days significantly;  $p=0.014$ .

**Conclusion.** The results reflect the potential role of VEGF level determination in the improvement of risk stratification of lethality or disability after AIS.

### ATRIAL NATRIURETIC PEPTIDE – PREDICTOR OF SURVIVAL AFTER CEREBRAL INFARCTION

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**Purpose.** Purpose of the study is to research the influence of atrial natriuretic peptide (ANP) levels in blood upon the patients survival after cerebral infarction (CI).

**Method.** It has been performed a prospective cohort study involving 95 patients with CI, the average age – 72.0 ± 11.7 years old. Determination of ANP level was performed by ELISA within 48 hours of stroke onset.

**Results.** ANP level at the first day of treatment was 22 {18; 27} pg/ml, what was significantly higher than the rate of control group – 6 {5; 7} pg/ml respectively ( $p<0.001$ ). By means of working characteristic curve it was defined the threshold ANP level regarding to prediction of survival during 1 year after CI, which was found to be 75-percentile ANP level. It was 27 pg/ml. Regression analysis of Cox proportional hazards showed that the relative risk of death in group with ANP level of 27–46 pg/ml during 1 year observation in 2.5 times (95% confidence interval from 1.1 to 5.8) was higher compared to patients group with ANP level 0–26.9 pg/ml.

**Conclusion.** Obtained results prove a potential role of ANP determination in improving the long-term mortality risk stratification in patients with CI. At the first 48 hours of stroke onset ANP level of the threshold value 27 pg/ml or higher is associated with high risk of death within 1 year of observation.

### PLATELET AGGREGATION ABILITY IN PATIENTS WITH CEREBRAL INFARCTION DEPENDING ON AGE

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The central part of cerebral infarction (CI) pathogenesis is thrombosis with platelet activation.

**Aim** of this work is studying the platelet agreeability in patients with CI depending on their age.

**Materials and Methods.** 215 patients with acute CI during 48 h after stroke onset were included into investigation. Patients were divided into three groups: 31 patients of middle age (average age 53.1 ± 4.0 yrs), 88 ones of advanced age (69.3 ± 4.3 yrs) and 96 old patients (80.0 ± 3.9 yrs). Three control groups of appropriate age categories were consisted of 40 healthy persons. The evaluation of platelet aggregation parameters (velocity, degree, time) was performed with light-transmission aggregometry and inductors: adenosine diphosphate (ADP) solutions with concentration of 0.5 and 1.5 μmol/l, collagen – 2.0 mg/ml. Statistical analysis was made with Mann-Whitney U-test, parameters were presented as Med {Q1; Q3}.

**Results.** It has been revealed significant differences between all age categories of patients and controls at all types of induced platelet aggregometry. The most marked difference with norm level was found in patients of middle age: 0.5 μmol/l ADP-induced aggregation rate exceeded control by 45%, aggregation degree – by 28.8% ( $p=0.001$ ). But maximal platelet aggregation was registered at old persons: aggregation velocity was 39.1 {35.8; 47.7} %/min, degree – 68.1 {57.7; 78.4} %. Differences between patients findings of middle and advanced age were not detected.

**Conclusion.** Obtained results prove differences between the state of primary hemostasis in middle/advanced and old age, which implies a differentiated approaches in antiplatelet therapy of patients with CI depending on their age characteristics.

## HIGH PREVALENCE OF RISK FACTORS AMONG YOUNG STROKE PATIENTS IN ESTONIA

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**Background.** Recent studies have identified a high frequency of traditional vascular risk factors among young stroke patients. The aim of this study was to determine the prevalence of risk factors of acute ischemic stroke in the young in Estonia.

**Methods.** Medical documents of all consecutive patients aged 15–54 with first-ever ischemic stroke from the two hospitals of Estonia (Tartu University Hospital and North Estonia Medical Centre) from 2008 to 2012 were retrospectively analyzed.

**Results.** Of the 381 patients, 255 (67%) were male. The mean age of patients was 45.9 (SD 7.7 years), without significant gender differences. The most frequent risk factors were hypertension (60%), current smoking (43%) and dyslipidemia (41%), followed by alcohol consumption (19%), obesity (14%), diabetes (11%), atrial fibrillation and carotid stenosis (both 9%). Treatment of hypertension, dyslipidemia, diabetes and atrial fibrillation prior to stroke was used in 43%, 11%, 71% and 19% of patients, respectively. Female patients had an average of 0.5 less risk factors at any age. The number of risk factors increased by 0.05 factors per one year of age. Only 5% of men and 13% of women did not have any risk factor despite of intensive investigations.

**Conclusions.** Stroke risk factors are highly prevalent among young stroke patients in Estonia. Moreover, the treatment of risk factors prior to stroke is underused. More effective primary prevention strategies are necessary to decrease the burden of stroke

## ANALYSIS OF CLINICAL AND DIAGNOSTIC DATA OF PATIENTS CURED IN A STROKE PREVENTION CENTERS IN LATVIA

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Patients suspected on having cerebrovascular disease or stroke risk factors have been examined in a stroke prevention centres in Riga All out-patients consulted by neurologists underwent US examination of precerebral and cerebral blood vessels, some of them underwent angiography, MRI or CT. Statistical analysis of clinical-diagnostic correlations of 1625 patients aged 7–89 years (65% female, 35% male) had been performed.

The percentage of defined vascular pathology in self-referred patients with the main complains of vertigo, tinnitus and headache was low (11.3%). Patients with arterial hypertension had atherosclerotic lesions in 24% of those cases. The most common diagnoses for patients sent to examination by doctors were: suspected occlusion or stenosis of precerebral and cerebral arteries (20.4%) and chronic cerebral ischemia (31.8%) where different degree stenotic lesions have been found consequently in 66.8% and in 23.3% of cases. Insignificant and

severe (70% reduction) stenoses were found with the similar frequency (22–23.2%) in patients aged 50–80 years.

Less frequently (15.3%) arterial pathology was defined in patients with chronic and acute headache (17.2% of all patients), although AVM, venous sinus thrombosis and artery dissections were detected in this group. Surprisingly rare (in 17%) arterial pathology has been found in patients with suspected TIA in a vertebral-basilar artery territory. IMT increase and minor sclerotic lesions in patients with arterial hypertension (14% from all patients) was found less then was expected similarly to more prominent arterial lesions (in 30.7%).

## EPIDEMIOLOGY OF INTRACEREBRAL HEMORRHAGE IN GRODNO, BELARUS

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**Introduction.** No population-based studies of incidence of intracerebral hemorrhage (ICH) have been performed yet in Belarus.

**Methods.** All suspected ICH occurred among 342,444 residents of Grodno-city during a 12-month period of 2011 were identified and assessed for all age groups. Multiple overlapping sources of notification were used to ascertain cases, and standard criteria for ICH and case-fatality were used. Patients with cerebral hemorrhages related to cerebral aneurism, tumour, trauma, or haematological malignancy were excluded.

**Results.** During the study period 114 cases of ICH were registered, with 103 being first-ever-in-a-lifetime strokes. The diagnosis of ICH were confirmed by CT/MRI/autopsy in 98%, patient age ranged from 20 to 89 years (meanSD age, 61.313.6 years). The crude incidence rate for ICH was 30.0 per 100,000 (95% confidence intervals [95% CI], 24.5 to 36.6); for men 35.2 (95% CI, 26.9 to 46.1) and for woman 25.8 (95% CI, 19.1 to 34.1). ICH incidence adjusted to the World Health Organization world standard population was 24.7 per 100 000 (95% CI, 22.8 to 32.9).

47 from 103 patients (45.6%) died within 28 days of ICH onset. The 28-day case-fatality rate was 41.8% for men and 50.0% for women.

**Conclusion.** ICH incidence and case-fatality rates in Grodno were found to be of highest among other studies.

## Topic 6: HEART, ATRIAL FIBRILLATION AND BRAIN

### ECG TELEMETRY DISCLOSES PREVIOUSLY UNKNOWN ATRIAL FIBRILLATION IN 24% OF PATIENTS WITH ISCHEMIC STROKE

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**Background.** Atrial fibrillation (AF) is a major cause of ischemic stroke and is probably often not recognized, with suboptimal secondary prophylaxis as a consequence.

**Material and methods.** We examined the files of all patients admitted with a diagnosis of acute cerebral infarction (ICD-10 diagnosis I63) in Nordland Hospital in Bodo from 01.01.2011 through 30.04.2012. Patients transferred from other hospitals were excluded.

**Results.** We found that 180 patients with a cerebral infarct were admitted directly to the stroke unit during this period. Mean age was 72.7 years of age (107 men and 73 women).

Five patients died during their stay in the hospital. ECG telemetry was performed in 112 of the 175 patients (64%) leaving the stroke unit alive. Exclusion criteria were previously known or ongoing atrial fibrillation at admission. Telemetry disclosed paroxysms of AF in 27 of 112 patients (24%), leading to anticoagulation treatment in 22 patients (20% of patients examined with telemetry). Of 180 patients treated in the stroke unit, fifty-one (29%) finally established a diagnosis of AF, more than half demonstrated by telemetry only. Fourteen patients with AF were not treated with anticoagulation, due to previous major bleeding (4), confusion or dementia (4), major infarct with NIHSS 17–23 (4) or general bad health.

**Conclusion.** ECG telemetry in a general stroke population in Northern Norway disclosed previously unrecognized AF in 24% of patients with ischemic stroke, leading to a change in secondary prophylaxis in about 20% of patients examined.

## THE CHALLENGE OF DETECTING ATRIAL FIBRILLATION

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**Background.** Atrial fibrillation (AF) increases the risk of stroke, thus early detection is important. The purpose of this review was to assess the different PAF detection methods, their AF detection rate, advantages and disadvantages, and to find the most efficient and cost-effective strategy.

**Methods.** Literature study using PubMed with key words 'atrial fibrillation detection monitoring'. 13 articles of which were of major interest in this report, supplemented with relevant articles quoted in the found papers.

**Results.** Several AF screenings and detection methods were examined; nurse pulse assessment, bipolar ECG, finger probe, modified blood pressure monitor (MBPM), Holter, cardiac telemetry, serial ECG, event loop recorders (ELR) and implantable loop recorders (ILR). ELR and ILR were considered some of the best PAF detection methods.

## Topic 7: MANAGEMENT OF HEMORRHAGIC STROKE

### LOST POTENTIAL OF KIDNEY AND LIVER DONORS AMONG INTRACEREBRAL HEMORRHAGE PATIENTS

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**Objective.** To identify potential kidney and liver donors among ICH patients. Do we miss them?

**Methods.** A retrospective single-center chart-review of consecutive ICH patients treated between 2005 and 2010 at the Helsinki University Central Hospital. All ICH patients who died

within 14 days of onset were assessed by a multi-professional team. Based on the results, acute service was restructured to increase organ donation.

**Results.** Of the 955 patients with follow-up data, 254 (27%) died within 14 days. Only 8 became organ donors. We identified 51 additional potentially suitable donors: 9 patients suitable for kidney donation, 11 for liver, and 31 for both. In 49/51 (96%) cases, Do-Not-Resuscitate (DNR) orders were issued early leading to refrainment from intensive care. These 51 potential donors differed from those ICH patients who survived a whole year (n=529) by male preponderance, more severe symptoms with median NIHSS of 25 (vs. 6) and GCS 7 (vs. 15) in addition to larger hematoma volumes of 24.8 cm<sup>3</sup> (vs. 6.7), and frequent finding of midline shift and intraventricular rupture of the hemorrhage on admission brain CT.

After revision of our guidelines on identification and treatment of potential organ donors based on these results, 8 ICH patients became organ donors in 2012 equaling to the total number of 6 during previous years.

**Conclusion.** A considerable number of ICH patients are potential organ donors if in-hospital practices are reorganized.

## Topic 8: MANAGEMENT OF POSTSTROKE SYMPTOMS

### THE EFFECT OF SOCIAL AND DEMOGRAPHIC CIRCUMSTANCES ON THE QUALITY OF LIFE OF STROKE SURVIVORS

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**The aim of the study.** Was to identify the associations between the quality of life (QOL) and social and demographic factors in stroke survivors and in the control group.

**Methods.** The studied groups consisted of 508 inhabitants (25–84 years) of Kaunas city and had survived a stroke. The control groups consisted of 508 age- and sex-matched inhabitants of Kaunas city randomly selected from the stroke-free population. SF-12 QOL questionnaire was used. We analyzed the QOL in physical and mental health domains with respect to social and demographic factors.

**Results.** We found a statistically significant inverse correlation between the evaluation of physical health and age. In the physical health domain, both in the control (p=0.01) and in the stroke survivor (p=0.008) groups, better evaluations were demonstrated by subjects who were not living alone. Employed subjects – both the controls and stroke survivors – presented better evaluations of their physical health.

**Conclusions.** QOL in the physical health domain worsened with age both in stroke survivors and in controls. In both the stroke survivor and the control groups, males and females with higher education levels, not living alone, and having employment demonstrated better evaluations of their QOL in the physical health domain.

## PAIN AND QUALITY OF LIFE IN STROKE PATIENTS

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**The aim of the study.** Was to compare the quality of life (QOL) among stroke survivors and healthy controls, and to evaluate the influence of age and sex on the QOL.

**Methods.** The case group consisted of 508 inhabitants (25–84 years) of Kaunas city and had experienced their first stroke. The control group consisted of age- and sex-stratified randomly selected 508 stroke-free inhabitants of Kaunas city. The QOL was evaluated using the SF-12 questionnaire. The study compared the QOL between stroke survivors and the controls in eight domains of the QOL.

**Results.** In the domain of physical and mental health, stroke survivors presented poorer evaluation of their QOL, compared to controls. Compared to healthy controls, stroke survivors presented poorer evaluation of their QOL in all domains except for pain. The evaluation of physical health in both groups worsened with age.

**Conclusions.** Compared to controls, stroke survivors presented poorer evaluations of their QOL in both the physical and the mental health domains except for pain. It was only in the control group that females evaluated their physical health worse than males did. In both studied groups, poorer evaluation of physical health was associated with older age.

## RELATIONSHIPS BETWEEN CLINICAL CHARACTERISTICS, TIME AND COSTS OF THE TREATMENT IN PATIENTS WITH POST-STROKE PNEUMONIA AND URO-INFECTION

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**Purpose.** To identify relationships between clinical characteristics, time and costs of the treatment in patients with post-stroke pneumonia and uro-infection.

**Methods.** Medical records of 256 patients with acute stroke who were treated in the stroke unit of Klaipeda university hospital in 2010 were used as a data source. The chi-square ( $\chi^2$ ) test and Spearman correlation coefficient ( $r$ ) were used to determine the relationship between characteristics. The linkage of complications to the type of stroke, gender, age and duration of treatment was established by applying logistic regression. The data difference was statistically significant at  $p < 0.05$ .

**Results.** 32 patients (12.5 percent) were diagnosed with post-stroke pneumonia and 6 patients (3.2 percent) with urinary tract infection accordingly. Older age (controlling sex) appeared to be linked to the development of after stroke pneumonia  $OR = 1.08$  (1.04 to 1.14),  $p < 0.001$ . Urinary tract infection, regardless of gender and age, was associated with hemorrhagic stroke ( $OR = 9.6$ ,  $p = 0.027$ ). Treatment duration of patients with pneumonia and urinary tract infection exceeded one and a half times that of patients without complications [ $OR = 1.52$  (1.29 to 1.78) and 1.51 (1.17 to 1.94) respectively]. Significantly higher treatment costs per patient were observed in patients with pneumonia ( $p < 0.001$ ) and urinary tract infection.

**Conclusions.** Treatment duration of patients diagnosed with after stroke pneumonia and urinary tract infection exceeded that of patients without complications. Treatment costs for patients with post-stroke pneumonia and uro-infection were significantly higher. Effective prevention and management of early complications is needed.

## CHRONIC BRAIN ISCHAEMIA. ATTEMPT TO CLASSIFY AND TREAT

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We examined 241 patients, 143 women and 93 men, the patients' age was from 56 to 84. All these patients were examined by head computer tomography and biomagnetic resonance and stroke was excluded. In 198 patients permanent syndromes of CBI were found and they were classified like this: a cephalgic syndrome in 73 patients, a vestibular syndrome in 43 patients, a pyramid syndrome in 8 patients, a light cognitive disorder in 20 patients, Parkinson's syndrome in 2 patients, a bulbar syndrome in 1 patient, an organic psychosyndrome in 51 patients. In the group of paroxysmic syndromes (43 patients) such kind of classification was received: transient global amnesia in 13 patients, drop attack in 8 patients, syncope in 4 patients, late epilepsy in 10 patients, falls by elderly people in 8 patients. For all these manifestations of CBI, we applied special treatment: anti-convulsants for late epilepsy, nootropes, cerebral metabolites and cholinesterasis inhibitors for a light cognitive disorder, analgetics for a cephalgic syndrome and so on, however, we administered medicaments to improve encephalon blood circulation, i.e., vinpocetin (cavinton), pentoxifillin, cinarisin, gynco preparations, for all our patients. During our observation period (120 days), episodes of transient global amnesia did not repeat, there were only 2 drop attacks for the patients with expressed encephalon vascular atherosclerosis and rough neck spinal osteochondrosis, we noticed much fewer falls by elderly people and better postural stability.

## Topic 10: REPERFUSION STRATEGIES IN ACUTE ISCHEMIC STROKE

### IS IT ALWAYS NECESSARY TO USE THROMBOLYTIC THERAPY IN ACUTE ISCHEMIC STROKE? POINT OF VIEW OF THE RADIOLOGIST

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One of the promising way of the brain revascularization in ischemic stroke is thrombolytic therapy.

**The purpose** of the study – to determine the criteria for thrombolysis based on transcranial Doppler (TCD).

**Methods.** The study included 40 patients aged 23 to 75 years who received thrombolytic therapy. In 36 (90%) patients lesion was localized in the basin of middle cerebral artery in 4 (10%) in the vertebrobasilar basin.

In 31 (77.5%) cases selective thrombolysis by Actilyse, and in 9 (22.5%) systemic thrombolysis with streptokinase were performed. TCD was performed before and after thrombolysis. Blood peak flow and Purcell index (PI) were estimated.

**Results.** Dopplerographic patterns before thrombolysis was allocated in the following way: normal perfusion – 5 (12.5%), hypoperfusion – 16 (40%), the flow of stenosis – 11 (27.5%), asymmetrical flow – 8 (20%). On CDS in 4 cases 'old' occlusion of the ICA and in 7 cases severe stenosis of the homolateral ICA were diagnosed. During thrombolysis was revealed the lack of lesion in the main trunk of MCA in nor-

mal perfusion. In hypoperfusion defined to the 'old' occlusion of the ICA attempts of thrombolysis and mechanical recanalization failed. In patients with asymmetrical flow and stenosis in most cases complete recanalization was achieved.

**Conclusion.** In our opinion, the indications for thrombolysis are flow of stenosis and asymmetric flow. Hypoperfusion may be the indication for thrombolysis in the absence of the 'old' occlusion of the ICA. Normal perfusion flow is not an indication for thrombolysis, so reflects M3–M4 segment lesion of MCA.

## EMERGENT ENDOVASCULAR RECANALIZATION FOR EXTRACRANIAL CAROTID STENO-OCCLUSIVE LESIONS IN ACUTE STROKE

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**Introduction.** The usefulness of emergent stenting or angioplasty of the extracranial carotid artery in acute stroke patients is not well established. The aim of this study was to determine the safety, feasibility, and efficacy of carotid artery stenting (CAS) or angioplasty in patients with acute stroke who have occlusion or high-grade stenosis of the extracranial internal carotid artery (ICA).

**Methods.** From November 2004 through December 2012, 40 consecutive patients presented to our center with acute strokes and severe steno-occlusion of the ipsilateral extracranial ICA. All were treated with emergent carotid stent placement. The medical records were reviewed and summarized. The outcome was measured by the modified Rankin scale (mRS) 3 months later and classified into favorable (mRS score, 0 to 2) or poor.

**Results.** Median NIHSS scores before emergency stent placement and at 7 days were 6.7 and 3.7, respectively, showing significant improvement ( $P < .019$ , Wilcoxon rank sum test). Twenty-six patients (65%) had favorable outcomes at 90 days. Two patients (5%) were failure of recanalization. Four patients (10%) were died due to malignant infarction, sepsis and acute myocardial infarction. Two patients (5%) have symptomatic hemorrhage.

**Conclusion.** Emergent CAS is a feasible and effective method in acute treatment of selected stroke patients with steno-occlusion of the proximal ICA.

## THROMBOLYSIS IN PRIVATE CLINIC: TUNISIAN EXPERIENCE

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**Background and aims.** The aim of this study is to report clinical, neuroimaging parameters and outcome of patients thrombolysed in the last 15 months at our new stroke-unit opened in a private clinic by September 2011.

**Methods.** We report clinical data (Age; gender; NIHSS; door to needle time; risk factors; outcome) and neuroimaging (Brain MRI and angio-MR at admission and WITHIN 24 hours after thrombolysis) of 16 patients, admitted at our stroke-unit and eligible for thrombolysis.

**Results.** 16 patients (8 males and eight females) were reported. The mean age was 67.513.5 [45–96 years]. The mean NIHSS at admission was 17.56.2 [7–27]. The mean NIHSS after thrombolysis was 7.87.6 [0–22]. The mean door to needle time was 200.6 mn 61.7 mn [90–300 mn]. Stroke interested the MCA in 15 patients and the PICA in one patient. Repermeabilisation was noted in 7 out of 13 patients for whom MRI showed occluded vessels. Three patients died between two and ten days after thrombolysis.

**Conclusion.** This is the first publication of stroke patients data from Tunisia. From this preliminary results and a review of the literature the authors will compare clinical and neuroimaging data with those previously reported in emergent countries.

## FIRST EXPERIENCE OF MECHANICAL THROMBECTOMY FOR ACUTE STROKE PATIENTS IN LITHUANIA

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**Background.** Intravenous thrombolysis is the first line treatment for acute ischemic stroke, but is less effective for occlusions of large arteries. The recent data has shown that the endovascular treatment is safe and effective as additional alternative method for patients with acute ischemic stroke. The aim of our work is evaluate the results of first mechanical thrombectomies in Lithuania.

**Methods, patients.** The consecutive patients with acute ischemic stroke who underwent mechanical thrombectomy from September 2012 to April 2013 were included. The baseline, demographic and logistic characteristics were analyzed. The primary endpoint was good outcome (modified Rankin scale score 0–2) after 3 months. The secondary endpoint was recanalization rate.

**Results.** 5 patients were included. The mean age was 6114 years, mean NIHSS score – 226. The 4 patients had anterior circulation stroke and 1 patient – posterior circulation stroke. All patients received intravenous thrombolysis before mechanical thrombectomy. The mean time from end of intravenous thrombolysis to puncture of groin artery was 8624 min, from puncture to begin of thrombectomy – 5212 min, and from begin of thrombectomy to restoration of blood flow – 138 min. The mean onset – recanalization time was 319111 min. The recanalization rate was 60%. No procedural complications and sICH were noted. 1 patient (20%) had good outcome. The 3 months mortality rate was 60%.

**Conclusion.** The mechanical thrombectomy is safe treatment for acute ischemic stroke patients. The more patients need to evaluate the clinical efficacy of mechanical recanalization. The door to thrombectomy time must be shortening.

## EFFECT OF ANTIPLATELET USE ON OUTCOME IN STROKE PATIENTS RECEIVING IV THROMBOLYSIS

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**Background.** Antiplatelet is widely used in prevention of stroke and the number of people using antiplatelet drugs is increasing. Few studies have examined the impact of pre-morbid antiplatelet use on stroke severity and outcomes,

but there is lacking data on antiplatelet use influence on IVT. The aim of our study was to examine whether prior antiplatelet use affects outcome and intracranial hemorrhage (ICH) rates in stroke patients receiving intravenous thrombolysis (IVT).

**Methods, patients.** The acute stroke patients treated with IVT in Republican Vilnius University hospital and Vilnius University hospital Santariskiu Clinics were included in this study. The demographic and baseline characteristics were collected. The patients were divided into 2 groups according to usage of antiplatelet before stroke. The primary endpoint was favorable outcome after 3 months (0–1 score on mRS). The safety profile includes rate of mortality and symptomatic ICH.

**Results.** 168 patients were included. 34 (20%) patients used and 132 (80%) did not use antiplatelet prior stroke. Females more often were on antiplatelet treatment. Antiplatelet users were older ( $p=0.027$ ), and more frequently had a congestive heart failure ( $p=0.01$ ). The good outcomes (19% vs. 21%,  $p>0.05$ ) or mortality after 3 month (27% vs. 24%,  $p>0.05$ ) were similar in both groups. There was no difference in symptomatic ICH in both groups (6% vs. 5%,  $p>0.05$ ). Only the age, NIHSS and glucose level on admission were independent predictors of outcomes on logistic regression analysis.

**Conclusions.** The prior antiplatelet treatment does not influence the functional outcome intracerebral hemorrhage or mortality after IVT.

## NEUROPROTECTION FOR ACUTE STROKE PATIENTS IN JAPAN

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Neuroprotection is essential for therapy in acute stage of stroke. Edaravone, a free radical scavenger, is the first clinical drug for neuroprotection in the world which has been used from 2001 in most ischemic stroke patients in Japan, and now in China and India too. Edaravone scavenges hydroxyl radicals both in hydrophilic and hydrophobic conditions, and is especially useful in thrombolytic therapy with tissue plasminogen activator (tPA). Combination therapy of Edaravone with tPA greatly increased survival of stroke animals, reduced infarct size, and inhibited molecular markers of oxidative damage in lipid, protein and DNA. Use of Edaravone greatly reduced hemorrhagic transformation accompanied by tPA treatment in human patients in Japan, and may also extend therapeutic time window with tPA therapy for more than 4.5 hr in human stroke patients. Our recent study suggested Edaravone also promoted a recanalization rate of tPA against thrombo-embolism of acute stroke patients.

It is important for regenerative therapy that the neural stem cells which are intrinsically activated or exogenously transplanted. Direct transplantation of iPS cells into ischemic brain caused a big tumorigenic mass in the brain, which have to be taken into account for the future human application of iPS cells. G-CSF may promote bone marrow cell migration into ischemic brain to reduce such a damage. Clinical trial with G-CSF for acute ischemic stroke patients (GENESIS-II) which are currently conducted with us showed a good preliminary results.

## Topic 11: RISK FACTORS OF STROKE

### SCREENING FOR ASYMPTOMATIC ATRIAL FIBRILLATION IN PATIENTS WITH LEFT ATRIAL ENLARGEMENT

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**Background.** Increased left atrial size has been linked to the development of atrial fibrillation (AF), although the exact relation is not clear.

**Objective.** To estimate the prevalence of undiagnosed atrial fibrillation (AF) in patients, with an enlarged left atrium (diameter 40 mm) compared to patients with a normal size left atrium.

**Material and methods.** Design: Comparative, cross-sectional study. Setting: Clinical Physiology, University Hospital. Patients: Patients, without known AF, 65years, thus having at least one risk factor associated with stroke (CHA2DS2-VASc), being referred for cardiac ultrasound (CU), were consecutively included. Interventions: After undergoing CU all patients additionally registered 30 second handheld-ECG (Zenicor EKG) recordings, twice daily and when having cardiac symptoms, during four weeks. Main outcome measures: Detection of AF in at least one registration 30 seconds or in two registrations 10 seconds.

**Preliminary results.** 248 patients, 133 men and 115 women, with an average age of 73.5 years were included, of these 143 had an enlarged left atrium (45.2 mm, +/-SD 4.9) and 105 a normal size atrium (36.2 +/-SD 3.1). Ten new AF patients were found, four men and six women, five of these had an enlarged left atrium; AF prevalence 3.5% (95% confidence interval [CI] 1.5–7.9). Five had a normal size left atrium; 4.8% (95% confidence interval [CI] 2.1–10.7). No statistic difference in AF prevalence was found between these two groups ( $p=0.598$ ).

**Conclusions.** Preliminary results from this study do not support AF screening of patients with an enlarged left atrium.

## CEREBROVASCULAR DISORDERS IN PULMONARY PATIENTS

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**Objective.** To analyse cerebrovascular disorders in pulmonary patients.

**Material and methods.** 82 patients (42 women and 40 men, the average age – 70.1 years) were examined at the Department of Internal diseases of Vilnius City Clinical Hospital. All patients passed neurological examination, general and biochemical blood test, spirometry, lung radiography or CT. Part of patients passed bronchoscopy, echoscopy of pleural cavities, cytological and bacteriological testing of pleural puncture samples, blood culture test, coagulogram. Cerebral (spinal) CT or MRI were performed in presence of indications.

**Results.** Cerebrovascular disorders and other neurological pathology in patients with lung diseases were analysed in Lithuania for the first time. Cerebrovascular disorders were di-

agnosed in 18 (22.0%) patients: 8 (9.8%) – ischemic stroke, 1 (1.2%) – minor stroke (RIND), 3 (3.7%) – transient ischemic attack (TIA), 1 (1.2%) – hypertensive encephalopathy, 5 (6.1%) – consequences of ischemic stroke. In 64 (78.0%) patients other neurological impairment was diagnosed (hypoxic encephalopathy, Pancoast syndrome, neuralgia of intercostals nerves, etc.). Ischemic stroke in all 8 (9.8%) cases and minor stroke occurred in patients with pneumonia in the arterial hypotension background. 4 (4.9%) patients suffering pneumonia and stroke died; those who survived experienced a high level of disability. In 3 (3.7%) out of 5 (6.1%) patients with previously diagnosed ischemic stroke and thromboembolism of pulmonary artery manifested ‘decompensation syndrome of old focus’.

**Conclusions.** Cerebrovascular disorders are the most frequent neurological impairment of pulmonary patients. The association between ischemic stroke, minor stroke and pneumonia in the arterial hypotension background was established. Thromboembolism of pulmonary artery deepens clinics of preceding stroke.

### THE PROBLEM OF HYPERTENSION AFTER STROKE: A CROSS-SECTIONAL ANALYSIS FROM A SINGLE CENTRE STROKE OUTPATIENT UNIT

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**Background.** Hypertension remains a crucial stroke risk factor. Stroke populations consist mainly of elderly individuals with polypharmacy and frequent side effects diminishing compliance. The aim of this cross-sectional analysis was to explore the extent of blood pressure control with antihypertensive medication after stroke.

**Method.** From a catchment’s area of 350,000 inhabitants, patients are seen in our specialized stroke outpatient after a first- or recurrent stroke. Newly referred patients during the 4th quarter 2012, were included. Patients with office blood pressure > 140/90 mmHg or already diagnosed with hypertension were defined as hypertensive. Also the dose and type of antihypertensive (AHM) were documented.

**Results.** A total of 226 patients had a first appointment in the stroke outpatient unit during the study period; 165 (73.0%) were hypertensive according to definition. 73 (44.2%) of the hypertensive patients were well-regulated on their respective medications, with 30 patients (41.1%) on 1 AHM, 23 (31.5%) on 2 AHM and 20 (27.4%) on 3 AHM.

85 patients (52.0%) were not adequately controlled, 21 patients (24.7%) were not on any AHM, 24 (28.2%) were on 1, 22 (25.9%) were on 2 and 18 (21.2%) were on 3 AHM.

**Conclusion.** This study found that 1 in 3 patients was hypertensive without effective treatment and more than 1 in 5 of these were on >2 AHM. This illustrates that hypertension control in patients after stroke remains a serious problem. The uniformity of 20–30% of uncontrolled hypertensive patients, despite increasing numbers of AHM, suggests inadequately compliance and/or resistant hypertension.

### TOOTH LOSS MAY BE A PREDICTOR OF SILENT CEREBRAL INFARCT AND WHITE MATTER CHANGE IN COMMUNITY-DWELLING ADULTS

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**Background & Objective.** Periodontal disease has been recognized as a predictor of stroke and cognitive impairment from previous epidemiologic studies. The association between number of tooth loss, one of indicators of periodontal diseases and silent infarcts and cerebral white matter changes on brain computed tomography (CT) scan was investigated among community-dwelling adults without dementia and stroke.

**Methods.** We performed dental examination by dentist for 438 subjects (315 female, mean age 637.8 years; 123 male, 61.58.5 years) among 650 stroke- and dementia-free adults older than 50 years recruited for early health check-up program, a part of PRESENT project between January 2009 and December 2010. Assessment of vascular risk factors and physical examination by in-person interview and were taken by neurologist, and trained nurses. We performed brain CT scan for subjects.

**Result.** In unadjusted analysis, odds ratio(OR) of subjects with the loss of 6 to 10 teeth and those with the loss of more than 10 were 2.3 (95% CI 1.38–4.39, p=0.006), 4.2 (95% CI 1.57–5.64, p<0.001) respectively for silent cerebral infarct and cerebral white matter changes when compared with subjects who has loss of 0 to 5 teeth. After adjusted for age, education, hypertension, DM, hyperlipidemia, and smoking, OR was 1.7 (95% CI, 1.08–3.69, p=0.12) for those who has loss of 6–10 teeth and was 3.9 (95% CI, 1.27–5.02, p<0.001) for more than 10.

**Conclusion.** These findings suggest that severe tooth loss may be a predictor of silent cerebral infarct and cerebral white matter changes among community-indwelling, stroke-and dementia-free adults.

### PRELIMINARY ANALYSIS OF STROKE IN PEOPLE TRAVELLING THROUGH DIFFERENT CLIMATE ZONES

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**Aim.** Most regions in China, such as north-east and north of China are located in the temperate zone, and very cold in winter, the average temperature is about -10 to -20°C. Whereas Sanya, the southern most city in China, falls in the tropical zone, is warm in winter, the average temperature is about 10 to 20°C. People travelling from the Chinese mainland to Sanya in winter have been found to have an increased risk of stroke. This study aimed at evaluating the mechanisms involved in the high incidence of stroke with respect to the changes in the different climate zones and at determining the preventive measures and treatments.

**Materials and Methods.** Data from 300 patients, aged 45 years, in 3 large hospitals in Sanya were collected. These patients had travelled from the northeast and north of China to Sanya in winter. The patients were divided into 2 groups on the basis of whether they had suffered a stroke within 20 days of arriving at Sanya: thus, 150 patients were included in the case group and 150 patients in the control group. Differences between the 2 groups were examined using Pearson  $\chi^2$  test, Student’s t test, or Raditi analysis, depending on the nature of

the variables being compared. Logistic regression analysis was applied to identify the independent factors of stroke related to the change in climate zones. P values <0.05 were considered statistically significant.

**Results.** Risk factors of stroke that were found to be related to the change in climate zones were male gender ( $p=0.045$ , OR=1.992), diabetes ( $p<0.001$ , OR=11.275), intracranial arterial stenosis ( $p<0.001$ , OR=11.544), hyperhomocysteinemia ( $p=0.009$ , OR=2.498), and a history of stroke ( $p=0.004$ , OR=2.620). Patients with intracranial arterial stenosis or diabetes had a higher risk of stroke if the temperature difference between the 2 regions was  $>20^{\circ}\text{C}$ . Other factors such as smoking, drinking, hyperlipemia, hypertension, and duration of travel did not differ between the 2 groups. The blood pressure of most travelers in our study decreased after they arrived at Sanya: systolic and diastolic pressure decreased by about 7.9 mmHg and 4.7 mmHg, respectively. Among the 112 patients from case group for whom MRI + DWI was performed, 61.6% (69/112) patients had cerebral watershed infarction, which is much higher than that reported in previous studies, in which watershed infarction accounted for approximately 10% of all brain infarcts.

**Conclusions.** Thus, stroke observed in people who had travelled to Sanya was found to be related to the change in climate zones. Hemodynamic changes due to the change in climate zones was result in stroke in these patients.

These are the results of the preliminary analysis; our study is still ongoing. Further research will be conducted in the future. Thank you for your time!

## MIDNOR TIA – A PROSPECTIVE COHORT STUDY OF 600 TIA PATIENTS IN THE MID-NORWAY REGION

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**Background.** Transient ischemic attack (TIA) is a predictor of stroke. The ABCD2 score is a widely used risk score for identifying patients with high risk of stroke after TIA.

**Objective.** To investigate stroke risk after TIA in both short (1 week) and long term (3 months/1 year), and to assess whether the ABCD2 score is a sufficient tool for predicting stroke risk, and whether adopting imaging modalities (ultrasound, DW-MRI) and biological markers of blood into a risk score could improve its predictive value and still be feasible in a daily clinical practice. Further on overall risk factors in TIA patients, and the incidence of other vascular events will be studied. A substudy designed as a randomized controlled trial evaluates pharmaceutical counseling in a subset of participants. A cost-benefit analysis, and a long-term follow-up (5 years) is planned.

**Method.** Designed as a prospective cohort study conducted from October 2012 until June 2014 with an estimated 600 TIA patients included from 8 hospitals in the Mid-Norway region. Data from clinical examination, imaging, blood samples and questionnaires, and end-point data from health registries are collected and analysed. Analysing methods used are Kaplan-Meier survival analysis, log-rank tests, and other standardised statistical methods.

**Results/Discussion.** Results will be presented in autumn 2015. The Mid-Norway region has a relatively stable population of 680,000 inhabitants, and together with well functioning health registries and the large size of the study it will provide important knowledge about TIA, and subsequent risk of vascular events based on risk scoring methods.

## GLOBAL BRIDGES EUROPE: A REGIONAL APPROACH TO IMPROVING TOBACCO DEPENDENCE TREATMENT TO REDUCE PREMATURE MORTALITY AND MORBIDITY

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**Introduction.** Tobacco use remains the most significant cause of preventable mortality and morbidity in Europe, and is a leading cause of CVD and stroke across the World, tripling the risk of stroke compared to non smokers; causing and exacerbating high Blood Pressure etc. Smoking cessation is not only a key element in reducing the risk of an initial stroke or CV incident; but also in recovery and secondary prevention. Health Care Professionals (HCPs) have a major role to play in identifying tobacco users and supporting them to quit using evidence based clinical practice, but there is significant variation in attitudes, knowledge and behaviour, and in policy and practice. Across Europe, there is wide variation in smoking prevalence and associated outcomes; as well as in HCP knowledge, attitudes and behaviours.

**Aims and objectives.** The Global Bridges: Healthcare Alliance for Tobacco Dependence Treatment network has been established to build a worldwide network of healthcare professionals and organisations dedicated to this issue. A European branch of this covers the 53 countries of Europe to spread good and evidence based practice, including the 3 As (Ask, Advise, Assist) which has been proven to double the natural quit rate when applied by HCPs to their patient populations. The network is open to all HCPs and those involved in policy or research.

**Methods.** Each WHO region has a tailored approach developed to reaching and engaging with HCPs, including reviewing and providing resources, training programmes, and linking together HCPs. In Europe, this also includes the recruitment of Global Bridges Tobacco Dependence Honorary National Advisers to share access to resources, policy makers and practitioners to engage them in the field.

**Results.** Across Europe, a scoping exercise by Global Bridges found significant variation in policy and practice amongst countries; and significant opportunities to engage with relevant leaders and professionals across the region. The results of this exercise will be discussed with particular reference to the Nordic and Eastern parts of the region.

**Conclusions.** Organisations that support the policy and practice of HCPs are integral to reducing variations in professional practice across countries. There is clear evidence that more work is required, and that many more lives could be positively affected, or saved from CV incidents and stroke, as well as premature death if more HCPs intervened and provided evidence based treatment. There is opportunity to work together across Europe and with HCPs to establish effective systems and professional practice to reduce tobacco dependence across the world.

## Topic 12: STROKE CONTROVERSIES

### REPEATED HYPOTHERMIA FOR REBOUND CEREBRAL EDEMA AFTER THERAPEUTIC HYPOTHERMIA IN MALIGNANT CEREBRAL INFARCTION

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Malignant cerebral infarction has a high risk of fatal brain edema and increased intracranial pressure (IICP) with cerebral herniation causing death. One of the major causes of death is a rebound cerebral edema during rewarming phase. A 66-year-old male patient presented with the right hemiplegia and global aphasia due to malignant cerebral infarction in the whole territory of middle cerebral artery with the occlusion of the proximal internal carotid artery. Being refused decompressive hemicraniectomy, he received the therapeutic hypothermia for 6 days. After rewarming for 6 hours, mentality was suddenly decreased and dilated pupil. Follow-up CT revealed that midline shifting was more aggravated. We decided on repeated hypothermia for rebound cerebral edema and successfully controlled. Therefore we reported our experience with repeated hypothermia for rebound cerebral edema following therapeutic hypothermia in malignant cerebral infarction.

### THE EFFECT OF CORTICAL ISCHEMIC INJURY ON DOPAMINERGIC NERVE SYSTEM IN STROKE ANIMAL MODEL

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**Background and aims.** Dopamine was the first neurotransmitter identified to play a role in ischemic damage. Several investigators determined that levels of dopamine and norepinephrine dropped following ischemia due to either decreased synthesis or increased release at the time of energy failure. However, it is not established that which particular dopaminergic neurons are involved after stroke. The purpose of the present study was to evaluate the effects of cortical ischemic injury on the dopaminergic nerve system in the brain.

**Methods.** Cortical infarcts were produced by focusing light on the sensori-motor cortex in Rose Bengal-treated male

Sprague-Dawley rats. To evaluate the alteration of dopaminergic system, an apomorphine test, behavior test and immunohistochemical study were performed.

**Results.** The stroke groups showed significantly decreased TH expression in periaqueductal gray, arcuate hypothalamic nucleus, substantia nigra pars compacta, ventral tegmental area, dorsal raphe nucleus, and locus coeruleus. The apomorphine test showed rotational movement in the stroke group. In the apomorphine-treated stroke group, the path length and average speed were increased, and resting time was decreased.

**Conclusion.** In our results, we suggest that cortical ischemic injury damaged the dopaminergic nerve system in the brain, and modulation of the dopaminergic nerve system affected the degree of neurological deficit and recovery after stroke.

### TWO CASES OF SPONTANEOUS INTRACRANIAL VERTEBROBASILAR ARTERY DISSECTION WITH DIFFERENT CLINICAL OUTCOME

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Spontaneous intracranial vertebrobasilar artery dissection is a rare clinical entity. Though anticoagulation has been recommended for patients with acute dissection of vertebrobasilar artery, the validity of such treatment has never been proved. We experienced two patients with anticoagulant therapy who had no consistent results. A 41-year-old man suddenly developed headache, dizziness and dysphagia 1 day before admission. Neurologic examination showed minimal dysarthria, left facial hypesthesia and left limb ataxia. Brain MRI showed left cerebellar infarction and left medullar was compressed by left vertebral artery dissection. After anticoagulant therapy, he complained chest pain and dyspnea six days after admission. Chest CT showed moderate amounts of pleural effusion and hematoma in right lung field. A 51-year-old healthy man was admitted to our hospital complaining of dizziness, dysarthria and right side weakness. These symptoms lasted for two hours, being mild and transient. There was no abnormality on the neurologic examination. MR angiography and transfemoral cerebral angiography findings were consistent with basilar artery dissection. After anticoagulant therapy, he had no more attacks of these symptoms. The therapeutic approach for spontaneous intracranial vertebrobasilar artery dissection has not yet been fully established. The risk/benefit rate of anticoagulation must be carefully weighed in patients with intracranial vertebrobasilar artery dissection. As many of them have serious underlying disorders, anticoagulation may carry increased risk.

## Topic 13: STROKE DIAGNOSTICS AND CEREBROVASCULAR NEUROIMAGING

### ASSOCIATION OF CEREBROVASCULAR PLAQUES WITH CEREBRAL MICROBLEEDS AND CEREBROVASCULAR ISCHEMIC EVENTS

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**Purpose.** The purpose of this study is to evaluate the correlation of cerebrovascular plaque characters, the presence of cerebral microbleeds (CMBs) and cerebrovascular ischemic (CVI) events.

**Materials and methods.** Thirty five consecutive patients (18 men; 17 women; mean age, 62.1 years) underwent vessel wall MRI studies including high resolution T1-, T2-, Proton density, and contrast-enhanced T1-weighted images and MR angiography for cerebrovascular plaque at 3T. CMBs were studied using T2\*-weighted GRE sequences and/or susceptibility weighted images. Plaques are characterized based on their composition. Intraplaque hemorrhage (IPH) and adventitial enhancement (AE) are categorized by T1 and T2 hyperintensity and contrast enhancement. Patients are classified with recent CVI events.

**Results.** IPH and AE are present in 29% and 82% of patients, which are associated with recent CVI events (P value <0.05). The prevalence of CMBs is 21%, which is significantly higher in the patients with recent CVI events (P value <0.05). A statistically significant association is observed between the presences of IPH, AE and CMBs (P value <0.05). Correlation analysis demonstrates an association between the number of CMBs and the recent CVI events (P value <0.05).

**Conclusion.** In conclusion, there are an association between the presence of IPH, AE, CMBs and recent CVI events. The presence of CMBs may represent an indicator of cerebrovascular symptom severity.

### ROLE OF STATIN IN ATRIAL FIBRILLATION-RELATED STROKE: A CONVENTIONAL ANGIOGRAPHIC STUDY FOR COLLATERAL FLOW

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**Background.** Intense lipid lowering is recommended in patients with atherosclerotic ischemic stroke or TIA. However, the role of statin has not been established in cardioembolic stroke. We investigated the role of statin in the development of collateral vessels in cardioembolic stroke.

**Method.** A collaborative study from two stroke centers in distinct geographic regions included consecutive patients with acute MCA infarction due to atrial fibrillation (AF) who underwent cerebral angiography. We focused on AF-related stroke in order to assess rapid poststroke collateral development after abrupt MCA occlusion. We assessed the relationship between pretreatment collateral grade and the use and dose of statin at the time of stroke onset.

**Results.** A total of 88 patients (66 statin-naïve patients and 22 statin-user) was included. Compared with statin-naïve patients, statin-users were older and more frequently had hyperlipidemia (p<0.05, in both cases). Good collaterals (collateral grade 3–4) were more frequently observed in statin-users (11 patients, 50%) than in statin-naïve patients (15 patients, 22.7%) (p=0.015). Prestroke statin use (odds ratio, 7.246; 95% CI, 1.932 to 27.181; p=0.003) was independently associated with good collateral. In statin-users, collateral grade was correlated with time interval after symptom onset (r=0.491, p=0.028), but not in statin-naïve patients.

**Conclusion.** Premorbid use of statin in AF patients is associated with good collateral flow. Although most statin trials excluded patients with cardioembolic stroke, our data raised the possibility that statin may be beneficial in this subtype, and further studies are required to answer this question.

### DIAGNOSTIC VALUE OF TRANSCRANIAL DOPPLER AND COMPUTED TOMOGRAPHIC ANGIOGRAPHY IN ACUTE BASILAR ARTERY ISCHEMIA

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**Objectives.** To assessment of diagnostic value of transcranial Doppler (TCD) and computed tomographic angiography (CTA) in acute basilar artery (BA) ischemia.

**Methods.** We prospectively studied 17 patients (47+9.7 years, 11 man, 6 women) with clinical features of BA occlusion. Prior TCD was performed in all cases (MT-1010). CTA were performed on Brilliance-40 (Philips). In 5 patients we performed digital subtraction angiography (Allura XPER FD 20, Philips). In 4 cases TCD were performed repeatedly 5–6 hours after CTA.

**Results.** CTA revealed BA occlusion in 14 patients and significant stenosis of BA with residual flow in 3 patients. In 2 cases CTA results were inconclusive because of severe BA calcification. The results of TCD were inconclusive in 7 patients. Certain BA occlusion was revealed in 8 patients. In an additional 2 cases TCD were diagnostic patency BA occlusion. TCD were false-negative in 3 patients with distal BA occlusion shown by digital subtraction angiography and CTA. In 3 patients with TCD were performed after CTA, recanalization were demonstrated. CTA results prompted indication for intra-arterial thrombolysis in 4 patients. After that, CTA provided information on the exact site and length of BA occlusion and collateral pathways.

**Conclusions.** CTA was superior to TCD in the assessment of BA occlusion in patients with acute basilar ischemia, especially in cases with distal BA occlusion. In our opinion, TCD is usefulness in the diagnosis and exclusion of proximal BA occlusion.

### PREDICTING EARLY LETHAL OUTCOME AFTER ACUTE ISCHEMIC SUPRATENTORIAL STROKE USING PARAMETERS OF QUANTITATIVE ELECTROENCEPHALOGRAPHY: DEVELOPMENT OF NEW PROGNOSTIC MODEL

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**Background and Purpose.** Statistical models to predict the lethal outcome of patients with acute ischemic supratentorial stroke (AISS) have several uses, but no adequate model exist.

We therefore developed new model using parameters of quantitative electroencephalography (QEEG).

**Methods.** Ninety-one patients (mean age  $65,6 \pm 1,6$  years) were studied within the first 72 hours of clinical evolution of middle cerebral artery territory ischemic stroke. Ninety-one QEEG recordings were obtained. Separately to affected and intact hemisphere the values of absolute spectrum rhythm power of  $\delta$ ,  $\theta$ ,  $\alpha$ ,  $\beta$  ranges, and lo- (4–6 Hertz), hi- (6–8 Hertz), lo- (8–10 Hertz), hi- (10–13 Hertz), lo- (13–25 Hertz) and hi- (25–35 Hertz) subranges in parieto-occipital regions were the QEEG selected variables for development of 14 coefficients and comparative predictive values of these coefficients for 21-th day death from stroke onset were calculated using receiver operating characteristic (ROC) curves and logistic regression modeling. Out of 91 stroke patients, 80 (87.8%) were followed up, 11 (12.2%) – were dead.

**Results.** Baseline value of  $\delta$  /  $\theta$  ratio [OR (95% CI)=1.55 (1.22–1.97),  $p < 0,0001$ ] and  $(\delta + \theta)$  /  $(\alpha + \beta)$  ratio [OR (95% CI)=1.55 (1.22–1.97),  $p < 0,0001$ ] of the affected hemisphere were independently associated with early lethal outcome of AISS (significance level of Hosmer & Lemeshew test for  $\delta$  /  $\theta$  ratio  $p = 0,77$ ,  $(\delta + \theta)$  /  $(\alpha + \beta)$  ratio –  $p = 0,28$ ). Using a comparative ROC-analysis, baseline value of  $\delta$  /  $\theta$  ratio of the affected hemisphere has the largest area under ROC curve [AUC (95% CI)=0.912 (0.835 to 0.962),  $p < 0,05$ ], a cut-off of 2.73 predicted early lethal outcome of AISS with 90.9% sensitivity, 81.2% specificity.

**Conclusions.** The value of  $\delta$  /  $\theta$  ratio of the affected hemisphere performed within the first 72 hours of AISS might be a powerful tool predicting early lethal outcome.

**Significance.** These findings may have an impact on stroke care.

## Topic 14: STROKE IN YOUNG AGE

### HEMODYNAMIC CHANGES DURING ORTHOSTATIC TESTING IN CHILDREN AFTER RECURRENT SYNCOPE: POSSIBILITY TO PREDICT RESULT

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**Objective.** Syncope is common problem in adolescents. Although it is mostly benign and reflex, but in some cases it may be the clue to underlying cardiovascular disease and may predict risk of sudden death. Orthostatic testing helps to simulate syncope and to explore hemodynamic changes during it, but is very uncomfortable for patient, extended for physician. Aim of this study was to determine hemodynamic predictors of response before losing of conscious in children with at least 3<sup>rd</sup> episode of syncope.

**Patients.** Orthostatic testing was performed in 205 children mean age  $13.45 \pm 2.68$  years after non-complicated clinical and ecg examination. Testing was divided into three periods: I – time to basic measures, II – from start of orthostasis to compensatory hemodynamic and III – from compensatory to the first complaint according to reflex.

**Results.** Statistically significant differences of systolic and diastolic blood pressure, and heart rate measurements were not established, at rest and basic stage among different hemodynamic patterns of syncope. But systolic blood pressure statistically significant differed ( $p = 0.003$ ;  $F = 4.07$ ), as diastolic blood pressure ( $p = 0.001$ ;  $F = 4.61$ ) and as heart rate ( $p = 0.000$ ;  $F = 6.07$ ) at compensatory stage. Changes of blood pressure and heart rate were statistically significant different

during the second period of orthostatic testing: systolic blood pressure ( $p = 0.000$ ;  $F = 5.78$ ), diastolic blood pressure ( $p = 0.008$ ;  $F = 3.53$ ), heart rate ( $p = 0.000$ ;  $F = 9.56$ ) among hemodynamic patterns of syncope.

**Conclusion.** Although syncope still has many questions to research and clear, but result of orthostatic testing is predictable without losing of conscious in children suffering from multiple syncope.

### PRECEDING AND POST-STROKE INFECTIONS IN YOUNG ADULTS WITH FIRST-EVER ISCHEMIC STROKE: IMPACT ON SHORT-TERM AND LONG-TERM OUTCOME

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**Background.** There are mixed results how preceding infection (PI) affects the prognosis of ischemic stroke, but it is well known that post-stroke infections (PSI) worsen the outcome in acute ischemic stroke. Our objectives were to characterize PI and PSI in young adults with first-ever stroke and to study, whether they are associated with unfavorable 3-month outcome. We studied also whether such infections are associated with long-term outcome, recurrent vascular events and death.

**Methods.** From our database of 1008 consecutive patients aged 15 to 49 we included in the present study those who had brain imaging done within the first two days from stroke onset. Outcomes were unfavorable 3-month outcome (modified Rankin Scale 2–6), and during long-term follow-up, vascular events and all-cause death. Logistic regression and Cox proportional models were used to find out associations between infections and clinical outcomes

**Results.** 681 patients (62.3% males) fulfilled the inclusion criteria. Of these, 73 (10.7%) had PI, most commonly upper respiratory tract infection and 103 (15.1%) had PSI, most commonly pneumonia. After adjusting for gender, age and risk factors, both PI (OR 2.86; 95% CI 1.48–5.54) and PSI (OR 2.26; 95% CI 1.08–4.76) were independently associated with unfavorable 3-month outcome. PSI was also associated with long-term (follow-up  $7.84 \pm 0$  years) higher risk of all-cause death.

**Conclusion.** In young stroke patients with ischemic stroke, both pre and post-stroke infections correlate with unfavorable short-term prognosis. Post-stroke infections were also associated with higher mortality in the long term.

### CEREBRAL VENOUS THROMBOSIS ASSOCIATED WITH LYME BORRELIOSIS DURING PREGNANCY. A CASE REPORT

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**Objectives.** Description of a patient with cerebral venous thrombosis (CVT) related with pregnancy and Lyme disease.

**Case description.** A 25-years-old pregnant woman at 8 week of first gestation was admitted to the Hospital of Lithuanian University of Health Sciences Kaunas clinics with com-

plaints of headache, nausea, vomiting, photophobia and fever. Her medical history was clear, any information of abortion, genetic or systemic diseases. On examination, she showed right abducens nerve palsy, had stiff neck and positive Kerning's sign, temperature was 37.8 C. The ophthalmological consultation: bilateral papilledema with retinal hemorrhages. Magnetic resonance imaging (MRI) scan and venography showed: filling defects, hyperintense in the superior sagittal, right transverse and straight sinuses, absent of signals flow void on these sinuses and bilateral cortical venous near superior sagittal sinus. These findings confirmed the diagnosis of CVT. A low molecular weight heparin (LMWH) 0.6 ml twice daily up to end of the pregnancy was prescribed. The infectious disease physician confirmed diagnosis of Lyme disease by Western blot test, the specific serum antibody index was 7.76 for IgG (normal <0.20) and 0.34 for IgM (normal <0.32) antibodies. Intravenous ceftriaxone 2 g/day was prescribed for 2 weeks. Other CVT causes, we did not find. Control MRT was done on the third weeks and showed a positive course of the disease. At 38 weeks gestation woman delivered a healthy baby without postpartum complication.

**Conclusion.** This is not very common pathology, but according to literature data pregnancy and Lyme disease may cause of CVT. LMWH are safe and effective during pregnancy.

## CAUSES OF ISCHAEMIC STROKE IN YOUNG ADULTS IN VILNIUS UNIVERSITY HOSPITAL SANTARISKIU KLINIKOS

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**Objectives.** To analyze prevalence of risk factors and etiology of ischaemic stroke (IS) in young adults.

**Methods.** We retrospectively evaluated 90 IS patients aged 18 to 50 admitted to our hospital during 2010–2012. All patients were divided into 2 groups: with (1st group, N 77) and without (2nd group, N 13) traditional risk factors. Performed diagnostic tests were grouped: a. standard laboratory; b. vascular investigations; c. search of cardioembolic sources; d. tests for paradoxical embolism; e. prothrombotic factors. Etiology was classified by TOAST criteria. Groups of patients were compared regarding performed diagnostic tests and possible etiology.

**Results.** Study included 52 (57.8%) men and 38 (42.2%) women. Mean age at stroke was 42.67.9, men were significantly older than women (44.275.92 vs. 40.219.61,  $p < 0.05$ ). Incidence increased exponentially with aging. The majority of patients had one or more traditional risk factors (85.5%,  $p < 0.05$ ). Diagnostic tests performed in the 1st group of patients: a. 100%, b. 89.6%, c. 88.3%, d. 22.1%, e. 28.6%; in the 2nd group: a. 100%, b. 92.3%, c. 84.6%, d. 30.8%, e. 30.8%. Presumable etiology of IS: large artery atherosclerosis – 24.4%, cardioembolism – 26.7%, small artery occlusion – 0%, other determined etiology – 15.6%, undetermined etiology – 33.3%.

**Conclusions.** The traditional risk factors are very frequent in young adult stroke patients. Cardioembolism and large artery atherosclerosis are the most prevalent etiologic subgroups. Strokes of undetermined etiology comprise more than 1/3 of all cases. Young stroke patients without traditional risk factors are inadequately evaluated, especially considering paradoxical embolism and prothrombotic factors.

## Topic 15: STROKE REHABILITATION

### THE EFFECT OF RESPIRATORY MUSCLE TRAINING ACCORDING TO PATIENT'S INITIAL PULMONARY FUNCTION IN SUBACUTE STROKE PATIENTS

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**Objective.** The aim of this study was to determine which subgroup showed more improvement of pulmonary function and functional status after respiratory muscle training according to their initial FEV1.

**Methods.** Patients with first episode of unilateral stroke were recruited. All subjects participated in conventional stroke rehabilitation program and pulmonary rehabilitation program. Pulmonary rehabilitation program consisted of inspiratory muscle training using volumetric incentive spirometer and expiratory muscle training using positive expiratory pressure breathing device. Subjects performed pulmonary function test and were assessed for modified Barthel index (MBI) and Brief Fatigue Inventory (BFI) at baseline and at the end of the training. The results were assessed in 5 groups according to initial relative FEV1.

**Results.** 24 stroke patients were enrolled. Patients with moderate pulmonary function (2nd, 3rd, 4th quintile) showed significant improvement in FEV1, BFI after the training. Patients with mild (5th quintile of FEV1) and severe (1st quintile of FEV1) pulmonary function had improved FEV1 and BFI, however there was no statistical significance. There was a statistically significant increase in MBI score in subjects in the 2nd, 3rd, 4th, and 5th quintile of FEV1. The improvement of FEV1, BFI, MBI score was different according to initial FEV1.

**Conclusion.** This study suggests that respiratory muscle training was effective for improvement of pulmonary function and recovery of functional status. Patients showed difference in results according to initial pulmonary function after pulmonary rehabilitation program. Patients with moderate pulmonary function showed more improvement than patients with severe and mild pulmonary function.

### COMBINED TREATMENT FOR MALES WITH SEXUAL DYSFUNCTION IN STROKE RECOVERY

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**Background.** Combined treatment program for males who suffer from sexual dysfunction after stroke with decreased libido and erectile dysfunction includes: new-generation blood thinners for prevention of stroke by use anticoagulant medicine treatment (AMT), cognitive hypnotherapy (CH) with mind-body relaxation, cognitive restructuring of depressed mood and fear of another stroke, and couple therapy (CT) for sexual rehabilitation.

**The aim** of this study was to evaluate the effectiveness of using AMT, CH and CT for males who suffer from sexual dysfunction after stroke.

**Material and methods.** During last year period 10 heterosexual males, aged 57–69, suffering from erectile dysfunction (ED), diminished libido and bad couple's well-being after

stroke compared to their sexual functioning before stroke, were treated and observed. Group A males (n=6) received five weeks oral anticoagulant medicine Xarelto – 20 mg tablet once a day, CH and CT twice a week. Group B males (n=4) received 5 weeks only AMT. The functional measures included IIEF domain EF. A stage of apathy, decreased libido was investigated by modified Montgomery-sberg Depression Rating Scale. Level of couple's well-being was measured by Visual Analogue Scale.

**Results.** After 5 weeks treatment course IIEF dimension EF improved significantly with restored libido, high-spirited mood – for 66% of group A males, intensity of the couple's well-being – improved for 83% of group A males ( $p < 0.05$ ).

**Conclusion.** New-generation anticoagulant medicine treatment with cognitive hypnotherapy and couple therapy in five weeks combined treatment course for males with sexual dysfunction is an effective treatment in stroke recovery.

## RELATIONSHIP BETWEEN BALANCE PERFORMANCE AND STEP WIDTH AMONG STROKE SURVIVORS

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**Introduction.** Stroke survivors usually have difficulties in maintaining static and dynamic balance due to typical hemiplegic gait. The gait parameters are therefore adversely affected.

**Purpose.** This study investigated relationship between static balance, dynamic balance performances and step width in hemiplegic stroke survivors.

**Methods.** This correlation study involved 25 stroke survivors (15 males, 10 females) recruited from 3 teaching hospitals with age range between 32 and 76 years. Berg balance scale was used to assess both static and dynamic balance performance. A piece of white paper measuring 6 m in length and 0.5 m in width, taped at the edges on a level floor to walk on and impress their footprint. Print was allowed to dry and step width was measured with an inelastic tape measure.

**Data Analysis.** Data were summarised using descriptive statistics of mean, range and standard deviation. Inferential statistics of spearman rank order correlation coefficient was used to determine the relationship between step width and balance (static and dynamic) performance at 0.05 level of significance.

**Results.** Step width did not correlate significantly with either the static balance performance ( $r = -0.19$ ,  $p > 0.05$ ) or dynamic balance performance ( $r = 0.37$ ,  $p > 0.05$ ).

**Conclusions.** Based on the outcome of the study it was concluded that step width does not affect balance (static and dynamic) performance in hemiparetic stroke patients. Changes in step width will not significantly influence balance performance in stroke patients with hemiparesis.

## PATIENTS' PERCEIVED PARTICIPATION AND SATISFACTION IN THE REHABILITATION PROCESS

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In the literature on stroke rehabilitation, there exist many studies that assess the effects of patient involvement on recovery rates. Most of these studies focus on the degree of

actual involvement in the process and the results of rehabilitation as estimated by the doctors in charge. Drawing on social science studies of people's participation in group decision-making processes, this paper suggests to ameliorate existing research by focussing more on patients' subjective estimates of the rehabilitation process and satisfaction rates.

## EFFECTS OF DUAL TRANSCRANIAL DIRECT CURRENT STIMULATION OVER PRIMARY MOTOR CORTEX WITH fMRI

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**Background and Objectives.** We observed modulation of motor networks induced by dual Transcranial direct current stimulation (tDCS) in healthy subjects using functional MRI (fMRI).

**Methods.** Twelve right handed healthy participants underwent two stimulation conditions: 1) Real dual-hemisphere – with anodal tDCS over right primary motor cortex (M1) 2) Sham tDCS. Before and after tDCS, fMRI were performed while both finger tapping task were performed in a conventional block design. Participants performed a finger-sequencing task with the non-dominant hand before and after real and sham stimulation outside MR scanner.

**Results.** In the real tDCS session, there was similar activation pattern before and after stimulation during right hand task. When fMRI images between the real and sham tDCS sessions were compared, there was no significant interaction in motor network. In the real tDCS session, there was increased activation in right M1 and decreased activation in left M1 and both SMA during left hand task. When fMRI images between the real and sham tDCS sessions were compared, the real tDCS session showed significantly increased activation in the both SMA and left M1 in motor network after applying tDCS. After real tDCS, there was significant improvement in reaction time and movement accuracy in finger-sequencing task ( $p < 0.05$ ).

**Conclusions.** Simultaneously dual tDCS over bilateral M1 modulated functional motor networks during motor task. Effective modulation of functional networks by dual tDCS might be a determinant to obtain functional improvements in healthy persons by direct or distant effect.

## CHANGES IN QUALITY OF LIFE OF STROKE PATIENTS: FINDINGS FROM MONGOLIAN STROKE PATIENTS

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**Background.** Stroke is a major health burden worldwide and it is a first leading cause of mortality in Mongolia. Even though patients who survived from stroke, the quality of life is still remained the concern. Longitudinal studies are limited in low and middle-income countries.

**Aims.** To study the changes of health-related quality of life (HRQOL) during six months after the stroke onset and to identify the factors associated with HRQOL changes.

**Methods.** Patients completed a questionnaire that included socioeconomic status, WHO-BREF questionnaire for HRQOL, rehabilitation, and caregiver characteristics. Charlson Comorbidity Index, Barthel Index, and Modified

Rankin Scale were also measured. Changes of HRQOL were calculated for before discharge and after 6-month follow-up. One-sample t-tests were performed to compare the scores at discharge and after 6 months. Multiple linear regressions were performed to identify the factors associated with these changes.

**Results.** 240 patients were interviewed at baseline and 82 were successfully followed-up for complete quality of life (QOL) and other measurements after 6 months. The changes of the mean scores improved in physical and environmental domains ( $p < .05$ ), however, declined in social domain ( $p < .05$ ). There were no statistical differences in psychological domain and overall HRQOL scores. Factors associated with changes of HRQOL were high activities of daily living scores, patients with caregivers, and patients who received rehabilitations.

**Conclusions.** Functional status, rehabilitation, and assistances from caregivers were identified as predictors for better QOL in physical and environmental domains. However, there is a need for psychosocial support to the patients who suffered by stroke.

## THE SYNERGISTIC EFFECTS OF MIRROR THERAPY AND FUNCTIONAL ELECTRICAL STIMULATION ON HAND FUNCTION IN SEVERE STROKE PATIENTS

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**Background and Objectives.** Our study was performed to investigate the synergic effects of mirror therapy and functional electrical stimulation on hand function in severe stroke patients.

**Methods.** Thirty patients with severe hemiplegia after stroke were included. Ten patients had FES applied and simultaneously underwent mirror therapy. Ten patients had FES applied only, and ten patients underwent mirror therapy only. Each treatment was done five days per week, 30 minutes per day, for four weeks. FES was applied on the surface of the extensor digitorum communis, flexor carpi radialis, biceps brachii, and triceps brachii for hand and arm motion. Muscle tone, Fugl-Meyer assessment were evaluated before and after treatment.

**Results.** There were significant improvements in the Fugl-Meyer assessment score, as well as power of wrist and hand in all groups after treatment. The mirror combined with FES group showed significant improvements in the Fugl-Meyer scores of hand, wrist, arm, coordination and power of wrist flexion compared to the other groups. However, the power of hand flexion, extension, wrist extension showed no significant differences among the three groups. Muscle tone also showed no significant differences in the three groups.

**Conclusion.** This study showed that there is a synergic effect of mirror therapy and FES on hand function. Therefore, a hand rehabilitation strategy combined with FES and mirror therapy may be more helpful for improving hand function in stroke patients than FES or mirror therapy only.

## Topic 16: TRANSLATIONAL APPROACHES TO STROKE

### SPINAL CORD PROTECTION EFFECT OF CEREBROLYSIN IN ISCHEMIC-REPERFUSION ANIMAL MODEL

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**Background.** The most sensitive organ to ischemic injury is the spinal cord, and ischemic injury can produce paraplegia after descending aorta surgery. There have been many efforts to protect the spinal cord against severe ischemic and/or reperfusion injury. Cerebrolysin has neuroprotective effect on brain injury and ischemic stroke. Now, we examined the neuroprotective effect of cerebrolysin on ischemic-reperfusion spinal cord injury in rat model.

**Methods.** Eight Sprague-Dawley male rats were randomly divided into two groups. Control group ( $n=4$ ) and Ischemic group (test group,  $n=3$ ) underwent spinal cord injury by trans-abdominal clamping of the aorta proximal to the right renal artery for 30 minutes. Cerebrolysin was injected intraperitoneally in test group. Neurologic evaluation for the locomotor function was checked according to the modified Tarlov score during 2 hours of ischemic period. The spinal cord was harvested for histopathologic examination and Tunnel assay. The numbers of red neuron were counted and compared between two groups.

**Results.** The spinal cord ischemic model with direct aortic ligation in rats was highly reproducible. The numbers of red neurons were **14.0 0.31**, in control group, **18.0 5.53** in test group with statistical significance ( $p=0.02$ ). Tunnel assay analysis in test group showed reduced neuronal cell death.

**Conclusions.** Cerebrolysin has potential protective effect in spinal cord ischemic-reperfusion model in rats.

## Topic 17: UPDATE ON THERAPY OF ACUTE ISCHEMIC STROKE

### INTRAVENOUS THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE: MAIN OUTCOMES AT THE HOSPITAL OF LITHUANIAN UNIVERSITY OF HEALTH SCIENCES (HLUHS) KAUNAS CLINICS

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**The aim** of this study was to present main outcomes of acute ischemic stroke patients treated with <iv thrombolysis at the HLUHS Kaunas clinics.

**Methods.** This was a retrospective study of ischemic stroke patients treated with i/v thrombolysis during 2009 to 2012 at HLUHS Kaunas Clinics. Clinical data, outcomes were collected and analyzed using SPSS.

**Results.** During this study period i/v thrombolysis was used for treatment of 104 patients with ischemic stroke. Of them 60 (60.6%) were men and 41 (39.4%) were women. Of on patient 13 (12.5%) have had a history of diabetes mellitus, 29 (27.9%) of atrial fibrillation, 7 (6.7%) of stroke, 69 (66.3%) of PAH, 19 (19.2%) were on aspirin or anticoagulant. Initial NIHSS score was 13.35.0, and on 7<sup>th</sup> day after thrombolysis 7.76.6. For more than a half of the patient (51.9%) a decrease in NIHSS by more than 4 points was observed. Complications related with thrombolysis were documented in 44 (42.3%) patients, including 7 (6.7%) symptomatic ICH. In hospital case lethality rate was 14.4%. The mean 'door to needle' time was 88.228.5 min, onset to needle time 149.132.2 min. Initial NIHSS score more than 15 (OR 1.3, 95% CI 1.1–1.5; P=0.001), symptomatic ICH (OR 21.7, 95% CI 3.7–127.1; P<0.001), early CT findings (OR 4.5, 95% CI 1.4–15.3; P=0.01), atrial fibrillation (OR 7.2, 95% CI 2.2–23.5; P=0.01), cerebral edema (OR 35.1, 95% CI 8.3–148.3; P=0.004) associated with increased risks of death in thrombolysed patient.

**Conclusion.** Main outcomes of thrombolysis in this set of patient may be treated as relatively good in terms of SICH and case-lethality rate.

## CLINICAL FEATURES OF NEUROGENIC BLADDER IN BRAIN INJURY PATIENTS: 6 MONTHS FOLLOW UP STUDY

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**Objective.** Some brain injury patients are suffering from neurogenic bladder. One of most common symptom is urinary retention. The therapy for urinary retention is medications such as alpha blocker, cholinergics or clean intermittent catheterization or indwelling urinary catheter. But neurogenic bladder can impair quality of life of patients. The purpose of this study is to investigate prognosis of neurogenic bladder in brain injury patients.

**Methods.** Urodynamic studies were performed in 18 patients with brain injury who were transferred to Department of Rehabilitation Medicine of Asan medical center. During hospitalization, urine volume, residual urine, voiding frequency were measured. In outpatients clinic, use of medication and method of voiding were documented until 6 months after discharge.

**Results.** In results of urodynamic studies of 18 patients, 12 (66.7%) patients were areflexic, and 6 patients were hyperreflexic. In 18 patients, 1 patient who was areflexic have to use clean intermittent catheterization. In 12 areflexic patients, 6 of them (50.0%) had to use medications until 6 months after discharge. In 6 hyperreflexic patients, 2 of them (33.3%) had to use medications until 6 months after discharge. Differences of usage of medications were statistically significant between two groups ( $p < 0.05$ ).

**Conclusion.** In brain injury patients who have acute urinary retention, most of them could void. After 6 months, some of them had to take medications such as alpha blocker and cholinergics. The usage of medication were different between areflexic and hyperreflexic patients. The urodynamic study would be helpful to determine prognosis.

## SINGLE CENTRE EXPERIENCE OF OFF-LABEL INTRAVENOUS THROMBOLYSIS IN ESTONIA

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**Introduction.** Licensed contraindications for intravenous tissue-type plasminogen activator (tPA) are based on expert opinion for the original tPA trial. Observational studies have demonstrated benefit from tPA with no significant safety concerns for patients with various licensed contraindications.

**Aim.** The aim of the study was to evaluate safety and efficacy of off-label thrombolysis for patients with acute stroke.

**Methods.** All stroke patients with licensed contraindications to tPA were evaluated for safety for off-label thrombolysis during 2012. Patients received tPA if benefit/risk ratio was considered acceptable by treating physician and when patients/relatives consented. Efficacy and safety data was analysed.

**Results.** 40/69 (58%) patients received off-label tPA. Off-label indications were age (more than 80) in 26 patients, time from onset (more than 3 hours) 13 patients, NIHSS score (NIHSS) 6 patients, significant hypertension 5, loss of consciousness or seizures at onset 4 patients, oral anticoagulation 3 patients, head trauma in less than 2 months 1 patient, 1 patient received tPA twice in 4 months. In 18 patients blood pressure was lowered before tPA. More than one contraindication was present in 14 patients. 5 patients (14%) had unfavourable outcome, 4 died and 1 patient with basilar artery occlusion was discharged with NIHSS of 20. Mean NIHSS for patients with favourable outcome (31/36) on arrival and discharge was 11,3 and 7,3 respectively. In 13 patients (42%) NIHSS improved 4 or more and in 13 (36%) NIHSS was below 4 on discharge.

**Conclusions.** Off-label thrombolysis is safe and effective in selected patient groups.

## HOSPITAL ACQUIRED PNEUMONITIS IN ACUTE STROKE UNIT PATIENTS AT GREAT WESTERN HOSPITAL, SWINDON

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The hospital acquired pneumonitis (HAP) might be diagnosed in up to 25% of patients suffering with acute stroke. Dysphagia is quite common complication of stroke and has been associated with increased risk of mortality due to chest infection. The National clinical guidelines for management of stroke recommend early assessment of swallowing and risk of aspiration by trained team member to prevent HAP.

According to Dr Foster analysis included in the trust's own reporting mechanism, of the 676 spells between October 2011 and September 2012 there were 50 cases coded for HAP versus 32.4 expected. The aim of study was to identify reasons for the apparent increased spells of HAP and to identify if they were any issues related to the quality of clinical care. A clinical review of case notes was undertaken for 44 patients according to the trust's standard process.

Patient age 46–98 years (mean 81 years). Definite HAP was identified in 19/44 (43%) cases, possible HAP –

8/44 (18.25%), pneumonia prior admission (not HAP) – 9/44 (20.5%), other infections – 8/44 (18.25%). 40% of patients with definite/possible HAP had major stroke with low conscious level on admission (Glasgow Coma Scale <7). 67% of patients were assessed for dysphagia within recommended time and nasogastric tube was inserted in 52% of all cases.

**Conclusions.** Audit results demonstrated that the number of HAP does not exceed expected numbers. Major stroke and depressed conscious level increase risk of aspiration and HAP. The setting the diagnoses and coding of primary condition and complications are not sufficiently accurate which resulted in skewing real figures at the Acute Stroke Unit. All patients with acute stroke and risk of aspiration should be promptly and timely assessed by speech and language therapist.

## Topic 18: VASCULAR COGNITIVE IMPAIRMENT

### TYPE OF FOCAL NEUROLOGIC DEFICIT AND VASCULAR COGNITIVE IMPAIRMENT AT 3 MONTHS AFTER ISCHEMIC STROKE

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**Background.** The Stroke severity has been well-known factors associated with vascular cognitive impairment (VCI). However, the types of focal neurological deficits (FNDs) related with VCI have been still on the debate. We tried to examine the relationship between initial FNDs evaluated with the subscale of NIH Stroke Scale (NIHSS) and cognitive impairments in post-stroke survivors.

**Methods.** We enrolled prospectively 353 subjects who were randomly selected among the consecutive patients admitted to 13 hospitals with the ischemic stroke within 7 days after onset in Korea. The cognitive status was evaluated using Korean-Vascular Cognitive impairment Harmonization Standard Protocol at 3 months after stroke onset and the initial FNDs were measured by NIHSS scores on admission.

**Results.** Of 353 patients, the prevalence of VCI at 3 months after stroke was 68.9% (N=226). Univariate analysis found that VCI was associated with increased age, low education, hypertension, diabetes, stroke subtypes, and total scores of NIHSS on admission. Among the NIHSS subscales, the correlates of VCI were only the visual field (CI 1.03–3.28, P=0.038), facial palsy (CI 1.15–2.40, P=0.007), left arm weakness (CI 1.02–1.73, P=0.037), ataxia (CI 0.37–0.84, P=0.006), and dysarthria (CI 1.00–2.24, P=0.048) in multivariable logistic regression analyses adjusted by age, sex, education, and risk factors.

**Conclusions.** Initial neurological severity as total scores of NIHSS on admission was expectedly associated with cognitive impairments, but not all of the FNDs in NIHSS subscales such as level of consciousness, best gaze, limb weakness (except left arm weakness), sensory change, aphasia, and extinction.

## ASSESSMENT OF CEREBRAL VENOUS HEMODYNAMICS IN PATIENTS WITH VASCULAR COGNITIVE IMPAIRMENT

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**Purpose.** The aim of this investigation is the cerebral venous hemodynamics of patients with cerebrovascular disease and vascular cognitive impairment.

**Methods.** 80 inpatients (women 68%, men 32%) with cerebrovascular disease were studied by means of neuropsychological tests that assessed cognitive state (MMSE, FAB), arbitrary memory (10 words Luria) and attention (sample Schulte), visuoconstruction (drawing of clocks). For estimation of the cerebral venous hemodynamics MR-venography (apparatus Signa Infinity GE 1,5 TI) and ultrasound duplex scanning of head and neck main veins (ultrasonograph Toshiba Aplio XG) were used.

**Results.** Mild cognitive impairment (MMSE  $27.3+0.24$ ) with the decrease of arbitrary regulation of the activities (FAB  $14.8+0.2$ ) were found among the majority of patients (average age  $57.5+1.4$ ). Besides we revealed the decrease of short-term memory ( $5.06+1.3$ ) and attention span ( $47.03+1.55$ ). Using MR venography we observed hypoplasia of one of the transverse sinus in 79.7% cases (15.9% – on the right and 40.57% – on the left). At the same time we revealed the reduction of flow from the ipsilateral sinus and the major intracranial veins. The dilatation of the occipital and vertebral veins were seen in 21.2% cases. The diameter increase of the veins and high-speed parameters of venous blood flow from the contralateral side were also revealed by means of the ultrasound. These data were correlated with MR venography.

**Conclusions.** This comprehensive assessment showed that patients with cerebrovascular disease and vascular cognitive impairment have single of intracranial venous insufficiency ( $p<0.05$ ), which intern must be corrected by changing of standard therapy.

## MENTAL DISORDERS IN PATIENTS WITH A STROKE DURING THE EARLY REHABILITATION PERIOD

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We assessed mental disorders (MD) in patients with stroke (S).

**The aim.** To study MD in patients in early rehabilitation period (ERP) of ischemic stroke (S) and to define gender features.

**Material and methods.** 25 patients, age 54.8 with S in pool of the carotid artery (19), in the vertebrobasilar system (VBA) (6), with atherothrombotic type. Patients were neurologically observed, Bartel scale. MD were estimated by Memory Self-assessments test, short scale of mental status assessment, batteries of frontal tests, test of clock drawing, test of 5 words reminder.

**Results.** Paresis of a look, facial muscles, in hands and legs, pathological reflexes and sensitivity disorders presented more in females, symptoms of cerebellum attack – more in males with S in VBA. Speech disorders (dizartriya, aphasia) – more in females. So functional condition in females was 37% worse. Mild MD were in all patients. All patients did the tests

for orientation in time, place, for memory and perception identically. There were getting nothing reliable data according to fluency of speech, dynamic praxis, simple and complicated choice reactions. Categorical generalization of subjects was better in females. Low points of direct and delayed reproduction in the patients also testified about presence of MD. Females were better in the test of clock drawing, making mistakes only in disposition of hands instead of showing absolutely wrong time as males. Thus, in females were mostly motor, sensitive and speech disorders, in males – coordination ones. Mild mental disorders were in all patients, but heaviness of it was less in females.

## **CORRECTION OF COGNITIVE IMPAIRMENT IN CHRONIC CARDIOCEREBRAL SYNDROME**

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**Introduction.** One of the main manifestations of discirculatory encephalopathy (DE) is a cognitive-mnemonic disorders (CMD), which are detected in 83.9% of people over 60 years old (Levin OS., 2009). Pathogenetic factor of DE is heart failure, which leads to the restriction of hemoperfusion brain (chronic cardiocerebral syndrome). Timely and long-term administration of non-toxic cardioprotectors elderly and natural nootropics should slow the progression of CMD.

**Materials and Methods.** 20 patients (14 men and 6 women, aged  $76 \pm 0.44$  years) with postinfarction cardiosclerosis, atrial fibrillation and the effects of cortical cardioembolic ischemic stroke in form of small limitation of movement and moderate CMD have conducted a three-month treatment with carnitini and cereloba plus (Grindex) (an extract of Ginkgo biloba, garlic, green tea) for 2 doses per day (295 mg carnitini in 1 capsule and 561 mg of plant mass in 1 tablet cereloba). Before and after treatment Mini-Cog test was using.

**Results.** 20% people have done the clock drawing test with result 10 points in the experimental group before the treatment and 50% people after treatment. The scores increased from an average of 6 to 8 points. In the control group (16 similar patients with the treatment of conventional drugs), the same figures were respectively 15% and 20% and the increase in scores was from 4 to 6. If the memorizing of words in the test MiniCog was satisfactory by almost all patients before and after treatment, and then deferred their reproduction in the experimental group improved by all patients, and in control – only half, herewith only 10% of the subjects remembered all the words in the comparison group, and in the experimental group – 80%.

**Conclusion.** The study of using levocarnitine in cerebrovascular pathology showed greater efficiency in cardioembolic stroke than atherothrombotic one that explained by improved myocardial metabolism (E.I. Gusev and etc., 1999). Especially important the role of levocarnitine (experimentally proved) in reducing of the development of apoptosis – the main mechanism of mass loss of the brain in cerebrovascular disease (Konyavko M., Adachi S., 2000).

The positive and combined effect of the amino acid levocarnitine, flavonoids and polyphenols of ginkgo biloba on CMD, apparently based on the neural and receptor processes that provide cognitive function.

## **ABSTRACTS OF THE SUMMER SCHOOL OF NEUROSONOLOGY FOR BALTIC AND SCANDINAVIAN COUNTRIES (BSSSN) with patronage of the European Society of Neurosonology and Cerebral Hemodynamics (ESNCH)**

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### **ULTRASOUND ASSESSMENT OF ATHEROSCLEROTIC PLAQUES AND THE GRADING CAROTID STENOSIS**

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The degree of stenosis is the main criterion for the decision upon invasive or non-invasive treatment in patients with extracranial carotid artery stenosis. Furthermore, the progression of the degree of stenosis is an important prognostic indicator for an increased stroke risk in asymptomatic stenoses. Therefore, a precise grading of a carotid stenosis is mandatory, but not trivial because of different radiological grading definitions used in ECST (European Carotid Surgery Trial) and NASCET (North American Symptomatic Carotid Endarterectomy Trial) and different grading scales between Europe and North-America (classification in 10%-strata versus dichotomous classification with thresholds at 50% and 70%). Main criteria for grading a carotid stenosis (according to the internationally more common NASCET definition) are the presentation of the stenosis in B-mode and color flow imaging, the peak-systolic velocity within the maximum of the stenosis and distally to the stenosis, and the presence of collateral flow. Accessory criteria are end-diastolic velocities within the stenosis and in the common carotid artery, and an increased intensity of lower frequencies within the Doppler spectrum ('bruits'). Non-stenotic atherosclerotic plaques are defined as any focal thickening of the intima-medial complex encroaching into the vessel lumen. They can be categorized according to their echogenicity, texture and surface.

### **SONOGRAPHIC DIAGNOSTICS IN NEUROLOGICAL EMERGENCY AND INTENSIVE CARE MEDICINE**

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This lecture gives an up-to-date overview of neurosonographic emergency and intensive care diagnostics based on current literature. Fast and valid diagnostics in acute stroke is the main field of application of neurosonography – from assessment of acute and chronic neurovascular occlusion to raised intracranial pressure. A large variety from B-mode brain sonography to orbital sonography to multiple Doppler based techniques can be employed, each adding alternative values in the respect disease. Specific monitoring methods bear great advantages for intensive care patients, especially "as-often-as-wanted" repetitive imaging under real-time conditions. A number of new developments make neurosonography an interesting area of research. Neurosonography has a key role in neurologic emergency and intensive care medicine since many years.

## ORBITAL SONOGRAPHY (OPTICAL NERVE SHEATH MEASUREMENTS, CENTRAL RETINAL ARTERY OCCLUSIONS)

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Orbital sonography is a not-so-new ultrasound technique that has gained new attention to the practicing neurologist. Application includes measurement of papilloedema and optic nerve sheath diameter in patients with suspicion of raised intracranial pressure including pseudotumor cerebri. Assessment of flow in the retro-orbital arteries may be performed in retinal ischemia, to measure the effect of carotid revascularization and in patients with microangiopathy. Orbital is easy to learn and safe when performed within the output power limits, and its potential far from being reached.

## MONITORING THE BRAIN DURING INVASIVE MEDICAL PROCEDURES AND SURGERY

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Transcranial Doppler (TCD) is the only method which provides beat-to-beat information regarding both blood flow and embolization in the major intracranial arteries. It is therefore an excellent method for monitoring the cerebral circulation during invasive cardiovascular examinations and cardiovascular operations.

Emboli may be detected since they cause an increase in the amount of reflected ultrasound compared to that normally caused by red blood cells. Mean blood flow velocities provide information regarding changes in blood flow and this method will hopefully be improved by the introduction of frequency-weighted Doppler power measurements.

A major risk during carotid endarterectomy (CEA) and stenting (CAS) is ipsilateral ischemic brain injury. Procedure-related ipsilateral ischemic diffusion-weighted MRI (DWI) lesions have been found in 12–24% after CEA and in 21–38% of patients after CAS. It has been shown that solid and gaseous microemboli during carotid endarterectomy and stenting are increased in patients with procedure-related ipsilateral ischemic strokes or new diffusion-weighted cerebral MRI (DWI) lesions. This suggests that both solid and gaseous emboli may be harmful to the brain during these procedures.

Coronary artery bypass grafting (CABG) is the most common major surgical procedure. Improvements in anesthetic and surgical techniques as well as in post-operative management have resulted in a significant reduction in mortality. However, this has not been accompanied by a reduction in cerebral injury as surgery is now being performed on an older population who have a significantly greater burden of disease and associated comorbidity. The two main pathophysiological mechanisms responsible for cerebral injury are microembolism and intraoperative decreases in cerebral perfusion pressure. Gaseous and solid microemboli detected using transcranial Doppler are frequent during CABG especially during manual manipulation, cannulation and clamping of the ascending aorta. Atheromatous disease of the thoracic aorta may therefore be a crucial factor for the development of cerebral microemboli and postoperative lesions on DWI. Diffusion-weighted MRI (DWI) studies have shown new ischemic lesions in 26–45% of patients after surgery. Off-pump CABG surgery significantly decreases the number of emboli entering the brain but this may in part be counteracted by more unstable cerebral hemodynamics.

Left heart catheterization with coronary angiography or percutaneous coronary intervention (PCI) also poses a threat to

the brain. Cerebral morphological changes demonstrated with DWI and acute cognitive impairment has been demonstrated following left heart catheterization. TCD monitoring has shown that cerebral injury in this situation is most likely due to cerebral microembolism, especially solid microemboli. These emboli are caused by mechanical fragmentation of atherosclerotic plaques or clots from the tip of the catheter.

There is also evidence which suggest that cognitive impairment following CABG and left heart catheterization is correlated with the degree cerebral ischemic injury demonstrated by pre-catheterization MRI. These findings suggest that a cumulative burden of ischemic brain injury may cause neuropsychological deficits and increase the patients risk for vascular cognitive impairment.

## PATENT FORAMEN OVALE DETECTION USING CONTRAST TCD

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Patent foramen ovale (PFO) is the most common right-to-left shunt (RLS). Transesophageal echocardiography (TEE) is very useful for defining the anatomy of a PFO and its relationship to surrounding structures, but it is semiinvasive, and expensive. Contrast transcranial Doppler (cTCD) is a potential alternative to TEE. Both methods have similar sensitivity and specificity for detection of right-to-left shunts. cTCD has advantages compared to TEE of being noninvasive and easy to perform at the bedside. On the other hand, cTCD can only detect a right-to-left shunt, not the location of the shunt.

In order to obtain comparable results, a strict standardization of the cTCD examination technique is required. The dosage of the contrast agent and the position of the patient can affect the number of microembolic signals. The International Consensus Criteria and Spencer Logarithmic Scale are available to grade the size of shunt.

## ULTRASOUND EVALUATION OF PERIPHERAL NERVES

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High-resolution ultrasonography of peripheral nerves has increasingly been used as an adjunctive examination technique in clinical neurophysiology laboratories. Ultrasonography permits direct assessment of pathologic changes in nerve structure and/or in the adjacent tissue, and thus, provides complementary information to the electrodiagnostic findings on nerve function. This presentation summarizes the clinical applications of ultrasonography for the evaluation of entrapment neuropathies, traumatic nerve lesions, nerve sheath tumors, and several types of polyneuropathies. In nerve compression syndromes, a disturbed vascular microcirculation and an impaired axonal transport cause edema within the nerve resulting in an enlargement of the cross-sectional area of the nerve proximally to the entrapment site. Traumatic neuroma, which occur at the site of either partial or complete dissection of the nerve, can be localized precisely with ultrasonography. It further allows one to localize nerve displacement or encasement by surrounding scar or callus formation. Schwannomas and solitary neurofibromas appear as well-defined hypoechoic masses with a fusiform shape and a normal-appearing nerve that enters and exits the tumor. Diffuse nerve enlargement which involves uniformly all fascicles of an individual nerve is typically for Charcot-Marie-Tooth disease, while in CIDP, some fascicles are more affected than others and additional areas of focal enlargement are seen.