Cerebrovascular diseases 2

EP1214
Clinical factors related to severity of post stroke dementia
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Introduction: The results of clinical studies about the severity of post stroke dementia patients are limited in Korea. We investigate clinical factors related to severity of dementia and to inspect the clinical factors related to the progression of dementia severity.

Methods: The patients who visited the hospital by first time between March 2010 and September 2012, among the patients with post stroke dementia admitted to 50 geriatric hospitals spread all over Korea, formed the analysis cohorts. Retrospective review of medical records was performed.

Results: A total of 2965 patients were included. The average duration of illness is 24.61±28.18 months. By the severity of illness, mild cases were 1032 patients (34.81%), moderate 1278 (43.10%), severe 655 (22.09%), and mean score of MMSE was 14.82±6.24. The severity of dementia is higher in patients with overweight by 3.10 times (p=0.017) existence of inmate by 5.92 times (p=0.0002), past history of aphasia symptom by 0.18 times (p=0.0004). Among the clinical factors related to the progression of dementia severity, female patients showed longer duration of illness by 2.89 times compared with average, by the results of univariate analysis of 120 severe dementia patients.

Conclusions: Among the clinical factors related to severity of post stroke dementia in inpatients of 50 geriatric hospital in Korea, severity of dementia is higher in patients with overweight, existence of inmate, past history of aphasia symptom. The progression speed of dementia is suggested to be slow in female, regarding longer duration of illness in severe dementia patients.

Disclosure: Nothing to disclose

EP1215
Changes in brain thyroid hormone receptors after permanent cerebral ischemia in male rats
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Introduction: Thyroid hormones (TH) may play an important role in the pathophysiology of acute cerebral ischemia. We investigated whether serum T3/T4 and brain thyroid receptors (TRα1, TRβ1) change during the subacute phase of experimental stroke.

Methods: Male adult Wistar rats were subjected to permanent filament middle cerebral artery occlusion (group P) and compared to sham-operated controls (group S). Clinical evaluation and blood sampling was performed on days 2, 7 and 14. On day 14, tissues were collected from the infarction (E1), peri-infarction hemisphere (E2) and non-infarcted hemisphere (E3) for Western-blot (WB) and confocal microscopy (CM) analysis of TRα and TRβ.

Results: Serum T4 was reduced in P vs S group (p<0.05) on day 2, while half of the animals in group P displayed "low-T3" serum values (p<0.05) on day 14. Compared to S group, TRβ1 (WB analysis) was reduced within the infarct core area (E1) (p<0.01) while TRβ1 nuclear fraction was increased in the peri-infarcted area (E2); TRβ1 protein expression did not differ in the contralateral, non-ischemic hemisphere (E3). TRα1 nuclear fraction (WB data) only demonstrated a mild, nonsignificant (p=0.1) reduction in the infarct core. CM analysis revealed that TRα1 was strongly expressed by the activated macrophages/microglia within the infarct core and weakly in the reactive astrocytes; TRβ was strongly expressed in the nucleus of reactive astrocytes in the infarct.

Conclusions: Our data support that brain ischemia induces a low-T3 and T4 response, associated with significant medium-term total and local changes in brain TRs expression.

Disclosure: Nothing to disclose
EP1216

Setting up a neuroscience stroke and rehabilitation centre 12,000 km away with the help of telemedicine – To teach to treat – to treat to teach

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Introduction: Due to the world-wide aging population there is a need for specialist neurological knowledge. Our project in Brunei Darussalam (BD) offers to overcome distances and also a long-time benefit for patients. It comprises the set up of a specialized local stroke unit, neurological intensive care units, normal wards and neurorehabilitation. This has been achieved by continuous medical education and telemedical consultation.

Methods: Set up of the Bruneian Neuroscience Stroke and Rehabilitation Centre (BNSRC) started 7/2010. In order to overcome the distance, a telemedical network between the Department of Neurology of Krankenhaus Nordwest, Frankfurt am Main, Germany (KHNW) and the BNSRC was established. This international cooperation includes the development of a “specialist in neurology” training program, accredited in BD and an international advisory board. Daily tele-teaching as well as 24/7 tele-neurology services are offered. All neurological laboratories have been set up on site, tele-cytology, tele-electrophysiology including EEG and ultrasound. Awareness campaigns, telescience have been successfully started.

Results: So far patients with stroke, intracerebral hemorrhage, aneurysms, myasthenia gravis, multiple sclerosis, Parkinson’s disease, encephalitis and other neurological diseases as in- and out-patients. We evaluated 85% ischemic strokes and 15% hemorrhagic. Thrombolysis, hemicraniectomy, hypothermia, invasive intracranial pressure measurement have been also performed. 1st intravenous thrombolysis had a door to needle time of 24 minutes. We have achieved world class neurological intensive care standards in a brief period. Training programs and the back up with telemedicine are ideal for teaching and treating in Neurology.

Conclusion: Stroke is a major disease at the present time and prevention is more important than ever. Treatment in a stroke unit has been proven to be effective. Setting up BNSRC is not only a useful tool, far more it proved to be feasible and successful to cooperate irrespective of distance, religion and culture

Disclosure: Nothing to disclose

EP1217

Hypomorphic NOTCH3 allele in an Italian family with CADASIL features

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Introduction: The cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a hereditary disease whose diagnosis may require a multidisciplinary approach to its clinical, radiological, pathological and genetic features. Significant efforts have been made to clarify whether hypomorphic NOTCH3 mutations are neutral polymorphisms, or, causative for a distinct cerebrovascular entity. In this view, we explored, for the first time, clinical, radiological, pathological, genetic and molecular findings in a family carrying a novel NOTCH3 nonsense mutation in exon 3 (c.307C>T, p.Arg103*).

Methods: A non-consanguineous family from Naples (Italy) was examined because of recurrent cerebrovascular disorders. All the recruited subjects underwent clinical evaluation, MRI scans, skin biopsy with ultrastructural analysis, genetic studies and protein activity evaluation.

Results: Seven members of the family were included in the present study, five of them carried the novel NOTCH3 mutation in exon 3 (c.307C>T, p.Arg103*). The clinical picture of the family was suggestive of CADASIL, with an autosomal dominant inheritance and a typical symptom timeline through generations. At MRI scans, mutation carriers presented significant cerebrovascular signs. Ultrastructural investigations did not show any granular osmiophilic material (GOM) but only non-specific signs of vascular damage. Furthermore, studies were performed to evaluate protein activity.

Conclusion: Clinical, radiological, pathological, genetic and molecular findings are widely discussed to clarify the importance of this NOTCH3 nonsense mutation. The present study broadens the spectrum of CADASIL mutations and, therefore, opens new insights about the mechanism of Notch3 signaling.

Disclosure: Nothing to disclose
**EP1218**

**Ischemic stroke in patients under anticoagulation therapy: new options, old problems!**

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**Introduction:** Anticoagulation with vitamin K antagonists or novel oral anticoagulants (NOACs) reduces acute ischemic stroke (AIS) in atrial fibrillation and other high-risk thrombogenic conditions. However, AIS remains a problem in patients under anticoagulation therapy (AT).

**Methods:** Hospital based retrospective descriptive study of cardio-embolic AIS in patients under AT during one year (2013).

**Results:** Of 632 hospitalized patients, 33 (5.2%) had AIS under AT. The majority were males (18/58%). Median age was 72 [53-82]. Patients were receiving warfarin/acenocumarol (25/80.6%), dabigatran (5/16.1%), and rivaroxaban (1/3.3%). Most (25/80.6%) had atrial fibrillation, with mean and median CHA2DS2-VASc score of 4.75 and 5 respectively. The majority 17 (68%) of patients on warfarin/acenocumarol were under-anticoagulated. Regarding the NOACs, all were receiving the lowest recommended dose, with adherence problems in all except one. At hospital presentation 25 (80.6%) patients were not eligible for thrombolysis: INR ≥1.7 (13/41.9%), delayed presentation (11/35.4%), miscellaneous factors (7/22.5%). There was no absolute contra-indication for thrombolysis in 6 (19.4%) patients under treatment with warfarin (3), dabigatran (2), and rivaroxaban (1). Two patients on warfarin were treated with alteplase without complications. Medication adherence reinforcement in all, dose escalation of anticoagulants (13), addition of an antiplatelet drug (2), and switch to a NOAC (3) were treatment strategies adopted.

**Conclusions:** Undercoagulation remains a major problem in patients receiving vitamin K antagonists. AIS in patients receiving NOAC is a new problem to be discussed. As with the older anticoagulants, perhaps even more important, adherence appears as a major issue in patients receiving NOACs.

**Disclosure:** Nothing to disclose

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**EP1219**

**Blood genomic signatures in extracranial- and intracranial atherosclerosis in ischemic stroke patients**

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**Introduction:** Extracranial- and intracranial atherosclerosis (ECAS and ICAS) have different pathogeneses. Blood genomic profiling may identify their unique molecular signatures.

**Methods:** Whole gene microarray of peripheral blood was performed in 24 patients with acute ischemic stroke (ECAS, n=12; ICAS, n=12) and 12 healthy controls. Differential gene expression and gene set enrichment analysis (GSEA) were conducted. Plasma resistin levels were compared across independent samples of stroke patients with ECAS (n=39), ICAS (n=20), and small vessel disease (SVD, n=57).

**Results:** Compared to controls, microarray revealed that 144 and 24 transcripts were altered in ECAS and ICAS, respectively. All of transcripts that were differentially expressed in ICAS were also differentially expressed in ECAS, and 120 transcripts were differentially expressed only in ECAS. Gene sets related to immune response and protein metabolism were altered in both ECAS and ICAS, but the magnitude of gene alteration was higher in ECAS than in ICAS. Several genes of interest that encode resistin (RETN, fold difference [FD]:2.11), interferon regulatory factor 5 (IRF5, FD: 1.59), CD163 (CD163 transcript variant 1, FD: 1.59, CD163 transcript variant 2, FD: 1.59), and CHST13 (carbohydrate sulfotranferase 13, FD: 1.55) showed higher gene expression in ECAS than ICAS. Circulating resistin levels were elevated in independent samples of ECAS, but not in those of ICAS, compared to those of SVD.

**Conclusions:** ECAS and ICAS had different blood genomic alterations in acute ischemic stroke. Several genes, including resistin, were more associated with pathogenesis of ECAS than ICAS.

**Disclosure:** Nothing to disclose
EP1220

Comparison of duplex ultrasonography with digital subtracation angiography in the assessment of symptomatic carotid artery stenosis

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Introduction: Conventional duplex ultrasonography (dUS) is a noninvasive imaging modality widely used as a first tool for the evaluation of carotid stenosis. Our aim was to assess the accuracy of dUS in the assessment of symptomatic carotid stenosis, compared to digital subtraction angiography (DSA) now considered to be a “gold standard”.

Methods: The study included 135 patients with anterior circulation stroke or transient ischemic attacks, which were admitted during a 6-year period and submitted to both dUS and DSA. Estimates of carotid stenosis obtained by dUS were compared to data from DSA. Stenosis was classified as mild (0-49%), moderate (50-69%), significant (70-79%), severe (80-99%) and total occlusion (100%).

Results: A very significant correlation between dUS and DSA was found when carotid stenosis was classified according to the aforementioned criteria (Spearman’s coefficient: 0.9, p<0.001). DUS showed the greatest sensitivity (96.8%) in the mild stenosis group (n=190 vessels) as well as in the total occlusion group (92.6%, n=27 vessels). In the intermediate groups, dUS underestimated the stenosis; its sensitivity was 36.4% in the moderate (n=22 vessels), 33.3% in the significant (n=9 vessels) and 22.7% in the severe stenosis group (n=22 vessels).

Conclusions: DUS is very reliable for the noninvasive assessment of carotid stenosis. However its accuracy is lower in severe, significant and most importantly in moderate stenosis, potentially affecting the appropriate surgical management. Further studies are needed for the potential use of combined noninvasive imaging techniques as a substitute of DSA in the assessment of carotid stenosis.

Disclosure: Nothing to disclose

EP1221

Decision analysis for thrombolysis in acute ischemic stroke of various degrees of severity

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Introduction: Thrombolysis for acute ischemic stroke (AIS) has proven results on decrease of disability/mortality. Mild and rapidly remitting AIS were excluded from clinical trials, and are often excluded during the therapeutic decision. We quantified 5-year’s gain with thrombolysis according to initial stroke severity.

Methods: We developed a decision analysis model on TreeAge Pro2011©, analysing gains as increased years of life expectancy (YLE) and lesser years lost to disability (YLD) at 5 years. It was applied to Code Stroke patients with AIS admitted during 2 years. Stroke severity was based on National Institutes of Health Stroke Scale (NIHSS): mild as NIHSS≤4, moderate as 5-10, and severe >10. Patients with rapidly remitting symptoms were included as mild if best score≤4.

Results: From 406 Stroke Code admissions, 261 (64.3%) were AIS (55.2% male, median age 71 years). In 254 patients with NIHSS information, mild stroke was found in 91 (35.8%), moderate in 77 (30.3%), and severe in 86 (33.9%). Ninety-four patients (36.0%) underwent thrombolysis. Estimated gains with thrombolysis in 5 years for mild stroke were more 0.39 YLE and less 0.05 YLD. For moderate stroke 0.70 YLE were gained with 0.02 less YLD. Severe stroke benefited with more 1.07 YLE and less 0.03 YLD, although the latter was less 0.22 YLD when mortality was discounted.

Conclusions: Thrombolysis benefits in YLE increased with stroke severity. Our model favours thrombolysis even in mild stroke, with additional YLD reduction. Decision analysis modelling may have a role supporting intravenous thrombolysis in all stroke severity groups.

Disclosure: Nothing to disclose
EP1222
Adherence with post-stroke follow-up clinic visits and factors influencing compliance in a large urban hospital in the United States of America
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Introduction: Referral to a Stroke Prevention Clinic (SPC) is associated with a one-quarter reduction in mortality after ischemic stroke or transient ischemic attack (TIA). We investigated adherence with post-stroke follow-up visits to SPC and tried to identify factors influencing compliance with such visits in a large urban hospital.

Methods: A retrospective chart review was performed in patients discharged in 2011 and 2012 who were admitted with an acute stroke (ischemic or intra-parenchymal hemorrhage) or TIA. Only patients who were provided with a documented follow-up appointment before discharge were analyzed. The patients were divided into “missed” and “visited” groups. Descriptive statistical tools and binary logistic regression forward conditional method was used for analysis of this data.

Results: 198 (41.9%) of 472 eligible patients returned to clinic, with an average duration of 51 days post-discharge. Regression analysis showed that gender, modified Rankin score at discharge, and insurance status did not affect SPC attendance, but several other factors did (Table 1). The likelihood of SPC attendance decreased by a factor of 0.976 for every 1 year increase in patient age. Patients discharged to home were more likely to visit SPC. Patients with a TIA were less likely to return for follow up than patients with a stroke (ischemic or hemorrhagic). Non African-American (AA) patients (25.6% of the patients) were more likely to attend SPC than AA patients (Table 1).

Conclusions: We found poor compliance with SPC visits, which seems to be influenced by age, discharge disposition, race and type of vascular event.

Disclosure: Nothing to disclose

EP1223
Inhibition of plasma kallikrein protects mice from ischemic stroke by combined antithrombotic, anti-inflammatory and anti-edematous mechanisms
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Introduction: Plasma kallikrein (PK) is an important component of the kallikrein-kinin system (KKS). The KKS contributes to stroke pathophysiology by mediating inflammation, edema and thrombus formation. Activation of PK triggers the cleavage of kininogen to release kinins - highly inflammatory mediators that participate in the attraction of immune cells and increase vascular permeability. In the present study we investigated the pathophysiological role of PK in mouse models of ischemic stroke.

Methods: Focal cerebral ischemia was induced by middle cerebral artery occlusion (MCAO) in PK-deficient (Pk-/-) and control (Pk+/+) mice as well as in mice receiving PK-specific blocking antibodies. Infarct volumes and neurological scores were assessed between day 1 and day 7, and findings were confirmed by magnet resonance imaging. Evans Blue tracer was applied to quantify the extent of blood-brain barrier (BBB) damage. Local inflammatory responses and thrombus formation were assessed post stroke by qRT-PCR, Western blot and histological approaches.

Results: Inhibition of PK by both targeted deletion (Pk-/-) and pharmacological blockade led to significantly smaller brain infarctions, improved neurological outcome and improved long-term survival. Reduced BBB damage, attenuation of the local inflammatory response and reduced intracerebral thrombus formation could be identified as underlying mechanisms.

Conclusions: The present together with our previous findings further corroborate the major pathophysiological relevance of the KKS during ischemic neurodegeneration. Selective inhibition of distinct members of the KKS might become a promising strategy to combat ischemic brain damage in the future.

Disclosure: Nothing to disclose
EP1224

Prognostic evaluation of cerebral vein and dural sinus thrombosis

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Introduction: Although the overall outcome of cerebral vein and dural sinus thrombosis (CVT) is good, about 25% of patients develop complications, and mortality rate is 3-15%. Identification of prognostic factors is crucial for selecting the proper treatment for each case (more aggressive versus conservative). A risk score comprising six clinical variables with different hazard ratios was proposed to predict CVT outcome (Ferro et al, Cerebrovasc Dis 2009).

Aim: To evaluate the ability of this prognostic score in predicting the prognosis of our population of CVT patients.

Methods: We conducted a retrospective analysis of consecutive adult patients diagnosed with CVT from 2006 to 2012. The prognostic score and the six variables were analysed and compared with the outcome at six months, using a simplified regression model (R>0.5 suggesting a stronger relationship).

Results: 60 patients were studied, 83.3% females; mean age: 39.8 years-old. The value of R between the result of the weighted risk scale and outcome was 0.345. When the 6 variables were combined but not weighted, and compared with outcome, the value of R was 0.529. For the combination of the variables “malignancy” and “intracranial haemorrhage on admission”, R was 0.460. There was no significant correlation between other variables independently or combined.

Conclusion: In our population, the proposed risk score did not show a strong correlation with prognosis. However, the combination of intracranial haemorrhage and malignancy had a stronger correlation with outcome, being probably the most important predictive factors in clinical practice.

Disclosure: Nothing to disclose

EP1225

The aetiology of spontaneous intracerebral haemorrhage - Insights from a neuropathological series

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Introduction: The therapeutic and prognosis of spontaneous intracerebral haemorrhage (ICH) depend on the underlying aetiology; however, it remains undetermined in many patients. We aim to assess the impact of the histopathology study in the etiologic diagnosis of encephalic ICH and describe the findings from a 10-year neuropathological series.

Methods: The setting is a tertiary hospital in Northern Portugal; all the patients with ICH admitted in the last 10 years were identified and histologic samples of surgically drained ICH retrieved. Blinded from histologic results, a presumable clinical aetiology was attributed to these patients, using clinical and imaging records. The histopathology samples were reviewed and immunohistochemistry to beta-amyloid was performed in undetermined cases.

Results: From 2003 to 2013, 52 patients with ICH underwent surgical drainage and had histopathology samples. The average age was 49.2 years (SD=19.5), 56% were men. Clinical and imaging data defined a presumable aetiology in 27.1%, including 7.9% under anticoagulation and 19.2% with suspected structural pathology. The histological data allowed definitive diagnosis in 65.4%. The arteriovenous malformations (28.6%) and cavernous hemangiomas (19.3%) represented the most common structural abnormalities. In 7 patients (13.5%) with average age of 67.1 years (SD=8.5) the vessels showed changes related to amyloid angiopathy.

Conclusions: The histopathology study established a definite aetiology in an additional 38.3% of patients than using the clinical and imaging data. Although the patients from this series are younger and with major bleedings, we identified a significant number of amyloid angiopathy, in agreement with what has been described in the few published series.

Disclosure: Nothing to disclose
EP1226
Diabetes and stroke: liraglutide is associated with a decreased risk of stroke in type 2 diabetes mellitus. A nested case-control study
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Introduction: Diabetes mellitus (DM) is associated with an increased risk of stroke. We investigated antidiabetic drugs and their effect on stroke incidence in DM patients.

Methods: We conducted a nested case-control study. Cases were DM patients who subsequently suffered from stroke; controls were DM patients with no subsequent stroke. Using the Danish National Hospital Discharge Register, we included DM patients with information on date of DM diagnosis, date of stroke, and comorbidities. From the Central Region of Jutland, Denmark, medication use and biochemical parameters were collected.

Results: 15,773 DM patients were included. Biguanides (OR: 0.592, 95%CI: 0.422-0.832), DPP-4 inhibitors (OR: 0.553, 95%CI: 0.339-0.903) and liraglutide (OR: 0.351, 95%CI: 0.208-0.592) decreased the risk of stroke, whereas insulin (OR: 0.923, 95%CI: 0.735-1.158), β-cell stimulating drugs (OR: 1.260, 95%CI: 0.879-1.808), pioglitazone (OR: 0.682, 95%CI: 0.166-2.805) and exenatide (OR: 0.848, 95%CI:0.390-1.843) had no significant effect. A dose- and duration-response trend was shown for liraglutide. When limited to type 2 DM patients (n = 11,202), the associations remained.

When results were adjusted for biochemical parameters (LDL, HDL, total cholesterol, HbA1c and creatinine), none of the antidiabetic drugs reduced the risk of stroke.

Conclusions: An association between liraglutide and a reduced risk of stroke in type 2 DM patients was present. Of the antidiabetic drugs, liraglutide had the most pronounced effect, which may indicate that liraglutide could be recommendable as part of first-line treatment in stroke prophylaxis in diabetic subjects.

Disclosure: none

EP1227
Persistent barriers to help seeking for stroke and TIA after a national media campaign (Face, Arm, Speech, Time to Call 999 (FAST))
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Introduction: National media campaigns (e.g. Face Arm Speech Time (FAST)) have encouraged the public to dial emergency services (“999”) immediately for stroke symptoms. However many patients still reach hospital too late for thrombolysis and optimal care. Reasons for delays in calling 999 after stroke/TIA are poorly understood.

Methods: We interviewed consecutive patients admitted to the stroke service in Sheffield, UK with stroke/TIA in August 2013 where informed consent was available. Carers were interviewed if they had called for help on the patients’ behalf. We recorded timings of symptoms and medical consultations, perceptions of symptoms and barriers to calling 999.

Results: 61 patients were included; 9 had major stroke (NIHSS >5), 38 minor stroke, and 14 TIA. 13 carers were also interviewed. 50 (82%) patients/carers were aware of the FAST campaign pre-admission, and 54 (89%) patients had ≥1 “FAST” symptom. The median (IQR) time between symptoms onset to first call for medical help was 57.5 mins (10-1021) but 30 (49%) called the family doctor first. Only 21 (34%) patients reached hospital within 4 hours of symptoms onset. There were several important barriers to calling 999 e.g. 35 (57%) callers had not thought the symptoms were serious, 21 (34%) did not want to trouble hospital services and 16 (26%) were embarrassed or afraid to call 999.

Conclusions: Despite widespread awareness of the FAST campaign, most patients/carers delay or avoid calling 999 after stroke/TIA. Future campaigns need to emphasize the seriousness of stroke/TIA and the need to call emergency services promptly.

Disclosure: Nothing to disclose
EP1228

Expansive arterial remodeling: risk factors for ischemic complication after carotid artery stenting?

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Introduction: Expansive artery remodeling and vulnerable plaque are considered risk factors of cerebral ischemic events. However it is not well known whether these can be risk factors of medical complication for carotid artery stenting (CAS). The purpose of this study is to investigate association between carotid artery remodeling ratio (RR) and ischemic complication in patients treated with CAS for their high grade carotid artery stenosis.

Methods: Forty-three patients with >50% stenosis (15 symptomatic and 28 asymptomatic) treated with CAS were included to the study.

Results: New ischemic signals on DWI-MRI were detected in 34.9% (15/43). Vulnerable plaques were detected 15/43 patients on T1-weighted MRI and associated significantly high new ischemic signals of 8/15 compared with patients with non vulnerable plaque (7/28). (p=0.063) Remodeling ratio (RR) was calculated by dividing the outer vessel circumference at the site of greatest stenosis by a normal reference-segment vessel circumference by using multidetector row CT. There is no statistical significant between RR and new ischemic signals (p=0.541) and also present of vulnerable plaque (p=0.558).

Conclusions: Remodeling Ratio has the potential for more accurate selection for CAS treatment.

Disclosure: Nothing to disclose