Cerebral Aneurysms

AB-14686-00

The constant release of nitric oxide (NO) is essential to maintain basal cerebrovascular tone. Oxyhaemoglobin, liberated by lysis of red blood cells after subarachnoid haemorrhage binds NO and prevents its entry into vascular smooth muscle cells. While endothelium-dependent vasoconstriction is preserved, decreased levels of NO inhibit endothelium-dependent relaxation and may cause vasospasm. S-nitrosothiols are potent vasodilators and precursors of NO. The authors’ aim was to determine whether S-nitroso-N-acetylpenicillamine (SNAP), a stable S-nitrosothiol compound, could reverse vasospasm in an experimental vasospas model in rabbit. Experimental subarachnoid haemorrhage (SAH) was induced in 37 New Zealand white rabbits. The animals were divided into four groups. Control (no SAH), SAH only, SAH plus saline and SAH plus SNAP. SNAP (15 μg/kg/min) or 0.09% saline (equal volume) was infused 46 hours after induction of SAH. All animals were killed by perfusion fixation 48 hours after SAH occurred. Basilar arteries were removed, sectioned and their cross sectional areas were evaluated in a blind manner, by light microscopy and by using computer assisted morphometry. Experimental SAH elicited vasospasm in all animals of SAH only and SAH plus saline group. In animals treated with SNAP, arterial narrowing was markedly attenuated without producing systemic hypotension. This widening achieved statistical significance when compared to the arteries of the SAH only and SAH plus saline group (p<0.01). This study indicates that the NO donor SNAP is a potentially useful drug to reverse cerebral vasospasm due to SAH.

AB-14687-00
Risk of Subarachnoid Haemorrhage in First Degree Relatives of Patients With Subarachnoid Haemorrhage: Follow Up Study Based on National Registries in Denmark—Gaist D (Epidemiology, Institute of Public Health, Univ of Southern Denmark, Odense Univ, DK 5000 Odense C, Denmark), Vaeth M, Tsiropoulou I, Christensen K, Corder E, Olsen J, Sørensen HT—BMJ 2000;320:141–145.

Objective To estimate the risk of occurrence of subarachnoid haemorrhage in first degree relatives (parents, siblings, children) of patients with subarachnoid haemorrhage.

Design Population based cohort study using data from the Danish National Discharge Registry and the Central Person Registry.

Subjects Incident cases of subarachnoid haemorrhage admitted to hospital from 1977 to 1995 (9367 patients) and their first degree relatives (14 781).

Main outcome measures The incidence rate of subarachnoid haemorrhage was determined for the relatives and compared with that of the entire population, standardised for age, sex, and calendar period. This process was repeated for patients discharged from neurosurgery units, as diagnoses from these wards had high validity (93%).

Results 18 patients had a total of 19 first degree relatives with subarachnoid haemorrhage during the study period, corresponding to a standardised incidence ratio of 2.9 (95% confidence interval 1.9 to 4.6).

Patients discharged from neurosurgery wards had a higher standardized incidence ratio (4.5, 2.7 to 7.3).

Conclusions First degree relatives of patients with subarachnoid haemorrhage have a threefold to fivefold increased risk of subarachnoid haemorrhage compared with the general population.

AB-14688-00

Objective: To assess the safety and feasibility of a clinical trial on the effectiveness of acetylsalicylic acid (ASA) in subarachnoid hemorrhage (SAH). Background: Several studies have indicated that increased platelet activity might be involved in the pathogenesis of delayed cerebral ischemia (DCI) after SAH. Method: Fifty patients who had early surgery (≤4 days) for a ruptured aneurysm were enrolled in this randomized, double-blind, placebo-controlled trial. Trial medication, consisting of suppositories with 100 mg ASA versus placebo, was started immediately after surgical clipping of the aneurysm and continued for 21 days. End points were functional outcome and quality of life at 4 months, clinical deterioration after operation, development of DCI, hypodense lesion on postoperative CT, and hemorrhagic complications. Results: One-third of all patients with aneurysmal SAH were eligible for the trial. Fifteen of 26 patients receiving placebo deteriorated clinically versus 10 of 24 patients receiving ASA; 4 patients in each group deteriorated from DCI. Postoperative hypodensities on CT were observed in 27 patients, distributed equally in both groups. Functional outcome and quality-of-life scores were slightly in favor of patients who had received ASA, but not to a significant degree (p=0.22). Two patients in the ASA group had an asymptomatic hemorrhagic complication, and one patient in the placebo group had a fatal and another a symptomatic hemorrhagic complication. Conclusion: This pilot study shows that a clinical trial of acetylsalicylic acid (ASA) in subarachnoid hemorrhage (SAH) is feasible and probably safe. The effectiveness of ASA on functional outcome and delayed cerebral ischemia has to be studied in a larger trial.

AB-14689-00

OBJECTIVE: Cerebral vasospasm is a potentially fatal consequence of aneurysmal subarachnoid hemorrhage and influences the prognosis of the patient. The purpose of this study was to evaluate the status of thin (actin) and thick (myosin heavy chain) filament regulation of smooth muscle contraction in the double-subarachnoid hemorrhage canine model of cerebrovasospasm and to determine the effects of a kinase inhibitor reported to be effective in vasospasm, HA1077, on thin and thick filament regulation.

METHODS: Cerebral vasospasm was assessed by vertebral angiography. Myosin regulatory light chain phosphorylation was measured using glycerol-urea gels, whereas protein levels of the thin filament-associated protein calponin were measured by Western blot.

RESULTS: The basilar arteries of dogs in which subarachnoid hemorrhage was induced narrowed to 36%±2.0% of their size on the first day (n=12). The phosphorylation of the regulatory light chain tended to increase, but the change did not reach statistical significance (35%±5.9% [n=12] versus 25%±4.8% [n=10] in control arteries). In contrast to this increase, significant degradation of calponin was ob-
served in the samples from vasospastic dogs (85.4%±5.45% [n=5] versus 15.2%±6.21% [n=5]; P<0.01). Prophylactic treatment with intravenous injections of HA1077 at 0.67 mg/kg b.i.d. significantly inhibited vasospasm (diameters, 65%±10.2% of Day 1 diameters [n=5]; P<0.05), and calponin degradation (57.8%±13.9% [n=4] was substantially reduced.

CONCLUSION: These data suggest that degradation of the thin filament-associated protein calponin plays a role in cerebral vasospasm and that the antivasospastic action of HA1077 is, at least in part, due to prevention of calponin degradation.

Clinical

AB-14690-00


Background Protruding atheromas in the aortic arch are an independent risk factor for ischemic stroke in the elderly. However, the role of atheroma morphologic characteristics (ulceration and mobility) has been less well characterized. Moreover, data have been obtained in predominantly white populations, and little is known about the association between atheromas and stroke in minorities.

Methods and Results We performed transesophageal echocardiography in 152 elderly patients with stroke (58 white, 45 black, 49 Hispanic) and in 152 age- and race/ethnicity-matched control patients. Atheromas were classified as small (<4 mm in thickness), large noncomplex (>4 mm, no ulceration or mobility), and complex (ulcerated or mobile). Logistic regression analysis was performed to assess the risk of stroke associated with different definitions of atheroma in the over-all group and in the race-ethnic strata after adjusting for the presence of other stroke risk factors. Complex atheromas were strongly associated with stroke in the overall group (22.4% in cases, 2.6% in control patients; adjusted odds ratio [OR] 17.1, 95% confidence intervals [CI] 5.1 to 57.3), whereas large noncomplex atheromas conferred a mildly increased stroke risk (22.4% vs 16.5%; adjusted OR 2.4, 95% CI 1.1 to 5.1). Complex atheromas also were strongly associated with stroke in whites (adjusted OR 24.3, 95% CI 3.9 to 150.6) and Hispanics (adjusted OR 13.9, 95% CI 1.4 to 136). In blacks, complex atheromas were significantly more frequent in cases (15.6% vs 9%; P=0.006), but their absence in control patients precluded the calculation of the OR. Complex atheromas were twice as frequent in white patients with stroke (32.5%) than in black or Hispanic patients (15.6% and 16.3%, respectively; P=0.05).

Conclusions Aortic atheroma complexity rather than size is strongly associated with ischemic stroke in the elderly. Complex atheromas are significantly associated with stroke in all 3 race-ethnic subgroups.

AB-14691-00


Background: Several studies have attempted to identify criteria for predicting functional prognosis after stroke, but often with contradictory results. The purpose of this study was to predict the functional outcome at discharge of first-time stroke patients included consecutively in the Lausanne Stroke Registry. Methods: We studied 3,628 sequential patients with first-ever stroke who were admitted consecutively to the Centre Hospitalier Universitaire Vaudois. Functional status was evaluated using the Rankin disability scale at discharge. We studied the prognostic value of historical, clinical and instrumental variables related to functional outcome at discharge. The factors studied were age, sex, risk factors, ECG results, occurrence of transient ischemic attacks (TIAs), extension of cerebral infarction, presumed cause of stroke, clinical findings and demographic characteristics. Univariate analysis was performed on each variable by comparing the number of functionally independent with that of dependent patients at the moment of discharge. The significant variables of the univariate analysis were subjected to multivariate analysis with a backward logistic regression procedure to find those with an independent effect on the outcome. Results: A total of 3,156 patients, excluding 117 patients with ischemic stroke who died during hospitalization and 355 with brain hemorrhage, were included; 2,867 patients belonged to the nil, mild or moderate disability groups (modified Rankin score 1–4; functionally at least partially independent patients), while 291 patients belonged to the severe disability group (modified Rankin score 5; functionally dependent patients). The mean duration of stay in hospital of the severe disability group was 31.2 days (SD=16.2). Multivariate analysis showed that impaired consciousness on admission, limb weakness, progressive worsening, infarct in the superficial and deep territory of the middle cerebral artery, ischemic heart disease and cardiac arrhythmia were predictors of severe disability at discharge. Age was not an independent predictor of poor outcome. Hypercholesterolemia was significantly related to a better outcome.

Conclusions: Some prognostic indicators associated with functional outcome at discharge are available during the first few hours after onset of stroke. This is important for the management of the individual stroke patient and for organizing suitable rehabilitation planning.

AB-14692-00


Objective: To examine whether the demonstrated efficacy of tissue-type plasminogen activator (t-PA) for acute ischemic stroke can be effective in a community setting. Methods: Sixty-eight consecutive patients with acute ischemic stroke treated with IV t-PA within 3 hours of symptom onset by attending general neurologists in a busy teaching hospital. Outcome measures at 3 months were the National Institute of Health Stroke Scale (NIHSS), functional outcome (independence [modified Rankin score 0–2], dependence [modified Rankin score 3–5], and death), and symptomatic hemorrhage. Appropriately treated patients were defined by adherence to the National Institute of Neurological Disorders and Stroke (NINDS) guidelines. Effectiveness is expressed as the absolute risk reduction in which the baseline risk is assumed to be similar to that of the NINDS control group. Results: Of 68 consecutively treated patients (with a mean baseline NIHSS score of 15±6), 26 (38%) made a full recovery and 39 (57%) made an independent recovery. The 11 patients who violated protocol had a lower probability of independence (p<0.02) and full neurologic recovery (p<0.02) and a higher probability of symptomatic hemorrhage (p<0.05) and death (p<0.01) compared with those of 57 patients treated according to NINDS guidelines. Conclusions: The use of t-PA for stroke in this community is effective with a number needed to treat of six. The risk of symptomatic hemorrhage is similar to that noted in randomized trials. Treating patients who violate protocol results in excess risk with no observable benefit.

AB-14693-00


Objective: To determine the prognosis of asymptomatic carotid artery occlusion. Background: As opposed to symptomatic carotid occlusion, little information is available on the prognosis of asymptomatic carotid occlusion. Method: Thirty never-symptomatic and 81 symptomatic
patients with carotid occlusion underwent baseline assessment of 15 risk factors together with PET measurements of oxygen extraction fraction (OEF). Every 6-month telephone contact recorded interval medical treatment and subsequent stroke occurrence during an average follow-up of 32 months. Patients, treating physicians, and an end point adjudicator were blinded to PET results. 

**Results:** Ischemic stroke occurred in 1 of 30 of never-symptomatic patients (3.3%) and 15 of 81 of symptomatic patients (18.5%; \( p = 0.03 \)). No strokes in the carotid territory distal to the occluded vessel occurred in the never-symptomatic patients. Multivariate analysis of baseline risk factors for all 111 patients revealed that age, plasma fibrinogen level, and PET findings of high OEF distal to the occluded carotid artery were the only independent predictors of subsequent stroke (\( p < 0.05 \)). Previous ipsilateral hemispheric or retinal symptoms was not a significant predictive variable. The lower risk of stroke in never-symptomatic patients was associated with a lower incidence of high OEF (4 of 30) as opposed to symptomatic patients (39 of 81; \( p = 0.002 \), but there was no significant difference in age or fibrinogen level. 

**Conclusions:** Never-symptomatic carotid occlusion carries a very low risk of subsequent ischemic stroke. This benign prognosis is associated with a low incidence of cerebral hemodynamic compromise in these patients. These data support further the importance of hemodynamic factors in the pathogenesis of ischemic stroke in patients with carotid occlusion.

**AB-14694-00**

**Early Lacunar Strokes Complicating Polyarteritis Nodosa: Thrombotic Microangiopathy—Reichhart MD, Bogousslavsky J (Service de Neurologie, CHUV 1011 Lausanne, Switzerland), Janzer RC—Neurology. 2000;54:883–889. Copyright © 2000 by the American Academy of Neurology.**

**Objective:** To determine the patterns and mechanisms of polyarteritis nodosa (PAN)-associated strokes (PANAS). 

**Background:** Strokes are reputed to be rare complications of PAN and to occur at a late stage (2 to 3 years). The cause of stroke is unknown but may be related either to atherosclerosis-like occlusive vasculopathy, caused possibly by hypertension or corticosteroid (CS) use, or to vasculitic arterial occlusion. 

**Methods:** Clinical and radiologic patterns, latencies, and current therapy at onset in 15 PANAS patients (4 of the authors’ and 11 published cases) were analyzed. 

**Results:** A lacunar stroke syndrome (11/15 cases, 73%) was the most frequent stroke pattern in PANAS (multiple, small, deep infarcts in 6, [55%], pontine lacunae in 3 [27%], and leukoaraiosis in 2 [18%]), followed by pure lobar hemiatrophy and bilateral, possibly cardio-embolic, large ischemic infarcts (2 cases each). A stroke latency shorter than that previously established (within 8 months in 73% of cases; mean latency, 6.5 months) and a close relationship between the use of CS and stroke in PAN also were found. Of the 77% of first-time or recurrent lacunar strokes that developed despite CS therapy, 80% appeared within 6 months and 50% within 3 weeks of CS initiation. 

**Conclusion:** Early lacunar stroke syndrome, related to deep small- or pontine-penetrating artery thrombotic microangiopathy rather than vasculitis, was the most frequent PANAS pattern. This vasculopathy may be aggravated by corticosteroid (CS) therapy enhancement of either platelet thromboxane \( A_2 \) production or arterial wall fibrosis. Thus, antiplatelet drugs in association with CS may be advisable for preventing stroke occurrence or recurrence in PAN.

**Epidemiology**

**AB-14695-00**

**Insulin Resistance Syndrome Predicts the Risk of Coronary Heart Disease and Stroke in Healthy Middle-Aged Men: The 22-Year Follow-up Results of the Helsinki Policemen Study—Pyörälä M, Miettinen H, Halonen P, Laakso M, Pyörälä K (Dept of Medicine, Univ of Kuopio, Puijonlaaksontie 2, PO Box 1627, 70211 Kuopio, Finland)—Atheroscler Thromb Vasc Biol. 2000;20:538–544. Copyright © 2000 American Heart Association, Inc.**

The interpretation of conventional multivariate analyses concerning the relation of insulin to the risk of atherosclerotic disease is complex because of correlations of insulin with other risk factors. Therefore, we applied factor analysis to study the clustering of risk factors in the baseline data of the Helsinki Policemen Study (970 healthy men aged 34 to 64 years) and investigated whether these clusterings predict coronary heart disease (CHD) and stroke risk. Areas under the glucose and insulin response curves (AUC glucose and AUC insulin) were used to reflect glucose and insulin levels during oral glucose tolerance tests. During the 22-year follow-up, 164 men had a CHD event, and 70 men had a stroke. Factor analysis of 10 risk factor variables produced 3 underlying factors: insulin resistance factor (comprising body mass index, subcapsular skinfold, AUC insulin, AUC glucose, maximal \( O_2 \) uptake, mean blood pressure, and triglycerides), lipid factor (cholesterol and triglycerides), and lifestyle factor (physical activity and smoking). In multivariate Cox models, the age-adjusted hazard ratio for insulin resistance factor during the 22-year follow-up was 1.28 (95% CI 1.10 to 1.50) with regard to CHD risk and 1.64 (95% CI 1.29 to 2.08) with regard to stroke risk. Lipid factor predicted the risk of CHD but not that of stroke, and lifestyle factor predicted a reduced CHD risk. Factor analysis including only 6 risk factor variables proposed to be central components of insulin resistance syndrome (body mass index, subcapsular skinfold, AUC insulin, AUC glucose, mean blood pressure, and triglycerides) produced only a single insulin resistance factor that predicted the risk of CHD and stroke independently of other risk factors.

**AB-14696-00**


**Purpose:** The purpose of this study was to determine the etiologic factors in the progression of carotid stenosis. 

**Methods:** We performed prospective serial duplex scan surveillance of 1470 carotid arteries in 905 asymptomatic patients during a 10-year period, with an average follow-up interval of 29 months and an average of 3.0 scans per carotid artery. Vascular laboratory and hospital records were used to collect risk factor information. The data were analyzed with proportional hazards modeling. 

**Results:** We examined several demographic, clinical, and laboratory risk factors that were chosen because of their potential relevance to atherosclerotic disease. These factors were analyzed with univariate proportional hazards modeling, in which time to progression of stenosis was the outcome variable. The six significant predictors (\( P < 0.05 \)) were age, sex, systolic pressure, pulse pressure (systolic pressure – diastolic pressure), total cholesterol, and high-density lipoprotein (HDL). All except HDL, were positive predictors of time to disease progression. With multivariate modeling, only pulse pressure and HDL remained as significant independent predictors of stenosis progression. The risk ratio for a 10-mm Hg rise in pulse pressure was 1.12, and the risk ratio for a 10-mg/dL decrease in HDL was 1.20. 

**Conclusion:** In this large cohort of patients who were followed prospectively for carotid stenosis, pulse pressure and HDL were found to be the key risk factors for carotid stenosis progression. The fact that pulse pressure superseded systolic pressure in multivariate modeling may shed light on the biology of carotid plaque progression. Further, our identification of these modifiable risk factors may help in the design of therapeutic trials for the prevention of progression of carotid atherosclerosis.

**Experimental Pathology**

**AB-14697-00**

**ACE-Inhibition Promotes Apoptosis After Balloon Injury of Rat Carotid Arteries—Holm AM (Dept of Medicine B2142, The Rigshos-
Objective: Angiotensin II stimulates vascular smooth muscle cells (VSMC) growth, and is considered to be an important mediator of intimal thickening after vascular injury. Recent evidence has indicated that VSMC apoptosis plays a major role in the response to balloon injury, and we therefore examined the effect of angiotensin converting enzyme (ACE)-inhibition on VSMC apoptosis and vascular lesion formation in the rat model of balloon injury. Methods: Male Sprague-Dawley rats were subjected to carotid artery balloon injury and randomized to a standard diet or a diet supplemented with 1 mg/ml captopril in the drinking water. Animals were sacrificed 2 and 14 days after injury for assessment of apoptosis and proliferation by in situ terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL) and proliferating cell nuclear antigen (PCNA) immunohistochecmetry, respectively. At 14 days post injury, vessel cross-sections were subjected to microscopic morphometry and total cell numbers were determined. Results: At 2 days after balloon injury, captopril-treated animals displayed a significant increase in the percentage of TUNEL-positive VSMCs in the medial area (12±4% vs. 1±1%; P<0.05) as compared to controls. This increase in early apoptosis was associated with decreased intimal cellularity 14 days post injury (238±47 cells/cross-section vs. 449±75 cells/cross-section; P<0.05), and a reduction of neointimal formation (0.13±0.02 mm² vs. 0.23±0.04 mm²; P<0.05). The fraction of PCNA-positive VSMCs per cross-section 2 or 14 days after injury was not significantly altered by captopril. Conclusion: Captopril inhibits neointimal formation in the rat model of arterial injury by mechanisms involving induction of VSMC apoptosis. © 2000 Elsevier Science B.V. All rights reserved.


A reduction in the apparent diffusion coefficient (ADC) of water measured by magnetic resonance imaging (MRI) has been shown to occur early after cerebrovascular occlusion. This change may be a useful indicator of brain tissue adversely affected by inadequate blood supply. The objective of this study was to test the hypothesis that loss of membrane on homeostasis and depolarization can occur simultaneously with the drop in ADC. Also investigated was whether elevation of extracellular glutamate ([GLU]) would occur before ADC changes. High-speed MRI of the trace of the diffusion tensor (15-second time resolution) was combined with simultaneous recording of the extracellular direct current (DC) potential and on-line [GLU]e from the striatum (15-second resolution) was combined with simultaneous recording of the extracellular direct current (DC) potential and on-line [GLU]e from the striatum and that high [GLU]e has no involvement in the early rapid ADC decrease.


Early overuse of a lesioned forelimb, induced by immediate immobilization of the intact forelimb after a cortical lesion, has been reported to increase tissue damage and delay functional recovery. To investigate if early training without immobilization of the intact forelimb could increase tissue loss and reduce recovery, the middle cerebral artery was ligated distal to the striatal branches in 25 male spontaneously hypertensive rats. Control rats were housed in standard cages, training rats were transferred to larger cages allowing various activities and received additional special training 1 hour a day starting either 24 hours or 7 days after the ligation. The rats were tested on a rotating pole, in a leg placement test, and in a water maze and they were killed 6 weeks after the ligation. Delayed training resulted in the best overall performance; however, both training groups performed better than standard rats on the rotating pole. The cortical infarct volume was larger in the early training group than in the other two groups (P<0.005), possibly related to increased glutamate release and peri-infarct cortical hyperexcitability.

Imaging


Background: Acetazolamide (AA) is used to determine the cerebral vasoreactivity (CVR). To investigate whether the usually applied standard dose of 1 g intravenously will guarantee stable test conditions, the dose-response relationship of AA on cerebral blood flow (CBF) and cerebral blood flow velocity (CBFV) in normal subjects was determined. Methods: In 59 healthy volunteers, rCBF was measured with a [13]Xenon inhalation device, and CBFV of the middle cerebral artery (MCA) by transcranial Doppler sonography. The first CBF measurement was taken at rest, the second 15 min after application of AA at a dosage of 5, 10, 13, 15 and 18 mg/kg of body weight, respectively. The CBFV (n=52) of the middle cerebral artery on the side of the better temporal window was taken 25 min after application of AA 13 mg/kg. In order to determine the side effects of AA, statements of an additional 172 patients were included. Results: A significant dosage dependence of AA on the CBFV (fast flow and initial slope index) exists between 5 and 18 mg/kg. After AA 13 mg/kg, the fast flow increases from 70.8±10.8 to 110.1±13.5 ml/100 g/min, the initial slope index from 46.5±5.4 to 62.8±5.8, and the CBFV from 51.5±8.5 to 85.4±14.2 cm/s. The CVR of CBF and CBFV ascertained that way shows an age dependence equivalent to the situation at rest. Severity and frequency of side effects are dosage-dependent, significantly in part, but reversible without exception. Conclusion: For the determination of CVR of CBF with AA, a dosage related to body weight is required. The usually applied standard dose of 1 g intravenously is not sufficient for standardized test conditions. For evaluation of the results obtained, the apparent age dependence of CVR must be taken into account. Because of the severity of side effects occurring at a higher dose, an AA dosage of 13 mg/kg intravenously is recommended.


Simultaneous registration of cerebral tissue oxygenation parameters obtained by near infrared spectroscopy (NIRS), intracranial blood flow velocity (CBFV) measured by transcranial Doppler sonography (TCD)
and basic cardiovascular parameters was carried out during a passive 80° head-up tilt table test in 15 patients with a history of orthostatic syncope and 20 control subjects. In normals, the cardiovascular parameters showed a specific course after changing to a vertical position: the heart rate increased, the mean arterial blood pressure remained unchanged, and the CBV decreased. The NIRS measurements showed an increase in deoxyhemoglobin (HHb) and a decline in oxyhemoglobin (O$_2$Hb) and the regional oxygen saturation (RSAT). Patients had a significantly more prominent decline in arterial blood pressure (p < 0.001), CBFV (p < 0.001) and RSAT (p = 0.04). Five patients experienced symptoms of (pre)syncope during the experiment, which were associated with a further sudden and marked (>10%) drop of O$_2$Hb. The results indicate that the combination of TCD and NIRS increases the understanding of hemodynamic and metabolic changes during orthostatic stress, which may lead to individually suited therapeutic procedures.

AB-14702-00

Objective: Ischemic lesions seen on diffusion-weighted imaging (DW) are reversible if reperfusion is performed within minutes after the onset of ischemia. This study was designed to determine whether acute reversibility of DWI abnormalities is transient following brief temporary focal brain ischemia and to characterize the temporal evolution of in vivo ischemic lesions. Methods: Eight rats were subjected to 30 minutes of temporary middle cerebral artery occlusion and underwent diffusion-, perfusion-, and T2-weighted MRI during occlusion; immediately after reperfusion; 30, 60, and 90 minutes after reperfusion; and 12, 24, 48, and 72 hours after reperfusion. Average apparent diffusion coefficient (ADC$_{av}$) and the cerebral blood flow index (CBFI) ratio were calculated in both the lateral caudoputamen and overlying cortex at each time point. The size of the in vivo ischemic abnormalities was calculated from the ADC$_{av}$ and the T2 maps. Postmortem triphenyltetrazolium chloride (TTC) staining was used to verify ischemic injury. Results: Both the CBFI ratio and ADC$_{av}$ values declined significantly in the two regions during occlusion. The CBFI ratio recovered immediately after reperfusion and remained unchanged over 72 hours. However, ADC$_{av}$ values returned to normal at 60 to 90 minutes and secondarily decreased at 12 hours after reperfusion as compared with those in the contralateral hemisphere. The extent of the in vivo ischemic lesions maximized at 48 hours and was highly correlated with TTC-derived lesion size. Conclusions: Acute recovery of initial ADC$_{av}$-defined lesions after reperfusion is transient, and secondary ADC$_{av}$-defined lesions develop in a slow and delayed fashion.

Neurology

AB-14703-00
Distribution of Cerebral Microembolism in the Anterior and Middle Cerebral Arteries—Wijman CAC, Babikian VL (Dept of Neurology, Boston Univ School of Medicine and Boston Veterans Administration Medical Center, 150 S Huntington Ave, Boston, MA 02130), Winter MR, Pochay VE—Acta Neurol Scand. 2000;101:122–127. Copyright © Munksgaard 2000.

Background and purpose—Cerebral infarcts occur more frequently along the middle (MCA) than the anterior cerebral artery (ACA) territory. The reason(s) for this difference remains speculative. The objective of this study was to investigate the distribution of cerebral microemboli as detected by transcranial Doppler ultrasound (TCD) along the MCA and ACA territories. Methods—Records of consecutive patients examined for the presence of cerebral microembolism during a 32-month period at the Neurovascular Laboratory were reviewed. Of the original 375 TCD studies in 268 patients, 28 studies in 24 patients demonstrated microembolic signals (MES) and monitored the MCA and ACA on the same side. TCD studies were performed on TC-2000 or TC-2020 instruments. MES positive studies were saved and off-line reviewed. MES satisfied previously established criteria. Results—MES were more frequent in the MCA than the ACA in 85.7% (24/28) of studies (P < 0.01). Of the total number of MES (n = 979), 29.6% (n = 290) were detected in the ACA and 70.4% (n = 689) in the MCA (P < 0.01). The mean (±SD) intensity of MCA MES of 12.2 (±2.4) dB was significantly lower than that of ACA MES of 14.8 (±3.2) dB (P = 0.05). The mean (±SD) duration of MCA MES of 38.1 (±45.3) ms was longer than that of ACA MES of 30.7 (±34.0) ms (P = 0.05). Conclusions—Cerebral microembolism occurs more frequently in the MCA than the ACA, which may explain the uneven distribution of cerebral infarcts along these arterial territories. Furthermore, there are significant differences in the characteristics of ACA and MCA MES.

AB-14704-00

Objective: To investigate the frequency of transcranial Doppler (TCD) waveform blunting in patients with severe (80–99%) symptomatic or asymptomatic extracranial carotid artery stenosis. Background: Severe carotid artery stenosis has been identified as a risk factor for ischemic stroke. Blunted Doppler flow waveforms (reduced systolic flow velocity and pulsatility) of the middle cerebral artery (MCA) are inferred to reflect hemodynamic impairment, possibly indicating an increased risk of stroke. Methods: The 114 consecutive patients (mean age 72.4 years, SD 9.0 years; 37% women; 46 clinically symptomatic, 68 asymptomatic) with 80–99% stenosis of the extracranial internal carotid artery (ICA), as determined by duplex sonography, were examined with TCD. Flow velocities, pulsatility index, and spectral waveforms of the MCA distal to the ICA stenosis were assessed blinded to the clinical status of the ICA: Doppler waveform blunting was defined as loss of the characteristic systolic peak. Odds ratio was 95% confidence intervals and chi² statistics were used to describe the association between waveform blunting and the symptomatic status of the ICA stenosis. Results: Among asymptomatic patients, 23 (50%) had completed strokes, and a further 23 (50%) had transient neurologic deficits in the territory of the stenotic ICA. Blunted spectral waveform was found in 37 (80%, 95% CI 68–92%) of the symptomatic and 25 (37%; 95% CI 25–49%) of the asymptomatic patients. Symptomatic patients had significantly increased odds of having blunted TCD waveforms (OR 7.5, 95% CI 3.1–18.1, p < 0.001). Conclusions: Our findings suggest that TCD waveform blunting in the MCA as here described may be an additional risk factor in the setting of severe extracranial carotid artery stenosis. A prospectively designed study to confirm our results seems warranted.

Pharmacology / Therapeutics

AB-14705-00

Observational data suggest that diets rich in fruits and vegetables and with high serum levels of antioxidants are associated with decreased incidence and mortality of stroke. We studied the effects of α-tocopherol and β-carotene supplementation. The incidence and mortality of stroke were examined in 28 519 male cigarette smokers aged 50 to 69 years without history of stroke who participated in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC Study). The daily supplementation of 50 mg α-tocopherol, 20 mg β-carotene, both, or...
placebo. The median follow-up was 6.0 years. A total of 1,057 men suffered from incident stroke: 85 men had subarachnoid hemorrhage; 112, intracerebral hemorrhage; 807, cerebral infarction; and 53, unspecified stroke. Deaths due to stroke within 3 months numbered 50, 65, and 7, respectively (total 160). α-Tocopherol supplementation increased the risk of subarachnoid hemorrhage 50% (95% CI 3% to 132%, \( P = 0.07 \)) but decreased that of cerebral infarction 14% (95% CI 25% to \( -1\% \), \( P = 0.03 \)), whereas β-carotene supplementation increased the risk of intracerebral hemorrhage 62% (95% CI 10% to 136%, \( P = 0.01 \)). α-Tocopherol supplementation also increased the risk of fatal subarachnoid hemorrhage 181% (95% CI 37% to 479%, \( P = 0.01 \)). The overall net effects of either supplementation on the incidence and mortality from total stroke were nonsignificant. α-Tocopherol supplementation increases the risk of fatal hemorrhagic strokes but prevents cerebral infarction. The effects may be due to the antiplatelet actions of α-tocopherol, β-Carotene supplementation increases the risk of intracerebral hemorrhage, but no obvious mechanism is available.

AB-14706-00


The aim of the randomized, double-blind, placebo-controlled trial was to assess the safety and the efficacy of the pharmacologic drug glycine in 200 patients with acute (<6 h) ischemic stroke in the carotid artery territory. Fifty patients received placebo, 49 glycine 0.5 g/day, 51 glycine 1.0 g/day and 50 glycine 2.0 g/day for 5 days in each group. The efficacy of glycine was assessed by clinical analysis, by an enzyme-linked immunosorbent assay of levels of blood serum autoantibodies to NMDA-binding proteins, by detection of excitatory (glutamate, aspartate) and inhibitory (glycine, GABA) amino acid concentrations and lipid peroxidation products (TBARS) in CSF. The trial confirmed the safety profile of the glycine treatment. Slight sedation was observed in 9 patients (4.5%) as a side-effect. Other marked side-effects of adverse events were absent. The glycine treatment at the dose of 1.0–2.0 g/day was accompanied by a tendency to a decreased 30-day mortality (5.9% in 1.0 g/day glycine and 10% in 2.0 g/day glycine groups vs. 14% in the placebo and 14.3% in 0.5 g/day glycine groups), to an improved clinical outcome on the Oggogoro Stroke Scale (\( p < 0.01 \)) and to a favorable functional outcome on the Barthel index (\( p < 0.01 \) in 1.0 g/day glycine vs. placebo group in patients with no mild disability). An early normalization of autoantibody titres to NMDA-binding proteins in serum was found (\( p < 0.01 \) vs. placebo), a reduction of glutamate and aspartate levels (\( p < 0.05 \) vs. placebo), an increase in GABA concentrations (\( p < 0.01 \) vs. placebo in severe stroke patients) and also a reduction of TBARS levels (\( p < 0.05 \) vs. placebo) in CSF by day 3. Thus, the trial suggests that sublingual application of 1.0–2.0 g/day glycine started within 6 h after the onset of acute ischemic stroke in the carotid artery territory is safe and can exert favorable clinical effects. These results will be verified in further trials with a larger number of patients.

Surgery

AB-14707-00


Object: The authors analyzed their series of carotid endarterectomies (CEAs), which were performed after administration of either a general or regional anesthetic, to determine whether the choice of anesthetic affected patients’ clinical outcomes and length of hospital stay.

Methods: A series of 803 consecutive CEAs performed between July 1990 and February 1999 was reviewed. Cases were analyzed for patient demographics, comorbid medical states, and perioperative complications. Contingency-table statistical analysis was used to compare the incidence of comorbid medical states and perioperative complications between patients who underwent CEA in which either a regional or general anesthetic was used. Student’s t-test was used to compare the length of hospital stay and mean patient age. A regional anesthetic was used for 632 CEAs, and a general anesthetic was used for 171 operations. There were no statistically significant intergroup differences in demographics or comorbid medical states. The incidence of perioperative stroke and death did not differ significantly between the regional (2.7%) and the general anesthetic groups (2.3%). However, the incidence of nonneurological, nonfatal complications was significantly less in the regional anesthetic (1.6%) than in the general anesthetic group (14.6%, \( p < 0.0001 \)). Patients undergoing CEA in which a regional anesthesia was used had a significantly lower incidence of cardiopulmonary complications (myocardial infarction and post-operative intubation), cervical complications (neck hematomas and cranial nerve injuries), and urological complications (urinary retention) than patients who underwent surgery after receiving a general anesthetic.

Conclusions: Patients undergoing CEA in which a regional anesthetic was used had significantly fewer nonneurological, nonfatal complications, particularly cardiopulmonary complications, than similar patients surgically treated after induction of general anesthesia.

AB-14708-00


Purpose: The purpose of this study was to identify the risk and outcome of reconstruction of the extracranial vertebral artery (ECVA).

Method: The study was conducted as a retrospective review of 369 consecutive ECVA reconstructions.

Results: The clinical presentations consisted of hemispheric symptoms alone in 4% of the cases, hemispheric and vertebrobasilar symptoms in 30%, and vertebrobasilar symptoms alone in 60%. The cause of the lesion was atherosclerosis (n = 300), extrinsic compression (n = 42), dissection (n = 7), radiation arteritis (n = 5), intimal hyperplasia (n = 3), fibromuscular dysplasia (n = 2), previous surgical ligation (n = 3), aneurysm (n = 2), and other (n = 5). All the patients underwent preoperative arteriography. There were 252 proximal ECVA reconstructions (218 transpositions, 42 bypass grafting procedures, and two other) and 117 distal ECVA reconstructions (85 bypass grafting procedures, 25 transpositions, and seven other). In 83 patients, the ECVA operation was performed concomitant with a carotid or supraaortic trunk reconstruction. This series was analyzed in two separate sets: before 1991 (n = 215), when changes in indications and management were occurring; and after 1991 (n = 154), when we acquired a dedicated anesthesia team and digital arteriography in the operating room and established uniform protocols for the management of ECVA disease. The stroke, death, and stroke/death rates for the period before 1991 were, respectively, 4.1%, 3.2% and 5.1%. The stroke, death, and stroke/death rates for the period after 1991 were, respectively, 1.9%, 0.6%, and 1.9%. The patency rate at 5 years was 80%. The survival rate at 5 years was 70%. Most of the deaths during the follow-up period were caused by cardiac disease. Among the survivors, the protection rate from stroke was 97%.

Conclusion: The changes in operative selection and management have improved the results of ECVA reconstruction. The data reported for ECVA reconstruction in patients who underwent operation since 1991 reflect the outcome of ECVA reconstruction today. In our experience, a reconstruction of the ECVA is less risky than a carotid reconstruction.

Objective: The durability of carotid endarterectomy (CEA) may be affected by carotid restenosis. The data from randomized trials show that the highest incidence of restenosis after CEA occurs from 12 to 18 months after surgery. The optimal CEA technique to reduce perioperative complications and restenosis rates is still undefined. This study examines the long-term clinical outcome and incidence of recurrent stenosis in patients who undergo eversion CEA. Previously published perioperative outcome between the eversion and standard techniques at the available follow-up examination.

Methods: From October 1994 to March 1997, 1353 patients with surgical indications for carotid stenosis were randomly assigned to undergo eversion (n=678) or standard CEA (n=675; primary closure, 419; patch, 256). Withdrawal from the assigned treatment occurred in 1.6% of the patients (in 13 assigned to eversion CEA, and in nine assigned to standard CEA). The clinical and duplex scan follow-up examination was 99% complete, and the mean follow-up interval was 33 months (range, 12 to 55 months). The primary outcomes were perioperative and late major stroke and death, carotid restenosis (stenosis ≥50% of the lumen diameter detected at duplex scanning), and carotid occlusion. The primary evaluation of study outcomes was conducted on the basis of an intention-to-treat analysis.

Results: Restenosis was found at duplex scanning in 56 patients (19 in the eversion group, and 37 in the standard group). Within the standard group, the restenosis rates were 7.9% in the primary closure population and 1.5% in the patched population. Of the patients with restenosis, 36% underwent cerebral angiography that confirmed restenosis in all cases. The cumulative restenosis risk at 4 years was significantly lower in the group that underwent treatment with eversion CEA as compared with the standard group (3.6% vs 9.2%; P=.01), with an absolute risk reduction of 5.6% and a relative risk reduction of 62%. Eighteen patients would have had to undergo treatment with eversion CEA to prevent one restenosis during the 4-year period. The incidence rate of ipsilateral stroke was 3.3% in the eversion population and 2.2% in the standard group. There were no significant differences in the cumulative risks of ipsilateral stroke (3.9% for eversion, and 2.2% for standard; P=.2) and death (13.1% for eversion, and 12.7% for standard; P=.7)) in the two groups. Of the 18 variables that were examined for their influence on restenosis, eversion CEA (hazard ratio, 0.3; 95% confidence interval, 0.2 to 0.6; P=.0004) and patch CEA (hazard ratio, 0.2; 95% confidence interval, 0.07 to 0.6; P=.002) were negative independent predictors of restenosis with multivariate Cox proportional hazards regression analysis.

Conclusion: The EVEREST (EVERsion carotid Endarterectomy versus Standard Trial) showed that eversion CEA is safe, effective, and durable. No statistically significant differences were found in late outcome between the eversion and standard techniques at the available follow-up examination.

Items of Interest


Abstracts of Literature
Askiel Bruno and Engin Y. Yilmaz

Stroke. 2000;31:1467-1473
doi: 10.1161/01.STR.31.6.1467

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/31/6/1467

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/