Cerebral Aneurysms

AB-14310-99


Endothelin participates in regulating the vascular tone, and it is also involved in the pathogenesis of vasospasm following subarachnoid hemorrhage (SAH). Endothelin-1 (ET-1) induced cerebral vasospasm is inhibited by ETA receptors specific antagonist—BQ-123; this protects the neurons from ischemic damage. The present study evaluates the dynamics of ET-1 concentration changes in the plasma of rats in the acute phase of vasospasm after SAH, which was induced by administering 100 microliters non-heparinized fresh autologous arterial blood into the brain cisterna magna (CM). The study also assesses the effect of blocking ETA receptors on the changes in ET-1 level. BQ-123, the specific ETA receptors antagonist, was administered to cerebrospinal fluid (CSF) through a cannula inserted into CM; the antagonist—40 nmol in 50 microliters CSF—was given 20 minutes prior to SAH. In the control group, sham SAH was induced by administering 100 microliters artificial CSF (aCSF) to CM. ET-1 concentration in the plasma of rats in the acute phase of vasospasm was assessed by radioimmunoassay 30 and 60 minutes after SAH or sham SAH. It has been shown that both SAH and sham SAH cause significant increase in the ET-1 concentration (p<0.05) in the rat plasma after 30 minutes; the concentration returns to an initial value after following 30 minutes, which may suggest that ET-1 released binds to its receptors in the acute phase of the vasospasm. On the other hand, in the two groups of rats with blocked ETA receptors there was a significant rise in ET-1 concentration 30 minutes after SAH or sham SAH, and a still further rise was observed 60 minutes after the procedure. The rise was significantly higher in animals with SAH (p<0.05). The dynamics of the ET-1 concentration changes observed in rats with blocked ETA receptor suggests that SAH is an ET-1 production stimulator significantly more potent than other factors assessed in the study, such as a rise in the intracranial pressure resulting from administering a CSF to CM. Blocking ETA receptors makes it impossible for the ET-1 released to bind to the receptors, which may be a factor preventing the occurrence of cerebral vasospasm following SAH.

AB-14311-99

Effects of Unilateral Intrathecal Administrations of Low Dose Tissue-Type Plasminogen Activator on Clot Lysis, Vasospasm and Brain Phospholipid Hydroperoxidation in a Primate Model of Bilateral Subarachnoid Hemorrhage—Suzuki H, Kanamori K (MIE Univ School of Medicine, Dept of Neurosurgery, Tsu, MIE 5148507 Japan), Kuroki M, Sun H, Waga S, Miyazawa T—Neurol Res. 1998;20:625–631.

In order to clarify the effect of clot lysis by recombinant tissue-type plasminogen activator (tPA) on the brain lipid peroxidation, we measured phosphatidylcholine hydroperoxide (PCOOH) and phosphatidylethanolamine hydroperoxide (PEOOH) levels in a primate model of subarachnoid hemorrhage (SAH). Monkeys were assigned into two groups; a tPA-treated group receiving intrathecal injections of 0.02 mg/CaP, and a placebo-treated group receiving saline. The tPA or placebo was injected into the right side of the basal cistern every 8 h for 6 days following bilateral SAH induction. The tPA cleared the right side clots (p<0.0001), but not the left side clots. The degree of vasospasm in the right middle cerebral artery and the rCBF decrease in the right parietal cortex were significantly attenuated in the tPA group (p<0.05). In the placebo group, more severe vasospasm and marked rCBF reduction were noted in comparison with those in the tPA group. PCOOH levels in the parietal cortex were significantly higher in the placebo group than in the tPA group (p<0.05). There were no significant changes in brain PEOOH levels. These results may explain the limitations for clinical application of unilateral intrathecal administration of tPA.

AB-14312-99


A polymorphism in the angiotensin I-converting enzyme (ACE) gene has been associated with cerebrovascular diseases as a new potent risk factor. The purpose of this study was to investigate an association of the gene polymorphism with intracranial saccular aneurysm patients. The study population consisted of 83 aneurysmal patients (age range 41–85 years) (the AN group) and 104 matched control subjects (age range 30–81 years) (the Control group). For detection of the ACE gene polymorphism, the standard PCR method was performed by using genomic DNA isolated from peripheral blood leukocytes. The PCR products were a 490-bp in the presence of the insertion (I) and a 190-bp fragment in the absence of the insertion (D). The ACE gene polymorphism was classified into three genotypes: I/I genotype (a 490-bp band); D/D genotype (a 190-bp band); or I/D genotype (both a 490-bp and a 190-bp band). The number of subjects with I/I, I/D, and D/D genotypes was 38, 40, and 5 in the AN group and 43, 45, and 16 in the Control group, respectively. The frequency of the D/D genotype in the AN group (5/83=0.06) than that in the Control group (16/104=0.15). There was no significant difference between the genotypes of hypertensive patients and normotensive patients in the AN group. Thus, this present study suggests that genetic heterogeneity of the ACE gene may be correlated with the etiology of intracranial aneurysms.

Clinical

AB-14313-99

Stroke and Cocaine or Amphetamine Use—Petitti DB (393 E Walnut St, Pasadena, CA 91188), Sidney S, Quesenberry C, Bernstein A—Epidemiol. 1998;9:596–600.

The association of cocaine and amphetamine use with hemorrhagic and ischemic stroke is based almost solely on data from case series. The limited number of epidemiologic studies of stroke and use of cocaine and/or amphetamine have been done in settings that serve mostly the poor and/or minorities. This case-control study was conducted in the defined population comprising members of Kaiser Permanente of Northen and Southern California. We attempted to identify all incident strokes in women ages 15–44 years during a 3-year period using hospital admission and discharge records, emergency department logs, and payment requests for out-of-plan hospitalizations. We selected controls, matched on age and facility of usual care, at random from healthy members of the health plan. We obtained information in face-to-face interviews. There were 347 confirmed stroke cases and 1,021 controls. The univariate matched odds ratio for stroke in women who admitted to...
using cocaine and/or amphetamine was 8.5 (95% confidence interval = 3.6–20.0). After further adjustment for potential confounders, the odds ratio in women who reported using cocaine and/or amphetamine was 7.0 (95% confidence interval = 2.8–17.9). The use of cocaine and/or amphetamine is a strong risk factor for stroke in this socioeconomically heterogeneous, insured urban population.

**AB-14314-99**

**Inherited Prothrombotic States and Ischaemic Stroke in Childhood**—Ganesan V, (Newcomen Centre, Guys Hospital, St Thomas St, London SE1 9RT, UK), McShane MA, Liesner R, Cookson J, Hann I, Kirkham, FJ—*Neur Neurosurg Psychiatry.* 1998;65:508–511.

**Objective:** To investigate the prevalence of currently recognised inherited prothrombotic states in a population of children with arterial stroke.

**Methods:** Children with arterial stroke presenting to a tertiary level paediatric neurology centre between 1990 and 1996 were investigated for inherited prothrombotic states.

**Results:** Sixty seven children with arterial stroke were investigated. Abnormalities were initially identified in 16 patients; however, only eight children (12%) had an inherited prothrombotic state. This was type 1 protein S deficiency in one patient, the factor V Leiden mutation in six, and activated protein C resistance (without the factor V Leiden mutation) in one. The prevalence of the factor V Leiden mutation was not significantly higher in children with arterial stroke (12%) than in a control population of children without thrombosis attending the same institution (5.2%; Fisher’s exact test, p = 0.19; difference in prevalence between patients and controls (95% confidence interval) = 6.8% (2.78% to 16.8%).

**Conclusions:** Currently recognised inherited prothrombotic tendencies were rarely associated with stroke in this group of children, although larger numbers of patients would be needed to confirm this. Age appropriate normal values should be used when interpreting the results of a prothrombotic screen. Prothrombotic abnormalities seen acutely are as often transient as inherited. Longitudinal assessment and family studies are required before low concentrations of an anticoagulant protein found acutely can be attributed to an inherited abnormality.

**AB-14315-99**


**Objective:** To correlate MRI and sensory changes in patients with spontaneous lesions in the cerebral “pain pathway.”

**Methods:** The authors used MRI and quantitative somatosensory testing in 73 patients with central poststroke pain (CPS) and in 13 patients with pain-free stroke with sensory deficit.

**Results:** Lesions in any part of the discriminatory somatosensory pathway may or may not produce CPS. Most CPS patients have multiple lesions, many probably unrelated to pain. Ventroposterior thalamic nuclear lesions are more likely to produce half-body pain than lesions elsewhere (including the brainstem). In supratentorial lesions, the greatest pain is more likely to be in an extremity, and in infratentorial lesions, the greatest pain is likely to be in the face. Supratentorial CPS patients have a deficit of sharpness and cold (peripherally mediated by Aδ fibers) than pain-free stroke patients, whereas patients with infratentorial CPS additionally have a deficit of C-fiber-mediated warmth and hot pain. Burning pain is more common than nonburning pain in younger patients. Warmth and cold, but not hot pain, exhibiting central convergence (spatial summation) are more affected in CPS patients with burning than nonburning pain. Alloedync CPS patients had a significantly greater deficit for warmth than patients without allodynia.

**Conclusions:** Different stroke sites produce different patterns of sensory deficit. The progression from painless sensory deficit to CPSP is not purely quantitative.

**AB-14316-99**

**Specificity, Isotype, and Titer Distribution of Anticardiolipin Antibodies in CNS Diseases**—D’Olhaberriague L, Levine SR (WSU School of Medicine, University Heath Center, 6E, 4201 Saint Antoine, Detroit, MI 48201), Salowich-Palm L, Tanne D, Sawaya KL, Aurora TK, Perry M, Day M, Spencer T, Schultz L—*Neurology.* 1998;51:1376–1380. Copyright © 1998 by the American Academy of Neurology.

**Background and purpose:** There is an association between anticardiolipin antibodies (aCL) and ischemic stroke. There are, however, also occasional reports linking aCL with other CNS diseases (OND), particularly with multiple sclerosis (MS). Hence, we studied the specificity of aCL for ischemic stroke.

**Methods:** Prospective, consecutively identified patients evaluated for aCL (immunoglobulin G [IgG] and immunoglobulin M [IgM] isotypes) were divided into two groups: ischemic stroke (first ever) and OND (stroke-free subjects affected by OND).

**Results:** The ischemic stroke group (n = 300) and the OND (n = 149) differed in the following risk factors: age (64±14 versus 58±15 years; p < 0.001) and proportions of African Americans (67% versus 29%; p < 0.001), current cigarette smoker (26% versus 17%; p = 0.028); hypertensive (69% versus 34%; p < 0.001); diabetic (18% versus 7%; p < 0.001); history of angina (16% versus 8%; p = 0.015) or myocardial infarction (15% versus 3%; p < 0.001). There were higher rates of aCL positivity (26% versus 17%; p = 0.050), IgG-aCL >10 GPL (23% versus 11%; p = 0.003) or IgG aCL >20 GPL (12% versus 4%; p = 0.012) among the stroke group than among the OND group. No differences in IgM-aCL positivity were found between the MS group and the rest of the OND group but the MS patients had a higher rate of IgM-aCL positivity than the other OND patients.

**Conclusion:** IgG-aCL positivity does not appear to be a marker for CNS disease generally but of ischemic stroke.

**AB-14317-99**


**Background:** Patients with cerebellar hematomas may appear stable but may worsen suddenly. Whether certain clinical or CT scan findings predict worsening is not known.

**Methods:** We reviewed clinical and neuroimaging data in 72 patients with cerebellar hematomas at the Mayo Clinic from 1973 through 1993 to identify predictive features for neurologic deterioration. Patients presenting in coma and patients with vascular malformations or malignancies were excluded. Data were analyzed using chi-square or Fisher’s exact test, with calculation of odds ratios with 95% confidence intervals. Multivariate logistic regression analysis was performed on appropriate variables.

**Results:** Thirty-three patients (46%) deteriorated, with a decrease in level of consciousness, new brainstem signs, or worsened motor response on the Glasgow Coma Scale. Clinical and neuroradiologic predictors for neurologic deterioration at p < 0.05 were admission systolic blood pressure greater than 200 mm Hg, pinpoint pupils and abnormal corneal or oculocephalic reflexes, hemorrhage extending into the vermis, hematoma size more than 3 cm in diameter, brainstem distortion, intraventricular hemorrhage, upward herniation, and acute hydrocephalus. Multivariate analysis demonstrated that hemorrhage located in the vermis (p = 0.03) and acute hydrocephalus (p = 0.006) on admission CT scanning independently predicted deterioration.

**Conclusion:** Patients with a cerebellar vermis hematoma or acute hydrocephalus are at high risk for neurologic deterioration. These patients should be carefully monitored and are more likely to require consideration for neurosurgical intervention.

**Epidemiology**

**AB-14318-99**

**Influence of Risk Factors on Peripheral and Cerebrovascular Disease in Men With Coronary Artery Disease in Men with Coronary Artery Disease, Low High-Density Lipoprotein Cholesterol Levels, Low Total Cholesterol Levels, High Low-Density Lipoprotein Cholesterol Levels, and Low High-Density Lipoprotein Cholesterol Levels.**

Background The Veterans Administration-HDL Intervention Trial is an ongoing, 20-center, randomized, double-blind, placebo-controlled study aiming to assess the effect of gemfibrozil-improved low high-density lipoprotein cholesterol levels on cardiovascular morbidity and mortality rates.

Methods and Results Eligible patients were men with low high-density lipoprotein cholesterol levels and demonstrable coronary heart disease. A total of 2531 patients (average age 63.5 years) were randomly assigned in this study, with a mean high-density lipoprotein cholesterol level of 0.83 mmol/L (32 mg/dL) and low-density lipoprotein cholesterol level of 2.87 mmol/L (111 mg/dL). Baseline data provided the opportunity to assess the interaction of several coronary heart disease risk factors and comorbid vascular diseases. Of these patients, 206 had diabetes mellitus (DM) alone, 1021 had hypertension (HTN) alone, 421 had both DM and HTN, and 883 had neither (“others”). Considering the influence of these risk factors on comorbidities independent of smoking status, patients with DM alone had a 2-fold increase in the prevalence of peripheral vascular disease and a 1.5-fold increase in congestive heart failure. Patients with HTN had a significant increase in the prevalence of cerebrovascular disease, stroke, and congestive heart failure. Patients with HTN and DM had a significant increase in all comorbidities. Smoking resulted in substantial increase of both peripheral vascular disease and cerebrovascular disease. Compared with nonsmoking patients with no DM or HTN, patients with DM and HTN and smoking had a 3-fold increase in the prevalence of peripheral vascular disease and a 3.5-fold increase in cerebrovascular disease (P<.001).

Conclusions We conclude that DM is a strong correlate of peripheral vascular disease, hypertension of cerebrovascular disease, and that there is a strong additive effect between DM, HTN, and smoking on both.

AB-14319-99
Risk Profile and Prediction of Long-Term Ischemic Stroke Mortality: A 21-Year Follow-Up in the Israeli Ischemic Heart Disease (IIHD) Project—Tanne D, Yaari S, Goldbourt U (Section of Epidemiology, Neufeld Cardiac Research Institute, Sheba Medical Center, Tel-Hashomer 52621, Israel)—Circulation. 1998;98:1365–1371. Copyright © 1998 by American Heart Association, Inc.

Background—Multinational comparisons demonstrate marked ethnic and regional variation in stroke mortality and risk-factor distribution. We assessed the role of ethnicity and estimated the cumulative effect of multiple risk factors on long-term ischemic stroke mortality.

Methods and Results—Civil servants and municipal employees in Israel (n=9734 men; age, ≥42 years), chosen by stratified sampling in 6 prespecified areas of birth (those born in Israel and those who were immigrants from 5 other regional-ethnic strata), were included in the Israeli Ischemic Heart Disease (IIHD) Project. Over a 21-year follow-up period, age-adjusted mortality rates per 10,000 person-years attributed to ischemic stroke (n=282; International Classification of Diseases [ICD]-9 codes 433 to 438) were higher among immigrants to Israel from northern Africa and the Mideast (17.1 to 19.0), than from 3 parts of Europe (11.3 to 12.4). Crude rates per 1000 subjects observed in those born in Asia or Africa (29.4 to 31.2) exceeded rates predicted by risk-factor profiles (21.4 to 24.9). Adjusted hazard ratios were 3.00 for age (per 10 years), 2.15 for left ventricular hypertrophy, 1.69 for systolic blood pressure (BP, per 20 mm Hg), 1.86 for diabetes mellitus, 1.83 for peripheral vascular disease, 1.79 for smoking (>20 cigarettes per day), 1.51 for coronary heart disease, 1.16 for percent cholesterol contained in the HDL fraction (% HDL, per 5% decrease), and 1.88 for diastolic BP (per 12 mm Hg; assessed in an alternative model). Accounting for regression dilution bias and assessed from repeat measurements, we found that hazard ratio estimates associated with diastolic BP, systolic BP, and percent HDL (per increments described) increased to 3.22, 2.23, and 1.23, respectively. Ischemic stroke mortality rates were 30-fold greater among subjects at the highest versus the lowest quintile of predicted probability according to risk-factor profiles (81.2 versus 2.6 per 1000 subjects).

Conclusions—Assessment of multiple risk factors provides useful quantitative prediction of long-term ischemic stroke mortality risk. Regional-ethnic variations are consistent with a hypothesis that other, undetermined inherent genetic or sociocultural factors act to increase ischemic stroke mortality rates in immigrants to Israel from the Mideast and northern Africa over that predicted by conventional risk factors.

Experimental Pathology

AB-14320-99

Delayed treatment with aminoguanidine (AG), a relatively selective inhibitor of inducible nitric oxide synthase, ameliorates brain damage produced by occlusion of the rat’s middle cerebral artery (MCA). We investigated whether the protection exerted by AG is dose-dependent and whether it is associated with improved neurologic outcome. We also studied the effect of the timing of administration of AG relative to the induction of cerebral ischemia. Halothane-anesthetized spontaneously hypertensive hypertensive rats underwent permanent MCA occlusion distal to the lenticulostriate branches. Neurologic deficits were assessed daily by the postural reflex test and beam balance test. Infarct volume was determined in thionin-stained sections 96 hours after ischemia and values corrected for swelling. Treatment with AG (intraperitoneally, twice daily), starting 24 hours after MCA occlusion, decreased necrotic infarct volume in comparison to vehicle-treated rats. After correction for swelling, the decrease was 8±12% at 50 mg/kg (n=8; P<.05; analysis of variance), 25±13% at 100 mg/kg (n=7; P<.05), 30±16% at 200 mg/kg (n=7; P<.05) and 32±9% at 400 mg/kg (n=5; P<.05). Twenty-four hours after induction of ischemia neurologic deficits scores did not differ between treated and untreated rats (P<.05). However, from 48 to 96 hours after ischemia, neurologic deficits improved significantly in rats treated with AG (100 to 400 mg/kg) compared to rats in which vehicle was administered (P<.05). The decrease in neocortical infarct volume was greatest when AG (100 mg/kg; twice daily) was administered 12 (26±17%; n=9) or 24 hours (25±13; n=7) after MCA occlusion. The findings show that AG decreases ischemic brain damage dose-dependently and improves neurologic recovery. Delayed treatment with AG may be a therapeutic strategy to selectively target the evolution of ischemic damage that occurs in the post-ischemic period.

AB-14321-99
Spatial Stability of Extracellular Potassium Ion and Blood Flow Distribution in Rat Cerebral Cortex After Permanent Middle Cerebral Artery Occlusion—Sick TJ (Dept of Neurology, Univ of Miami School of Medicine, South Campus, Blvdg B, 12500 SW 152 St, Miami FL 33177), Feng Z-C, Rosenthal M—J Cereb Blood Flow Metab. 1998;18:1114–1120. Copyright © 1998 The International Society of Cerebral Blood Flow and Metabolism.

Extracellular potassium ion activity ([K+]o) increases precipitously during brain ischemia when blood flow falls below threshold values less than approximately 15 mL/100 g/min. This flow threshold for increase of [K+]o occurs also in focal ischemia producing gradient from ischemic core to adjacent normally perfused brain. In this study we investigated the spatial and temporal stability of extracellular potassium ion and blood flow gradients after permanent middle cerebral artery occlusion (MCAO) in rats. [K+]o and regional CBF were measured, respectively, with [K+]o-sensitive and polarographic hydrogen-sensitive microelectrodes at different cortical locations in the middle cerebral artery distribution...
region. Spatial assessment of $[K^+]_o$ and regional CBF was conducted at 30, 90, and 180 minutes after MCAO. $[K^+]_o$ in the more lateral cortex (core) increased from near 3 mmol/L before MCAO to greater than 50 mmol/L and was associated with flow values less than 25% of pre-ischemic levels. Measurements medial to the core (penumbra) indicated progressively decreasing levels of $[K^+]_o$ and improvement of CBF. There was a tendency for $[K^+]_o$ in penumbraal zones to decrease toward normal levels with time, but there was little dissipation of $[K^+]_o$ in core regions. In contrast, the spatial CBF profile remained remarkably constant for the entire recording period. Thus, unlike infarction which has been reported to expand with time after focal ischemia, the spatial $[K^+]_o$ disturbance tends to contract primarily due to decreasing $[K^+]_o$ with time in the penumbra. Thus, steady state levels of $[K^+]_o$ after focal ischemia may not be a valuable predictor of cell viability.

AB-14322-99


Transgenic mice, which had been transfected with the human extracellular superoxide dismutase gene, causing an approximate five-fold increase in brain parenchymal extracellular superoxide dismutase activity, were used to investigate the role of extracellular superoxide dismutase in ischemic brain injury. Transgenic (n=21) and wild-type (n=19) mice underwent 90 min of intraluminal middle cerebral artery occlusion and 24 h of reperfusion. Severity of resultant hemiparesis and cerebral infarct size were measured. Wild-type mice had larger infarcts (cortex: wild type=37±14 mm³, transgenic=27±13 mm³, P=0.03; subcortex: wild type=33±14 mm³, transgenic=23±10 mm³, P=0.02). Neurological scores, however, were similar (P=0.29). Other mice underwent autodiagnostic determination of intra-ischemic cerebral blood flow. The volume of tissue at risk of infarction (defined as volume of tissue where blood flow was <25 ml/100 g/min) was similar between groups (cortex: wild type=51±15 mm³, transgenic=47±9 mm³, P=0.65; subcortex: wild type=39±16 mm³, transgenic=37±17 mm³, P=0.81).

These results indicate that antioxidant scavenging of free radicals by extracellular superoxide dismutase plays an important role in the historical response to a focal ischemic brain insult.

AB-14324-99


We have developed a new method for estimation of regional CBF (rCBF) and cerebrovascular reserve capacity on a pixel-by-pixel basis by means of dynamic magnetic resonance imaging (MRI). Thirteen healthy volunteers, 8 patients with occlusion and/or high grade stenosis of the internal carotid artery (ICA), and 2 patients with acute stroke underwent dynamic susceptibility-weighted enhanced MRI. Using principles of indicator dilution theory and deconvolution analysis, maps of rCBF, regional cerebral blood volume, and of the mean transit time (MTT) were calculated. In patients with ICA occlusion/stenosis, cerebrovascular reserve capacity was assessed by the rCBF increase after acetazolamide stimulation. Mean gray and white matter rCBF values in normals were 67.1 and 23.7 ml.100g−1 min−1, respectively. Before acetazolamide stimulation, six of eight patients with ICA occlusions showed decreased rCBF values; and in seven patients increased MTT values were observed in tissue ipsilateral to the occlusion. After acetazolamide stimulation, decreased cerebrovascular reserve capacity was observed in five of eight patients with ICA occlusion. In acute stroke, rCBF in the central core of ischemia was less than 8 ml.100g−1 min−1. In peri-infarct tissue, rCBF and MTT were higher than in unaffected tissue but rCBF was normal. Dynamic MRI provides important clinical information on the hemodynamic state of brain tissue in patients with occlusive cerebrovascular disease or acute stroke.

AB-14325-99


Background and purpose: Diagnosis of brain death requires confirmation of the clinical diagnosis by appropriate tests, generally electroencephalography (EEG) and angiography. The diagnostic limitations or logistical problems inherent to these tests indicate the need to develop other more appropriate methods. The results obtained with transcranial Doppler (TCD) led us to conduct this prospective study of TCD recordings in brain dead patients. Methods: 130 patients, aged 2–88
years were diagnosed as brain dead between July 1987 and June 1993. Clinical criteria were confirmed in all cases by EEG (n=88) and or angiography (n=64). Intracranial anterior circulation was insonated via temporal windows or, when impossible, via a transorbital approach. The posterior circulation was studied only in more recent patients. Examinations were made as soon as possible after brain death diagnosis and repeated for about 30 min. Vital parameters and treatments were taken into account. Results: There was only one false negative result, in a patient with an extended skull defect, who retained TCD and angiographic intracranial circulation despite confirmed irreversible brain death. All other patients displayed typical ultrasonic patterns of cerebral circulation arrest: an oscillating signal (n=190, 73%), a systolic spike (n=62, 24%) or a unilateral absence of signal (n=5). Despite a total correlation for positive diagnosis, TCD and angiography may differ as to the level of circulation arrest. TCD is useful for patients under sedative drugs. No false positive result was encountered but we were unable to insonate any intracranial artery in 5 patients. Conclusion: Data from previous studies and the results of this study indicate that TCD is a very sensitive and safe method for diagnosing cerebral circulatory arrest. TCD may be used as a confirmatory test alongside EEG and angiography. TCD is more widely applicable than EEG and may be earlier and safer than angiography.

AB-14326-99

The effect of cardioinhibition and/or vasodepression on cerebral hemodynamics assessed by transcranial Doppler has been investigated during carotid massage in 11 patients (62–87 years, mean age 72) with carotid sinus syndrome. The patients were tested in the OOO mode (n=11) with six tested in the DDD mode. Carotid massage in the OOO mode decreased mean arterial pressure by 44% (P<0.01) and mean cerebral blood flow velocity by 50% (P<0.01). Although not significant, cerebrovascular resistance increased transiently by 17% during massage, then decreased by 31% upon recovery. Carotid massage in the DDD mode decreased arterial pressure by 30% (P<0.01), cerebral blood velocity by 23% (P<0.01), and resistance by 15% (P<0.05). The decreased cerebral perfusion induced by cardioinhibition and/or vasodepression results from the delayed onset of cerebral autoregulation. Pacing in the DDD mode temporarily assists the critical period preceding the onset of cerebral autoregulation that plays a key role in preventing the deleterious effects of vasodepression.

Pharmacology / Therapeutics

AB-14327-99

Background—Antiplalet agents presently used in the secondary prevention of cardiovascular disease fail to prevent the majority of cases of recurrent stroke and systemic embolization. An evaluation of the efficacy of new agents is hampered by a lack of in vivo models in humans. Asymptomatic cerebral embolic signals (ES) may be detected with the use of transcranial Doppler ultrasonography. These signals are particularly common after carotid endarterectomy, and this provides a situation in which new antiplatelet agents can be evaluated. With this model, we determined the effectiveness of S-nitrosoglutathione (GSNO), a nitric oxide donor with relative platelet specificity, in reducing cerebral embolization.

Methods and Results—Transcranial Doppler ultrasound recordings from the ipsilateral middle cerebral artery were made after carotid endarterectomy in 12 control patients and 12 patients receiving intravenous GSNO from the induction of anesthesia until 2 hours after skin closure. Recording times were 0.5 to 3.5, 6 to 7, and 24 to 25 hours after skin closure. The Doppler signal was recorded onto tape, and analysis for ES was performed, with the investigators blinded to treatment group. All patients received aspirin 300 mg/d before surgery and 5000 IU of heparin during surgery. The median (range) number of ES detected during the initial 3-hour postoperative recording was markedly reduced in the GSNO group compared with the control group: 7.5 (0 to 61) versus 38.5 (1 to 219) (P=0.018). This difference persisted until 6 hours after surgery.

Conclusions—Despite the administration of aspirin and heparin, frequent embolization occurred and was markedly reduced after the administration of GSNO. This demonstrates the potential use of platelet-specific nitric oxide donors in the treatment of thromboembolic disease. This model of cerebral embolism may allow determination of the effectiveness of new antiplatelet agents in humans.

AB-14328-99
Prevalence of Atrial Fibrillation and Eligibility for Anticoagulants in the Community—Suklow M (Dept of Medicine, School of Clinical Medical Sciences, Univ of Newcastle upon Tyne, Newcastle upon Tyne NE2 4AA, UK), Thomson R, Thwaites B, Rodgers H, Kenny RA—Lancet. 1998;352:1167–1171.

Background: Anticoagulants are effective in the prevention of stroke in atrial fibrillation and flutter (AF). We aimed to find out the prevalence of AF in the UK and to estimate the proportion of patients with AF who might benefit from anticoagulation.

Methods: We screened with electrocardiography a random sample of 4843 people from the community aged 65 years and older for AF. Participants with AF had further investigations to identify risk factors for stroke and contraindications to anticoagulants. We used three sets of criteria to assess risk and eligibility for anticoagulation.

Findings: 228 (4.7%) participants had AF. According to analyses derived from risk stratifications based on the Stroke Prevention in Atrial Fibrillation (SPAF) study 61% of these patients would have benefited from anticoagulation, 49% according to pooled analysis of trial results, and 41% according to the inclusion criteria for the SPAF 3 study. Anticoagulants were used by 1114 (23%) of all patients and were least used among elderly women, who may be the most likely to benefit. Echocardiography would be useful to assess the need for anticoagulation only in patients younger than 75 years with no contraindications to treatment and no clinical risk factors for stroke.

Interpretation: Anticoagulants seem to be underused and misdirected in treatment of AF, according to various criteria. Efforts to promote and support wider and more appropriate use of anticoagulants would seem to be justified, and should decrease the incidence of stroke amongst elderly patients.

AB-14329-99

Objective: To perform a single-center pilot investigation of early hematoma removal in patients with intracerebral hemorrhage (ICH).

Background: Considerable debate remains regarding the utility of surgical clot evacuation for ICH. Methods: This was a prospective trial of open craniotomy within 12 hours of ICH symptom onset versus best medical therapy. Patients were eligible if they had a nontraumatic ICH >9 mL with significant neurologic impairment and were prepared for surgery within 12 hours of symptom onset. The study included a prospective registry of patients and a randomized trial. Results: The registry group included 34 medical and seven surgical patients. The surgical group had larger hemorrhages (median, 96 mL) and a lower
Glasgow Coma Scale (GCS) score (median, 10) compared with the medical group (33 mL; GCS score, 13). Six-month mortality was less in the medical group (36%) compared with the surgical group (54%). In the randomized series, median ICH volumes were similar in the surgical group (n = 17; 49 mL) compared with the medical group (n = 17; 44 mL). Median GCS score was also similar (medical, 10; surgical, 11). Mortality was lower in the surgical group (6%) compared with the medical group (24%) at 1 month, but similar at 6 months (surgical group, 17%; medical group, 24%). Conclusion: A trial of early surgery for ICH is feasible. This study represents the largest prospective, randomized series of surgery for ICH. A modest early mortality benefit for surgery is possible, but long-term benefit for surgery was not established in this single-center pilot investigation.

Surgery

AB-14330-99

Background: Carotid endarterectomy may be performed under cervical plexus block with local anesthetic supplementation by the surgeon as necessary during surgery. It is unclear, however, whether deep or superficial cervical plexus block offers the best operating conditions or patient satisfaction. Therefore, the authors compared the two in patients undergoing carotid endarterectomy.

Methods: Forty patients undergoing carotid endarterectomy were randomized to receive either a superficial or a deep cervical plexus block with 20 ml bupivacaine, 0.375%. Outcomes subjected to statistical analysis included supplemental anesthetic supplementation with lidocaine, 1%, by the surgeon, dermatomes affected by the block, paresthesia during block placement, postoperative pain scores, and analgesic requirements.

Results: Median supplemental lidocaine requirements were 6 ml (range, 0.5 to 20 ml) in the deep block group and 6 ml (range, 0 to 20 ml) in the superficial block group (P = 0.7323). Patients in the deep block group who reported paresthesia during block placement required less lidocaine supplementation (median, 2; range, 0.5 to 20 ml) than the 9.5 ml (range, 6 to 15.5 ml) required by those who did not experience paresthesia (P = 0.0113). Compared with patients in the superficial block group, those in the deep block group were less likely to need analgesia in the first 24 h after operation (P = 0.047), and those who required analgesia received it later (6.6 ± 4.1 vs. 3.9 ± 1.4 h after operation; Student’s t test, P = 0.02). One patient in each group expressed dissatisfaction with the technique.

Conclusions: Carotid endarterectomy may be performed satisfactorily during superficial or deep cervical plexus block placement with no differences in terms of supplemental local anesthetic requirements, although this is influenced by whether paresthesia is elicited during placement of the deep block. Therefore, the clinician’s decision to use one block rather than another need not be based on any assumed superiority of one block based on intraoperative conditions or patient satisfaction.

AB-14331-99

Purpose: This study is an analysis of the outcome of a common method of management of the external carotid artery (ECA) during routine carotid endarterectomy (CEA).

Methods: Between 1986 and 1997, 1069 primary CEAs were performed with a combination of proximal eversion technique and blind distal endarterectomy on the ECA. Of these, 973 CEAs (91%) had 1 or more postoperative duplex scans that included the ECA. Both preoperative and early postoperative studies were performed on 313 of these CEAs. Intraoperative post-CEA continuous-wave Doppler scans identified low flow or occlusion of the ECA in 37 CEAs (4%). These CEAs were isolated and repaired.

Results: The early post-CEA duplex scan velocities were 143 ± 81 cm/s (mean ± 1 standard deviation of the mean). In the first 6 months after the CEAs, 692 ECAs (72%) had <50% stenosis, 175 (18%) had 50% to 74% stenosis, 90 (9%) had ≥75% stenosis, and 9 (1%) were occluded. Of the 37 repaired ECAs, 20 (54%) had <50% stenosis, 10 (27%) had 50% to 74% stenosis, 5 (14%) had ≥75% stenosis, and 2 (5%) were occluded. The cumulative life-table ≥50% stenosis rate was 36% at 1 year, 40% at 3 years, 48% at 5 years, and 81% at 10 years. The cumulative ≥75% stenosis rate was 12% at 1 year, 12% at 3 years, 15% at 5 years, and 37% at 10 years. Preoperative studies showed <50% stenosis in 152 of the 313 ECAs (48%). In the early postoperative period, 102 of these ECAs (66%) had <50% stenosis, 35 (23%) had 50% to 74% stenosis, 13 (9%) had ≥75% stenosis, and 3 (2%) were occluded. Of the 161 ECAs with ≥50% preoperative stenosis, 66 (41%) had <50% stenosis in the first 6 months after CEA, 61 (38%) had 50% to 74% stenosis, 32 (20%) had ≥75% stenosis, and 2 (1%) were occluded.

Conclusions: Combined proximal eversion technique and blind distal ECA endarterectomy during routine CEA gives poor and unacceptable early and late outcomes. The repair of severely obstructed or occluded ECA identified during surgery after CEA has a similarly poor outcome. The technique and management of the ECA during routine CEA needs further investigation and modification.

AB-14332-99

Purpose: Myocardial infarction and other comorbidities contribute to complications after carotid endarterectomy (CEA). However, because the combined stroke and death rate after CEA is less than 5%, even relatively large series have small numbers of adverse events that preclude a detailed analysis of the association between the outcome and the patient factors, such as comorbidity and age. We sought to overcome this limitation by studying patients who underwent CEA in a large random sample of Medicare beneficiaries.

Methods: We used a database that contained a 20% random sample of all Medicare beneficiaries to identify patients who underwent CEA between the years 1988 to 1990 (n = 22,165), and we followed these cases until 1992. With multivariate logistic regression and Cox proportional hazards regression models, we examined the impact of age, race, gender, geographic location, hospital characteristics, and comorbidity, including acute myocardial infarction (AMI) and congestive heart failure (CHF), on the risk of stroke and death after CEA.

Results: AMI and CHF had the greatest negative impact on the long-term survival rates (adjusted hazard ratio [HR]: 2.40, P < .0001, and 2.85, P < .0001, respectively). Other variables with a significant impact on the long-term survival rates were an age of >80 years (HR, 2.16, P < .0001), an acute stroke (HR, 1.51; P < .0001), diabetes mellitus (DM; HR, 1.52; P < .0001), and male sex (HR, 1.32; P < .0001). In addition, AMI, CHF, DM, and advanced age were associated with an increased risk of perioperative stroke and death.

Conclusion: Patients with AMI, CHF, DM, and an age of >80 years have diminished perioperative and long-term survival rates after CEA. These results may alter the risk/benefit analysis for such patients, especially those with asymptomatic disease.
Items of Interest


Abstracts of Literature
Askiel Bruno and Alfredo M. Lopez-Yunez

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