Cerebral Aneurysms

AB-14125-98


PURPOSE: Our goal was to determine the accuracy of MR angiography at 0.5 T for the diagnosis of intracranial aneurysms.

METHODS: We retrospectively studied 140 patients, 70 with acute subarachnoid hemorrhage, who were either at high or low risk for intracranial aneurysm. Three-dimensional time-of-flight MR angiography was typically performed to cover the circle of Willis, with a volume thickness of 30 mm. Conventional spin-echo MR images and MR angiograms were reviewed together, and the results were compared with those obtained at intraarterial cerebral angiography to determine the sensitivity and specificity of MR angiography.

RESULTS: Eighty-nine aneurysms (size range, 2 to 27 mm; 25 aneurysms \( \leq 5 \) mm) were identified at intraarterial cerebral angiography. Six aneurysms were missed by MR angiography and two were doubtful (sensitivity, 91% to 93%; specificity, 100%). Missed aneurysms were located outside the MR angiographic acquisition volume (n=3) or on the carotid siphon (n=3; size=2, 3, and 5 mm).

CONCLUSION: Even if MR angiography presents some restrictions in acquisition volume and spatial resolution, the detection rate of intracranial aneurysms is excellent at 0.5 T in both asymptomatic patients and in those with subarachnoid hemorrhage. A midfield system is not a restriction to the detection of intracranial aneurysms by MR examination.

AB-14126-98


PURPOSE: Our goal was to evaluate the utility of subtraction three-dimensional CT angiography for the detection of intracranial aneurysms.

METHODS: Thirty-six patients with intracranial aneurysms were examined using newly devised controlled-orbit helical scanning. Three-dimensional CT angiograms and subtraction 3-D CT angiograms were compared with conventional angiograms for their characterization of intracranial aneurysms.

RESULTS: Fifty aneurysms were depicted on conventional angiograms, of which 48 (96%) were seen on the 3-D CT angiograms. Three-dimensional CT angiography was superior or equivalent to conventional angiography for depicting the shape, direction, and location of 33 (66%) of 50 aneurysms; however, it was often less useful than conventional angiography in delineating intracranial aneurysms adjacent to bone. Subtraction 3-D CT angiograms were obtained in 32 patients with a total of 46 aneurysms (in four cases, aneurysms were not depicted owing to excessive motion artifacts), and were superior or equivalent to conventional angiograms in all 46 cases.

CONCLUSIONS: Subtraction 3-D CT angiography with the use of controlled-orbit helical scanning is effective in the detection of intracranial aneurysms.

AB-14127-98


Object: The aim of this study was to determine the prevalence of cerebral saccular aneurysms in patients with carotid artery and/or vertebral artery (VA) fibromuscular dysplasia (FMD).

Methods: A metaanalysis was performed using data from 17 previously reported controlled-orbit scan series included in the metaanalysis; the prevalence of incidental, asymptomatic aneurysms in patients with ICA and/or VA FMD that included information on the prevalence of cerebral aneurysms. In addition, the authors retrospectively evaluated their own series of 117 patients with ICA and/or VA FMD to determine the prevalence of cerebral aneurysms. The metaanalysis of the 17 earlier series, which included 498 patients, showed a 7.6±2.5% prevalence of incidental, asymptomatic aneurysms in patients with ICA and/or VA FMD. The authors' series of patients with FMD, 6.3±4.9% of patients harbored an incidental, asymptomatic aneurysm. When the authors' series was combined with those included in the metaanalysis, the prevalence was found to be 7.3±2.2%. The prevalence of aneurysms in the general population would have to be greater than 5.6% for there to be no statistically significant difference (chi-square test, \( p<0.05 \)) when compared with this 7.3% prevalence in patients with FMD.

Conclusions: The prevalence of intracranial aneurysms in patients with cervical ICA and/or VA FMD is approximately 7%, which is no higher than the 21 to 51% prevalence that has been previously reported.

AB-14128-98


Hemoglobin released from hemolyzed erythrocytes has been postulated to be responsible for delayed cerebral vasospasm after subarachnoid hemorrhage (SAH). However, the evidence is indirect and the mechanisms of action are unclear. Cerebrovascular tone is regulated by a dynamic balance of relaxing and contracting factors. Loss of the endothelium-derived relaxing factor-nitric oxide in the presence of oxyhemoglobin and overproduction of endothelin-1 stimulated by oxyhemoglobin have been postulated as causes of delayed cerebral vasospasm after SAH.

Object: The authors aimed to investigate this hypothesis using in vivo microdialysis to examine time-dependent changes in the perivascular concentrations of oxyhemoglobin, deoxyhemoglobin, and methemoglobin in a primate model of SAH.

Methods: Nine cynomolgus monkeys underwent right-sided frontotemporal craniectomy and placement of a semipermeable microdialysis catheter adjacent to the right middle cerebral artery (MCA). Saline (control group, three animals) or an arterial blood clot (SAH group, six animals) was then placed around the MCA and the catheter. Arteriographically confirmed vasospasm had developed in all animals with SAH but in none of the control animals on Day 7. The dialysate was collected daily for 12 days. Levels of oxyhemoglobin, deoxyhemoglobin, and methemoglobin were measured by means of spectrophotometry.

The abstracts in this section have been typeset for consistency with journal format but otherwise appear as in the original articles.
Perivascular concentrations of oxyhemoglobin, deoxyhemoglobin, and methemoglobin peaked on Day 2 in the control monkeys and could not be detected on Days 5 to 12. Perivascular concentrations of oxyhemoglobin and deoxyhemoglobin peaked on Day 7 in the SAH group, at which time the concentrations in the dialysate were 100-fold higher than in any sample obtained from the control animals. Methemoglobin levels increased only slightly, peaking between Days 7 and 12, at which time the concentration in the dialysate was 10-fold higher than in samples from the control animals.

Conclusions: This study provides in vivo evidence that the concentrations of oxyhemoglobin and deoxyhemoglobin increase in the cerebral subarachnoid perivascular space during the development of delayed cerebral vasospasm. The results support the hypothesis that oxyhemoglobin is involved in the pathogenesis of delayed cerebral vasospasm after SAH and implicated deoxyhemoglobin as a possible vaso spasmod agent.

Clinical

AB-14129-98


Background: Antibodies to cardiolipin and other phospholipids have been associated with recurrent thrombotic events, including stroke.

Methods: Over a 16 month period we assessed an unselected cohort of 151 ischemic stroke patients for the presence of antiphospholipid antibodies. Patients with known systemic lupus erythematosus, systemic sclerosis, or Sjögrens Syndrome were excluded. Sera from patients admitted to hospital with a diagnosis of ischemic stroke (n=151) and from controls (n=111) assessed during the same period were tested for antiphospholipid antibodies (APLA) using 3 assays; anticardiolipin antibodies (ACA) by ELISA, prolonged activated partial thromboplastin time (APTT), and VDRL.

Results: The average age of ischemic stroke cases was 68 years (range 29 to 91) and of controls 63 years (range 29 to 86). The prevalence of APLA detected by at least one of the three methods was 12% for IS cases and 10% for controls. After correcting for known risk factors such as age, gender, diabetes mellitus, heart disease, hypertension, and smoking, the odds ratio for risk of stroke fell to 0.8 (C.I. 0.4 to 1.2).

Conclusions: Our findings suggest that APLA may not be an independent risk factor for ischemic stroke in unselected persons who do not have known systemic lupus erythematosus or systemic sclerosis but further evaluation of the role of lupus anticoagulant is indicated.

AB-14130-98

Comparison of the Three Strategies of Verbal Scoring of the Glasgow Coma Scale in Patients With Stroke—Prasad K (Rm 704, CN Centre, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India), Menon GR—Cerebrovasc Dis. 1998;8:79–85. © 1998 S. Karger AG, Basel.

Presence of aphasia in patients with stroke poses a problem in the use of the full form (eye-motor-verbal) Glasgow Coma Scale (GCS). Stroke investigators and clinicians have used three different strategies to deal with the untestable verbal subscale, i.e. eliminating the verbal subscale, pseudoscorings with ‘one’, and median value substitution; but the predictive accuracy of the strategies has not been compared. To compare the predictive accuracy of the three strategies for acute mortality in stroke, we prospectively applied the GCS to 275 consecutive patients with acute stroke and recorded their survival status before discharge from hospital. 95 (33.8%) patients died. 32 (12%) patients had untestable verbal score. Receiver-Operator-Characteristic curves for predicting mortality were constructed with the GCS sum score and with the multivariate logistic models, and areas under the curves were measured to compare the predictive accuracy. They were all found to be similar (0.87–0.88 sq unit). Specifically, the GCS with eye and motor subscale had 87% accuracy compared to 88% for the model with eye, motor and verbal scale. We conclude that the short-form (eye-motor) GCS is as good a predictor of early mortality (within 2 weeks) as the full form (eye-motor-verbal) GCS in patients with stroke.

AB-14131-98


Background: Several reports suggest that the incidence of stroke and atrial fibrillation is reduced in patients receiving physiologic pacemakers, compared with patients receiving a ventricular pacemaker.

Hypothesis: The study was undertaken to address the impact of different pacing modalities on the incidence of stroke and atrial fibrillation.

Methods: We prospectively analyzed 210 consecutive patients. Those with previous episodes of cerebral ischemia and/or atrial fibrillation were excluded from the study. The study population included 100 patients paced for total atrioventricular (AV) block or second-degree AV block (type II Mobitz) and 110 patients paced for sick sinus syndrome (SSS). The pacing mode was randomized. All patients underwent a brain computed tomography (CT) scan at the date of enrollment and after 1 and 2 years. Patients were followed for 2 years, and the incidence of atrial fibrillation and stroke was evaluated.

Results: The incidence of atrial fibrillation was 10% at 1 year and 11% at 2 years. Comparing the different pacing modalities, we reported an increase in the incidence of atrial fibrillation in patients receiving ventricular pacing (p<0.05). On the other hand, no difference was found between patients paced for AV block and those paced for SSS. At the end of follow-up, we reported 29 cases of cerebral ischemia; 9 patients had AV block while 20 had SSS (p<0.05). Comparing the different pacing modalities, there was an increase in the incidence of stroke in patients receiving ventricular pacing (p<0.05).

Conclusion: There was an increase in the incidence of stroke and atrial fibrillation in patients with ventricular pacing.

AB-14132-98


Context: Warfarin is highly effective in preventing thromboembolism, but increases the risk of hemorrhage, particularly at an international normalized ratio (INR) greater than 4.0. Identifying causes of excessive anticoagulation in clinical practice could help target patients at risk for elevated INRs.

Objective: To determine causes of INRs greater than 6.0 in a clinical practice setting.

Design: Case-control study.

Setting: Outpatient anticoagulant therapy unit.

Patients: Outpatients followed up prospectively from April 1995 to March 1996 who had been taking warfarin for more than 1 month, had a target INR of 2.0 to 3.0, and were able to be interviewed within 24 hours of their reported INR. Case patients had INRs greater than 6.0; controls were randomly selected from patients having INRs between 1.7 and 3.3.

Main Outcome Measures: Factors associated with INRs greater than 6.0, including medication use, recent diet, illness, alcohol consumption, and actual warfarin use.

Results: A total of 93 cases and 196 controls were interviewed; they did not differ in age, indication for warfarin, length of therapy, warfarin dose, number of prescription medications, or previous INR or long-term INR variability. Acetaminophen ingestion was independently associated in a dose-dependent manner with having an INR greater than 6.0 (P for trend <0.01). For the highest-dose category of acetaminophen intake, 9100 mg/wk or more, the odds of having an INR greater than 6.0 were...
increased 10-fold (95% confidence interval [CI], 2.6–37.9). Other factors independently associated with an INR greater than 6.0 were new medication known to potentiate warfarin (odds ratio [OR], 8.5; 95% CI, 2.9–24.7), advanced malignancy (OR, 16.4; 95% CI, 2.4–111.0), recent diarrheal illness (OR, 3.5; 95% CI, 1.4–8.6), decreased oral intake (OR, 3.6; 95% CI, 1.3–9.7), and taking more warfarin than prescribed (OR, 8.1; 95% CI, 2.2–30.0). Higher vitamin K intake (OR, 0.7; 95% CI, 0.5–0.9) and habitual alcohol consumption of 1 drink every other day to 2 drinks a day (OR, 0.2; 95% CI, 0.1–0.7) were associated with decreased risk.

Conclusions—These data suggest that acetaminophen is an underrecognized cause of overanticoagulation in the outpatient setting. Several other clinically important risk factors were identified. Increased monitoring of INR values when such risk factors are present or modification of the risk factors themselves should reduce the frequency of dangerously high levels of anticoagulation.

AB-14133-98

OBJECTIVE: To determine the association between asymptomatic carotid bruits and the development of subsequent stroke in older adults with isolated systolic hypertension.

DESIGN: Retrospective cohort study.

SETTING: The Systolic Hypertension in the Elderly Program (SHEP), a 5-year randomized trial testing the efficacy of treating systolic hypertension with isolated systolic hypertension.

OBJECTIVE: To determine the association between asymptomatic carotid bruits and the development of subsequent stroke in older adults with isolated systolic hypertension.

CONCLUSIONS: Although we cannot rule out a small increased risk of stroke associated with bruits in asymptomatic SHEP enrollees aged 60 to 69 years, there was a trend ($p = 0.08$) toward increased risk (relative risk [RR] 2.05; 95% CI 0.92, 4.68) of subsequent stroke in persons with, compared to those without, carotid bruits. However, among enrollees aged 70 years or over, there was no relation between carotid bruit and subsequent stroke (RR 0.98; 95% CI 0.55, 1.76). In no other subgroup of SHEP enrollees did the presence of carotid bruit independently predict stroke.

AB-14134-98

We investigated the association between cerebral venous thrombosis and hereditary resistance to activated protein C (APC) in 12 consecutive German patients with non-fatal cerebral venous thrombosis and in 187 controls without a history of thrombotic disorder. Three patients (25%) had a mutation in the factor V Leiden gene against only one subject in the control group. This difference was significant ($P < 0.05$), with an odds ratio of 11.7 (1.5–87; 95% confidence interval). Two patients carrying the mutation had additional common risk factors for thrombosis, and 2 had a positive family history of thromboembolism. We conclude that inherited APC resistance by a mutation in factor V Leiden is an important risk factor in non-fatal cerebral venous thrombosis. We recommend testing for APC resistance and, if abnormal for factor V Leiden mutation in patients with cerebral venous thrombosis.

AB-14135-98
IgA Anticardiolipin Antibodies: Relation With Other Antiphospho-

Objective: To evaluate the usefulness of IgA antiphospholipid antibodyodies as markers of thrombosis and/or antiphospholipid antibody syndrome. Patients and Methods: A cross-sectional study design in a tertiary, university-based, autoimmune reference hospital. Seven-hun-
dred ninety-five patients classified into five different groups—autoim-
mune diseases (255), deep vein thrombosis (153), transitory ischemic attacks (108), obstetric complications (196), infectious diseases (83) and controls (81)—were tested for IgA, IgG, and IgM aPL, and lupus anticoagulant. Plasma and serum samples were drawn for detection of aPL using an internationally standardized ELISA method and LA was carried out using coagulometric assays. Results: True IgA aPL were found only in two patients with systemic lupus erythematosus; these patients were also positive to IgG aPL. Conclusion: The incidence of true positivity to IgA antiphospholipid antibodies is extremely low. Their determination was not helpful in diagnosing the antiphospholipid syn-
drome or in explaining thrombotic events or aPL related manifestations—fetal loss—in the groups studied.

Epidemiology

AB-14136-98
Atrial Fibrillation As A Risk Factor For Stroke: A Retrospective Cohort Study of Hospitalized Medicare Beneficiaries—Yuan Z, Bowlin S, Einstadter D, Cebul RD, Conners AR, Rimm AA (Dept of Epidemiology and Biostatistics, School of Medicine, Case Western Reserve University, 10900 Euclid Ave, Cleveland, OH 44106-4945)—Am J Public Health. 1998;88:395–400.

Objective: This study examined the relationship between atrial fibrillation and (1) stroke and (2) all-cause mortality.

Methods: All eligible Medicare patients older than 65 years of age hospitalized in 1985 were followed up for 4 years. Kaplan-Meier and Cox proportional hazards models were used for assessment of risk of stroke and mortality.

Results: A total of 4 282 607 eligible Medicare patients were hospital-
ized in 1985. The mean age was 76.1 (±7.7) years; 58.7% were female; 7.2% were Black; and 8.4% had a diagnosis of atrial fibrillation. During the follow-up period, 66 063 patients (32.6/1000 person-years) developed nonembolic stroke and 7285 (3.6/1000 person-years) developed embolic stroke. After adjustment for age, race, sex, and comorbid conditions, atrial fibrillation remained a significant risk factor for both nonembolic stroke (relative risk [RR] = 1.56) and embolic stroke (RR = 5.80) and for mortality (RR = 1.31). Approximately 4.5% of nonembolic and 28.7% of embolic strokes among hospitalized Medicare patients aged 65 years and older were attributable to atrial fibrillation.

Conclusions: This study demonstrates that atrial fibrillation is asso-
ciated with an appreciable increase in the risk of stroke (both embolic and nonembolic) and in the risk of mortality from all causes.

AB-14137-98
Hyperinsulinaemia and Cardiovascular Disease in Elderly Men: The Honolulu Heart Program—Burchfiel CM (Division of Epidemiology...

Hyperinsulinemia has been associated with cardiovascular disease (CVD), but whether this relation is independent of other CVD risk factors is uncertain. Most studies have focused on coronary heart disease (CHD), but few have included peripheral vascular disease (PVD) and stroke. Moreover, evidence in elderly and minority populations is limited. Between 1991 and 1993, 3562 elderly (71 to 93 years) Japanese-American men from the Honolulu Heart Program were examined and had fasting insulin levels measured. Hyperinsulinemia, defined as a fasting insulin ≥95th percentile among nonobese men with normal glucose tolerance and no diabetic history or medication use, was observed in 22% of the population. Subjects with hyperinsulinemia had a more adverse CVD risk factor profile and had higher age-adjusted prevalences of CHD, angina, PVD, thromboembolic stroke, and hemorrhagic stroke compared with those without hyperinsulinemia. Age-adjusted fasting insulin levels but not 2-hour levels were also significantly elevated (P<0.01) in those with prevalent CVD compared with those without. In logistic regression analyses, adjustment for multiple CVD risk factors attenuated the relations of hyperinsulinemia with CHD, angina, and PVD to nonsignificant levels, whereas those involving thromboembolic and hemorrhagic stroke were strengthened and remained significant (odds ratios=2.27 and 7.53, 95% confidence intervals=1.25 to 4.13 and 1.65 to 34.25, respectively). When multivariate analyses were restricted to nondiabetic subjects, associations were slightly weaker and in general nonsignificant. Nondiabetic men with thromboembolic stroke were twice as likely to have hyperinsulinemia as those who were stroke-free, although this association was of borderline significance (odds ratio=1.99, 95% confidence interval=0.95 to 4.17, P=0.069). In subjects with elevated total cholesterol levels, somewhat stronger associations were observed for PVD and stroke but not for CHD. Although further prospective studies are indicated, particularly for PVD and stroke, these cross-sectional results are consistent with an indirect role for insulin in CVD, wherein hyperinsulinemia or an underlying insulin-resistant state may adversely affect other CVD risk factors or serve as a marker for an atherogenic or thrombogenic state.

AB-14138-98

Background—A high plasma homocysteine concentration is a risk factor for atherosclerosis, and circulating concentrations of homocysteine are related to levels of folate and vitamin B6. This study was performed to explore the interrelationships between homocysteine, B vitamins, and vascular diseases and to evaluate the role of these vitamins as risk factors for atherosclerosis.

Methods—In a multicenter case-control study in Europe, 750 patients with documented vascular disease and 800 control subjects frequency-matched for age and sex were compared. Plasma levels of total homocysteine (before and after methionine loading) were determined, as well as red cell folate, vitamin B12, and vitamin B6. Between 1991 and 1993, 3562 elderly (71 to 93 years) Japanese-American men from the Honolulu Heart Program were examined and had fasting insulin levels measured. Hyperinsulinemia, defined as a fasting insulin ≥95th percentile among nonobese men with normal glucose tolerance and no diabetic history or medication use, was observed in 22% of the population. Subjects with hyperinsulinemia had a more adverse CVD risk factor profile and had higher age-adjusted prevalences of CHD, angina, PVD, thromboembolic stroke, and hemorrhagic stroke compared with those without hyperinsulinemia. Age-adjusted fasting insulin levels but not 2-hour levels were also significantly elevated (P<0.01) in those with prevalent CVD compared with those without. In logistic regression analyses, adjustment for multiple CVD risk factors attenuated the relations of hyperinsulinemia with CHD, angina, and PVD to nonsignificant levels, whereas those involving thromboembolic and hemorrhagic stroke were strengthened and remained significant (odds ratios=2.27 and 7.53, 95% confidence intervals=1.25 to 4.13 and 1.65 to 34.25, respectively). When multivariate analyses were restricted to nondiabetic subjects, associations were slightly weaker and in general nonsignificant. Nondiabetic men with thromboembolic stroke were twice as likely to have hyperinsulinemia as those who were stroke-free, although this association was of borderline significance (odds ratio=1.99, 95% confidence interval=0.95 to 4.17, P=0.069). In subjects with elevated total cholesterol levels, somewhat stronger associations were observed for PVD and stroke but not for CHD. Although further prospective studies are indicated, particularly for PVD and stroke, these cross-sectional results are consistent with an indirect role for insulin in CVD, wherein hyperinsulinemia or an underlying insulin-resistant state may adversely affect other CVD risk factors or serve as a marker for an atherogenic or thrombogenic state.

AB-14139-98
Prevalence, Detection, and Management of Cardiovascular Risk Factors in Different Ethnic Groups in South London—Cappuccio FP (Blood Pressure Unit, Dept of Medicine, St George’s Hospital Medical School, Cranmer Terrace, London SW17 ORE, UK, or email f.cappuccio@sghms.ac.uk), Cook DG, Atkinson RW, Strazzullo P—Heart. 1997;78:555–563.

Objective—To assess the prevalence of cardiovascular risk factors and their level of detection and management in three ethnic groups.


Setting—Former Wandsworth Health Authority in South London.

Subjects—1578 men and women, aged 40 to 59 years; 524 white, 549 of African descent, and 505 of South Asian origin.

Main outcome measures—Age adjusted prevalence of hypertension, diabetes, obesity, raised serum cholesterol, and smoking

Results—Ethnic minorities of both sexes had raised prevalence rates of hypertension and diabetes compared to white people. Age and sex standardised prevalence ratios for hypertension were 2.6 (95% confidence interval 2.1 to 3.2) in people of African descent and 1.8 (1.4 to 2.3) in those of South Asian origin. For diabetes, the ratios were 2.7 (1.8 to 4.0) in people of African descent and 3.8 (2.6 to 5.6) in those of South Asian origin. Hypertension and diabetes were equally common among Caribbeans and West Africans and among South Asian Hindus and Muslims. Prevalence of severe obesity was high overall, but particularly among women of African descent (40% (35% to 45%)). In contrast, raised serum cholesterol and smoking rates were higher among white people. Of hypertensives, 49% (216 of 442) had adequate blood pressure control. Overall, 18% (80 of 442) of hypertensives and 33% (62 of 188) of diabetics were undetected before our survey. Hypertensive subjects of African descent appeared more likely to have been detected (p=0.034) but less likely to be adequately managed (p=0.085).

Conclusions—Hypertension and diabetes are raised two- to threefold in South Asians, Caribbeans, and West Africans in Britain. Detection, management, and control of hypertension has improved, but there are still differences between ethnic groups. Obesity is above the Health of the Nation targets in all ethnic groups, particularly in women of African descent. Preventive and treatment strategies for different ethnic groups in Britain need to consider both cultural differences and underlying susceptibility to different vascular diseases.

Experimental Pathology

AB-14140-98

Objectives—To study whether nitric oxide (NO) affects the CBF response to hypoxia and carbon monoxide (CO) hypoxia. Material and methods—We incrementally reduced arterial oxygen content in rats, by decreasing the concentration of inspired oxygen (20 rats) or by repeated CO inhalation (20 rats), and measured local CBF using the hydrogen clearance method. Ten animals of each group received 80 mg/kg NO synthase (NOS) inhibitor N-nonomethyl-L-arginine intravenously prior to hypoxia, while 10 rats served as controls. Results—Inhibition of NOS decreased mean CBF by 30% and increased cerebrovascular resistance by 70%. Under hypoxic hypoxia, mean oxygen reactivity of CBF
(relative change of CBF to a change of arterial oxygen content) was 7.8% / vol% in control animals and 3.3% / vol% after NOS inhibition ($P < 0.02$). Under CO hypoxia, mean oxygen reactivity was 7.3% / vol% in control animals and 5.1% / vol% after NOS inhibition ($P < 0.05$). Inhibition of NOS diminished significantly the cerebral vasodilatory response during hypoxic hypoxia ($P < 0.05$) but only to a lesser extent during CO hypoxia. Conclusion—These observations suggest that NO is involved in cerebral oxygen vasoreactivity, particularly in severe hypoxia.

**AB-1441-98**


Elevated plasma homocysteine is an established risk factor for vascular disease although the mechanisms are unclear. Homocysteine has been reported to stimulate DNA synthesis and proliferation in rat aortic smooth muscle cells. Human vascular smooth muscle cells (HVSMC) from saphenous veins (n = 8), internal mammary arteries (n = 6) and umbilical arteries (n = 2) were studied. To reflect DNA synthesis, 3H-thymidine incorporation, during 24 h exposure to homocysteine in concentrations from 0.0625 to 10 mM, was studied. Incorporation was significantly increased up to 0.5 or 1 mM and thence was progressively higher. The incorporation fell to approximately 25% of the control values at 10 mM ($P < 0.005$). Qualitatively similar results were obtained in umbilical arteries. Homocysteine had a biphasic effect on DNA synthesis in cultured HVSMC but the higher inhibitory concentrations are well above the levels reported to stimulate DNA synthesis and proliferation in rat aortic smooth muscle cells. Human vascular smooth muscle cells (HVSMC) from saphenous veins (n = 8), internal mammary arteries (n = 6) and umbilical arteries (n = 2) were studied. To reflect DNA synthesis, 3H-thymidine incorporation, during 24 h exposure to homocysteine in concentrations from 0.0625 to 10 mM, was studied. Incorporation was significantly increased up to 0.5 or 1 mM and thence was progressively depressed, the maximum stimulation being 24 ± 5 (S.E.% in vein ($P < 0.005$) and 34 ± 4% in mammary artery ($P < 0.001$)) while incorporation fell to approximately 25% of the control values at 10 mM ($P < 0.001$). Qualitatively similar results were obtained in umbilical arteries. Homocysteine had a biphasic effect on DNA synthesis in cultured HVSMC but the higher inhibitory concentrations are well above those commonly found in vivo. While the conditions of exposure to homocysteine render close analogy to the clinical situation impossible, homocysteine can stimulate HVSMC, offering one possible mechanism for the involvement of homocysteine in the pathogenesis of atherosclerosis.

**AB-14142-98**


**OBJECTIVE:** To characterize changes in regional blood flow (rCBF) during and after a period of arterial occlusion and determine the effect on rCBF and on the extent of infarction when the mean arterial blood pressure is increased during the period of occlusion.

**METHODS:** rCBF in the middle cerebral artery (MCA) territory of rabbits was monitored using laser Doppler perfusion imaging before, during, and after a 1- or 2-hour period of MCA occlusion, and the size of the infarction was assessed by 2,3,5-triphenyltetrazolamine chloride staining after 2 hours of reperfusion. Test animals, the mean arterial blood pressure of which was increased by 65 mm Hg with intravenous phenylephrine during the ischemia, were compared with control animals that remained normotensive. The laser Doppler perfusion imager (Lica Developments Co., Linköping, Sweden) scanned a 3-cm² area of cortex with a resolution of 4 mm² every 15 minutes.

**RESULTS:** MCA occlusion reduced rCBF to 71 ± 2% of the control level ($n = 24$, $P < 0.001$). Hypertension (HTN) restored rCBF to 84 ± 3% of the control level ($n = 12$, $P < 0.01$), but the HTN-induced improvement diminished with time, so that after 1 hour, there was no longer a significant difference between hypertensive and normotensive animals. HTN during the MCA occlusion caused a 97% reduction in infarct size ($P < 0.05$) in the animals subjected to 1 hour of occlusion but caused only a 45% reduction ($P = 0.1$) in the animals subjected to 2 hours of occlusion.

**AB-14143-98**


The antiphospholipid syndrome (APS) is characterised by both arterial and venous thrombosis, recurrent pregnancy loss and thrombocytopenia in association with antiphospholipid antibodies (aPL). To explore further the pathogenesis of thrombosis in APS, we evaluated the behaviour of tissue factor (TF) pathway in patients with APS. Plasma antigen levels of soluble TF and tissue factor pathway inhibitor (TFPI), a physiological regulator of TF dependent coagulation activation, were measured in 57 APS patients (36 primary and 21 secondary to systemic lupus erythematosus). Significantly elevated levels of both TF and TFPI were found in APS patients compared with 25 healthy controls (27.9 ± 15 vs. 217 ± 17 pg/ml, $p = 0.01$; 56.2 ± 2.0 vs. 47.9 ± 2.2 ng/ml, $p = 0.01$, respectively), suggesting in vivo upregulation of TF pathway in patients with APS. By flow-cytometry, monocytes from a healthy donor displayed higher TF antigen expression when incubated in the presence of APS plasmas than in control plasmas (24.2 ± 3.11 vs. 12.7 ± 1.57%, $p = 0.002$). Peripheral blood mononuclear cells (PBMC) also expressed more procoagulant activity (PCA) when incubated in the presence of APS plasmas than in control plasmas (1.80 ± 0.12 vs. 1.35 ± 0.054, $p = 0.001$) implying that TF up-regulation in APS was reproducible in vitro. Human monoclonal anticardiolipin antibodies induced PCA on PBMC and also TF mRNA on both PBMC and human umbilical vein endothelial cells shown by reverse-transcription polymerase chain reaction. These data strongly suggest that the TF pathway is implicated in the pathogenesis of aPL related thrombosis.

**AB-14144-98**


**Purpose:** This study examines the long-term clinical outcome and the incidence of recurrent stenosis (≥50%) after carotid endarterectomy (CEA) with primary closure (PC) versus vein patch closure (VPC), saphenous (SVP), and jugular vein (JVP) and polytetrafluoroethylene patch closure (PTFE-P).

**Methods:** A total of 399 CEAs were randomized into the following groups: 135 PC, 134 PTFE-P, and 130 VPC (SVP alternating with JVP). A total of 399 CEAs were randomized into the following groups: 135 PC, 134 PTFE-P, and 130 VPC (SVP alternating with JVP). Postoperative duplex ultrasound scans were performed at 1, 6, and 12 months and every year thereafter. The mean follow-up was 30 months with a range of 1 to 62 months, and demographic characteristics were similar in all groups. Kaplan-Meier analysis was used to estimate the risk of restenosis and the stroke-free survival.

**Results:** The incidence of ipsilateral stroke was 5% (seven of 135) for PC, 1% (one of 134) for PTFE-P, and 0% for VPC (PC vs VPC, $p = 0.008$; PC vs PTFE-P, $p = 0.034$). Seven strokes occurred in the perioperative period. All three groups had similar mortality rates. The cumulative stroke-free survival rate at 48 months was 82% for PC, 84% for PTFE-P, and 88% for VPC ($p < 0.01$; PC vs PTFE-P or VPC). PC had a higher incidence of recurrent stenosis and occlusion (34%) than PTFE-P (2%) and VPC (9%) (SVP 9%, JVP 8%) ($p < 0.001$). PTFE-P had a lower recurrent stenosis rate than VPC ($p < 0.045$). Restenoses necessitating a redo CEA were also higher for PC (11%) than for PTFE-P.
(1%) and VPC (2%) (p<0.001). Women with PC had a higher recurrent stenosis rate than men (46% vs 23%, p=0.008). Kaplan-Meier analysis showed that freedom from recurrent stenosis at 48 months was 47% for PC, 84% for VPC, and 96% for PTFE-P (p<0.001). The SVP and JVP results were comparable. The mean operative diameter of the internal carotid artery was similar in patients with or without restenosis. Significantly more late internal carotid artery dilations occurred in the VPC group compared with the PC group.

Conclusions: Patch closure (VPC or PTFE-P) is less likely than PC to cause perioperative stroke. Patching was also superior in lowering the incidence of late recurrent stenoses, especially in women.

AB-14145-98

OBJECTIVE: To identify clinical and angiographic factors of cerebral arteriovenous malformations (AVMs) associated with hemorrhage to improve the estimation of the risks and help guide management in clinical decision making.

METHODS: We conducted a retrospective analysis of 100 consecutive adults who have presented during the past 3 years to our institution with cerebral AVMs. Angiographic and clinical parameters were evaluated using multivariate logistic regression analysis to analyze factors associated with hemorrhagic presentation.

RESULTS: The group had a mean age of 37.8 years; 53% were men, 48% presented with intracranial hemorrhage, and 40% presented with seizures. All 10 patients with cerebellar AVMs presented with hemorrhage. The following factors were independently associated with AVM hemorrhage: history of hypertension (P=0.019; odds ratio [OR]=5.36), nidal diameter <3 cm (P=0.023; OR=4.60), and deep venous drainage (P=0.009; OR=5.77). Dural arterial supply (P=0.008; OR=0.15) was independently associated with decreased risk of bleed. Location, nidal aneurysms, patient age, and smoking were not associated with increased or decreased bleeding risk.

CONCLUSION: In this study, we found small AVM size and deep venous drainage to be positively associated with AVM hemorrhage. Dural supply was associated with a decreased likelihood of hemorrhagic presentation. Hypertension was found to be the only clinical factor positively associated with hemorrhage, a finding not previously reported. Smoking, although associated with increased risk of aneurysmal subarachnoid hemorrhage, was not associated with a higher risk of AVM hemorrhage.

Imaging

AB-14145-98

PURPOSE: Our goal was to describe the prevalence and types of cerebral vascular malformations (CVMs) seen with MR imaging in patients with hereditary hemorrhagic telangiectasia (HHT).

METHODS: We reviewed retrospectively the brain MR images of 184 consecutive patients with HHT. Catheter angiography was performed in 17 patients with CVMs detected on MR images.

RESULTS: MR imaging revealed 63 CVMs in 42 patients. Classic arteriovenous malformation (n=10) had a conspicuous network of vessels with flow voids and enlarged adjacent pial vessels. Apparent venous malformations (n=5) were best seen after administration of contrast material as a prominent vessel coursing through normal brain parenchyma. Indeterminate vascular malformations (n=48) had a spectrum of appearances characterized by variable combinations of heterogeneous signal intensity, enhancement, or hemosiderin. Angiography in 17 patients revealed 47 CVMs. Forty-six were arteriovenous malformations (AVMs), including 25 CVMs not seen with MR imaging and 21 CVMs that by MR criteria included 8 AVMs and 13 indeterminate vascular malformations. Angiography confirmed 1 venous malformation seen with MR imaging but failed to detect 3 indeterminate lesions revealed by MR imaging.

CONCLUSION: MR imaging of a large cohort of consecutive patients with HHT revealed a CVM prevalence of 23% (42/184). Most CVMs (48/63) have an atypical appearance for vascular malformations on MR images. Angiographic correlation suggests that MR imaging underestimates the prevalence of CVMs and that the majority of indeterminate CVMs, despite their variable MR appearance, are AVMs.

AB-14146-98

PURPOSE: The purpose of this study was to assess the value of three-dimensional fast imaging with steady-state precession (FISP) MR sequences relative to contrast-enhanced CT and spin-echo MR imaging in the diagnosis of carotid cavernous fistula (CCF).

METHODS: Seventeen patients with 19 angiographically proved CCFs had contrast-enhanced CT, spin-echo MR imaging, and 3-D FISP imaging. Three observers assessed these imaging studies as well as those of 43 control sides in a blinded manner for the presence or absence of CCF. Receiver operating characteristic analysis was used to assess the diagnostic utility of each imaging technique. In a nonblinded study, contrast-enhanced 3-D FISP images were also evaluated.

RESULTS: Higher diagnostic accuracy was obtained with 3-D FISP sequences, as the shunt flow within the cavernous sinus was well seen. Sensitivity of 3-D FISP images was 83% and specificity was 100% in the blinded study. In the receiver operating characteristic analysis, the diagnostic performance of observers was found to be better with the 3-D FISP images than with the spin-echo MR images. Although there were no significant differences between 3-D FISP and contrast-enhanced CT, higher diagnostic performance was obtained with 3-D FISP images. In three CCFs without anterior drainage, a diagnosis was made only from the 3-D FISP images. The contrast-enhanced 3-D FISP images were not helpful, since the cavernous sinuses enhanced.

CONCLUSION: Three-dimensional FISP imaging is superior to spin-echo MR imaging and contrast-enhanced CT in the diagnosis of CCF. Contrast-enhanced 3-D FISP images are not helpful for the evaluation of CCF.

AB-14147-98

PURPOSE: Our objective was to determine whether a multisection technique, diffusion-weighted half-Fourier single-shot turbo spin-echo (HASTE) imaging, can compensate for the drawbacks common to other diffusion-weighted techniques; specifically, the need for echo-planar technology and the presence of susceptibility artifacts in areas close to the skull base.

METHODS: Forty subjects who were referred to the stroke service with signs of acute (less than 24 hour) neurologic dysfunction were included in this prospective study. MR imaging of the brain was...
performed with diffusion-weighted echo-planar and diffusion-weighted HASTE sequences. The images obtained with both sequences were analyzed for the presence of hyperintensities corresponding to ischemic lesions as well as for the presence of image artifacts and distortions.

RESULTS: Diffusion-weighted HASTE images showed areas of hyperintensity corresponding to the infarcts present on diffusion-weighted echo-planar imaging studies without distortion or susceptibility artifacts in all the patients who had a stroke. Twelve patients had no acute ischemic lesions; of these, five had other findings, six had normal findings, and in one patient, a hyperintensity seen on diffusion-weighted echo-planar images proved to be an artifact on diffusion-weighted HASTE images.

CONCLUSIONS: Diffusion-weighted echo-planar imaging in the detection of early ischemia. Because of the absence of significant image distortions and other artifacts, diffusion-weighted HASTE permits fast multiplanar imaging in artifact-prone regions, such as the posterior fossa and the inferior frontal and temporal lobes. Diffusion imaging can be performed on conventional systems with strengths of 1.5 T that do not have echo-planar imaging capabilities.

AB-14148-98
Magnetic Resonance Angiography in Patients With Brain Infarction: Qureshi AI (Division of Neurosciences Critical Care, The Johns Hopkins Hospital, Meyer 8-140, 600 N Wolfe St, Baltimore, MD 21287-7840), Isa A, Cinnamon J, Fountain J, Ottenlips JR, Brainah J, Frankel MR—J Neuroimag. 1998;8:65–70. Copyright © 1998 by the American Society of Neuroimaging. This study evaluated the role of magnetic resonance angiography (MRA) in detecting extra- or intracranial vascular disease in 118 patients with brain infarction and the accuracy of MRA diagnosis when compared with conventional angiography in patients who had both investigations. Magnetic resonance angiography ruled out extra- and intracranial large vessel disease in 36% of the patients. MRA also demonstrated extra- or intracranial disease in 56% (probably asymptomatic in 31, possibly symptomatic in 18, and asymptomatic in 17 patients), and provided no information in 8% of the 118 patients. Among the 176 major vessels visualized by both MRA and conventional angiography confirmed the presence of 9/10 extracranial and 32/40 intracranial large vessel abnormalities detected on MRA. There were two false-negative findings on MRA: occlusion of a distal branch of middle cerebral artery, and an asymptomatic posterior cerebral artery stenosis. Magnetic resonance angiography is a clinically useful method for screening extra- and intracranial disease in patients with brain infarction and selecting high-yield patients for conventional angiography.

AB-14149-98
Distinguishing Silent Lacunar Infarction From Enlarged Virchow-Robin Spaces: A Magnetic Resonance Imaging and Pathological Study: Bokura H (Dept of Internal Medicine III, Shimane Medical University, 89-1 Enay-cho Izumo, 693 Japan), Kobayashi S, Yamaguchi S—J Neuroil. 1998;245:116–122. © Springer-Verlag 1998. We studied clinicopathological correlations between magnetic resonance imaging (MRI) appearances of postmortem brains and pathological findings in 12 patients to identify simple criteria with which to distinguish lacunar infarctions from enlarged Virchow-Robin spaces. In vivo MRI was also available for 6 of the 12 patients. We focused on small, silent, focal lesions including lacunar infarctions and enlarged Virchow-Robin spaces that were confirmed pathologically. From a total of 114 lesions, enlarged Virchow-Robin spaces were most often found in the basal ganglia and had a round or linear shape. Lacunar infarctions also were most frequent in the basal ganglia, but 47% of these were wedge-shaped. In the pathological studies, excluding lesions from the lower basal ganglia region, enlarged Virchow-Robin spaces were usually smaller than 2×1 mm. The shapes and sizes of the lesions detected by MRI (in vivo and post-mortem) concurred with the pathological findings, except that on MRI the lesions appeared to be about 1 mm larger than found in the pathological study. When lesions from the lower basal ganglia and the brain stem regions are excluded, the sensitivity and specificity for discriminating enlarged Virchow-Robin spaces from lacunar infarctions are optimal when their size is 2×1 mm or less in the pathological study (79%/75%, respectively), 2×2 mm or less in both of the MRI studies: postmortem (81%/90%), and in vivo (86%/91%). In conclusion, we were able to differentiate most lacunar infarctions from enlarged Virchow-Robin spaces on MRI on the basis of their location, shape and size. We stress that size is the most important factor used to discriminate these lesions on MRI.

Neurosonology

AB-14150-98
Frequency and Determinants of Microembolic Signals on Transcranial Doppler in Unselected Patients With Acute Carotid Territory Ischemia: Koennecke HC (Neurologische Abteilung, Universitätsklinikum Benjamin Franklin, Hindenburgdamm 30, D-12200 Berlin, Germany), Mast H, Trocio SH Jr, Sacco RL, Ma W, Mohr JP, Thompson JLP—Cerebrovasc Dis. 1998;8:107–112. © 1998 S. Karger AG, Basel. Background and Purpose: Few data exist regarding to the occurrence of microembolic high-intensity transient signals (HITS) on transcranial Doppler ultrasound (TCD) in unselected acute stroke patients. The aim of this study was to investigate prospectively the frequency and determinants of HITS in acute carotid territory ischemia. We hypothesized that carotid artery disease, cardiac abnormalities, and nonlacunar infarcts were independent predictors of HITS in acute stroke. Methods: We investigated 145 consecutive patients with acute internal carotid artery territory ischemia. The median interval time between stroke and TCD examination was 2 days. TCD monitoring was performed for 30 min on each middle cerebral artery. The frequency of HITS was class-cross-classified with carotid artery status, potential cardiac sources of embolism, and nonlacunar infarct subtype. Multivariate logistic regression models determined the independent relationship of these variables to HITS. Results: Microembolic signals were detected in 35 patients (24.1%). Ipsilateral carotid artery disease was significantly and independently associated with HITS (odds ratio 3.3, 95% confidence interval 1.4–7.8, p=0.007), whereas potential cardiac sources (OR 1.07, 95% CI 0.48–2.4, p=0.84) and infarct subtype (OR 0.84, 95% CI 0.29–2.4, p=0.75) were not. Conclusions: High-intensity transient signals can be found in almost 25% of patients with acute anterior cerebral circulation ischemia and are significantly more prevalent among those with symptomatic carotid artery disease. Future clinical studies are required to determine whether HITS are a marker of increased stroke recurrence and can help to clarify stroke etiology in patients with competing stroke mechanisms.

AB-14151-98
Emboli Detection During Continuous-Wave Doppler Sonography of Internal Carotid Artery Stenosis: Klotzsch C (Dept of Neurology, Rheinisch-Westfälische Technische Hochschule, Pauwelsstr 30, 52057 Aachen, Germany), Popescu O—J Stroke Cerebrovasc Dis. 1998;7:109–112. Copyright © 1998 by National Stroke Association. Background and Purpose: Continuous-wave (cw)-Doppler sonography is a well-established noninvasive method for examining the extracranial vessels. It is extremely rare for an acute ischemic event to occur during cw-Doppler sonography of carotid stenosis. However, no data are available concerning the influence of mechanical stress connected with this procedure on the emboli rate distal to the stenosis. Methods: The study involved 46 patients (28 men, 18 women) aged 66±10 years with an unilateral moderate (n=10) or severe (n=36) stenosis of the internal carotid artery (ICA). Twenty patients had a symptomatic stenosis and the remaining 26 were asymptomatic. Patients with other embolic sources, such as atrial fibrillation or mechanical heart valves, were excluded. All patients underwent bilateral emboli detection of the middle cerebral artery for a period of 29±8 minutes. In a second step, emboli detection (5±1 minutes) was performed simultaneously with cw-Doppler sonography.
raphy of the carotid stenosis. Results: Seven of 46 patients (15%) had a median emboli rate of 5 emboli per hour distal to the carotid stenosis before the procedure. During cw-Doppler sonography of the carotid stenosis, 6 patients (13%) had a median emboli rate of 14 emboli per hour without clinical symptoms of cerebral ischemia. One patient had no change of the emboli rate and 2 patients showed a nonsignificant increase in emboli rate during cw-Doppler sonography. Three patients had no emboli before cw-Doppler sonography, but between 12 and 15 emboli per hour during the extracranial examination (P<.001). Conclusions: It must be presumed that patients with severe stenoses of the ICA represent a subgroup with fragile atheromatous plaques, which are more vulnerable to mechanical stress. The observations support the hypothesis that mechanical stress associated with routine ultrasound examinations of carotid stenosis may, in rare cases, evoke asymptomatic artery-to-artery embolism.

Pharmacology and Therapeutics

AB-14152-98

Patients with acute hemispheric stroke and ensuing urinary incontinence were randomly allocated to a ward using conventional methods of rehabilitation (n=13) or to a ward practicing rehabilitation governed by Functional Independence Measure (FIM) (n=21). All patients were assessed on admission and on discharge using the Katz activities of daily living (ADL) index, the psychological general well-being index, item G of the FIM index (FIM-G), and a mobility score. Patients admitted to the ward utilizing FIM were additionally evaluated using the total FIM on admission, repeatedly during the rehabilitation period and on discharge. An individual rehabilitation programme based on the latest FIM score was used throughout rehabilitation.

There were no differences on admission between groups regarding clinical and demographic characteristics, ADL, mobility and mood. Twenty patients in the intervention group regained continence before discharge compared to 3 (p<0.01) in the control group. There was also a greater improvement in well-being in the intervention group compared to the control group (p<0.01). This study has indicated that rehabilitation governed by the use of FIM reduced urinary incontinence and enhanced well-being better than conventional methods of rehabilitation. The results warrant a larger study to further investigate rehabilitation of incontinent stroke patients using FIM.

Items of Interest


Role of Infection as a Risk Factor for Atherosclerosis, Myocardial Infarction, and Stroke: Mattila KJ (Bayer Finland, Suomalaisentie 7, 02270 Espoo, Finland), Valtosen VV, Nämänen MS, Asikainen S—CID. 1998;26:719–734. © 1998 by the University of Chicago.


Abstracts of Literature
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