Cerebral Aneurysms

AB-14558-00

OBJECT: This study was undertaken to evaluate the long-term angiographic outcome of surgically treated aneurysms, which is unknown. Specifically, the incidence of recurrent aneurysms, the fate of residual necks, and the de novo formation of aneurysms were evaluated.

METHODS: One hundred two patients (80 females and 22 males; mean age 49 years; range 12–78 years) harboring a total of 167 aneurysms underwent late follow-up angiography; 160 aneurysms were surgically treated. Late angiographic follow-up review was obtained at a mean of 4.4±1.6 years postsurgery (range 2.6–9.7 years). Late follow-up angiography revealed two recurrent aneurysms (1.9%) of 135 clipped aneurysms without residua. Of 12 aneurysms with known residua, there were eight “dog-ear” residua, of which two (25%) enlarged. One hemorrhage was noted, yielding a hemorrhage risk of 1.9% per year. A second subgroup with broad-based residua revealed dramatic regrowth in three of four cases. Eight de novo aneurysms were found in six patients, for an annual risk of 1.8% per year. A history of multiple aneurysms was associated with de novo aneurysm formation (p=0.049, chi-square analysis). CONCLUSIONS: This study confirms the long-term efficacy of aneurysm clip ligation. In addition, the authors found there is a small but significant risk of de novo aneurysm formation, particularly in patients with multiple aneurysms. Most residual aneurysm rests appear to remain stable, although a subset may enlarge or rupture. These findings support the rationale for late angiographic follow-up review in patients with aneurysms.

AB-14559-00

OBJECT: This study was conducted to define neuropsychological changes following operation for subarachnoid hemorrhage (SAH) caused by rupture of an anterior communicating artery (ACoA) aneurysm and to assess the influence of the timing of surgery to clip the aneurysm.

METHODS: Cognitive outcome was evaluated using the Cambridge Neuropsychological Test Automated Battery in patients with an ACoA aneurysm that had caused an SAH. Adult patients younger than 70 years of age who had achieved a favorable neurological outcome (Glasgow Outcome Scale scores of 4 or 5) were studied 24 months postsurgery. Patients were divided into early (Days 0–3) and late surgery groups (after Day 3) according to the timing of surgery after the ictus. Neuropsychological analysis was performed by reviewers who were blinded to the timing of surgery. Forty-seven patients whose mean age was 51.5 years were tested. They were compared with age- and intelligence quotient (IQ)-matched controls by using premorbid IQ as estimated on the National Adult Reading Test. Patients showed deficiencies in several tasks of verbal fluency, pattern recognition, and spatial working memory; this profile of deficits was similar to that seen in patients who underwent temporal lobe excisions. However, there was no significant difference in cognitive performance between the early and late surgery groups.

CONCLUSIONS: After open surgery for ruptured ACoA aneurysms, patients who have achieved a favorable neurological outcome still exhibit significant cognitive deficits, primarily in tests sensitive to temporal lobe dysfunction. However, early surgery does not carry a higher risk of neuropsychological disability.

AB-14560-00

OBJECT: The authors confirm the usefulness of extravasation detected on three-dimensional computerized tomography (3D-CT) angiography in the diagnosis of continued hemorrhage and establishment of its cause in patients with acute intracerebral hemorrhage (ICH). METHODS: Thirty-one patients with acute ICH in whom noncontrast and 3D-CT angiography had been performed within 12 hours of the onset of hemorrhage and in whom conventional cerebral angiographic studies were obtained during the chronic stage were prospectively studied. Noncontrast CT scanning was repeated within 24 hours of the onset of ICH to evaluate hematoma enlargement. Findings indicating extravasation on 3D-CT angiography, including any abnormal area of high density on helical CT scanning, were observed in five patients; three of these demonstrated hematoma enlargement on follow-up CT studies. Thus, specificity was 60% (three correct predictions among five positives) and sensitivity was 100% (19 correct predictions among 19 negatives). Evidence of extravasation on 3D-CT angiography indicates that there is persistent hemorrhage and correlates with enlargement of the hematoma. Regarding the cause of hemorrhage, five cerebral aneurysms were visualized in four patients, and two diagnoses of moyamoya disease and one of unilateral moyamoya phenomenon were made with the aid of 3D-CT angiography. Emergency surgery was performed without conventional angiography in one patient who had an aneurysm, and it was clipped successfully.

CONCLUSIONS: Overall, 3D-CT angiography was found to be valuable in the diagnosis of the cause of hemorrhage and in the detection of persistent hemorrhage in patients with acute ICH.

AB-14561-00
Results of Early Surgical Evacuation of Packed Intraventricular Hemorrhage From Aneurysm Rupture in Patients With Poor-Grade Subarachnoid Hemorrhage—Shimoda M (Dept of Neurosurgery, Tokai Univ School of Medicine, Kanagawa 2591193, Japan), Oda S, Shibata M, Tominaga J, Kittaka M, Tsugane R—J Neurosurg. 1999;91:408–414.

OBJECT: The goal of this study was to evaluate the results of early surgical evacuation of “packed” intraventricular hemorrhage (IVH) in patients with poor-grade subarachnoid hemorrhage (SAH). METHODS: The authors performed surgery within 24 hours after onset of SAH, identified on neuroimaging as a cast distending the ventricular system, in 74 patients with poor-grade SAH (World Federation of Neurosurgical Societies Grades IV and V) without intracerebral hemorrhage. Eighteen of these patients had packed IVH; in these patients the intraventricular clots were extensively evacuated via frontotemporal corticotomy performed under microscopic view. CONCLUSIONS: Overall, 42% of the 74 patients undergoing craniotomy in the acute stage had favorable outcomes, whereas 30% died. Using multivariate analysis, variables significantly associated with favorable outcome in patients with poor-grade SAH included absence of a packed intraventricular clot on computerized tomography scanning; absence of a history of cardiac disease; and a Glasgow Coma Scale score of 11 or 12. None of the 18 patients who had
packed IVH had favorable outcomes and seven of these died. In six recently treated patients with packed IVH, which was examined using fluid-attenuated inversion recovery imaging, extensive periventricular brain damage was found both immediately after surgery and during the chronic stage. Accordingly, the authors believe that irreversible periventricular brain damage is already complete immediately after packed IVH occurs.

AB-14562-00

OBJECTIVE: Balloon-assisted technique is a promising technical adjunct to use of Guglielmi detachable coils for embolization of wide-necked aneurysms. In this study using experimental aneurysms in swine, the safety and long-term efficacy of this technique were evaluated.

METHODS: Sixteen wide-necked aneurysms (sidewall model) were surgically created in common carotid arteries of swine. In the acute study of eight aneurysms, intra-aneurysmal pressure changes were recorded during balloon inflation in different positions of the balloon relative to the neck of the aneurysm. In the chronic study, eight aneurysms were treated with this technique, and follow-up angiography was performed 14 days postembolization. The animals were then killed for macroscopic evaluation.

RESULTS: In the acute study, the systolic intra-aneurysmal blood pressure increased with balloon inflation at the distal portion of the neck and with balloon inflation/occlusion across the entire neck of the aneurysm. In the chronic study, seven of eight cases were embozized with satisfactory occlusion, and six showed no coil displacement on the follow-up angiogram. In five cases, macroscopic evaluation of the aneurysm showed that the coils were compacted at the neck of the aneurysm with a concave shape consistent with the shape of the inflated balloon across its neck.

CONCLUSION: This preliminary study indicates that balloon-assisted Guglielmi detachable coiling technique may produce a temporary increase of pressure within the aneurysm while occluding the aneurysmal neck during coil delivery. This sudden change of intra-aneurysmal pressure may potentially be the cause of aneurysm rupture in the clinical setting. The balloon must be inflated and deflated very slowly to minimize these potentially risky hemodynamic changes. Although angiographic follow-up showed successful obliteration of aneurysms, further long-term angiographic studies are necessary to establish the durability of this technique.

Clinical

AB-14563-00

BACKGROUND: Several markers of hemostatic function and inflammation have been associated with increased risk of coronary heart disease, but prospective evidence for their role in ischemic stroke is scant. METHODS AND RESULTS: The Atherosclerosis Risk in Communities (ARIC) Study measured several of these markers in more than 14 700 participants 45 to 64 years old who were free of cardiovascular disease and were followed up for 6 to 9 years for occurrence of ischemic stroke (n=191). There was no apparent association between ischemic stroke incidence and factor VIIc, antithrombin III, platelet count, or activated partial thromboplastin time. After adjustment for multiple cardiovascular risk factors, von Willebrand factor, factor VIIIc, fibrinogen, and white blood cell count were positively associated and protein C was negatively but nonsignificantly associated with ischemic stroke incidence in regression analyses based on either continuous variables or fourths of the variable distributions. The adjusted relative risk (and 95% CI) for ischemic stroke in those in the highest versus lowest fourth were: von Willebrand factor, 1.71 (1.1 to 2.7); factor VIIIc, 1.93 (1.2 to 3.1); white blood cell count, 1.50 (0.9 to 2.4); fibrinogen, 1.26 (0.8 to 2.0); and protein C, 0.65 (0.4 to 1.0). CONCLUSIONS: This study offers modest support for the hypothesis that some markers of hemostatic function and inflammation can identify groups of middle-aged adults at increased risk of stroke. These factors may play a role in the pathogenesis of ischemic stroke.

AB-14564-00

We aimed to study in-hospital mortality after a first-ever stroke (brain infarction or parenchymatous hemorrhage) and to determine its predictors using easily obtainable variables. The main outcome measure was vital status at hospital discharge. Clinical features and type of stroke, with a particular emphasis on age, stroke topography and presumed causes of stroke, were studied in 3362 consecutive patients from the Lausanne Stroke Registry. Overall mortality was 4.8%. Brain hemorrhage mortality was 14.4% (48/333) and brain infarction mortality was 3.70% (112/3029). Localizations with high mortality included infratentorial (17.5%) and deep hemispheric (15.9%) territories for brain hemorrhage and, for brain infarction, multiple localizations in the posterior circulation (18.4%) and large middle cerebral artery territory (15.5%). Presumed causes of stroke associated with high mortality included saccular aneurysm (58.3%) and hypertensive arteriopathy (13.0%) for brain hemorrhage and, for brain infarction, dissection (10.4%), arteritis (8.3%), hematologic conditions (6.7%) and coexisting arterial and cardiac sources of embolism (5.2%). Multivariate logistic analysis showed that impaired consciousness on admission and limb weakness were good predictors of mortality for brain hemorrhage, while impaired consciousness and the cumulative effect of progressive worsening, limb weakness, left ventricular hypertrophy, past history of cardiac arrhythmia and previous transient ischemic attack were predictors of mortality for brain infarction. Age was not an independent predictor of stroke mortality, but for brain infarction the number of cumulative factors considered in the model increased with age. Our study shows that several factors associated with death risk are available during the first few hours after onset of stroke. Age alone is not critical, although its interaction with other factors should be considered.

AB-14565-00

BACKGROUND: Previous studies link posterior border-zone cerebral infarcts between the middle cerebral artery (MCA) and the posterior cerebral artery (PCA) to hemodynamic causes, not embolism. OBJECTIVE: To study the cause of these infarcts. METHODS: We studied 21 patients (unilateral=18, bilateral=3) with acute, symptomatic posterior border-zone infarcts shown on CT or MRI to clarify stroke mechanisms. Patients were identified by review of CT and MRI logs and medical records during a 35-month period. An embolic mechanism was assigned when a source of embolism from either the heart, aorta, or parent large artery was present in the absence of intrinsic MCA or PCA disease. A hemodynamic mechanism was assigned when a particular emphasis on age, stroke topography and presumed causes of stroke, were studied in 3362 consecutive patients from the Lausanne Stroke Registry. Overall mortality was 4.8%. Brain hemorrhage mortality was 14.4% (48/333) and brain infarction mortality was 3.70% (112/3029). Localizations with high mortality included infratentorial (17.5%) and deep hemispheric (15.9%) territories for brain hemorrhage and, for brain infarction, multiple localizations in the posterior circulation (18.4%) and large middle cerebral artery territory (15.5%). Presumed causes of stroke associated with high mortality included saccular aneurysm (58.3%) and hypertensive arteriopathy (13.0%) for brain hemorrhage and, for brain infarction, dissection (10.4%), arteritis (8.3%), hematologic conditions (6.7%) and coexisting arterial and cardiac sources of embolism (5.2%). Multivariate logistic analysis showed that impaired consciousness on admission and limb weakness were good predictors of mortality for brain hemorrhage, while impaired consciousness and the cumulative effect of progressive worsening, limb weakness, left ventricular hypertrophy, past history of cardiac arrhythmia and previous transient ischemic attack were predictors of mortality for brain infarction. Age was not an independent predictor of stroke mortality, but for brain infarction the number of cumulative factors considered in the model increased with age. Our study shows that several factors associated with death risk are available during the first few hours after onset of stroke. Age alone is not critical, although its interaction with other factors should be considered.
with bilateral posterior border-zone lesions had perioperative hypoten-
sion. Prolonged lethargy, bilateral limb weakness, and cortical blindness
were common. CONCLUSIONS: Embolism, either cardiac or from the
parent carotid artery, is the predominant stroke mechanism in unilateral
posterior border-zone infarcts, not distal field perfusion failure. Bilateral
posterior border-zone infarcts have a distinctive clinical presentation and
are caused by systemic hypotension. Variability of irradiation of the major
arteries, passage of emboli to border-zone areas, and decreased clearance of
emboli in these areas explain the findings in the patients with unilateral
lesions.

AB-14566-00
Major Bleeding During Anticoagulation After Cerebral Ischemia: Patterns and Risk Factors—Gorrier JW (Dr A. Algra, Univ Hospital Utrecht, PO Box 85500, 3508 GA Utrecht, Netherlands) for the Stroke Prevention In Reversible Ischemia Trial (SPIRIT) and European Atrial Fibrillation Trial (EAFT) Study Groups—Neurology. 1999;53:1319–1327. Copyright © by American Academy of Neurology.

OBJECTIVE: To assess independent predictors of hemorrhage in 651 anticoagulated patients. BACKGROUND: An excess incidence of major bleeding (7% per year) in patients with nondisabling cerebral ischemia of presumed arterial origin treated with oral anticoagulation led to early termination of the Stroke Prevention In Reversible Ischemia Trial (SPIRIT). METHODS: The relationship between known risk factors and hemorrhage was assessed by univariate and multivariate analyses. We compared the risk factors with those in 225 patients anticoagulated because of cerebral ischemia with atrial fibrillation in the European Atrial Fibrillation Trial (EAFT). RESULTS: Leukoaraiosis (hazard ratio [HR] 2.7, 95% confidence interval [CI] 1.4 to 5.3) and age older than 65 years (HR 1.9, 95% CI 1.0 to 3.4) were independent predictors of all anticoagulation-related hemorrhages in SPIRIT. The incidence of intracranial bleeding in SPIRIT was 3.7% per year; this incidence increased by a factor of 1.37 for each 0.5 unit international normalized ratio (INR). Patients with cerebral ischemia of presumed arterial origin had a 19 times (95% CI 2.4 to 150) higher risk of intracranial hemorrhages than those with atrial fibrillation after correcting for baseline differences between SPIRIT and EAFT patients. CONCLUSIONS: In addition to the intensity of anticoagulation, leukoaraiosis and age older than 65 years are independent risk factors for bleeding in patients anticoagulated because of cerebral ischemia of presumed arterial origin. These patients have a higher inherent risk of anticoagulation-related intracranial hemorrhages than patients with atrial fibrillation.

AB-14567-00

To determine the yield of brain biopsy and the predictive value of clinical features and ancillary studies, we retrospectively analyzed hospital chart data from 61 consecutive patients suspected of having primary angitis of the CNS (PACNS). Biopsies disclosed PACNS in 22 (36%), alternative diagnoses in 24 (39%), and no diagnosis in 15 (25%). Clinical indicators and angiography were not useful predictors of PACNS. Brain biopsy should be the primary diagnostic tool in this setting because of the poor reliability of other indicators and because of the high yield of alternative diagnoses requiring different management.

Epidemiology

AB-14568-00

The authors investigated whether two objective allergy markers, peripheral blood eosinophilia and skin tests for common allergen, were associated with cardiovascular death. Of 5,382 subjects in the Vlagtwedde-Vlaardingen Study (the Netherlands) with data on allergy markers in 1965–1972, 507 subjects died from cardiovascular disease during 30 years of follow-up. Subjects with eosinophilia had an increased risk of cardiovascular death (relative risk [RR] = 1.7; 95% confidence interval [CI]: 1.4, 2.2), including ischemic heart disease death (RR = 1.6; 95% CI: 1.2, 2.2) and cerebrovascular death (RR = 2.3; 95% CI: 1.4, 3.8), independent of major risk factors. This association was limited to subjects with a percentage of the predicted forced expiratory volume in 1 second (FEV1 % predicted) of <100%. Positive skin tests were associated with a significantly reduced cardiovascular mortality in subjects with normal lung function and weight who did not smoke (RR = 0.15; 95% CI: 0.05, 0.46). Conversely, when subjects with positive skin tests had a body mass index of ≥25 kg/m2, had an FEV1 % predicted of <80%, or smoked, they had an increased risk for cardio-
vascular mortality. These results were not restricted to asthmatics. Our data suggest a possible link between eosinophilia and positive skin tests and cardiovascular mortality, especially in combination with other risk factors associated with its mortality.

AB-14569-00
Increased Carotid Intimal-Medial Thickness and Coronary Calcification Are Related in Young and Middle-Aged Adults: The Musca-
tine Study—Davis PH (Div of Cerebrovascular Diseases, Dept of Neurology, Univ of Iowa College of Medicine, 200 Hawkins Dr, Iowa City, IA 52242), Dawson JD, Mahoney LT, Lauer RM—Circulation. 1999;100:838–842. Copyright © 1999 American Heart Association Inc.

BACKGROUND: Increased carotid intimal-medial thickness (IMT) and coronary artery calcification (CAC) are used as 2 markers of early atherosclerosis. Our objectives were to assess whether increased IMT and CAC are related and to determine the relationship between cardiovascular risk factors and carotid IMT in young adults. METHODS AND RESULTS: A sample of 182 men and 136 women aged 33 to 42 years living in Muscatine, Iowa, underwent B-mode carotid ultrasound to determine the mean of 12 measurements of maximal carotid IMT. CAC was defined as calcification in the proximal coronary arteries in ≥3 contiguous pixels with a density of ≥130 Hu. The mean IMT was 0.788 mm (SD 0.127) for men and 0.720 mm (SD 0.105) for women. CAC was present in 27% of men and 14% of women and was significantly associated with IMT in men (P = 0.025) and women (P = 0.005). With multivariate analysis, after adjustment for age, significant risk factors for carotid IMT were LDL cholesterol (P = 0.001) and pack-years of smoking (P = 0.05) in men and LDL cholesterol (P = 0.001) and systolic blood pressure (P = 0.01) in women. These risk factors remained significant after CAC was included in the multivariate model. CONCLUSIONS: There is an association between increased carotid IMT and CAC and between cardiovascular risk factors and increased IMT in young adults. Carotid IMT may provide information in addition to CAC that can be used to identify young adults with premature atherosclerosis.

AB-14570-00

BACKGROUND: Chronic Chlamydia pneumoniae infection has been implicated in the pathogenesis of atherosclerosis but whether it plays a role at an early stage in the disease is uncertain. An early estimate of atherosclerosis can be obtained by ultrasonic imaging of the carotid artery to determine intima-media thickness (IMT) and the thickness of any atheroma plaques. METHODS AND RESULTS: In 983 normal population individuals aged 30 to 70 years, we measured common carotid artery (CCA) and carotid bulb IMT, and also carotid plaque thickness and the degree of internal carotid artery stenosis. C. pneumoniae IgA
 AB-14571-00

OBJECTIVE: The SPARC (Stroke Prevention: Assessment of Risk in a Community) study was designed to identify risk factors for stroke and cardiovascular disease using transesophageal echocardiography and carotid ultrasonography. This protocol was undertaken to establish a cohort in which putative risk factors for stroke were identified so that subsequent follow-up could discern the roles these risk factors play in stroke incidence. SUBJECTS AND METHODS: This was a prospective, population-based study. A randomly selected cohort comprised 1475 Olmsted County, Minnesota, residents aged 45 years or older, of whom 588 agreed to participate. Transesophageal echocardiography and carotid ultrasonography were used for evaluation of the subjects. Prevalences of various cardiovascular and cerebrovascular conditions were determined. RESULTS: Transesophageal echocardiography was successfully completed in 581 subjects. The prevalence (±SE) of patent foramen ovale was 25.6% (±1.9%), and that of atrial septal aneurysm was 2.2% (±0.6%). The prevalence of aortic atherosclerosis increased with age and was most common in the descending aorta, particularly in subjects 75 to 84 years old. The prevalence of strands on native valve was 46.4% (±2.2%). Carotid ultrasonography data for 567 participants revealed minimal atherosclerotic disease. Most subjects had minimal or mild carotid occlusive disease. The prevalence of moderate (50%–79%) and severe (80%–99%) stenosis was 7.7% (±1.1%) and 0.3% (±0.2%), respectively. CONCLUSIONS: This prospective study defines the prevalence of multiple potential cardiovascular and cerebrovascular risk factors, providing population-based data for ongoing follow-up of the risk of stroke.

AB-14572-00

Objective: To determine whether a specific apolipoprotein E (APOE) polymorphism is a risk factor for ischemic cerebrovascular disease (CVD; stroke or TIA). Background: The APOE ε4 allele is overrepresented in AD, atherosclerosis, and ischemic heart disease. In addition, ε4 carriers have higher plasma cholesterol levels than non-ε4 carriers. Methods: Using Medline (OVID and PubMed), a search was performed for all studies that examined APOE in ischemic CVD. The authors identified nine case–control studies that were suitable for analysis. Results: There were 926 patients with ischemic stroke or TIA’s and 890 age- and sex-matched control subjects. Overall analysis revealed a significantly higher APOE-ε4 allele frequency in affected patients compared with control subjects (0.14 versus 0.09; odds ratio, 1.68; 95% CI, 1.36 to 2.09; P<0.001). There was a significant excess of the ε3 allele (0.85 versus 0.80) but not the ε2 allele (0.06 versus 0.06) in the control subjects compared with the ischemic CVD patients. Seven studies had data on APOE genotypes. Carriers of ε4 were more frequent among ischemic CVD patients than control subjects (27% versus 18%; odds ratio, 1.73; 95% CI, 1.34 to 2.23; P<0.001). Conclusions: The APOE-ε4 allele and carriers of ε4 are more frequent among patients with ischemic CVD compared with control subjects. The ε2 allele does not appear to be protective for ischemic CVD. These findings imply a role for the APOE genotype in the pathogenesis of some cases of ischemic CVD.

Experimental Pathology

AB-14573-00

Advanced atherosclerosis is often associated with dystrophic calcification, which may contribute to plaque rupture and thrombosis. In this work, the localization and association of the noncollagenous bone matrix proteins osteonectin, osteopontin, and osteocalcin with calcification, lipoproteins, thrombus/hemorrhage (T/H), and matrix metalloproteinases (MMPs) in human carotid arteries from endarterectomy samples have been determined. According to the recent American Heart Association classification, 6 of the advanced lesions studied were type V (fibroatheroma) and 16 type VI (complicated). Osteonectin, osteopontin, and osteocalcin were identified by monoclonal antibodies IIIA(3)A(8), G12, and MPIIIIB10(1) and antiserum LF-123. Apolipoprotein (apo) A1, B, and E; lipoprotein(a); fibrinogen; fibrin; fragment D/D-dimer; MMP-2 (gelatinase A); and MMP-3 (stromelysin-1) were identified with previously characterized antibodies. Calcium phosphate deposits (von Kossa’s stain) were present in 82% of samples (3 type V and 15 type VI), Osteonectin was localized in endothelial cells, SMCs, and macrophages and was associated with calcium deposits in 33% of type V and 88% of type VI lesions. Osteopontin was distributed similarly to osteonectin and was associated with calcium deposits in 30% of type V and 94% of type VI lesions. Osteocalcin was localized in large calcified areas only (in 17% of type V and 38% of type VI lesions). ApoB colocalized with cholesterol crystals and calcium deposits. Lipoprotein(a) was localized in the intima, subintima, and plaque shoulder. Fibrin (T/H) colocalized with bone matrix proteins in 33% of type V and 69% of type VI lesions. MMP-3 was cytoplastic in most cells and colocalized with calcium and fibrin deposits. MMP-2 was less often associated with calcification. The results of this study show that osteonectin, osteopontin, and osteocalcin colocalized with calcium deposits with apoB, fibrin, and MMP-3 in advanced, symptomatic carotid lesions. These data suggest that the occurrence of T/H might contribute to dystrophic arterial calcification in the progression and complications of atherosclerosis.

AB-14574-00

By means of magnetic resonance imaging (MRI) we longitudinally monitored the evolution of ischemic injury, changes in cerebral hemodynamics and alterations of the blood-brain barrier (BBB) during permanent or temporary middle cerebral artery occlusion (MCAO) in rats. Using the intraluminal suture occlusion model, male Sprague-Dawley rats were subjected to either permanent MCAO (Group A, n=6), reperfusion after 1 h (Group B, n=5), or reperfusion after 3 h (Group C, n=5). Diffusion- and perfusion-weighted MRI and Gd-DTPA enhanced...
T1-weighted images were performed at six time points from 0.5 to 6 h post-MCAO. The lesion volume increased progressively in group A, decreased significantly in group B (P < 0.01), and only showed a tendency toward reduction in group C. Perfusion-weighted MRI delineated severe perfusion deficits in the ischemic core, confirmed early and late reperfusion, and was able to demonstrate postischemic hyperperfusion in group C. Gd-DTPA extravasation was found in all animals with permanent MCAO and initially became grossly visible between 4.5 and 6 h post-MCAO. While only 2 animals demonstrated contrast enhancement in group B, widespread BBB changes were detected immediately following late reperfusion (Group C). Our results demonstrate that with advanced MRI techniques, alterations of the BBB can be correlated with the hemodynamic and biophysical consequences of reperfusion.

**Imaging**

**AB-14575-00**


**PURPOSE:** To compare conventional MR imaging, echo-planar diffusion-weighted imaging (EP-DWI) and spin-echo diffusion-weighted imaging (SE)-DWI at radiological diagnosis of acute stroke. MATERIAL AND METHODS: Twenty-seven patients (30–85 years old) were examined. Clinical examination was performed before MR imaging. All MR examinations were assessed by an experienced neuroradiologist blinded to clinical findings. RESULTS: In EP-DWI, every patient had a lesion corresponding to the clinical findings. EP-DWI was used as the gold standard. In conventional PD+T2 imaging, 23/59 focal lesions were interpreted as acute, which was false in 11 lesions, and 36/59 lesions were considered to be old, 6 were in fact acute. Nine acute lesions were only detected retrospectively and 12 acute lesions were not detected at all on PD+T2. SE-DWI including the apparent diffusion coefficient correlated fairly well with EP-DWI but the procedure was impractical. CONCLUSION: EP-DWI is reliable for diagnosis of early ischemic stroke, while SE-DWI performs reasonably well. Conventional PD+T2 imaging is not reliable for diagnosis of early ischemia.

**AB-14576-00**

MR Imaging of Experimentally Induced Intracranial Hemorrhage in Rabbits During the First 6 Hours—Gustafsson O, Rossitti S (Dept of Diagnostic Radiology, Univ Hospital, FIN-90220 Oulu, Finland), Ericsson A, Raininko R—Acta Radiol. 1999;40:360–368.

**PURPOSE:** To evaluate the MR appearance of intracranial, especially intraparenchymal, hemorrhage during the first 6 hours after bleeding with various pulse sequences in an animal model. MATERIAL AND METHODS: Intracerebral hematomas and subarachnoid hemorrhage were created by injecting autologous blood in 9 rabbits. MR studies were performed using a 1.5 T scanner with pixel size and slice thickness created by injecting autologous blood in 9 rabbits. MR studies were performed using a 1.5 T scanner with pixel size and slice thickness comparable to those used in clinical practice before blood injection, immediately after injection, and at regular intervals during 6 hours. The images were compared with the hematoma sizes on formalin-fixed brain slices. RESULTS: In every animal, susceptibility-weighted gradient-echo (GRE) pulse sequences depicted the intraparenchymal hematomas and blood escape in the ventricles or subarachnoid space best as areas of sharply defined, strong hypointensity. The findings remained essentially unchanged during follow-up. The sizes corresponded well to the post-mortem findings. Gradient- and spin-echo (GRASE) imaging revealed some hypointensities, but these were smaller and less well defined. Spin-echo (SE) sequences (proton density-, T1- and T2-weighted) as well as a fluid-attenuated inversion recovery turbo spin-echo sequence (fast FLAIR) depicted the hemorrhage sites as mostly isointense to brain. CONCLUSION: Susceptibility-weighted GRE imaging at 1.5 T is highly sensitive to both hyperacute hemorrhage in the brain parenchyma and to subarachnoid and intraventricular hemorrhage.

**AB-14577-00**


The capability of diffusion-weighted (DW) magnetic resonance imaging (MRI) to identify very early ischemic brain injury better than conventional MRI is well known. This technique, which successfully discriminates acute from old infarcts, is particularly useful in patients with multiple brain infarcts (MBI). Among 142 patients with acute stroke consecutively admitted to our primary care center, we selected 43 patients with two or more brain infarcts on conventional MRI. All patients presented with clinical deficits consistent with acute cerebral ischemia and underwent conventional spin echo for T1 (T1-WI) and T2-weighted images (T2-WI), T1-W gadolinium-enhanced images, and echo-planar technique for DW MRI sequences. Patients underwent DW MRI examinations within 15 days of stroke onset (mean ± SD: 3 ± 3 days). In all but 1 case, the infarcts detected on DW MRI were also visible on T2-WI. The different signal pattern on DW MRI, compared with T2-WI, facilitated the detection of acute infarcts in all patients. T1-WI with gadolinium enhancement was only helpful in 5 (11.6%) patients. DW MRI enabled precise clinicotopographic correlations in 79% of our patients and provided additional clinically relevant findings in 72% of the patients. Based on the neuroradiological findings, patients were divided into three clinicotopographic types of MBI as follows: 13 patients (30.2%) presented with multiple acute infarcts, 24 patients (55.8%) with a single acute infarct and multiple old infarcts, and 6 patients (13.9%) with multiple acute and old infarcts. In conclusion, DW MRI can easily be added to conventional MRI in order to be able to distinguish acute from old infarcts, and to identify acute multiple lesions. Therefore, a better correlation between clinical symptoms and the site of lesions can be obtained, considerably improving patient care.

**AB-14578-00**


**PURPOSE:** To (a) determine the optimal choice of a scalar metric of anisotropy and (b) determine by means of magnetic resonance imaging if changes in diffusion anisotropy occurred in acute human ischemic stroke. MATERIALS AND METHODS: The full diffusion tensor over the entire brain was measured. To optimize the choice of a scalar anisotropy metric, the performances of scalar indices in simulated models and in a healthy volunteer were analyzed. The anisotropy, trace apparent diffusion coefficient (ADC), and eigenvalues of the diffusion tensor in lesions and contralateral normal brain were compared in 50 patients with stroke. RESULTS: Changes in anisotropy in patients were quantified by using fractional anisotropy because it provided the best performance in terms of contrast-to-noise ratio as a function of signal-to-noise ratio in simulations. The anisotropy of ischemic white matter decreased (P < .01). Changes in anisotropy in ischemic gray matter were not significant (P = .63). The trace ADC decreased for ischemic gray matter and white matter (P < .001). The first and second eigenvalues decreased in both ischemic gray and ischemic white matter (P < .001). The third eigenvalue decreased in ischemic gray (P = .001) and white matter (P = .03). CONCLUSION: Gray matter is mildly anisotropic in normal and early ischemic states. However, early white matter ischemia is associated with not only changes in trace ADC values but also significant changes in the anisotropy, or shape, of the water self-diffusion tensor.

**Neurosonology**

**AB-14579-00**

Effect of An Internal Carotid Stenosis on Orbital Blood Velocity—Päivänsalo M (Dept Diagnostic Radiology, Univ Hospital, FIN-90220 Oulu, Finland)

PURPOSE: To examine how an internal carotid artery (ICA) stenosis influences the orbital blood velocity and to determine which velocity parameters are most useful. MATERIAL AND METHODS: The study group comprised 94 randomly selected patients examined with orbital US; most of the patients had a carotid artery stenosis. There were 58 men and 36 women, ranging in age from 22 to 88 years with a mean age of 63.1 years. The ICA stenosis grade was determined with carotid US. Peak systolic (Vp) and end-diastolic blood velocities, systolic acceleration, mean velocity, pulsatile index (PI) and resistance index (RI) were measured within the central retinal artery (CRA) and the ophthalmic artery (OA), and peak velocity was measured within the central retinal vein (CRV). The area under the ROC curve was used to compare the outcome of diagnostic tests. RESULTS: Only a severe (≥80%) ICA stenosis decreased orbital blood velocity significantly, while milder stenoses did not cause significant flow decrease or side differences. According to ROC curve analysis, the threshold values giving the highest accuracy in detecting a ≥80% ICA stenosis were Vp ≥0.08 cm/s for the CRA and Vp ≥0.14 cm/s for the OA. The sensitivities for detecting a ≥80% ICA stenosis were 45% for Vp CRA and 60% for Vp OA. Systolic acceleration also decreased in severe stenoses, but RI, PI and velocity in the CRV did not correlate with CRA pathology. Reversal of OA flow was seen in 92% of ICA occlusion and in 47% of severe ICA stenosis.

CONCLUSION: Orbital Doppler combined with carotid Doppler can be helpful in the diagnosis of the ocular ischaemic syndrome and in the evaluation of whether the symptoms are related to occlusion of the ophthalmic or central retinal vessels or are a consequence of carotid artery stenosis.


PURPOSE: This study was undertaken to determine the appropriate timing and frequency of duplex ultrasound scanning after carotid endarterectomy (CEA) for the detection of high-grade stenosis caused by recurrent carotid stenosis or contralateral atherosclerotic disease progression. METHODS: In 221 patients who underwent 242 CEs, duplex scanning was performed before, during, and after operation (in 3-month to 6-month intervals). High-grade internal carotid artery (ICA) stenosis (peak systolic velocity, >300 cm/s; diastolic velocity, >125 cm/s; ICA/common carotid artery ratio, >4) prompted the recommendation for repair. An average of four postoperative scanning procedures was performed during a mean follow-up period of 27.4 months. RESULTS: Intraoperative duplex scan results prompted the immediate revision of 12 repairs (4.9%), and one perioperative stroke (<1%) occurred. Six CEs (2.7%) had asymptomatic recurrent stenosis (>50% diameter-reduction [DR]); systolic velocity, >125 cm/s) develop. Only one of six patients had >75% DR stenosis develop and underwent reoperation (<1% yield for CEA surveillance). The yield of surveillance of the unoperated ICA was higher (P = .003), and 12% of unoperated sides had progressive stenosis (n = 21) or occlusion (n = 3) develop, which led to seven CEs for high-grade stenosis. Disease progression to >75% DR stenosis was five times as frequent (P = .002) in patients with >50% DR stenosis initially. All patients but one who required contralateral endarterectomy for disease progression had >50% ICA stenosis when first seen. During the follow-up period, no disabling strokes ipsilateral to an operated carotid artery occurred, but three strokes occurred in the hemisphere of the contralateral unoperated ICA. CONCLUSION: The yield of duplex scan surveillance after CEA was low. Only 13 patients (5.9%) had severe disease develop to warrant additional intervention. Progression of contralateral disease rather than restenosis was the most common abnormality that was identified. Duplex scanning at 1-year to 2-year intervals after CEA is adequate when a technically precise repair is achieved and minimal contralateral disease (<50% DR) is present. A policy of duplex scan surveillance and reoperation for high-grade stenosis was associated with a 1.6% incidence rate of disabling stroke during the follow-up period.

Pharmacology / Therapeutics


Clopidogrel is an effective new antiplatelet agent useful for the treatment of ischemic cerebrovascular, cardiac, and peripheral arterial disease. However, the mechanism of clopidogrel action is not well understood, although it is known to inhibit ADP-evoked platelet aggregation. In the current study, the effect of clopidogrel on recently identified human platelet ADP receptors and their signaling pathways was investigated by using platelets from clopidogrel-treated subjects, 6 healthy volunteers (2 females and 4 males) who received 75 mg of clopidogrel daily for 7 days. Blood was taken and various platelet receptor signaling pathways were analyzed before treatment, after 7 days of medication, and 4 weeks after treatment had ceased. Platelet tests included the analysis of aggregation, rapid calcium influx, calcium mobilization from intracellular stores, adenyl cyclase, and phosphorylation of vasodilator-stimulated phosphoprotein (VASP). The data indicate that clopidogrel does not affect those platelet ADP receptors coupled to cation influx (P2X1 ADP receptors) or calcium mobilization (P2Y1 ADP receptors). In contrast, clopidogrel treatment specifically impairs the ADP receptor coupled to G/adenyl cyclase (P2Y$_{12}$ ADP receptors). Clopidogrel abolishes the inhibitory P2Y$_{12}$ receptor-mediated ADP effects on prostaglandin E$_1$–stimulated, cAMP-dependent phosphorylation of VASP without affecting epinephrine, thrombin, and thromboxane signaling. VASP phosphorylation is known to be closely correlated with the inhibition of platelet and fibrinogen receptor (glycoprotein IIB/IIIa) activation. Therefore, inhibition of the platelet P2Y$_{12}$ ADP receptor and its intracellular signaling, including decreased VASP phosphorylation, is suggested as a molecular mechanism of clopidogrel action.

AB-14582-00 Percutaneous Transluminal Angioplasty for Intracranial Atherosclerotic Lesions: Evolution of Technique and Short-Term Results—Connors JJ III (Dept of Radiology, INOVA Fairfax Hospital, 3300 Gallows Rd, Falls Church, VA 22046), Wojak JC—J Neurosurg. 1999;91:415–423.

Objective. A retrospective analysis of a 9-year experience with balloon angioplasty for intracranial atherosclerotic stenosis was undertaken with the goals of illustrating development of a safe technique for treatment of intracranial atherosclerotic disease and reporting the immediate results in this series of patients.

Methods. Three distinct periods are defined, based on the technique used. In the early period, in which eight patients were treated, the angioplasty balloon size approximated the vessel size, but was always smaller. Angioplasty was moderately rapid and brief (15–30 seconds). Clinical improvement occurred in seven (87.5%) of eight patients, dissection without consequence occurred in four (50%) of eight, and residual stenosis greater than 50% was found in three (37.5%) of eight. No neurological complications occurred.

In the middle period, in which 12 patients were treated, the balloon size approximated the vessel size, but oversizing by up to 0.25 mm was permitted. Angioplasty was extremely rapid and brief. Angiographically visible dissection occurred in nine (75%) of 12 patients, necessitating urokinase infusion in five (41.7%) of 12 and producing abrupt occlusion in one (8.3%) of 12, resulting in death. Occlusion secondary to the
recessing of the lesion occurred in one (8.3%) of 12, resulting in stroke. Good outcome was eventually achieved in 10 (83.3%) of 12.

In the current period, in which 50 patients have been treated, the balloon is always undersized and inflation is extremely slow (several minutes). Dissection occurred in seven (14%) of 50 patients, necessitating fibrinolysis in two of 50 (4%, both uneventful) and producing no abrupt occlusion or stroke. Residual stenosis greater than 50% occurred in eight (16%) of 50, with no stenosis greater than 70%. Late restenosis occurred in four (9%) of 44 and successful repeated angioplasty was performed in all four. One guidewire vessel perforation occurred (2%), resulting in the patient’s death. Good angiographic and short-term clinical outcome was achieved in the other 49 patients (98%).

Conclusions. Extremely slow balloon inflation combined with balloon undersizing results in decreased intimal damage, decreased acute platelet/thrombus deposition, and decreased acute closure. This technique sometimes yields suboptimal angiographic results but achieves the clinical goal safely. Intracranial angioplasty can be safely performed using this technique and modern equipment.

AB-14583-00

OBJECTIVE: To determine whether recanalization, coma at presentation, or clot location in the basilar artery influences the relative mortality risk after intra-arterial thrombolytic therapy for acute vertebrobasilar artery occlusions.

METHODS: Studies were identified using the MEDLINE database for January 1987 to November 1997. Series were included if they involved 10 or more patients with basilar or vertebrobasilar artery occlusions, used urokinase and/or recombinant tissue plasminogen activator, and were written in English. A fixed-effect meta-analysis approach was used to estimate the risk of death with the aforementioned risk factors. Each study was weighted according to sample size. Relative risks were calculated with 95% confidence intervals.

RESULTS: As calculated from peer-reviewed published data, the relative mortality risk for patients for whom recanalization was attempted but not achieved was 2.34 (95% confidence interval, 1.48–3.71; n = 126). Coma at presentation was associated with a relative mortality risk of 1.95 (95% confidence interval, 1.26–2.99; n = 145). Clot locations in the distal one-third of the basilar artery were shown to favor survival, compared with clots located in the proximal and/or middle portions of the basilar artery (relative risk, 0.52; 95% confidence interval, 0.31–0.86; n = 126).

CONCLUSION: The combined data suggest that coma at presentation has an independent and adverse effect on survival rates. Complete recanalization, distal clot location, and responsiveness at the time of presentation are statistically significant factors for increased patient survival rates.

Surgery

AB-14584-00

OBJECTIVE: Although fixed dosage of heparin is frequently used during vascular surgery, there are very few studies that document the appropriateness of this type of dosing. We have undertaken a prospective study to determine the physiological response to a fixed dose of heparin, using a conventional measure of anticoagulation, and have correlated this measure with complications.

METHODS: We studied 140 consecutive patients undergoing elective carotid endarterectomy. Serial activated clotting times (ACT values) were obtained in duplicate before administration of heparin, 15 minutes after application of a carotid artery cross-clamp, and 1 hour after administration of 5000 U of heparin by intravenous bolus. Postoperatively, patients were assessed for new neurological deficits (transient ischemic attack and stroke) and neck hematoma. A battery of neuropsychometric tests was performed in 49 patients at baseline and on the day after carotid endarterectomy to identify subtle new neurological deficits.

RESULTS: ACT values were found to be highly reproducible, with less than a 1.5% difference between duplicate baseline samples. Although all patients received 5000 U of heparin, the dose received per kilogram of body weight varied considerably (44–116 U/kg), as did ACT values at both 15 minutes (178–423 s) and 1 hour (173–390 s). Nevertheless, there was a significant correlation between heparin dose per kilogram and ACT values at 15 minutes (r = 0.45) and at 1 hour (r = 0.38) postinfusion, as well as ACT ratios (final ACT/initial ACT) at 15 minutes (r = 0.43) and at 1 hour (r = 0.34) after heparin bolus. Eight patients (5.7%) developed postoperative wound hematomas, one of which (0.7%) required reoperation. No patient had a stroke, but one patient had a transient ischemic attack, and 19 (39%) of 49 patients demonstrated significant early postoperative neuropsychometric deficits. Although the incidence of neck hematoma was not influenced by the heparin dose (P = 0.23), the ACT value at 15 minutes (P = 0.71) or 1 hour (P = 0.61), or the ACT ratio (P = 0.68), the only severe hematoma requiring reoperation occurred when the maximal ACT value was more than 400 seconds. Although performance on neuropsychometric tests did not appear to be statistically influenced by heparin dosing, the ACT value, or the degree of ACT elevation, there was a trend for deficits to be associated with lower heparin doses.

CONCLUSION: Fixed heparin dosing achieves safe and efficacious anticoagulation in the great majority of patients having carotid endarterectomy, with 5000 U expected to result in 15-minute and 1-hour ACT values of 175 to 425 seconds and 170 to 390 seconds, respectively. Although weight-based heparin dosing may reduce the incidence of subtle complications (hematoma formation or decline on neuropsychometric tests) and may result in more predictable 15-minute and 1-hour ACT values (85 U/kg; 225–375 and 200–340 s, respectively), no statistically compelling clinical advantage could be demonstrated. Therefore, either weight-based or fixed dosing is acceptable, with both obviating the need for routine pre-clamp ACT confirmation, thereby saving operative time and expense.

Items of Interest

Dipyridamole Plus Aspirin in Cerebrovascular Disease—Wilerdin JK, Easton JD (Dept of Neurology, Rhode Island Hospital, 110 Lockwood St #324, Providence, RI 02903)—Arch Neurol. 1999;56:1087–1092.


Abstracts of Literature
Askiel Bruno and Engin Y. Yilmaz

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