Cerebral Aneurysms

AB-14638-00
Improved Efficiency of Hypervolemic Therapy With Inhibition of Natriuresis by Fludrocortisone in Patients With Aneurysmal Subarachnoid Hemorrhage—Mori T, Katayama Y (Dept of Neurological Surgery, Nihon Univ School of Medicine, 30-1 Oyaguchi Kamimachi, Itabashi-ku, Tokyo 173, Japan), Kawamata T, Hirayama T—J Neurosurg. 1999;91:947–952.

Object. To reduce the risk of ischemic complications in patients with subarachnoid hemorrhage (SAH), hypervolemic therapy is generally advocated. However, such conventional treatment cannot always ensure the maintenance of an effective intravascular volume expansion, because excessive natriuresis and osmotic diuresis occur after SAH. In this prospective study the authors examined the effects of inhibition of natriuresis with fludrocortisone acetate on intravascular volume expansion during hypervolemic therapy.

Methods. Thirty patients with SAH were randomized and divided into two groups: controls (Group 1, 15 patients) and patients treated with 0.3 mg/day of fludrocortisone (Group 2, 15 patients). In all patients sodium and fluid intake levels were in excess of maintenance requirements in an attempt to maintain a positive water balance and a central venous pressure (CVP) of 8 to 12 cm H2O. The mean sodium and water intake levels for 14 days after SAH were significantly reduced by fludrocortisone in Group 2 (487±34.52 mEq/day and 5159.2±249.29 ml/day, respectively; p<0.01) compared with Group 1 (634.2±42.86 mEq/day and 661.7±365.67 ml/day). Fludrocortisone significantly reduced the urinary sodium excretion (p<0.01) and urine volume (p<0.01) in parallel, and effectively prevented a negative shift in the sodium as well as water balance (p<0.001). The serum sodium level tended to decrease in Group 1, reaching 135 mEq/L on average, but not in Group 2 (p<0.01). Hyponatremia in Group 1 was always observed at the optimal range of CVP values. A decrease in serum potassium level within the range of 2.8 to 3.5 mEq/L was transiently noted in 11 patients (73.3%) of Group 2, but was easily corrected. Possible side effects of fludrocortisone, such as pulmonary edema, were not encountered.

Conclusions. Intravascular volume expansion in the presence of excessive natriuresis requires a large sodium and water intake and is often associated with hyponatremia. Inhibition of natriuresis with fludrocortisone can effectively reduce the sodium and water intake required for hypervolemia and prevent hyponatremia at the same time.

AB-14639-00
Antifibrinolytic Treatment in Subarachnoid Hemorrhage: A Randomized Placebo-Controlled Trial—Roos Y, for the STAR Study Group (Dr M. Vermeulen, Dept of Neurology, Academic Medical Center [AMC], Univ of Amsterdam, PO Box 22700, 1100 DE Amsterdam, Netherlands)—Neurology. 2000;54:77–82. Copyright © 2000 by the American Academy of Neurology.

Objective. To investigate whether antifibrinolytics in combination with treatment to prevent cerebral ischemia improve outcome in patients with subarachnoid hemorrhage (SAH) in whom occlusion of the aneurysm is delayed. Background. Antifibrinolytic treatment reduces rebleeding, but outcome does not improve because of a concurrent increase in the occurrence of cerebral ischemia. Because treatment of ischemia has improved, antifibrinolytics might now have a beneficial effect. Methods. A prospective, double-blind, placebo-controlled multicenter clinical trial was performed. Randomized were 462 patients (229 received tranexamic acid, 233 placebo) admitted within 96 hours after onset of SAH, in whom treatment of the aneurysm was delayed beyond 48 hours after SAH. All patients were treated with calcium antagonists and hypervolemia. At 3 months, outcome was assessed with the Glasgow Outcome Scale. The occurrence of cerebral ischemia and other complications were recorded, and the effects of treatment were related to the clinical condition on admission. Results. Antifibrinolytic treatment had no beneficial effect on outcome (relative risk [RR], 1.10; 95% confidence limits [CL], 0.91–1.34). Antifibrinolytics significantly reduced the occurrence of rebleeding (RR, 0.58; 95% CL, 0.42–0.80); the occurrence of ischemic and other complications was the same in the two groups. Conclusions. Antifibrinolytic treatment combined with treatment to prevent cerebral ischemia does not improve outcome.

AB-14640-00

OBJECTIVE: Computed tomographic angiography (CTA) is a rapid and minimally invasive method of detecting intracranial aneurysms. We wished to determine whether CTA could replace digital subtraction angiography (DSA) in the diagnosis and operative planning of ruptured cerebral aneurysms.

METHODS: In a prospective study, patients with subarachnoid hemorrhage diagnosed by plain computed tomography underwent CTA, DSA, or both. Computed tomographic scans and CTA studies were first reviewed by the treating surgeon, along with a neuroradiologist, and a decision to proceed to DSA or directly to surgery was made on the basis of the type and quality of information provided by CTA. All patients underwent postoperative DSA.

RESULTS: A total of 173 patients were studied. In 24 patients, both CTA and DSA were negative for a source of subarachnoid hemorrhage. Twelve patients underwent DSA without prior CTA because a technologist capable of performing CTA was not available when the patient was evaluated. Nine patients in poor neurological condition underwent CTA, and all tested positive for aneurysms but died without surgical intervention. Of the 126 patients who underwent CTA and surgery, 65 (52%) also required postoperative DSA. The decision to proceed to DSA after CTA was influenced by aneurysm location; posterior communicating artery (62%) and posterior circulation locations (67–75%) more commonly proceeded to DSA than middle cerebral artery aneurysms (34%; 0.025>P=0.01). The sensitivity and specificity of CTA for the detection of all aneurysms, ruptured and unruptured, in the group of patients who underwent both types of angiograms preoperatively were 84 and 100%, respectively. In the group of 61 patients in whom aneurysm surgery was performed on the basis of CTA results alone, the sensitivity and specificity for the detection of all aneurysms, as compared with postoperative DSA, were 90 and 100%, respectively. Missed aneurysms (n=24) were always small (<4 mm) and were usually found in patients with multiple aneurysms in whom the larger, ruptured aneurysm was identified by CTA. In one patient, the aneurysm missed by preoperative CTA would have resulted in a different operation if detected preoperatively.

CONCLUSION: It is possible to proceed to ruptured aneurysm repair entirely on the basis of good-quality CTA studies that demonstrate an aneurysm consistent with the pattern of bleeding observed on plain computed tomography (48% of the patients in this series and most common middle cerebral artery aneurysms). However, detection of small unruptured aneurysms in patients with multiple lesions remains a problem.
Clinical

AB-14641-00

Objectives—Stroke seems to be related to dementia more often than previously assumed and vascular factors are also related to Alzheimer’s disease. The pathophysiology of poststroke dementia includes ischaemic changes in the brain, a combination of degenerative and vascular changes, and changes only related to Alzheimer’s disease. Some cognitive decline recognised after a stroke may be due to pre-existing cognitive decline. The aim of this study was to determine the clinical and radiological determinants of pre-stroke cognitive decline.

Methods—The study group comprised 337 of 486 consecutive patients aged 55 to 85 years who 3 months after ischaemic stroke completed a comprehensive neuropsychological test battery; structured medical, neurological, and mental status examination; interview of a knowledgeable informant containing structured questions on abnormality in the cognitive functions; assessment of social functions before the index stroke; and MRI.

Results—Frequency of pre-stroke cognitive decline including that of dementia was 9.2% (31/337). The patients with pre-stroke cognitive decline were older, more often had less than 6 years of education, and had history of previous stroke. Vascular risk factors did not differ significantly between these two groups. White matter changes (p=0.004), cortical entorhinal, hippocampal, and medial temporal atrophy (p<0.001), cortical frontal atrophy (p=0.008); and any central atrophy (p<0.01), but not the frequencies or volumes of old, silent, or infarcts on MRI differentiated those with and without pre-stroke cognitive decline.

The correlates of pre-stroke cognitive decline in logistic regression analysis were medial temporal cortical atrophy (odds ratio (OR) 7.5, 95% confidence interval (95% CI) 3.2–18.2), history of previous ischaemic stroke (OR 4.4, 95% CI 1.8–10.6), and education (OR 0.9, 95% CI 0.8–0.9).

Conclusions—History of previous stroke, but not volumes or frequencies was found to correlate with pre-stroke cognitive decline. Other associating factors were rather those usually associated with degenerative dementia: white matter changes and cerebral atrophy; and in multiple models temporal cortical atrophy and education. The possible overlap between two or more underlying diseases must be remembered in diagnosis and treatment of patients with vascular cognitive impairment.

AB-14642-00

Recent studies suggest that high plasma levels of tissue-type plasminogen activator (tPA) and its inhibitor (plasminogen activator inhibitor-1, PAI-1) are markers of an increased risk of atherothrombotic ischemic events such as stroke and myocardial infarction. In this prospective study, we measured tPA antigen, PAI-1 antigen and activity, as well as tPA/PAI-1 complex in patients with acute stroke. Stroke subtypes were classified according to the TOAST criteria. From 132 consecutively screened patients, 89 (100%) were enrolled in this study, including 42 patients (47%) with large artery atherosclerosis (LAA), 32 (36%) with small vessel occlusion (SVO), and 15 (17%) with cardioembolism (CE). Nineteen age-matched neurologic patients without manifestations of cerebrovascular disease served as control subjects (CS). Patients with acute stroke had significantly higher plasma levels of tPA antigen (p<0.001), PAI-1 antigen (p<0.05) and PAI activity (p<0.05) than patients in the control group. t-PA antigen, PAI activity and tPA/PAI-1 complex levels were similar regardless of stroke etiology. Only PAI-1 antigen was lower in patients with cardioembolic stroke than in stroke patients with LAA (p<0.05). Plasma tPA antigen, PAI-1 antigen, and PAI activity are significantly increased in patients with acute ischemic stroke. Except for PAI-1 antigen, this increase appears not to be related to the underlying stroke etiology.

AB-14643-00
Postoperative Brainstem High Intensity Is Correlated With Poor Outcomes for Patients With Spontaneous Cerebellar Hemorrhage—Yanaka K (Dept of Neurosurgery, Institute of Clinical Medicine, Univ of Tsukuba, Tsukuba, Ibaraki 305-8575, Japan), Meguro K, Fujita K, Narushima K, Nose T—Neurosurgery. 1999;45:1323–1328.

OBJECTIVE: The outcomes for patients with cerebellar hemorrhage are thought to be influenced by anatomic damage to the brainstem. In this study, we investigated the magnetic resonance imaging findings in the brainstem, to examine the relationship between the degree of brainstem damage and the outcomes for patients with spontaneous cerebellar hemorrhage who are in poor-grade condition.

METHODS: The results for 31 patients with spontaneous cerebellar hemorrhage, with Glasgow Coma Scale scores of 8 or less at admission, who underwent magnetic resonance imaging examinations were reviewed. All patients underwent surgical intervention. The patients were divided into two groups according to their Glasgow Outcome Scale scores at the time of discharge, i.e., patients who experienced good recoveries or exhibited moderate disabilities (Group I, n=8) and patients who exhibited severe disabilities, were in a persistent vegetative state, or had died (Group II, n=23). We investigated obliteration of the fourth ventricle and the perimesencephalic cistern and the presence of hydrocephalus in initial computed tomographic scans and the presence of areas of high signal intensity in the brainstem in T2-weighted images.

RESULTS: Eight patients experienced good outcomes, and 23 patients experienced poor outcomes. The overall mortality rate was 32.3%. There were no significant differences between groups with respect to computed tomographic findings such as hematoma size, but the incidence of high signal intensities in the pons and midbrain in T2-weighted images for Group II was significantly higher than that for Group I (p<0.01).

CONCLUSION: Magnetic resonance imaging clearly demonstrated brainstem damage, and high signal intensity in the brainstem was a significant prognostic factor for determining outcomes for patients with spontaneous cerebellar hemorrhage who were in poor-grade condition.

Epidemiology

AB-14644-00
Dietary Sodium Intake and Subsequent Risk of Cardiovascular Disease in Overweight Adults—He J (Dept of Epidemiology, Tulane Univ School of Public Health and Tropical Medicine, 1430 Tulane Ave SL 18, New Orleans, LA 70112), Ogden LG, Vupputuri S, Bazzano LA, Loria C, Whelton PK—JAMA. 1999;282:2027–2034.

Context Dietary sodium is positively associated with blood pressure, and ecological and animal studies both have suggested that high dietary sodium intake increases stroke mortality.

Objective To examine the risk of cardiovascular disease associated with dietary sodium intake in overweight and nonoverweight persons.

Design Prospective cohort study.


Participants Of those aged 25 to 74 years when the survey was conducted in 1971–1975 (14,407 participants), a total of 2688 overweight and 6797 nonoverweight persons were included in the analysis.

Main Outcome Measures Dietary sodium and energy intake were estimated at baseline using a single 24-hour dietary recall method. Incidence and mortality data for cardiovascular disease were obtained from medical records and death certificates.
Results  For overweight and nonoverweight persons, over an average of 19 years of follow-up, the total number of documented cases were as follows: 680 stroke events (210 fatal), 1727 coronary heart disease events (614 fatal), 680 stroke events (210 fatal), 1727 coronary heart disease events (614 fatal), 895 cardiovascular disease deaths, and 2486 deaths from all causes. Among overweight persons with an average energy intake of 7452 kJ, a 100 mmol higher sodium intake was associated with a 32% increase (relative risk [RR], 1.32; 95% confidence interval [CI], 1.07–1.64; P = .01) in stroke incidence, 89% increase (RR, 1.89; 95% CI, 1.31–2.74; P < .001) in stroke mortality, 44% increase (RR, 1.44; 95% CI, 1.14–1.81; P = .002) in coronary heart disease mortality, 61% increase (RR, 1.61; 95% CI, 1.32–1.96; P < .001) in cardiovascular disease mortality, and 39% increase (RR, 1.39; 95% CI, 1.23–1.58; P < .001) in mortality from all causes. Dietary sodium intake was not significantly associated with cardiovascular disease risk in nonoverweight persons.

Conclusions Our analysis indicates that high sodium intake is strongly and independently associated with an increased risk of cardiovascular disease and all-cause mortality in overweight persons.

AB-14645-00 Smoking and Atherosclerotic Cardiovascular Disease in Men With Low Levels of Serum Cholesterol: The Korea Medical Insurance Corporation Study—Lee SH, Suh I, Kim IS, Appel LJ (Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins Univ, 2024 E Monument St, Suite 2-600, Baltimore, MD 21205-2223)—JAMA. 1999;282:2149–2155.

Context Few studies have examined the interactive effects of smoking and serum cholesterol level on morbidity and mortality from cardiovascular diseases. In East Asia, where the prevalence of smoking is among the highest in the world, morbidity and mortality from ischemic heart disease (IHD) is rapidly escalating.

Objectives To determine whether cigarette smoking is an independent risk factor for atherosclerotic cardiovascular disease (ASCVD) in the Republic of Korea (South Korea), a population that has relatively low levels of serum cholesterol, and to determine whether serum cholesterol levels modify the risk relationship between smoking and ASCVD.


Setting and Subjects A total of 106 745 Korean men aged 35 to 59 years who received health insurance from the Korea Medical Insurance Corporation and who had biennial medical evaluations in 1990 and 1992.

Main Outcome Measures Hospital admissions and deaths from IHD, cerebrovascular disease (CVD), and total ASCVD.

Results At baseline, 61 389 (58%) were current cigarette smokers and 64 482 (60%) had a total cholesterol level of less than 5.17 mmol/L (200 mg/dL). Between 1993 and 1998, 1006 IHD events (176 per 100 000 person-years), 1364 CVD events (238 per 100 000 person-years), and 716 other ASCVD events (125 per 100 000 person-years) occurred. In multivariate Cox proportional hazard models controlling for age, hypertension, hypercholesterolemia, and diabetes, current smoking increased the risk of IHD (risk ratio [RR], 2.2; 95% confidence interval [CI], 1.8–2.8), CVD (RR, 1.6; 95% CI, 1.4–1.8), and total ASCVD (RR, 1.6; 95% CI, 1.5–1.8). For each outcome, there were significant dose-response relationships with amount and duration of smoking. Throughout the range of serum cholesterol levels, current smoking significantly increased the risk of IHD and CVD. In the lowest quartile of serum cholesterol levels (<4.42 mmol/L [171 mg/dL]), the RR from current smoking was 3.3 (95% CI, 1.7–6.2) for IHD and 1.6 (95% CI, 1.2–2.3) for CVD. There was no evidence of an interaction between smoking and serum cholesterol (P for interaction = .75, .87, and .92 for IHD, CVD, and total ASCVD, respectively).

Conclusions This study demonstrates that in Korea smoking is a major independent risk factor for IHD, CVD, and ASCVD and that a low cholesterol level confers no protective benefit against smoking-related ASCVD.

Experimental Pathology


Object. The authors sought to ascertain the nature of the hemodynamic and metabolic derangement underlying acute pathophysiological events that occur after intracerebral hemorrhage (ICH).

Methods. Cerebral perfusion pressure (CPP), flow velocity (FV) of the middle cerebral artery, and the arteriovenous contents of oxygen and lactate were investigated in 24 dogs subjected to sham operations (Group A, four animals) or intracerebral injections of 3 ml (Group B, 11 animals) or 5 ml (Group C, nine animals) autologous arterial blood. Twelve additional dogs received intravenous injections of 2% Evans blue or trypan blue dye to evaluate blood-brain barrier (BBB) changes. Within 1 hour, animals with ICH exhibited a rise in FV associated with significant reductions (P<0.05) in CPP and the arteriovenous content difference (AVDO2). In Group C animals significant increases in lactate concentration were found in arterial and superior sagittal sinus (SSS) samples compared with those in the other two groups (P<0.05). Additionally, perihematomal dye extravasation was observed in animals subjected to ICH and trypan blue dye injections, with profound and mild leakages in Group C and Group B animals, respectively, but not in Group A and Evans blue dye–injected animals. During the subsequent 4 hours, the FV and AVDO2 returned to normal in Group B animals, indicating a balanced cerebral metabolic rate for oxygen (CMRO2) compared with a deranged CMRO2 in Group C animals due to their lowered FV and AVDO2. However, no coupling increase in brain lactate clearance in Group C animals accounted for either the early lactate elevation in SSS or the decrease in CMRO2.

Conclusions. Profound reductions in CPP and brain oxygenation after ICH may rapidly exhaust hemodynamic compensation and, thus, impede cerebral homeostasis; however, these reductions only modestly enhance anaerobic glycolysis. Furthermore, the data suggest that a selective increase in permeability, rather than anatomical disruption, of the BBB is involved in the acute pathophysiological events that occur after ICH, which may provide a possible gateway for systemic arterial lactate entering the SSS.


Purpose: An elevated plasma homocysteine level has been identified as an independent risk factor for atherosclerosis. Whether this represents a marker for vascular disease or a direct effect on the vasculature remains unclear. Because vascular smooth muscle cells (VSMCs) play an integral role in the atherosclerotic process, we studied the effect of homocysteine on human infragenicular VSMC proliferation and the role of folic acid in reversing the homocysteine effect.

Methods: Human infragenicular VSMCs harvested from amputation specimens were studied. Various cell groups were exposed to physiologic (6.25 μmol/L and 12.5 μmol/L) and pathologic (25 μmol/L to 500 μmol/L) concentrations of homocysteine. Similar groups were simultaneously exposed to 20 μmol/L of folic acid. Cell counts and DNA synthesis, as reflected by [methyl-3H]-thymidine incorporation, were performed at 6 days and 24 hours, respectively. Additional groups were exposed to various combinations of folic acid (20 μmol/L), vitamin B6 (145 nmol/L), and vitamin B12 (0.45 nmol/L) in the presence of homocysteine (25, 50, and 250 μmol/L).
Results: Homocysteine resulted in a dose-dependent increase in DNA synthesis and cell proliferation. Cell counts increased significantly at homocysteine concentrations ranging from 25 μmol/L to 500 μmol/L (P<0.05), with a maximal increase of 98% at 500 μmol/L of homocysteine. The addition of 20 nM/L folic acid resulted in significant inhibition of cell proliferation at all homocysteine concentrations studied (P<0.001). Maximal inhibition of 70% occurred in the cells exposed to 50 μmol/L of homocysteine. The increases in [methyl-3H]-thymidine incorporation ranged from 36% at 6 μmol/L homocysteine to a maximum of 247% at 500 μmol/L homocysteine. All increases were statistically significant (P<0.05). The addition of 20 nM/L folic acid resulted in significant inhibition of DNA synthesis (P<0.002). Vitamins B₆ and B₁₂ did not demonstrate significant antiproliferative properties.

Conclusion: A possible role of homocysteine in the formation of atherosclerotic lesions is through a direct proliferative effect on VSMCs in a dose-dependent fashion. Folic acid intake at levels available in dietary supplements may prove protective in hyperhomocysteinemia-induced atherosclerosis. Vitamins B₆ and B₁₂ alone do not appear to exhibit a substantial inhibitory effect in the setting of elevated homocysteine levels.

Imaging

AB-14648-00

Objectives—To examine the relationship between atherosclerotic lesions of the middle cerebral artery (MCA) detected on MRA and vascular risk factors. Material and methods—We retrospectively assessed 279 patients (mean age, 69.0±11.3 years) who visited the Department of Neurology of Masuda Red Cross Hospital and underwent three-dimensional, time-of-flight MRA of the head between January 1996 and October 1998. Cases of cerebral embolism and internal carotid artery occlusion were excluded. Diagnoses were cerebral infarction (n=152) and others (n=127). We evaluated stenotic or occlusive lesions of the MCA (M1 portion), using MRA. Age, sex, history of hypertension, HbAlc, total cholesterol, fasting triglyceride, high density lipoprotein, lipoprotein(a), blood pressure, hematocrit, smoking and left ventricular hypertrophy (LVH) on ECG were included in the analysis. Results—36 patients (12.9%) had stenotic or occlusive lesions of the MCA on MRA. Univariate analysis showed that age, hypertension and HbAlc were significantly correlated with MCA lesions. Multiple logistic regression analysis showed that HbAlc and hypertension were significant and independent predictors for MCA lesions. Conclusion—Hypertension and high serum HbAlc levels may contribute to the development of atherosclerotic lesions of the MCA in Japanese people.

AB-14649-00

BACKGROUND AND PURPOSE: One major limitation of current functional MR (fMR) imaging is its inability to clarify the relationship between sites of cortical neuronal activation, small parenchymal venules that are in close proximity to these sites, and large draining veins distant from the active parenchyma. We propose to use gradient-echo blood oxygenation level-dependent (BOLD) fMR time courses to differentiate large draining veins from parenchymal microvasculature.

METHODS: In eight research subjects, five of whom presented with space-occupying lesions near the central sulcus, gradient-echo fMR imaging was performed during alternating periods of rest and motor activation. MR signal time courses from parenchymal regions and draining veins of different diameters, which were identified using contrast-enhanced T1-weighted scans, were evaluated. Percent signal changes (ΔS) and the time to the onset of MR signal rise (T₀) were calculated.

RESULTS: Mean ΔS for all subjects was 2.3% (SD±0.7%) for parenchymal activation, 4.3% (SD±1.0%) for sulcal macrovasculature, and 7.3 (SD±1.1%) for large superficial bridging veins. The mean time to onset of MR signal increase was 4.4 seconds for parenchymal task-related hemodynamic changes and 6.6 seconds for venous hemodynamic changes, regardless of vessel size. Both the differences in ΔS and T₀ between micro- and macrovasculature might lead to a more accurate description of the spatial distribution of underlying neuronal activity.

AB-14650-00

BACKGROUND AND PURPOSE: The treatment algorithm for acute cerebrovascular accidents has traditionally sorted these accidents as either hemorrhagic or nonhemorrhagic, and MR imaging, with its ability to allow expedient assessment of vascular substrates and regional blood volume, is well suited for this purpose. Our purpose was to delineate the accuracy of MR imaging in acute, hemorrhagic forms of stroke during the time frame considered beneficial for intervention in an animal model.

METHODS: Eighteen dogs with small, lobar parenchymal, subarachnoid hemorrhage (SAH), or both were serially scanned over the initial 6-hour postictal period. Confirmatory pathologic specimens and 3-hour postictal CT scans were obtained in all animals. The MR and CT studies were then interpreted in a blinded fashion by two neuroradiologists for the presence of hemorrhage. The results were subjected to receiver operating characteristic analysis.

RESULTS: MR imaging depicted acute parenchymal hemorrhage and SAH with a high degree of accuracy at 1.5 T. This finding was independent of each of the time points studied during the 6-hour window. For SAH, the MR accuracy for reader 1 was 0.86 (95% CI, 0.76–0.97); for reader 2, accuracy was 0.85 (95% CI, 0.71–0.99). The CT accuracy for the two readers was 0.42 (95% CI, 0.26–0.58) and 0.66 (95% CI, 0.43–0.89), respectively. Fluid-attenuated inversion-recovery images improved the conspicuity of SAH on MR images and, along with spin-density-weighted spin-echo sequences, helped to establish the hemorrhagic nature. For parenchymal hemorrhage, the MR accuracy for reader 1 was 0.90 (95% CI, 0.81–0.99); for reader 2, accuracy was 0.93 (95% CI, 0.84–1.00). With CT, the accuracy of reader 1 was 0.91 (95% CI, 0.85–0.97) whereas for reader 2 accuracy was 0.76 (95% CI, 0.69–0.83). Parenchymal hemorrhage detection and diagnosis was best with T2*-weighted gradient-echo images.

CONCLUSION: MR imaging with appropriately selected sequences appears able to provide information regarding the presence (or absence) of hemorrhage in an acute stroke model requisite to the initiation of treatment.

Objective: To determine whether leukoaraiosis predicts morbidity and mortality. Background: Gait disturbance and leukoaraiosis both are common in the elderly. Gait disturbance predicts mortality. Leukoaraiosis may be a unifying factor to both gait disturbance and mortality. Our study suggests that increased accuracy can be achieved in the interpretation of carotid artery sonography by meticulous attention to the color image. When color Doppler sonography is technically limited by tortuosity or ulceration, or if significant contralateral disease is present, misinterpretation is more likely.

Neurosonology


Objective: This study compared carotid artery sonography with angiography to determine, in retrospect, which types of sonographic errors arose from incorrect interpretation of sonographic images and which errors could be ascribed to the limitations of sonographic imaging.

Materials and Methods. A review of all patients who underwent carotid artery sonography and angiography between 1993 and 1997 at our institution revealed 66 patients with complete sets of studies, yielding 132 examinations (right or left). Studies were not reinterpreted and angiography was considered to be the gold standard. Only stenoses of 60% or greater were included in our study. If the degree or location of stenosis differed on the two imaging studies, they were reviewed together to classify the type of sonographic error.

Results. We found complete agreement of sonography and angiography in 115 cases (87%) and discrepancies in 17 (13%). Thirteen of 17 sonographic errors were false-positive interpretations and three were false-negative interpretations. One was an error in location. Retrospective review showed seven interpretive errors. In all these cases, the color Doppler image better revealed the degree of stenosis. Other complicating factors included inconsistencies between absolute velocities, velocity ratios, and waveforms obtained while a patient was being treated with an intraaortic balloon pump. In the other 10 discrepancies, the sonographic interpretation was accurate. Seven of these cases were false-positive interpretations in patients with contralateral occlusions or stenoses. The other three cases in this group showed long segments of stenosis, ulcerations, or tortuous vessels on angiography.

Conclusion. Our study demonstrates that increased accuracy can be achieved in the interpretation of carotid artery sonography by meticulous attention to the color image. When color Doppler sonography is technically limited by tortuosity or ulceration, or if significant contralateral disease is present, misinterpretation is more likely.
show significant changes at the age of ~50 years, suggesting an adverse effect of menopause on atherosclerosis. The higher proportion of soft plaques in men compared with women increases with age and may partly account for the prevailing male excess risk of coronary heart disease in the elderly despite a similar prevalence of atherosclerosis in elderly men and women.

**AB-14655-00**


There is conflicting evidence in the literature as to the potential effect of continuous positive airway pressure (CPAP) on cerebral perfusion. Compromising cerebral perfusion could possibly outweigh the benefit of improved oxygenation. Patients with the obstructive sleep apnea syndrome (OSAS) have been claimed to have a higher cerebrovascular reactivity to changes in end-tidal pCO₂. In this study, we investigated 23 patients with OSAS and 16 healthy young adults in the waking state. Both groups performed a series of 10 min of normal breathing, 20 min with 9 cmH₂O nasal CPAP, and then 10 min of normal breathing while wearing a nasal CPAP mask. The following parameters were assessed: bilateral transcranial Doppler signal of the middle cerebral artery, systolic and diastolic blood pressure assessed manually, and cerebrovascular reactivity to changes in pCO₂ during hyperventilation and rebreathing into an airbag. Continuous end-tidal pCO₂ measurements were performed in 14 subjects. As compared with normal breathing middle cerebral artery blood flow velocity and pCO₂ remained unchanged during CPAP. Systolic and diastolic blood pressure increased slightly by 1.2 mmHg (p = 0.015) and 1.1 mmHg (p = 0.007), respectively. Cerebrovascular reactivity did not differ in the two groups. Nasal CPAP of 9 cmH₂O is a safe treatment with respect to the maintenance of cerebral blood flow. Our study gives further evidence for the autoregulation’s capacity to maintain cerebral blood flow velocity constant during different levels of intrathoracic pressure and different cerebral perfusion pressures. We could not demonstrate any difference in cerebrovascular reactivity between patients with OSAS and healthy persons.

**Pharmacology / Therapeutics**

**AB-14656-00**

Recombinant Tissue-Type Plasminogen Activator (Alteplase) For Ischemic Stroke 3 to 5 Hours After Symptom Onset—The ATLANTIS Study: A Randomized Controlled Trial—Clark WM (Oregon Stroke Center, UHS 44, Oregon Health Sciences Univ, 3181 SW Sam Jackson Park Rd, Portland, OR 97201), Wissman S, Albers GW, Hamilton S, Hamilton S, for the ATLANTIS Study Investigators—JAMA. 1999;282:2019–2026.

**Context** Recombinant tissue-type plasminogen activator (rt-PA) improves outcomes for patients with acute ischemic stroke, but current approved use is limited to within 3 hours of symptom onset. This restricts the number of patients who can be treated, since most stroke patients present more than 3 hours after symptom onset.

**Objective** To test the efficacy and safety of rt-PA in patients with acute ischemic stroke when administered between 3 and 5 hours after symptom onset.

**Design** The Alteplase ThromboLysis for Acute Noninterventional Therapy in Ischemic Stroke (ATLANTIS) study is a phase 3, placebo-controlled, double-blind randomized study conducted between December 1993 and July 1998, with up to 90 days of follow-up.

**Setting** One hundred forty university and community hospitals in North America.

**Patients** An intent-to-treat population of 613 acute ischemic stroke patients was enrolled, with 547 of these treated as assigned within 3 to 5 hours of symptom onset. A total of 39 others were treated within 3 hours of symptom onset, 24 were treated more than 5 hours after symptom onset, and 3 never received any study drug.

**Intervention** Administration of 0.9 mg/kg of rt-PA (n = 272) or placebo (n = 275) intravenously over 1 hour.

**Main Outcome Measures** Primary efficacy was an excellent neurologic recovery at day 90 (National Institutes of Health Stroke Scale [NIHSS] score of ≤1); secondary end points included excellent recovery on functional outcome measures (Barthel index, modified Rankin scale, and Glasgow Outcome Scale) at days 30 and 90. Serious adverse events were also assessed.

**Results** In the target population, 32% of the placebo and 34% of rt-PA patients had an excellent recovery at 90 days (P = 0.65). There were no differences on any of the secondary functional outcome measures. In the first 10 days treatment with rt-PA significantly increased the rate of symptomatic intracerebral hemorrhage (ICH) (1.1% vs 7.0% [P < 0.001]), a symptomatic ICH (4.7% vs 11.4% [P = 0.004]), and fatal ICH (0.3% vs 3.0% [P < 0.001]). Mortality at 90 days was 6.9% with placebo and 11.0% with rt-PA (P = 0.09). Results in the intent-to-treat population were similar.

**Conclusions** The study found no significant rt-PA benefit on the 90-day efficacy end points in patients treated between 3 and 5 hours. The risk of symptomatic ICH increased with rt-PA treatment. These results do not support the use of intravenous rt-PA for stroke treatment beyond 3 hours.

**AB-14657-00**

Long-Term Outcomes After Carotid Stent Placement For Treatment of Carotid Artery Dissection—Liu NY, Paulsen RD, Marcellus ML, Steinberg GK, Marks MP (Stanford Univ Medical Center, 300 Pasteur Dr, Stanford, CA 94305-5105).—Neuro. 1999;45:1368–1374.

**OBJECTIVE:** To assess the long-term outcomes after stent placement for the treatment of carotid artery dissections.

**METHODS:** Between 1992 and 1998, seven patients underwent stenting procedures for treatment of extracranial carotid artery dissections resulting from various causes, including trauma (n = 2), iatrogenesis (n = 2), spontaneous development (n = 2), and fibromuscular dysplasia (n = 1). Stenting procedures were performed for large, nonhealing, dissection-induced pseudoaneurysms (four cases) or severe preocclusive stenosis (three cases). A total of 11 stents were placed (Palmaz stents, n = 8; Wallstents, n = 3). Radiological follow-up examinations were performed after a mean period of 17.7 months (range, 1–67 mo), using conventional or computed tomographic angiography. Clinical follow-up data were obtained after a mean period of 42.9 months (range, 13–72 mo).

**RESULTS:** All stent placements resulted in complete resolution of dissection-induced stenosis. For two of the four patients with aneurysms, the lesions occluded spontaneously at the time of the procedure. The third patient required coil embolization of the pseudoaneurysm. One patient exhibited progressive shrinkage of the aneurysm in serial follow-up examinations, with healing after 18 months. No clinical complications were associated with the procedures. One patient exhibited progression to asymptomatic occlusion 3 months after stenting. The remaining six patients exhibited no significant changes in luminal diameters. All patients remained in clinically stable condition, with no ischemic symptoms, during more than 3.5 years (mean period) of follow-up monitoring.

**CONCLUSION:** This experience suggests that stents placed for treatment of extracranial carotid artery dissections remain patent and patients remain free of symptoms on a long-term basis. Additional studies will be required to determine the optimal types of stents and intervals for follow-up monitoring using imaging.

**AB-14658-00**

Intra-Arterial Prourokinese For Acute Ischemic Stroke: The PROACT II Study: A Randomized Controlled Trial—Furlan A (Cerebro-

Context: Intravenous tissue-type plasminogen activator can be beneficial to some patients when given within 3 hours of stroke onset, but many patients present later after stroke onset and alternative treatments are needed.

Objective: To determine the clinical efficacy and safety of intra-arterial (IA) recombinant prourokinase (r-proUK) in patients with acute stroke of less than 6 hours’ duration caused by middle cerebral artery (MCA) occlusion.

Design: PROACT II (Prolyse in Acute Cerebral Thromboembolism II), a randomized, controlled, multicenter, open-label clinical trial with blinded follow-up conducted between February 1996 and August 1998.

Setting: Fifty-four centers in the United States and Canada.

Patients: A total of 180 patients with acute ischemic stroke of less than 6 hours’ duration caused by angiographically proven occlusion of the MCA and without hemorrhage or major early infarction signs on computed tomographic scan.

Intervention: Patients were randomized to receive 9 mg of IA r-proUK plus heparin (n=121) or heparin only (n=59).

Main Outcome Measures: The primary outcome, analyzed by intention-to-treat, was based on the proportion of patients with slight or no neurological disability at 90 days as defined by a modified Rankin score of 2 or less. Secondary outcomes included MCA recanalization, the frequency of intracranial hemorrhage with neurological deterioration, and mortality.

Results: For the primary analysis, 40% of r-proUK patients and 25% of control patients had a modified Rankin score of 2 or less (P=0.04). Mortality was 25% for the r-proUK group and 27% for the control group. The recanalization rate was 66% for the r-proUK group and 18% for the control group (P<0.001). Intracranial hemorrhage with neurological deterioration within 24 hours occurred in 10% of r-proUK patients and 2% of control patients (P=0.06).

Conclusion: Despite an increased frequency of early symptomatic intracranial hemorrhage, treatment with IA r-proUK within 6 hours of the onset of acute ischemic stroke caused by MCA occlusion significantly improved clinical outcome at 90 days.

Surgery

AB-14659-00

Background: Mobile atheromas of the aortic arch are associated with otherwise unexplained strokes and transient ischemic attacks (TIA). They are associated with increased perioperative strokes in patients undergoing coronary artery bypass surgery. Peripheral embolization is an additional risk. Transesophageal echocardiography (TEE) accurately identifies mobile atheroma. Anticoagulant therapy may have therapeutic considerations in the management of this condition. However, the risk of significant carotid artery disease associated with mobile atheromas is unknown.

Methods: Between March 1994 and July 1998, 40 patients with mobile atheromas by TEE and evidence of embolization were studied. All patients were captured prospectively in a vascular registry and were retrospectively reviewed. Carotid artery disease was evaluated using carotid duplex imaging in an accredited vascular laboratory. All patients with significant carotid disease, 70% or greater stenosis, underwent arteriography. Patients with significant carotid artery stenosis then underwent carotid endarterectomy. All patients with mobile atheromas were maintained on anticoagulation.

Results: Forty patients with mobile atheromas of the aortic arch were diagnosed with TEE. All 40 patients had evidence of embolization. Patient age ranged from 57 to 73 years (mean 68.4). There were 22 men and 18 women. Twenty of 40 (50%) patients presented with symptoms of TIA. Eleven of 40 (28%) patients presented with diffuse atheroembolization (lower extremity embolization and renal insufficiency). Six of 40 (15%) patients presented with a completed stroke. Three of 20 (7%) patients presented with acute extremity ischemia secondary to a peripheral embolus. Twenty-three of 40 (58%) of patients had significant carotid artery stenosis, 70% or greater stenosis. These 23 patients underwent both arteriography and carotid endarterectomy without complication. All patients were treated with anticoagulation and have remained anticoagulated. Clinical follow-up between 2 to 48 months (mean 18) has demonstrated no further evidence of systemic embolization in these 40 patients. Repeat TEE was performed in 6 of 40 patients. These follow-up studies no longer visualized mobile atheromas.

Conclusions: Mobile atheromas are recognized sources for embolization. Routine carotid duplex imaging should be performed in patients found to have mobile atheromas of the aortic arch. Carotid endarterectomy appears to be safe in patients who have combined carotid artery stenosis and mobile atheromas. Anticoagulation may have therapeutic considerations in the management of this condition.

AB-14660-00

Objective: Recently published data from the North American Carotid Endarterectomy Trial revealed a benefit for carotid endarterectomy (CEA) in symptomatic patients with moderate (50% to 69%) carotid stenosis. This benefit was significant but small (absolute stroke risk reduction at 5 years, 6.5%; 22.2% vs 15.7%), and, thus, the authors of this study were tentative in the recommendation of operation for these patients. To better elucidate whether CEA in symptomatic patients with moderate carotid stenosis is a proper allocation of societal resources, we examined the cost-effectiveness of this intervention.

Methods: A decision-analytic Markov process model was constructed to determine the cost-effectiveness of CEA versus medical treatment for a hypothetical cohort of 66-year-old patients with moderate carotid stenosis. This model allowed the comparison of not only the immediate hospitalization but also the lifetime costs and benefits of these two strategies. Our measure of outcome was the cost-effectiveness ratio (CER), defined as the incremental lifetime cost per quality-adjusted life year saved. We assumed an operative stroke and death rate of 6.6% and a declining risk of ipsilateral stroke after the ischemic event with medical treatment (first year, 9.3%; second year, 4%; subsequent years, 3%). The hospitalization cost of CEA ($6420) and the annual costs of major stroke ($26880), minor stroke ($798), and aspirin therapy ($63) were estimated from a hospital cost accounting system and the literature.

Results: CEA for moderate carotid stenosis increased the survival rate by 0.13 quality-adjusted life years as compared with medical treatment at an additional lifetime cost of $580. Thus, CEA was cost-effective with a CER of $4462. Society is usually willing to pay for interventions with CERs of less than $60,000 (eg, CERs for coronary artery bypass grafting at $9100 and for dialysis at $53,000). CEA was not cost-effective if the perioperative risk was greater than 11.3%, if the ipsilateral stroke rate associated with medical treatment at 1 year was reduced to 4.3%, if the age of the patient exceeded 83 years, or if the cost of CEA exceeded $13,200.

Conclusion: CEA in patients with symptomatic moderate carotid stenosis of 50% to 69% is cost-effective. Perioperative risk of stroke or death, medical and surgical stroke risk, cost of CEA, and age are important determinants of the cost-effectiveness of this intervention.
Items of Interest


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Abstracts of Literature
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Stroke. 2000;31:993-1000
doi: 10.1161/01.STR.31.4.993
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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