Abstracts of Literature

Abstracts Editor: Askiel Bruno
Assisted by: Engin Y. Yilmaz

Cerebral Aneurysms

AB-14710-00
Subarachnoid Hemorrhage Induced Sympathoexcitation Arises Due to Changes in Endothelin and/or Nitric Oxide Activity—Lambert E (Baker Medical Research Institute, PO Box 6492, St Kilda Rd, Central Melbourne, Vic 8008, Australia), Lambert G, Fassot C, Friberg P, Elghozi J-L.—Cardiovasc Res. 2000;45:1046–1053. Copyright © 2000 Elsevier Science BV.

Objective: The demonstration of the effectiveness of endothelin antagonists and nitric oxide donors in managing vasospasm following subarachnoid hemorrhage is encouraging. Whether such drugs can modify the sympathoexcitation that accompanies this condition remains unknown and was the basis for the present report. Methods: Subarachnoid hemorrhage was induced in conscious rats by injecting blood via a catheter placed along the surface of the brain and directed towards the circle of Willis. We combined measurements of arterial plasma catecholamines with the spectral analysis of blood pressure variability in order to examine sympathetic nervous activation following subarachnoid hemorrhage. Experiments were performed in untreated animals and in rats following pretreatment with either bosentan or sodium nitroprusside.

Results: Indicative of a pronounced sympathoexcitation, the 0.2–0.6 Hz frequency components of blood pressure were markedly elevated following subarachnoid hemorrhage (2.5±0.5 vs. 8.9±2.6 mmHg², P<0.01). Parallel changes in plasma norepinephrine concentration were observed (1.0±0.2 vs. 2.4±0.4 nmol/l, P<0.01). The subarachnoid injection of saline did not modify blood pressure variability or plasma norepinephrine concentrations. Pretreatment with either bosentan or sodium nitroprusside completely prevented the subarachnoid hemorrhage induced sympathoexcitation. Conclusions: Experimental subarachnoid hemorrhage is associated with a pronounced activation of the sympathetic nervous system. It would appear that this sympathoexcitation has its roots enounced in either the release of endothelin or an impairment in nitric oxide mediated vasodilation.

AB-14711-00

Object:—The clinical and radiological features of patients admitted with SAH after a preceding bout of headache did not differ from those without such an episode, and are clearly dissimilar from those after documented rebleeds. The findings challenge the existence of minor “warning headaches”.

AB-14712-00

Object: The pathogenesis of cerebral vasospasm and delayed ischemia after subarachnoid hemorrhage (SAH) seems to be complex. An important mediator of chronic vasospasm may be endothelin (ET), with its powerful and long-lasting vasoconstricting activity. In this study the author investigated the correlation between serial plasma concentrations of ET and ischemic symptoms, angiographically demonstrated evidence of vasospasm, and computerised tomography (CT) findings after aneurysmal SAH.

Methods: Endothelin-1 immunoreactivity in plasma was studied in 70 patients with aneurysmal SAH and in 25 healthy volunteers by using a double-antibody sandwich-enzyme immunoassay (immunometric) technique.

On the whole, mean plasma ET concentrations in patients with SAH (mean±standard error of mean, 2.1±0.1 pg/ml) did not differ from those of healthy volunteers (1.9±0.2 pg/ml). Endothelin concentrations were significantly higher (p<0.05) in patients who experienced delayed cerebral ischemia with fixed neurological deficits compared with those in other patients (post-SAH Days 0–5, 3.1±0.8 pg/ml compared with 2.1±0.2 pg/ml; post-SAH Days 6–14, 2.5±0.4 pg/ml compared with 1.9±0.2 pg/ml). Patients with angiographic evidence of severe vasospasm also had significantly (p<0.05) elevated ET concentrations (post-SAH Days 0–5, 3.2±0.8 pg/ml; post-SAH Days 6–14, 2.7±0.5 pg/ml) as did those with a cerebral infarction larger than a lacuna on the follow-up CT scan (post-SAH Days 0–5, 3.1±0.8 pg/ml; post-SAH Days 6–14, 2.5±0.4 pg/ml) compared with other patients. Patients in whom angiography revealed diffuse moderate-to-severe vasospasm had significantly (p<0.05) higher ET levels than other patients within 24 hours before or after angiography (2.6±0.3 compared with 1.9±0.2 pg/ml). In addition, patients with a history of hypertension or cigarette smoking experienced cerebral infarctions significantly more often than other patients, although angiography did not demonstrate severe or diffuse vasospasm more often in these patients than in others.

Conclusions: Endothelin concentrations seem to correlate with delayed cerebral ischemia and vasospasm after SAH. The highest levels of ET are predictive of the symptoms of cerebral ischemia and vasospasm, and ET may also worsen ischemia in patients with a history of hypertension. Thus, ET may be an important causal or contributing factor to vasospasm, but its significance in the pathogenesis of vasospasm remains unknown.

Clinical

AB-14713-00
The Athens Stroke Registry: Results of a Five-Year Hospital-Based Study—Vemmos KN (Dept of Clinical Therapeutics, Univ of Athens...
Universita ` di Roma Tor Vergata, Via della Ricerca Scientifica, 00133—Mauriello A, Hyperl fibrinogenemia Is Associated With Specific Histocytological
AB-14714-00

11.9 years. Forty-six percent of the patients
orrhage were excluded. There were 613 male and 429 female patients,
subgroup of stroke as well. We investigated 1,042 consecutive patients
addition, during the last decades, strategies for the modification of risk
factors and primary prevention may have changed the prevalence of each
subgroup of stroke as well. We investigated 1,042 consecutive patients
who had first strokes, during a period of 5 years (from June 1992 to May
1997) and classified them prospectively based on etiopathogenic mech-
anisms. Patients with transient ischemic attacks and subarachnoid hem-
orrhage were excluded. There were 613 male and 429 female patients,
with a mean age of 70.2±11.9 years. Forty-six percent of the patients
arrived within 3 h from stroke onset. The probable mechanisms were:
large-artery atherosclerosis, 156 (15%); lacunes, 177 (17%); cardioem-
bolic, 335 (32.1%); infarct of unknown cause, 182 (17.5%); miscella-
neous causes, 35 (3.3%), and intracerebral hemorrhage (ICH), 157
(15.1%). In the cardioembolic group, nonvalvular atrial fibrillation
(NVAF) was the probable cause in 225 patients, especially in patients
older than 75 years (65%). The overall hospital mortality was 15.2%
(from 0.6% for lacunar stroke to 34% for ICH). In our population,
endoembolism is the most frequent subtype of stroke. NVAF is the most
likely source, especially in older patients.

AB-14714-00
Hyperfibrinogenemia Is Associated With Specific Histocytological

Background—Epidemiological studies have demonstrated that hyper-
fibrinogenemia is an independent risk factor for cerebrovascular athero-
sclerosis. However, the underlying mechanisms are poorly understood.
We studied whether hyperfibrinogenemia could modify the histological
composition of atherosclerotic plaque and precipitate carotid thrombosis
resulting from rupture of the plaque.

Methods and Results—We studied the histological composition of 71
carotid atherosclerotic plaques from patients who had undergone surgical
endarterectomy after a first episode of transient ischemic attack. Patients
were divided into 3 groups corresponding to the teritiles of plasma fibrinogen values. Hypercholesterolemia, hypertriglyceridemia, hyper-
tension, diabetes, and smoking habit were also assessed. At the histologi-
cal analysis, plaques of patients in the highest tertile of fibrinogen (>407
mg/dL) were characterized by a high incidence of thrombosis (66.7% of
cases) compared with plaques of subjects in the lower (21.7%)
(P<0.002) and middle (29.2%) (P=0.009) teritiles. Plaque rupture was
significantly associated with high fibrinogen levels (54.2%, P=0.003).
Multivariate logistic regression indicated that hyperfibrinogenemia was an
independent risk factor for a decrease in cap thickness (P=0.0005),
macrophage foam cell infiltration of the cap (P=0.003), and thrombosis
(P=0.003). When the presence of other risk factors was accounted for,
hyperfibrinogenemia remained an independent predictor of carotid
thrombosis with an odds ratio of 5.83, compared with other risk factors.

Conclusions—The results of the present study add to the evidence that
hyperfibrinogenemia, independently of other risk factors, is associated
with a specific histological composition of carotid atherosclerotic plaques
that predisposes them to rupture and thrombosis.

AB-14715-00

Objective. To determine whether patients who have silent cerebral infarction are more likely to develop pneumonia than are controls without silent cerebral infarction.

Design. We examined 269 community-residing participants of the senior day-care centre without history of previous stroke, and then followed them over a two-year period to assess pneumonia. On the basis of computerized tomography scans, they were divided into two groups: no infarction (n=102) and cerebral hemispheric infarction (n=167).

Cerebral infarcts were further divided into deep and superficial infarcts.

Results. The incidence of pneumonia was significantly higher in subjects with silent cerebral infarction (19.8%) than in controls (4.9%)
(odds ratio, 4.67 [95% CI, 1.87–11.67]; P<0.01). Deep infarcts were more closely associated with the incidence of pneumonia (29.1%) than
superficial infarcts (7.6%) (odds ratio, 5.00 [CI, 1.91–13.08]; P<0.01).

Conclusions. Elderly subjects with silent cerebral infarction were more likely to develop pneumonia than were controls without silent cerebral infarction. Amongst hemispheric silent cerebral infarcts, those located in the deep brain structures may be an important predictor of the development of pneumonia.

AB-14716-00
Frequency and Clinical Determinants of Dementia After Ischemic Stroke—Desmond DW (SUNY Downstate Medical Center, 450 Clark-

Objective: To investigate the frequency and clinical determinants of dementia after ischemic stroke. Methods: The authors administered
neuropsychological, and functional assessments to 453 pa-
tients (age 72.0±8.3 years) 3 months after ischemic stroke. They
diagnosed dementia using modified Diagnostic and Statistical Manual
of Mental Disorders, 3rd ed., revised criteria requiring deficits in memory
and two or more additional cognitive domains as well as functional
impairment. Results: The authors diagnosed dementia in 119 of the 453
patients (26.3%). Regarding dementia subtypes, 68 of the 119 patients
(57.1%) were diagnosed with vascular dementia, 46 patients (38.7%)
were diagnosed with AD with concomitant stroke, and 5 patients (4.2%)
had dementia for other reasons. Logistic regression suggested that
dementia was associated with a major hemispheral stroke syndrome (OR
3.0), left hemisphere (OR 2.1) and right hemisphere (OR 1.6) infract
locations versus brainstem/cerebellar locations, infarcts in the pooled
anterior and posterior cerebral artery territories versus infarcts in other
vascular territories (OR 1.7), diabetes mellitus (OR 1.8), prior stroke (OR
1.7), age 80 years or older (OR 12.7) and 70 to 79 years (OR 3.9) versus
60 to 69 years, 8 or fewer years of education (OR 4.1) and 9 to 12 years
of education (OR 3.0) versus 13 or more years of education, black race
(OR 2.6) and Hispanic ethnicity (OR 3.1) versus white race, and northern
Manhattan residence (OR 1.6). Conclusions: Dementia is frequent after
ischemic stroke, occurring in one-fourth of the elderly patients in the
authors’ cohort. The clinical determinants of dementia include the
location and severity of the presenting stroke, vascular risk factors such
as diabetes mellitus and prior stroke, and host characteristics such as
older age, fewer years of education, and nonwhite race/ethnicity. The
results also suggest that concomitant AD plays an etiologic role in
approximately one-third of cases of dementia after stroke.

Epidemiology

AB-14717-00
Relation of Low Body Mass to Death and Stroke in the Systolic
Hypertension in the Elderly Program—Wassertheil-Smoller S (Dept
of Epidemiology and Social Medicine, Albert Einstein College of
Medicine of Yeshiva Univ, 1300 Morris Park Ave, Rm 1312 Belfer,

Background: There are scant data on the effect of body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters) on cardiovascular events and death in older patients with hypertension.

Objective: To determine if low body mass in older patients with hypertension confers an increased risk of death or stroke.

Patients: Participants were 3975 men and women (mean age, 71 years) enrolled in 17 US centers in the Systolic Hypertension in the Elderly Program trial, a randomized, double-blind, placebo-controlled clinical trial of low-dose antihypertensive therapy, with follow-up for 5 years.

Main Outcome Measures: Five-year adjusted mortality and stroke rates from Cox proportional hazards analyses.

Results: There was no statistically significant relation of death or stroke with BMI in the placebo group (P = .47), and there was a U- or J-shaped relation in the treatment group. The J-shaped relation of death with BMI in the treated group (P = .03) showed that the lowest probability of death for men was associated with a BMI of 26.0 and for women with a BMI of 29.6; the curve was quite flat for women across a wide range of BMIs. For stroke, men and women did not differ, and the BMI nadir for both sexes combined was 29, with risk increasing steeply at BMIs below 24. Those in active treatment, however, had lower death and stroke rates compared with those taking placebo.

Conclusions: Among older patients with hypertension, a wide range of BMIs was associated with a similar risk of death and stroke; a low BMI was associated with increased risk. Lean, older patients with hypertension in treatment should be monitored carefully for additional risk factors.

**AB-14718-00**


Activated leukocytes are believed to be involved in the pathogenesis and progression of atherosclerotic vascular disease and its consequences. In a 4-year observational follow-up study, we investigated whether markers for systemic leukocyte activation (leukocyte-derived inflammatory mediators) were related to cardiovascular mortality after cerebrovascular ischemia. Using enzyme-linked immunosorbent assays, we measured the plasma levels of soluble tumor necrosis factor receptor protein-1 (sTNFR-1), neutrophil gelatinase-associated lipocalin (NGAL) and neutrophil protease-4 (NAP) in 144 patients (90 stroke, 54 transient ischemic attack) 1–3 days after cerebral ischemia. During the 4 years of follow-up, 42 (29%) of the 144 patients died; 38 of cardiovascular causes and 4 of other causes. Patients with evidence of higher leukocyte activation (n = 47) had a higher 4-year cardiovascular mortality rate than those without evidence of leukocyte activation (n = 97; p < 0.005). Logistic regression analysis with age, sex and other significant predictors as covariates showed higher plasma levels of sTNFR and NGAL both to be significant independent predictors of cardiovascular mortality, the respective odds ratio, 95% confidence intervals, and p values being 2.0, 1.2–3.4, p < 0.01, and 3.6, 1.2–10.5, p = 0.02, respectively. We concluded that in patients with acute cerebral ischemia, plasma markers of leukocyte activation were significant predictors of long-term cardiovascular mortality. This may indicate an important role of activated leukocytes in the progression of these diseases.

**AB-14719-00**


The effect of focal ischemia on tissue pH was studied at various times up to 6 hours after permanent middle cerebral artery occlusion in rats. Tissue pH was imaged by using umbelliferone fluorescence and correlated with cerebral blood flow, ATP content, and recordings of the steady potential. Circumscribed foci of alkalosis (pH 7.32 ± 0.11) were detected with increasing frequency in penumbral regions having near-to-normal ATP concentrations and cerebral blood flow values between 20% and 40% of control. Both the infarct core, defined by ATP loss and cerebral blood flow values of less than 20% of control, and the inner peri-infarct rim were consistently acidic (pH 6.03 ± 0.36 and 6.53 ± 0.24, respectively). Treatment with the glutamate antagonist dizocilpine (MK-801) suppressed negative shifts of the steady potential and reduced significantly the occurrence of alkalosis observed in 90% of untreated but only in 44% of treated animals. Penumbral alkalosis appeared to be a time-dependent event occurring 30 to 60 minutes after the passage of peri-infarct depolarizations. The diversity of penumbral pH changes reflects the local disturbance of pH regulation and, possibly, the differential fate of penumbral subareas.

**AB-14720-00**


The authors examined the effect of selective endothelin (ET) receptor type A (ET_A) antagonism on histological and functional recovery in cat. At 24 hours after reversible middle cerebral artery occlusion (MCAO). A novel and specific ET_A antagonist, Ro 61-1790 [5-methylpyridine-2-sulfonic acid-6-(2-hydroxyethoxy)-5-(2-methoxyphenoxo)-2-(2-H-tetrazol-5-yl-pyridin-4-yl)-pyrimidin-4-ylamide sodium salt (1:2)] (Roche, Basel, Switzerland), was used at doses that produced steady-state plasma concentrations and abolished ET-induced pial arteriolar vasoconstriction. In a cranial window preparation, 8 mmol/L ET constricted pial arteries by 33 ± 18% (mean ± SD), but this response was ablated by intravenous Ro 61-1790 treatment (10-mg/kg bolus, 4-mg/kg/h infusion). In additional animal cohorts, halothane-anesthetized cats were treated with 90 minutes of MCAO and 24 hours of reperfusion. Animals received Ro 61-1790 infusion beginning at the onset of reperfusion and continuing for 6 or 24 hours (n = 41). Control cats were treated with 0.9% saline by intravenous infusion throughout reperfusion. There was no difference in injury volume or necrologic evaluation score in saline-treated cats (n = 11; caudate 24 ± 28%, cortical injury 7.5 ± 5% of ipsilateral structure; score 52 ± 8) versus the results in cats treated with Ro 61-1790 for either 24 hours (n = 6; caudate 22 ± 23%, cortex 6.2 ± 5%, injury volume of ipsilateral structure; score 55 ± 3) or 6 hours (n = 11; caudate 33 ± 30%, cortex 12 ± 14%, injury volume of ipsilateral structure; score 50 ± 10). Mortality was greatest in the 24-hour drug treatment group. These data suggest that blockade of ET_A receptor activity is not beneficial to tissue or functional outcomes from experimental stroke in cat.

**AB-14721-00**

519. Copyright © 2000 The International Society for Cerebral Blood Flow and Metabolism.

Insulin-like growth factor (IGF-1) is induced in damaged brain tissue after hypoxia–ischemia, and exogenous administration of IGF-1 shortly after injury has been shown to be neuroprotective. However, it is unknown whether treatment with IGF-1 delayed by more than a few hours after injury may be protective. Hypothermia after brain injury has been reported to delay the development of ischemic neuronal death. The authors therefore hypothesized that a reduction in the environmental temperature during recovery from hypoxia–ischemia could prolong the window of opportunity for IGF-1 treatment. Unilateral brain damage was induced in adult rats using a modified Levine model of right carotid artery ligation followed by brief hypoxia (6% O₂ for 10 minutes). The rats were maintained in either a warm (31°C) or cool (23°C) environment for the first 2 hours after hypoxia. All rats were subsequently transferred to the 23°C environment until the end of the experiment. A single dose of IGF-1 (50 μg) or its vehicle was given intracerebroventriculally at either 2 or 6 hours after hypoxia. Histologic outcome in the lateral cortex was quantified 5 days after hypoxia. Finally, cortical temperature was recorded from 1 hour before and 2 hours after hypoxia in separate groups of rats exposed to the “warm” and “cool” protocols. In rats exposed to the warm recovery environment, IGF-1 reduced cortical damage (P<0.05) when given 2 hours but not 6 hours after insult. In contrast, with early recovery in the cool environment, a significant protective effect of IGF-1 in the lateral cortex (P<0.05) was found with administration 6 hours after insult. In conclusion, a reduction in cerebral temperature during the early recovery phase after severe hypoxia–ischemia did not significantly reduce the severity of injury after 5 days’ recovery; however, it markedly shifted and extended the window of opportunity for delayed treatment with IGF-1.

AB-14722-00


In focal cerebral ischemia the plasminogen–plasmin system plays a role in the fibrinolysis of vessel-occluding clots and also in the proteolysis of extracellular matrix components, which potentially contributes to brain edema and bleeding complications. The authors investigated the plasminogen activation after middle cerebral artery occlusion with and without reperfusion (reperfusion intervals 9 and 24 hours) in rats by histologic zymography and compared areas of increased plasminogen activation to areas of structural injury, which were detected immunohistochemically. After 3 hours of ischemia, increased plasminogen activation was observed in the ischemic hemisphere. The affected area measured 5.2% ± 8.5% and 19.4% ± 30.1% of the total basal ganglia and cortex area, respectively. Reperfusion for 9 hours after 3 hours of ischemia led to a significant expansion of plasminogen activation in the basal ganglia (68.8% ± 42.2%, P<0.05) but not in the cortex (43.0% ± 34.6%, P=0.394). In the basal ganglia, areas of increased plasminogen activation were related to areas of structural injury (r=0.873, P<0.001). No such correlation was found in the cortex (r=0.299, P=0.228). In this study, increased plasminogen activation was demonstrated early in focal cerebral ischemia. This activation may promote early secondary edema formation and also secondary hemorrhage after ischemic stroke.

AB-14723-00


In the immature brain, postischemic metabolism may be influenced beneficially by the effect of inducing hypercarbia or hypothermia. With use of 31P nuclear magnetic resonance spectroscopy, intracellular pH (pHᵢ) and cellular energy metabolites in ex vivo neonatal rat cerebral cortex were measured before, during, and after substrate and oxygen deprivation in vitro ischemia. Early postischemic hypothermia (fall in temperature −3.2±1.0°C) delayed the normalization of pHᵢ after ischemia by inducing an acid shift in pHᵢ (P<0.01). Postischemic hypercarbia (Kreb’s–Henselet bicarbonate buffer equilibrated with 10% carbon dioxide in oxygen) and hypothermia induced separate, but potentially additive, reversible decreases in pHᵢ, each of approximately −0.16 pH unit (P<0.05). When these postischemic perturbations were applied in isolation, there was significant improvement of ~20% in the recovery of β-ATP (P<0.05). In combination, however, hypercarbia and hypothermia worsened recovery in ATP by ~20% (P<0.05). In control tissue, which had not been exposed to ischemia, ATP content was also significantly reduced by co-administration of the two treatments (P<0.05), an effect that persisted even after discontinuing the perturbing conditions. Therefore, in this vascular-independent neonatal preparation, early postischemic modulation of metabolism by hypercarbia or hypothermia appears to confer improved bioenergetic recovery, but only if they are not administered together.

AB-14724-00


Objective. We used MR angiography to examine and follow up the changes of dissecting aneurysms of the extracranial internal carotid artery (ICA).

Materials and Methods. We retrospectively reviewed the records of 101 consecutive patients with dissecting aneurysms of the extracranial ICA. Twenty patients with 26 spontaneous dissecting aneurysms were followed up with MR angiography every 1–2 years (men, 16; women, four; age range, 28–67 years; mean age, 51 years).

Results. The mean duration of follow-up was 41 months (range, 10–93 months). At MR angiography follow-up, 20 aneurysms did not change, four decreased from their original size by 33–53% (mean, 43%), and two resolved. One patient had an asymptomatic recurrent dissecting aneurysm of the extracranial ICA. Clinically, no patient had a thromboembolic stroke or transient ischemic attack during the follow-up period.

Conclusion. MR angiography revealed that dissecting aneurysms of the extracranial ICA remain stable, decrease in size, or resolve—but they do not increase in size.

AB-14725-00


It remains unclear as to whether dynamic and static cerebral autoregulation (CA) are impaired in acute ischaemic stroke, and whether these changes are related to stroke subtype. This could have important implications with regard to post-stroke prognosis and the management of blood pressure (BP) in the acute post-ictal period. Using transcranial Doppler ultrasonography and non-invasive manipulation of BP, we compared both mechanisms in 61 patients with ischemic stroke within 96 h of ictus, and 54 age- and sex-matched controls. There was no difference in static and dynamic CA indices between the various stroke...
subtypes. Combining all stroke subtypes dynamic autoregulation, as measured using thigh cuff release, was significantly impaired in both the affected and non-affected stroke hemispheres compared to controls (mean autoregulation index 4.1±3.3, 4.8±3.1 and 6.2±2.3, respectively, p<0.05). By comparison static autoregulation, assessed using isometric hand grip and thigh cuff inflation, was not significantly different. In conclusion, dynamic but not static CA appears to be globally impaired in acute ischaemic stroke. This deserves further study and may identify possibilities for therapeutic intervention.

**AB-14726-00**


White-matter hyperintensities (WMH) are frequently associated with cerebrovascular risk factors in the elderly, particularly hypertension, and have been interpreted as a subclinical form of ischemic brain damage. WMH, clinical stroke and blood pressures show significant genetic influences. The objective of this study was to determine whether a relationship exists between family history of stroke and/or hypertension in first degree relatives and WMH in the elderly. WMH and stroke (CVA) volumes were quantified from brain MRI performed on 414 white, male twins born between 1917 and 1927 (average age 72.3±2.9 years). WMH, adjusted for age and head size, was significantly correlated with the family history score (r=0.21, p<0.001). Dividing the family history scores into quintiles revealed significant differences in WMH by quintile mean (p<0.05). Subjects in the highest quintile of family history score had the highest mean WMH. Recalculation of the family history score, by only counting relatives reported to have had a clinical stroke as a positive event, revealed a nonsignificant correlation with WMH, but the correlation of the family history score with MRI CVA volume was significant (p<0.05). Stepwise multivariate analysis including ApoE status, current smoking status, smoking packyear history, Doppler ankle/arm blood pressure ratios, current and long term hypertensive status and current systolic and diastolic pressures indicated that the stroke/hypertension family history score was the single best predictor (p<0.01) of WMH volumes. Family history was not an independent predictor of CVA volume.

**AB-14727-00**


Neurovascular compression (NVC) of the left ventrolateral medulla (VLM) has been implicated as a cause of essential hypertension. We investigated whether high-resolution MRI of the posterior cranial fossa could identify patients with essential hypertension who may benefit from surgery. A retrospective analysis of imaging and clinical records from 162 patients was performed. There were 38 patients with essential hypertension and 124 who were normotensive. Contact or compression of the VLM was present in 42.1% (16/38) of the hypertensive group on the left and 47.3% (18/38) on the right. In the normotensive group it was seen in 32.2% (40/124) on the left and 26.6% (33/124) on the right. There was no significant difference between the hypertensive and control groups with regard to contact or compression of the left VLM. The results support the contention that neurovascular compression (NVC) of the left or right VLM is a common finding on MRI in normotensive individuals. We therefore believe that high-resolution MRI cannot be used as a screening tool to identify patients who may benefit from surgery.

**Neurosonology**

**AB-14728-00**


**BACKGROUND AND PURPOSE:** Several recent studies have shown that sonographic contrast agents may affect transcranial Doppler evaluation of the arterial peak systolic velocity (PSV). Some investigators reported an increase in PSV, and others reported no change in PSV compared with baseline values. This study was conducted to determine the effect of sonographic contrast agent on PSV measured in normal middle cerebral arteries.

**METHODS:** Continuous spectral Doppler sonography was performed on the right middle cerebral artery of 20 participants with angiographically proven normal intracranial vasculature. Videotaping was performed in each case from the initiation of the administration of contrast medium until the effect of the contrast agent on the PSV subsided. The PSV values were normalized for each participant, were pooled, and were plotted as a function of time.

**RESULTS:** PSV increased in all participants after the administration of contrast material; the mean maximum increase was 24±7.4% (mean±standard deviation) (range, 15–36%). The mean duration of PSV increase was 320±97 s (range, 165–465 s).

**CONCLUSION:** The middle cerebral artery PSV increased substantially after the administration of contrast material. This effect needs to be considered if velocity thresholds developed for disease detection without the use of contrast materials are used when contrast agents are administered.

**Pharmacology / Therapeutics**

**AB-14729-00**


**Objective** To establish if a brief programme of domiciliary occupational therapy could improve the recovery of patients with stroke discharged from hospital.

**Design** Single blind randomised controlled trial.

**Setting** Two hospital sites within a UK teaching hospital.

**Subjects** 138 patients with stroke with a definite plan for discharge home from hospital.

**Intervention** Six week domiciliary occupational therapy or routine follow up.

**Main outcome measures** Nottingham extended activities of daily living score and “global outcome” (deterioration according to the Barthel activities of daily living index, or death).

**Results** By eight weeks the mean Nottingham extended activities of daily living score in the intervention group was 4.8 points (95% confidence interval — 0.5 to 10.0, P=0.08) greater than that of the control group. Overall, 16 (24%) intervention patients had a poor global outcome compared with 30 (42%) control patients (odds ratio 0.43, 0.21 to 0.89, P=0.02). These patterns persisted at six months but were not statistically significant. Patients in the intervention group were more likely to report satisfaction with a range of aspects of services.

**Conclusion** The functional outcome and satisfaction of patients with stroke can be improved by a brief occupational therapy programme carried out in the patient’s home immediately after discharge. Major benefits may not, however, be sustained.
AB-14720-00

We performed a meta-analysis of randomized clinical trials of more than 6 months duration to describe how fatal and nonfatal strokes are related to cholesterol lowering and to the type of intervention. A total of 41 individual trials including approximately 80,000 subjects and followed for an average of about 4 years were included in the overview. There was a 16% (95% CI, 7.2–25%) reduction in risk of stroke among treated patients compared to control patients (test for heterogeneity, p=0.76). When trials that used different interventions were separately examined, a significant reduction in stroke occurrence was observed only for those using statins as active treatment (risk reduction 23%; 95% CI 13–33%). A variance-weighted regression analysis of the logarithmic odds ratios for stroke incidence against the percentage of cholesterol reduction indicated that a reduction of fatal and nonfatal stroke can be obtained for a cholesterol reduction of 9% (95% CI 6.8–13.6%). The combined data of primary and secondary prevention trials indicate that a large reduction of blood cholesterol, achievable with statin drugs, can reduce the incidence of stroke.

AB-14721-00

Context: Tissue-type plasminogen activator (tPA) is the only therapy for acute ischemic stroke approved by the Food and Drug Administration.

Objective: To assess the safety profile and to document clinical outcomes and adverse events in patients treated with intravenous tPA for acute stroke in clinical practice.

Design and Setting: Prospective, multicenter study of consecutive patients enrolled between February 1997 and December 1998 at 57 medical centers in the United States (24 academic and 33 community).

Intervention: Intravenous tPA (recombinant alteplase).

Patients: Three hundred eighty-nine patients with a mean age of 69 years (range, 28–100 years); 55% were men.

Main Outcome Measures: Time intervals between stroke symptom onset, hospital arrival, and treatment with tPA; pretreatment computed tomographic scan results, intracerebral hemorrhage, and major systemic bleeding. The modified Rankin Scale score was used to assess clinical outcomes at 30 days.

Results: Median time from stroke onset to treatment was 2 hours 44 minutes, and the median baseline National Institutes of Health Stroke Scale score was 13. The 30-day mortality rate was 13%. At 30 days after treatment, 35% of patients had favorable outcomes (modified Rankin score, 0–1) and 43% were functionally independent (modified Rankin score, 0–2). Thirteen patients (3.3%) experienced symptomatic intracerebral hemorrhage, including 7 who died. Twenty-eight patients (8.2%) had asymptomatic intracerebral hemorrhage within 3 days of treatment with tPA. Protocol violations were reported for 127 patients (32.6%), and included treatment with tPA more than 3 hours after symptom onset in 13.4%, treatment with anticoagulants within 24 hours of tPA administration in 9.3%, and tPA administration despite systolic blood pressure exceeding 185 mm Hg in 6.7%. A multivariate analysis found predictors of favorable outcome to be a less severe baseline National Institutes of Health Stroke Scale score, absence of specific abnormalities (effacement or hypodensity of >33% of the middle cerebral artery territory or a hyperdense middle cerebral artery) on the baseline computed tomographic scan, an age of 85 years or younger, and a lower mean arterial pressure at baseline.

Conclusions: This study, conducted at multiple institutions throughout the United States, suggests that favorable clinical outcomes and low rates of symptomatic intracerebral hemorrhage can be achieved using tPA for stroke treatment.

AB-14732-00

Context: Little is known regarding outcomes after intravenous tissue-type plasminogen activator (IV tPA) therapy for acute ischemic stroke outside a trial setting.

Objective: To assess the rate of IV tPA use, the incidence of symptomatic intracerebral hemorrhage (ICH), and in-hospital patient outcomes throughout a large urban community.


Setting: Twenty-nine hospitals in the Cleveland, Ohio, metropolitan area.

Patients: A total of 3948 patients admitted to a study hospital with a primary diagnosis of ischemic stroke (International Classification of Diseases, Ninth Revision, Clinical Modification code 434 or 436).

Main Outcome Measures: Rate of IV tPA use and occurrence of symptomatic ICH among patients treated with tPA; proportion of patients receiving tPA whose treatment deviated from national guidelines; in-hospital mortality among patients receiving tPA compared with that among ischemic stroke patients not receiving tPA and with mortality predicted by a model.

Results: Seventy patients (1.8%) admitted with ischemic stroke received IV tPA. Of those, 11 patients (15.7%; 95% confidence interval [CI], 8.1–26.4%) had a symptomatic ICH (of which 6 were fatal) and 50% (95% CI, 37.8–62.2%) had deviations from national treatment guidelines. In-hospital mortality was significantly higher among patients treated with tPA (15.7%) compared with patients not receiving tPA (5.1%, P<.001) and compared with the model’s prediction (7.9%; P<.006).

Conclusions: A small proportion of patients admitted with acute ischemic stroke in Cleveland received tPA; they experienced a high rate of ICH. Cleveland community experience with tPA for acute ischemic stroke may differ from that reported in clinical trials.

AB-14733-00

Objective: To evaluate neurologic complications in patients with immune-mediated heparin-induced thrombocytopenia (HIT) with respect to incidence, clinical characteristics, outcome, and therapy. Methods: One hundred and twenty consecutive patients with immune-mediated HIT were recruited over a period of 11 years and studied retrospectively for the occurrence of neurologic complications. Diagnosis of HIT was based on established clinical criteria and confirmed by detection of heparin-induced antibodies using functional and immunologic tests. Results: Eleven of the 120 patients (9.2%) presented with neurologic complications; 7 suffered from ischemic cerebrovascular events, 3 from cerebral venous thrombosis, and 1 had a transient confusional state during high-dose heparin administration. Primary intracerebral hemorrhage was not observed. The relative mortality was much higher (Chi-square test, p<0.01) in HIT patients with neurologic complications (55%) as compared to patients without neurologic complications (11%). The mean platelet count nadir in neurologic patients was 38±25×10^9/L on average, and was lower in patients with fatal outcome compared to
those who survived (21 \pm 13 \times 10^9/l versus 58 \pm 21 \times 10^9/l; p<0.05, Wilcoxon test). In three patients neurologic complications preceded thrombocytopenia. There was a high coincidence of HIT-associated neurologic complications with other HIT-associated arterial or venous thrombotic manifestations. Conclusion: Neurologic complications in HIT are relatively rare, but associated with a high comorbidity and mortality. HIT-associated neurologic complications include cerebrovascular ischemia and cerebral venous thrombosis. They may occur at a normal platelet count.

Surgery

AB-14734-00


Background and purpose. In carotid artery disease, the relationship between carotid plaque morphology and the patient’s neurologic symptoms is reportedly conflicting. The aim of this study was to correlate gross carotid plaque characteristics with the presenting symptoms in a relatively large series of patients who underwent carotid endarterectomy (CEA).

Methods. Four hundred and five patients who underwent 461 CEAs were divided into three groups: (1) transiently symptomatic [transient ischemic attack (TIA) or amaurosis fugax]; (2) prior stroke; and (3) asymptomatic. The degree of stenosis based on the preoperative angiograms was used in association with the presenting symptoms as the primary criterion in the decision to operate. Carotid plaque characteristics, including ulcerated plaque (UP), intraplaque hemorrhage (IH), uncomplicated plaque, and degree of stenosis, were recorded prospectively for 457 CEAs, since 4 CEAs were excluded from the study. All CEA specimens were grossly evaluated at surgery.

Results. There was a statistically higher incidence of UP in transiently symptomatic (P=0.008) or prior stroke (P=0.006) patients than in the asymptomatic group. When IH was considered independently, its incidence did not differ significantly between the three groups. Previously symptomatic patients tended to have higher-grade stenosis than asymptomatic patients, although the difference failed to reach statistical significance (P=0.06). Although the incidences of UP and IH were higher in the higher-grade stenosis group, the difference was again not significant.

Conclusions. Carotid UP correlates closely with an initial presentation of TIA, amaurosis fugax, or prior stroke, while the association between IH and presenting symptoms is less clear. Although there is an insignificant trend toward a correlation between the higher degrees of stenosis and the onset of transient symptoms, the degree of stenosis appears unaffected by the morphology of the plaque. These findings suggest that plaque morphology may play an important role in the presentation of carotid artery disease.

Items of Interest


Abstracts of Literature
Askiel Bruno and Engin Y. Yilmaz

*Stroke*. 2000;31:1791-1797
doi: 10.1161/01.STR.31.7.1791

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2000 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/31/7/1791

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

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

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