Review of Critical Care and Emergency Approaches to Stroke

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The past year has brought steady progress in our understanding of the emergent treatment of stroke. Substantial clinical information has come from post hoc and hypothesis-generated analyses of prior trials, as well as population-based ischemic stroke experiences. The main focus of ischemic stroke investigations in the past year has been to realize the benefits apparent in the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA trial on much broader routine care. Clearly, this involves developing a professional consciousness regarding the precise requirements of emergency stroke management. In addition, human studies have explored therapeutic and pathophysiological mechanisms in the major form of untreated stroke, intracerebral hemorrhage (ICH). The present overview will focus on the evolving knowledge in these 2 areas as pertains to emergency and intensive care unit (ICU) management.

Emergency Care Ischemic Stroke

A population-based, state-wide assessment of diagnostic and treatment capabilities for the state of Illinois was performed by Ruland et al. Although this survey demonstrated that 93% of Illinois residents lived in a county with at least one acute care facility using a rt-PA treatment protocol, almost 30% of hospitals did not have such a protocol, and many were lacking in specialized personnel and equipment for stroke diagnostic technology such as MRI, transcranial Doppler, and consultation from Neurology and Neurosurgery. This survey demonstrates that substantial barriers to stroke care continue to exist at the personnel, diagnostic technology, and programmatic level. It remains clear that a systematic approach to emergency care for stroke has the potential to improve these deficits greatly.

Two evaluations of the National Institute of Health Stroke Scale (NIHSS) have suggested some potential alterations in this important emergency stroke evaluation tool. First, Tirschwell et al. have identified a subset of the NIHSS tests that can lead to a more rapid evaluation in the prehospital setting. This set includes leg strength, gaze, visual fields, language, level of consciousness, facial palsy, and dysarthria. Substantial correlations between the full NIHSS and these shorter 8- and 5-test versions were demonstrated. The utility of this scale, in prospective use, has yet to be demonstrated. Similarly, Fink et al. compared the difference in NIHSS values for a set of 153 patients with concurrent diffusion/perfusion MRIs. The goal of this analysis was to test whether there were differences in NIHSS scoring of right and left hemispheric stroke. Patients with right-sided stroke seem to have systematically lower NIH stroke scores, despite similar diffusion-weighted lesion volumes. This study confirms the apparent hemispheric bias of weighting language functions in the NIHSS. The second interesting finding was the low degree of correlation between the NIHSS and the absolute volume of lesions on diffusion-weighted imaging. Quite remarkably, the NIHSS accounts for only 25% to 35% of the variance attributable to different volumes of acute ischemic lesions. This finding suggests potential improvements in patient selection could occur if diffusion-weighted imaging was performed more routinely in the emergency setting.

Deterioration

Not all stroke patients improve in the initial hours after presentation. Two recent studies have described deterioration in the initial 1 to 7 days after hospitalization. Both studies demonstrate a 25% to 30% occurrence rate for decline in neurological function, as measured by either decreased NIHSS or decreased Canadian Neurologic Scale. These patients have substantially higher mortalities. Deterioration occurs with high frequency in patients experiencing total anterior circulation infarct and/or posterior circulation infarct. As a group, these patients tend to require more intensive care. More effective methods of assuring early reperfusion are needed if these patients are to avoid high degrees of morbidity or mortality. Large infarcts with mass effects seem to be the factors most strongly associated with deterioration.

Studies by Koh et al. and Kasner et al. clearly demonstrate the high sensitivity of routine, early computed tomography (CT) imaging to detect large infarct and mass effect. The odds ratios for various CT findings range from 4.5 to 26, strongly suggesting a diagnostic value for early and repeat CT imaging of infarct size in a deteriorating patient.

The importance of infarct size in the initial CT at the time of thrombolytic therapy is less clear, however. Both the retrospective analysis of European Cooperative Acute Stroke Study (ECASS) data and that of the Australian streptokinase trial did not demonstrate a statistical association of ICH with prolonged time to treatment (6-hour versus 3-hour window) or with enlarged area of vascular infarct on early CT. Thus, neither time of presentation nor early CT lucency in more than a third of the vascular territory of the ischemic hemisphere are absolute contraindications to thrombolytic treatment.
ICU Treatments

Initial stroke severity and clinical deterioration after initial stroke are reasons for the aggressive ICU care of stroke patients. Significant interest has developed in the use of cooling to provide neuroprotection during stroke therapy. Kasner and colleagues7 report the results of a randomized clinical trial on a small cohort of patients using 650 mg of acetaminophen every 4 hours to limit hypothermia. Only a small reduction of 0.22°C was demonstrated, and no differences in NIHSS over the initial 48 hours of treatment were noted. Endovascular cooling has also been explored. Initial reports of small series undergoing open-label endovascular cooling are reported by Georgiadis et al9 and Krieger et al10 Both series demonstrate the feasibility of cooling to a target temperature of 32±1°C for 48 to 72 hours. Side effects reported include pulmonary infection, arterial hypertension, bradycardia, tachyarrhythmia, gastrointestinal bleeding, and myocardial infarction. Thus, although cooling can be performed, side effects are possible and may be significant. A much larger series of patients will be required to assess the role of lowered body temperature in producing these side effects, because they are also associated with severe stroke and critical care therapy in general.

Georgiadis et al9 also reported an open-label series of 36 patients that allowed direct comparison between moderate hypothermia and hemicraniectomy for a group of severely impaired stroke patients (NIHSS ≥ 17).11 It is noteworthy that the duration of mechanical ventilation and neurointensive care stay was not significantly different between the surgically treated group and the moderate hypothermia group. However, the duration of catecholamine use and the maximum catecholamine dosage were significantly higher in the moderate hypothermia group, thus suggesting a greater need for circulatory support. Ventilation is another form of critical care support required by some stroke patients. Mayer et al12 evaluated the cost-effectiveness of mechanical ventilation. The cost of ventilation for stroke patients discharged alive was $89,000. The cost per year of life saved was $37,000, and the cost of quality-adjusted life-year saved was $174,000. The functional status of most survivors was poor at 6 months; half were severely disabled.

Two physiological studies were performed on stroke patients in the ICU. Georgiadis et al13 used a controlled paradigm to demonstrate that positive end-expiratory pressure between the levels of 4 and 12 mm Hg has no effect on either intracranial pressure or middle cerebral artery blood flow velocity in a cohort of 20 ventilated patients. Using similar methodology, Schwartz et al14 demonstrated that induced hypertension (norepinephrine infusion) was associated with substantial rises in mean arterial blood pressure (25 mm Hg increase), cerebral perfusion (25 mm Hg increase), and middle cerebral artery blood flow velocity (25 cm/s increase). These data suggest that induced hypertension may have the ability to augment flow velocity in stroke patients.

Intracerebral Hemorrhage

Long-term prognosis for patients experiencing spontaneous ICH remains dismal.15 A retrospective study in the Netherlands of 1,731 patients from 1986 to 1995 demonstrated a 57% one-year mortality with only 19% of all patients returning to their home environment. Within the group of 243 patients returning to the home environment, there was a 2.1% annual recurrence rate for ICH and an 8% annual recurrence rate between ICH and other vascular events. ICH patients seem to have ≈ 4 times the risk of other patients for experiencing a second ICH. A similar study was performed prospectively in 1996 for a 12-hospital region of Sweden, with defined population slightly greater than one million individuals. This study demonstrated an overall mortality rate of 47% at 1-year follow up. The initial level of consciousness (ie, severity of injury) was the single strongest predictor of fatal outcome.16 A small prospective series by Nasser et al17 offers some hope for developing treatment. This selected group of 10 patients with basal ganglia hematomas was treated with stereotactic rt-PA infusion and spontaneous clot drainage. An 80% hematoma reduction was observed on day 3, with 9 of the 10 patients experiencing a high level of functional outcome (Glasgow Outcome score 4 or 5) at 3 months.

A prospective evaluation of minimally invasive surgery plus clot lysis would be required to evaluate the true benefit of such a surgical procedure on a controlled group of patients in whom the initial severity of hemorrhage was equal. A similar evaluation of 26 consecutively treated patients at the Mayo Clinic was performed by Rabenstein et al18 This group evaluated the efficacy of craniotomy for infratentorial intracerebral hematomas in patients with rapidly deteriorating clinical conditions. Fifty-six percent of patients died, 22% remained severely disabled, and 22% regained independence. Comatose patients who had lost upper brain stem reflexes and demonstrated extensive posturing died despite surgery. Although this single hospital experience suggests that ≈ 22% of patients can return to functional independence after emergency craniotomy, the overall results do not seem different from the natural history of this disease, as reported in the Netherlands and Sweden. It remains obvious that ICH treatments that improve mortality and achieve a higher degree of functional morbidity are necessary.

Pathophysiology of Brain Injury

The absence of effective therapies for ICH has led to a more extensive evaluation of pathophysiological factors that would lend themselves to treatment. Significant progress seems to be occurring in both human and animal studies. Gebel et al19 reported a secondary analysis from a prospective, population-based study of hematoma growth performed in Cincinnati. This evaluation demonstrates a correlation between the relative amount of edema on presentation and subsequent poor outcome, as measured by the 12-week Barthel Index score. Interestingly, in this study, absolute edema volume did not predict mortality. In a companion article, the same group demonstrated that perihematoma edema volume increased by ≈ 75% during the first 24 hours, with the greatest increase occurring in patients who had the least edema initially.20 Carhuapoma et al21 used diffusion-weighted MRI to evaluate perihematoma edema more precisely in a prospectively studied cohort of 9 patients. This report demonstrates the
possibility of a direct correlation between intracerebral hematoma volume and the degree of apparent diffusion coefficient elevation in the perihematomal region. Thus, the findings suggest that a dose-effect relationship exists between volume of edema and the volume of blood products within the hematoma.

Summary
The human evidence seems to suggest that edema occurs and progressively worsens with ICH. There may be a relationship between the production of relative amounts of edema and the size of hematoma. This relationship could be important to predicting functional outcome. Further direct and prospective evaluation of this hypothesis in animal models and further evaluation of the natural history of edema production in response to human hematoma volume may help to refine an appropriate target for treatment.

References

KEY WORDS: hemorrhage ■ ischemia ■ stroke
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Stroke. 2003;34:362-364
doi: 10.1161/01.STR.0000054629.76247.EA
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 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:
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