In the past year there have been clinical trial advances in many areas that will impact the way stroke care is practiced in the intensive care unit (ICU). These include: (1) the long-term follow-up results of the International Subarachnoid Aneurysm Trial (ISAT) comparing clipping versus coiling for ruptured intracranial aneurysms, (2) the results of a phase 2 trial of prophylactic balloon angioplasty for Fisher Grade III subarachnoid hemorrhage (SAH), and (3) a variety of studies from the general critical care literature that have helped define best medical practices in the neuro-ICU.

**Long-Term ISAT Results**

ISAT was a landmark trial that compared long-term functional outcome in patients with aneurysmal SAH randomly assigned to surgical clipping or endovascular coiling. The study population consisted of 2143 primarily good-grade patients with small-to-medium–sized anterior circulation aneurysms. The initial results of the trial indicated that clipping was safer than coiling: there was a relative risk reduction of 22.6% and an absolute risk reduction of 6.9% in the rate of death or dependency (modified Rankin Scale score of 3 to 6) at 1 year. Most of this was due to a reduction in morbidity; the absolute reduction in mortality at 1 year was just 2.0% lower with coiling compared to clipping.

The generalizability of the ISAT trial has since been hotly debated, but the impact of the trial has been dramatic, with an ever-increasing proportion of SAH patients undergoing endovascular as opposed to surgical repair since 2002 when the study results were published. From a scientific point-of-view, the most vexing aspect of the ISAT trial has been that no data were presented to explain why coiling may be safer than clipping. Possible reasons include the lack of physical damage to the brain from retraction injury, a lower risk of vasospasm caused by exposure and manipulation of the brain, or less frequent intraoperative aneurysm rupture.

With this background, the long-term results of the ISAT trial were published earlier this year in *Lancet Neurology.* Patients were followed for a mean of 9 years (range 6 to 14 years). The main findings are as follows: (1) there was no longer any difference in the frequency of death or dependency at 5 years, (2) this was the case despite a 3% absolute increase in mortality at 5 years ($P = 0.03$) in clipped patients, and (3) the risk of rebleeding from the treated aneurysm more than 1 year after treatment was higher in coiled than clipped aneurysms, but in both groups the risks were small ($<1\%$).

These findings seem to indicate that in the long run, clips and coils are equivalent therapies for the treatment of ruptured intracranial aneurysms. Each has strengths and weaknesses. Clipping is slightly more durable in terms of the risk of rebleeding, but even more importantly does not require the long-term serial angiography that most interventionalists perform in patients they have coiled. The advantage to coils is that the procedure is less invasive, and appears to be associated with less short-term procedural morbidity.

The implications for clinical practice are clear: good-grade SAH patients with small-to-medium–sized anterior circulation aneurysms should be given a choice, after the risks and benefits of each form of therapy have been explained. More than anything, the long-term results of the ISAT trial further support the idea that aneurysm care should be centralized in high-volume centers that can offer the full spectrum of therapies, including clips, coils, interventional treatments for vasospasm, emergency neurosurgical intervention, and neurocritical care. The less-invasive nature of endovascular therapy still makes this treatment modality particularly attractive in patients with large posterior circulation aneurysms, or in patients with severe medical comorbidity.

**Prophylactic Balloon Angioplasty for Vasospasm**

Vasospasm remains an important cause of poor outcome in patients with ruptured aneurysms. Transuminal balloon angioplasty (TBA) has played an important role as a rescue therapy in treating cases that are refractory to medical treatment, with good short-term clinical response rates reported in approximately 50% of patients in single-center case series. Significantly, early treatment within 2 hours of symptom onset has been associated with better results.

The role of prophylactic TBA in high-risk patients with thick cisternal clot remains less well-defined. To address this issue, Zwienenberg-Lee et al randomly assigned 170 patients with Fisher Grade III SAH to prophylactic TBA within 96 hours of hemorrhage onset. The frequency of neurological attributed to vasospasm was lower in the TBA group (24% versus 32%), but this difference was not statistically significant, and the risk of death or severe disability at 3 months was...
the same in the 2 groups. More concerning was the fact that 4 of the prophylactic TBA-treated patients experienced intracranial vessel perforation as a complication of the procedure (a risk of 5%), and 3 of these cases were fatal.

This study has important implications for clinical practice. TBA is a powerful but dangerous intervention, with a risk of vessel perforation of 3% to 5% when all vessels in spasm are treated. This risk seems to be too high in good-grade patients with asymptomatic vasospasm, because it is well-established that the majority of patients will not develop delayed cerebral ischemia by imaging or clinical criteria. A more intriguing question is whether prophylactic TBA can prevent delayed cerebral ischemia in stuporous or comatose poor grade SAH patients, who were not included in the Zwienenberg-Lee study. These patients have a higher risk of delayed cerebral ischemia, and are at higher risk for clinically “silent” cerebral infarction from vasospasm, due to lack of sensitivity of the clinical examination and the frequent use of sedation to promote ventilator synchrony.6 Some centers routinely perform surveillance angiography in poor-grade patients between day 4 and 7 after SAH and deploy prophylactic TBA when moderate-to-severe vasospasm is identified. Alternately, multimodality monitoring techniques including continuous electroencephalography, brain tissue oxygen, and microdialysis can be used to trigger interventional therapy for vasospasm in poor-grade patients.7 These strategies eventually will need to be put to the test.

Critical Care of the Patient With Stroke

Prevention of Infections

Last year brought several pathbreaking investigations in general critical care medicine. Prevention of hospital-acquired infections is now a hot topic, and patients at stroke are at particularly high risk, particularly for hospital-acquired pneumonia. The effectiveness of selective digestive tract decontamination (SDD) and selective oropharyngeal decontamination (SOD) has been debated for almost 20 years. A large randomized trial of almost 6000 critically ill patients compared the impact of standard care, SDD, or SOD on mortality at 28 days.8 SDD consisted of 4 days of intravenous cefotaxime and topical application of tobramycin, colistin and amphotericin B in the oropharynx and stomach; SOD consisted of the topical treatment alone. Both treatments were associated with a small but significant reduction in mortality. Mortality was 27.5% at day 28 in the standard care group, and was reduced by 3.5 absolute percentage points with SDD and 2.9 percentage points with SOD. These results indicate that in critically ill stroke patients with an anticipated ICU length-of-stay exceeding 3 days, SOD and SDD can reduce mortality due to nosocomial infections. We agree with the author’s conclusion that in environments with a high prevalence of multidrug-resistant colonization, SOD seems to be the superior choice because it involves less selection pressure favoring the long-term development of resistant organisms.

Ventilator Weaning

Another important issue in the critical care of neurological patients is difficulty in liberating patients from the ventilator. Levine and colleagues9 investigated whether the combination of diaphragm inactivity and mechanical ventilation leads to disuse atrophy of myofibers in the human diaphragm. They compared those who had only short-term mechanical ventilation, which was limited to 2 to 3 hours, to those patients who had longer periods of ventilatory support. Patients with longer periods of mechanical ventilation showed decreased cross-sectional areas of slow switch and fast switch fibers, and decreased expression of other markers of muscle cell integrity. This finding gives further insight into the question how weaning failure can develop in our patients. One reason that daily spontaneous breathing trials might promote earlier weaning from mechanical ventilation10 is that daily “exercise” of the diaphragm might prevent accelerated disuse atrophy.

Glycemic Control

Whether or not intensive insulin therapy (IIT) in critical ill patients is beneficial has been a matter of intense debate since the van den Berge study in the New England Journal of Medicine in 2001.11 This year the results from NICE-SUGAR were published.12 In this trial, mortality in adults in the ICU treated with IIT to maintain target levels of 80 to 110 mg/dL had a higher mortality compared to those with a more liberal blood glucose target of 180 mg/dL or less. Whether the observed harm resulted from appropriately reduced glucose levels, increased administration of insulin, or episodic critical hypoglycemia is still unclear. However, on the basis of this 6000-patient trial, the use of IIT to maintain strict normoglycemia cannot be advocated at the moment in critically ill neurological patients. A more liberal target of 120 to 180 mg/dL seems more prudent, particularly in light of recent evidence based on microdialysis that has linked IIT with critical brain tissue hypoglycemia and brain energy crisis in comatose patients.13

Disclosures

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References


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