Outcome in neurocritical care: Advances in monitoring and treatment and effect of a specialized neurocritical care team

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Objective: To review current advances in the treatment of critically ill neurologic patients, including specialized care by neurointensivists.

Design: Review article.

Main Discussion and Conclusions: Significant developments in the fields of neurology and neurosurgery have led to improved treatments for the critically ill neurologic patient. The major areas reviewed include neuromonitoring, disease-specific treatments, and specialized neurocritical care units and team. The current trend is for the application of the so-called multimodality neuromonitoring, which includes the use of several monitoring techniques, including intracranial pressure, brain electrophysiology, brain metabolism and oxygenation, and cerebral blood flow, among others. Many new therapies that have been introduced are discussed, including thrombolytic therapy for acute ischemic stroke, induced hypothermia for comatose survivors of cardiac arrest, and endovascular coiling for ruptured cerebral aneurysms. Lastly, the introduction of neurointensivists and neurocritical care units has been associated with reduced hospital mortality and resource utilization without changes in readmission rates or long-term mortality rates. (Crit Care Med 2006; 34[Suppl.]:S232–S238)

KEY WORDS: neurologic critical care; neurointensivist; outcome and process assessment; intensive care unit; length of stay; hospital mortality; critical illness; organization; neurological; neurosurgical

Important developments in the fields of neurology and neurosurgery have greatly improved therapeutic modalities for the critically ill neurologic patient. Such enhancement is the result of improved monitoring techniques, microsurgical approaches, and novel and effective treatments for complex neurologic conditions. This article contains an overview of the field of neurocritical care, therapeutic advances including neuromonitoring, and emphasizes the role of specialized neurocritical care teams.

Overview of Neurocritical Care: Brief History and Outcome Measures Used

Neurocritical care is a relatively new discipline dedicated to the advancement of care of the critically ill neurologic patient (1). The birth of neurocritical care stemmed from the appreciation that an already affected brain (primary injury) is greatly influenced by systemic alterations that may adversely affect its function (secondary injury). The group of practitioners that are specially trained to recognize and treat such injuries are called neurointensivists. The first neurocritical care fellowships in the United States were set up in the late 1970s to early 1980s. Since then, neurocritical care has grown and is being increasingly recognized as a separate subspecialty within critical care. In fact, the Neurocritical Care Society, an international multidisciplinary enterprise, was founded in 2003 with the support of the Society of Critical Care Medicine (2). Also, most major academic medical centers in the United States have developed dedicated specialized neurocritical care units.

The main argument for the necessity of neurointensivists is that the care of the critically ill neurologic patient requires training in clinical physiology of intracranial pressure, cerebral blood flow and metabolism, brain and neuromuscular electrophysiology, postoperative care, and systemic complications of nervous system diseases. Neurointensivists would typically care for patients with acute ischemic stroke, intracerebral and subarachnoid hemorrhage, intracranial neoplasms, traumatic brain and spinal cord injury, status epilepticus, and neuromuscular respiratory failure, among others. Many advances in therapeutics and neuromonitoring have made it possible for neurointensivists to affect outcome of these patients.

Outcome of neurocritically ill patients is usually determined by using a combination of scales, including severity of illness scales, general functional scales, global health status scales, and disease-specific scales (3–14). A common feature of most of these outcome measures is their crudeness. However, with the advent of newer treatments, more sensitive scales have been developed. A summary of outcome measures commonly used in neurocritical care is presented in Table 1. The severity of illness scoring system most widely used is the Acute Physiology and Chronic Health Evaluation score (APACHE II and III) (8). APACHE score has been used mainly for stratification of patients with similar severity of disease in clinical studies, comparison of performance of multiple intensive care units (ICUs) with similar case mix, and for resource allocation. Despite the fact that disease-specific neurologic scales, such as the Glasgow Coma Scale, (9) have predicted patients' outcome, many studies have included general severity of disease

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Table 1. Scales and outcome indicators commonly used in neurocritical care

Indicator	Type of Scale/Outcome	Advantages	Disadvantages
Mortality (4–7)	General	Easy to obtain	Lack of indication of quality of life of survivors; greatly influenced by discharge practices
Length of stay (4–7)	General	Easy to obtain; surrogate for resource utilization	Crude measure of resource utilization; greatly influenced by discharge practices
APACHE Score (8)	Severity of illness	Widely used in critical care; risk adjustment	Neurologic information is limited to GCS
GCS (9)	Disease specific; measures level of consciousness	Easy to obtain; good interobserver and intraobserver reliability	Crude measure of neurologic injury
GOS (10)	Disability scale	Easy to obtain; good interobserver and intraobserver reliability	Crude measure of disability
Barthel index (11)	Functional scale; measures ability to perform activities of daily living	Easy to obtain; good interobserver and intraobserver reliability	Lack of measurement of quality of life
Rankin Scale Score (12)	Disability scale	Easy to obtain; good interobserver and intraobserver reliability	Lack of measurement of quality of life
SF-36 (13)	Multidimensional health status	Attempts to measure quality of life	Floor effect in the physical function and role domains in neurologic patients
NIHSS (14)	Disease specific; measures stroke severity	Easy to obtain; good interobserver and intraobserver reliability	It applies to stroke patients only

APACHE, Acute Physiology and Chronic Health Evaluation; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; SF-36, Short-Form 36 Health Survey; NIHSS, National Institutes of Health Stroke Scale.

scoring systems such as the APACHE in neurologic outcome predictive models. The advantage of such approach is the inclusion of underlying medical comorbidities that may affect final outcome. The main outcomes that have been studied in the neurocritically ill include mortality, length of stay, and long-term functional outcome (4–7, 11, 12, 14). More recent outcome research studies have also incorporated measures of health status and quality of life (14).

Neuromonitoring

The monitoring of the neurocritically ill patient has become increasingly complex (15). Besides the close evaluation of cardiac and respiratory functions common to all critically ill patients, several techniques have become available for whole and regional brain monitoring (16–32). A complete description of all the neuromonitoring techniques available is beyond the scope of this review. A brief overview of such techniques is presented in Table 2.

The simplest and most commonly used monitoring technique is the serial neurologic assessment performed at the patient's bedside. Despite its importance, neurologic examinations have several limitations, including the inability to detect changes in patients who are receiving sedatives and the fact that it provides a qualitative rather than a quantitative assessment of brain functions. Other disadvantages are the lack of sensitivity at detecting some important conditions such as nonconvulsive status epilepticus or early changes in intracranial pressure or cerebral metabolism.

Because of these drawbacks, various other techniques have been developed to aid the neurointensivist in the management of the critically ill neurologic patient. As can be glanced from the information provided in Table 2, there is no ideal technique, and many of their indications still need to be explored further. However, the most useful clinical application of the neuromonitoring techniques has been in the early detection and treatment of secondary insults that may not be otherwise obvious on physical examination. Such secondary insults may be due to derangements in cerebral hemodynamics that lead to deleterious effects on brain oxygenation and metabolism. Derangements in cerebral hemodynamics in turn may be due to systemic hypotension, intracranial hypertension, hypoxemia, or anemia, among others. All these factors will ultimately result in brain tissue damage and worse clinical outcome.

Therefore, it seems logical to envision that the best clinical results would result from reliance on a multimodal monitoring approach (33, 34). For instance, a typical patient with severe traumatic brain injury would be monitored with continuous systemic blood pressure, intracranial pressure, cerebral perfusion pressure, jugular venous and brain tissue oxygenation, systemic and brain temperature, electroencephalography, and microdialysis. Some studies have addressed the issue of multimodal monitoring (15). Although the sample sizes have been small, it has become increasingly clear that by using such approach neurointensivists may be able to apply new technology more judiciously. Information that is corroborated by various techniques can be more reliably acted on, whereas spurious readings can be more easily discarded. The main challenge for the future is the validation of all available techniques in a large sample of patients and, more importantly, their correlation with clinical outcome.

Therapeutic Advances

Many significant developments have occurred over the past decade that have changed the way we view and treat acute neurologic conditions. These are mostly due to the design and execution of clinical trials that have been bridging the gap between knowledge of brain function and effective therapeutic interventions when such function is disturbed. This section presents a succinct description of new treatments for common neurologic emergencies such as acute ischemic stroke, intracerebral hemorrhage, subarachnoid

Table 2. Major neuromonitoring techniques used in the neurocritical care unit

Technique	Variable Measured	Major Indications	Disadvantages
Whole-brain monitoring			
Serial neurologic examination (15)	Qualitative assessment of brain function	All neurocritically ill patients	Constricted by pharmacologic interventions; operator dependent; qualitative
Intracranial pressure devices (16, 17)	Intracranial pressure; cerebral perfusion pressure	Coma and abnormal head CT; cerebral edema; midline shift; acute hydrocephalus	Invasive; ICH (<3%); infection (<14%); malfunction
Internal jugular bulb catheters (18, 19)	Oxygen saturation of venous return from the brain; cerebral oxygen extraction can be derived	Severe traumatic brain injury; diffuse cerebral edema	Line sepsis; venous thrombosis; carotid puncture; does not measure regional oxygenation
Continuous electroencephalography (20)	Brain electrical activity with close relationship to cerebral metabolic rate	Status epilepticus; altered level of consciousness to detect nonconvulsive status epilepticus; pentobarbital coma	Qualitative evaluation; frequent artifacts; interference with head imaging studies
Regional/focal brain monitoring			
Transcranial Doppler ultrasound (21, 22)	Cerebral blood flow velocity	Monitoring of cerebral vasospasm; vessel recanalization after thrombolytic therapy; confirmation of brain death	Operator dependent; may be limited by cranial anatomy
Near-infrared spectroscopy (23, 24)	Cerebral tissue oxymetry	Severe traumatic brain injury	Sensitivity to extraneous light; motion artifact; signal drift
Xenon-133 clearance (25, 26)	Regional cerebral blood flow	Severe traumatic brain injury; subarachnoid hemorrhage	Measures superficial blood flow; unreliable with abnormal blood-brain partition coefficient
Laser-Doppler flowmetry (27)	Qualitative regional cerebral blood flow	Under study for severe traumatic brain injury and massive cerebral edema	Probe malfunction requiring replacement
Thermal diffusion flowmetry (28)	Regional cerebral cortical blood flow	Under study for severe traumatic brain injury and massive cerebral edema	Infection (low risk); signal distortion; small region monitored
Microdialysis catheters (29, 30)	Various substances in the extracellular space	Severe traumatic brain injury; subarachnoid hemorrhage	Infection (low risk); may not detect all ischemic regions
Brain tissue probes (31, 32)	Regional brain Po_2, Pco_2, pH, and temperature	Severe traumatic brain injury; subarachnoid hemorrhage; diffuse cerebral edema	ICH and infection (low risk)

ICH, intracerebral hemorrhage; CT, computed tomography.

hemorrhage, traumatic brain injury, hypoxic-ischemic brain insult, and fever.

Acute Ischemic Stroke. The most important therapy for ischemic stroke introduced in the past decade has been thrombolysis. The administration of intravenous thrombolytic agents (mainly rt-PA) within 3 hrs of symptom onset can result in clinical and statistical significant improvement (35). At least 30% of treated patients will be completely independent 3 months after treatment. Other approaches to thrombolysis include the intraarterial route (which increases the window treatment to 6 hrs) (36), the combination administration of intravenous followed by intraarterial medications (37), and ultrasound-enhanced systemic thrombolysis (38). The latter incorporates the use of continuous transcranial Doppler ultrasound that augments thrombolysis-induced arterial recanalization. The future of acute ischemic stroke management will be in the development of newer neuroprotective therapies that could be administered along with thrombolytic medications.

Intracerebral Hemorrhage. One of the major discoveries has been the realization that intraparenchymal hematomas grow in about 38% of patients within 3 hrs of onset (39). Such growth may result in increased mortality. The most promising intervention to limit hematoma growth with resulting improved mortality and functional outcome thus far has been the administration of recombinant activated factor VIIa (39, 40). Surgical evacuation of intracerebral hematomas within 24 hrs has not shown benefit when compared with initial conservative treatment (41). The one group of patients who may benefit from surgery with improved functional outcome is that with cerebellar hematomas. Another issue that has generated controversy is the blood pressure management in the acute setting after intracerebral hemorrhage. On the one hand, there is the risk of increasing the size of the hematoma if blood pressure remains elevated, and on the other, there may be the theoretical risk of causing cerebral ischemia if blood pressure is reduced. Recent preliminary evidence suggests that blood pressure reductions may be safe (42). A prospective study is under way to evaluate the optimal blood pressure control level in these patients.

Subarachnoid Hemorrhage. Subarachnoid hemorrhage is a devastating disease. It carries a significant number of medical and neurologic complications. The results of several clinical trials have led to improved care and outcome of these patients. Cerebral vasospasm is a frequent cause of cerebral ischemia after subarachnoid hemorrhage. Calcium antagonists, particularly nimodipine and possibly magnesium, reduce the risk of poor outcome and cerebral ischemia (43).

Current management protocols for patients with subarachnoid hemorrhage incorporate the routine use of nimodipine for all patients. Circulatory volume expansion has been commonly used under the assumption that hypovolemia is related to cerebral ischemia. However, convincing evidence of its benefit is lacking (44). The use of intraoperative (i.e., during aneurysm clipping) hypothermia does not improve clinical outcome as was previously predicated (45). Lastly, treatment of ruptured aneurysm has been revolutionized with the advent of endovascular detachable coiling as an alternative to craniotomy and aneurysm clipping. A recent multiple-center, randomized trial revealed that in patients with ruptured cerebral aneurysms, for which both endovascular coiling or surgical clipping are treatment options, the outcome in terms of disability at 1 yr is better for patients undergoing endovascular coiling (46). Currently ruptured aneurysms are best treated by a team of professionals with experience in both surgical clipping and endovascular coiling who can decide on the proper therapeutic option.

Hypoxic–Ischemic Insult. Sudden death from cardiac arrest is a frequent health problem. Few patients survive a cardiac arrest with acceptable neurologic recovery. Traditionally, for the past 40 yrs, treatment of cardiac arrest patients concentrated on resuscitative efforts to try to limit both systemic and neurologic damage. However, it has become evident that neurologic injury occurs during and after resuscitation. The most significant novel treatment for comatose survivors of cardiac arrest has been induced hypothermia (47–49). Evidence from randomized controlled trials has demonstrated that institution of mild-to-moderate hypothermia results in improved survival and functional outcome of these patients. Based on these results, the American Heart Association has recommended the inclusion of hypothermia intervention into the management of post–cardiac arrest patients.

Traumatic Brain Injury. Severe traumatic brain injury still remains an important public health issue, particularly among the young. Mortality rates have decreased over the past decade. One major factor that may have accounted for this is the establishment of trauma centers (50, 51). Patients admitted to specialized trauma centers are more likely to experience a reduced hospital length of stay and mortality, with improved functional outcome. Another important issue is the aggressive management of hypotension in the prehospital setting. A recent randomized clinical trial of aggressive fluid management in the prehospital setting revealed decreased mortality, most likely related to avoidance of hypotension (52).

Induced hypothermia has also been applied to patients with severe traumatic brain injury (53). Clinical trial results have not been as convincing as in comatose survivors of cardiac arrest. Studies have revealed that induced hypothermia may confer benefit particularly to those patients with elevated intracranial pressure. However, the routine use of this treatment remains controversial.

Fever. Elevated core body and brain temperature is associated with worsening neurologic injury and functional outcome of critically ill neurologic patients, regardless of the type of injury (54). Such association is very important because fever is a frequent occurrence in neurologic patients while in the ICU. It has also become evident that traditional methods of fever treatment such as administration of acetaminophen and traditional cooling blankets are not that effective at reducing fever. Therefore, newer cooling techniques have been developed. Both novel surface cooling and catheter-based heat-exchange systems have been found to be more beneficial than traditional cooling methods in febrile patients in the neurocritical care unit (55, 56). What remains to be answered is whether effective fever reduction results in significantly improved functional outcome and mortality rates in these patients.

High-Intensity Staffing with a Specialized Neurocritical Care Team

Care of the critically ill is expensive. It has been estimated that approximately 1% of the U.S. gross domestic product is directly utilized in the ICU (57). There is a lack of uniformity in how ICU care is delivered. The organization of an ICU is important because it can potentially reduce costs and improve outcomes. One such example is the availability of intensivists. Staffing general and surgical ICUs with intensivists has been associated with improved outcomes and reduced resource utilization (57–60).

ICU staffing has been classified as low intensity (i.e., no intensivist available or elective intensivist consultation) or high intensity (i.e., mandatory intensivist consultation or closed ICU) (57). Pronovost et al. (57) reported on a systematic review of the literature of physician staffing patterns and clinical outcomes in critically ill patients. A total of 26 observational studies were included in their review. The authors found that high-intensity staffing was associated with lower hospital mortality in 94% of the studies and reduced hospital length of stay in all the studies that adjusted for case mix. Most of these studies were reported in general medical or surgical ICUs.

A review of MEDLINE (January 1, 1965, through September 1, 2005) revealed four studies specifically addressing the issue of the effect of specialized neurocritical care teams or specialized neurocritical care units on outcome of the critically ill neurologic patient (4–7). The main features of these four studies are summarized in Table 3. Two of the studies evaluated the effect of the availability of specialized neurocritical care teams (high-intensity staffing) on mortality and length of stay (4, 5). Both studies reported improved outcomes as given by decreased hospital mortality rates and reduced hospital length of stay. There was also a reduced number of significant medical complications after the teams were introduced. Mirski et al. (7) reported on the effect of a neuroscience intensive care unit on outcome of patients with intracerebral hemorrhage within the same institution. The authors found that admission to a dedicated neuroscience critical care unit was associated with reduced mortality and hospital length of stay for these patients. Diringer and Edwards (6) analyzed data prospectively collected by Project Impact over a period of 3 yrs from 42 participating ICUs. The authors compared outcomes of patients with intracerebral hemorrhage admitted to general ICUs vs. those admitted to specialized neurocritical care units. They found that not being admitted to a neurocritical care unit was associated with increased hospital mortality. As opposed to the other three previous studies, the latter found that admission to a neurocritical care unit was also associated with increased length of stay in patients with intracerebral hemorrhage. In summary, the availability of specialized neurocritical care teams or neurocritical care units is associated with improved outcomes of critically ill neurologic patients, including decreased hospital mortality and resource utilization. The study by Suarez et al. (4) also evaluated the effect of a spe-

Table 3. Studies reporting on the effect of neurocritical care unit admission or availability of neurocritical care teams on outcomes of critically ill neurologic patients

Source	Population	Study Design	ICUs Studied	No. of Patients	Adjustment for Confounding Variables	Hospital Mortality	Hospital Length of Stay	Readmission Rates	Long-Term Mortality
Suarez et al. (4)	Mixed critically ill neurologic and neurosurgical	Cohort with historical control	One neurocritical care unit (before and after neurocritical care team introduction)	2381 adults	APACHE III score and other variables	Reduced from 10.6% to 8.0% (p =.04)	−13.8% change in mean length of stay (95% CI, −18.2 to −9.1)	Unchanged (7.7% vs. 6.4%, p = .3)	Unchanged
Varelas et al. (5)	Mixed critically ill neurologic and neurosurgical	Cohort with historical control	One neurocritical care unit (before and after neurocritical care team introduction)	2366 adults	Several variables, including expected mortality from University Hospitals Consortium	Unchanged, 10.1% and 9.1% (p = .4), but different from expected increase of 1.4% (p = .048)	Decreased from 8.5 ± 8.9 to 7.6 ± 8.1 days (p = .012)	Not reported	Not reported
Diringer and Edwards (6)	Intracerebral hemorrhage patients	Outcomes, cross-sectional with concurrent control	42 ICUs (comparing two neurocritical units with other medical and surgical ICUs)	1038 adults	APACHE II score and other variables	Increased if admitted to general ICU (OR, 3.4; 95% CI, 1.65–7.6)	Increased from 4.5 ± 6.2 to 7.8 ± 12.5 (p < .05)	Not reported	Not reported
Mirski et al. (7)	Intracerebral hemorrhage patients	Cohort with historical control	Two (general ICU compared with specialized neurocritical care unit)	128 adults	Mortality compared with national benchmarks for general ICUs	Decreased from 36% to 19% (p < .05)	Unchanged	Not reported	Not reported

ICU, intensive care unit; APACHE, Acute Physiology and Chronic Health Evaluation; OR, odds ratio; CI, confidence intervals.

cialized neurocritical care team on readmission rates and long-term mortality at 1 yr after discharge. The authors reported no changes in either outcome after the team was introduced.

The availability of neurocritical care teams as reported in all of the four studies mentioned led to significant organizational changes in the care of critically ill neurologic patients (4–7). There were changes in discharge and admission patterns, including enforcement of triage criteria. The authors also reported development of management protocols and educational programs for all the personnel involved in the care of these patients. The improved outcome associated with the presence of the neurocritical care team is likely multifactorial and may be related to the ability of these practitioners to standardize management of common medical problems and organize and manage the ICU environment (61, 62).

All studies investigating physician staffing patterns and outcomes of critically ill patients have limitations that are worth considering (4, 61). Most of these studies published so far include retrospective analysis of prospectively collected data. No randomized controlled trial has been designed to evaluate this issue due to both practical and ethical dilemmas. Other limitations include temporal trends and lack of control over pre- and post-ICU care, including changes in patient management and discharge practices over time. Lastly, none of these studies analyzed quality of life of survivors, which would be more meaningful for the everyday activities of survivors. Despite all these limitations, the evidence is very strong for the implementation of specialized neurocritical care units staffed by neurointensivists.

Conclusions

Critically ill neurologic patients present special challenges related to the interaction between systemic derangements and intracranial processes that require special attention. Significant advances have occurred over the past few years with regard to the care of these patients. It has become increasingly clear that neurocritical care units staffed by specially trained neurointensivists have a significant favorable effect on clinical outcome of patients and resource utilization. Neurointensivists are capable of providing an integrative care of neurologic patients requiring critical care. More importantly, neurointensivists can interpret multimodality monitoring that these patients often need and correct abnormalities in a timely fashion. Neurocritical care is a growing discipline. The creation of the Neurocritical Care Society will provide a means to enhance cooperation among neurointensivists. Such cooperation will undoubtedly have a significant effect on patient care, including better clinical trial design and execution.

REFERENCES

1. Bleck T: Critical care and emergency neurology. *In:* The American Academy of Neurology: The First 50 Years 1948–1998. Cohen MM (Ed). St Paul, American Academy of Neurology, 1998, pp 225–227
2. Neurocritical Care Society Web site. Available at: http://www.neurocriticalcare.org
3. Sung G: Outcomes in neurosciences critical care. *In:* Critical Care Neurology and Neurosurgery. Suarez JI (Ed). Totowa, NJ, Humana Press, 2004, pp 581–587
4. Suarez JI, Zaidat OO, Suri MF, et al: Length of stay and mortality in neurocritically ill patients: Impact of a specialized neurocriti-

cal care team. *Crit Care Med* 2004; 32:2311–2317

5. Varelas PN, Conti MM, Spanaki MV, et al: The impact of a neurointensivist-led team on a semi-closed neurosciences intensive care unit. *Crit Care Med* 2004; 32:2191–2198
6. Diringer MN, Edwards DF: Admission to a neurologic/neurosurgical intensive care unit is associated with reduced mortality rate after intracerebral hemorrhage. *Crit Care Med* 2001; 29:635–640
7. Mirski MA, Chang CW, Cowan R: Impact of a neuroscience intensive care unit on neurosurgical patient outcome and cost of care: Evidence-based support for an intensivist-directed specialty ICU model of care. *J Neurosurg Anesthesiol* 2001; 13:83–92
8. Knaus WA, Wagner DP, Draper EA, et al: The APACHE III prognostic system: Risk prediction of hospital mortality for critically ill hospitalized adults. *Chest* 1991; 10:1619–1636
9. Teasdale G, Jennett B: Assessment of coma and impaired consciousness: A practical scale. *Lancet* 1974; 2:81–84
10. Jennett B, Bond M: Assessment of outcome after severe brain damage. *Lancet* 1975; 1:480–484
11. Mahoney FI, Barthel DW: Functional evaluation: The Barthel Index. *Md State Med J* 1965; 14:61–65
12. Rankin J: Cerebral vascular accidents in patients over the age of 60. *Scott Med J* 1957; 2:200–215
13. Ware JE, Sherbourne CD: The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Med Care* 1992; 30:473–483
14. Brott T, Adams HP, Olinger CP, et al: Measurements of acute cerebral infarction: A clinical examination scale. *Stroke* 1989; 20:864–870
15. Miller DW, Suarez JI: Neurologic and systemic monitoring in the NSU. *In:* Critical Care Neurology and Neurosurgery. Suarez JI (Ed). Totowa, NJ, Humana Press, 2004, pp 101–122
16. Lang EW, Chestnut RM: Intracranial pressure: Monitoring and management. *Neurosurg Clin North Am* 1994; 5:573–588
17. The Brain Trauma Foundation. The American Association of Neurological Surgeons. The Joint Section on Neurotrauma and Critical Care. Indications for intracranial pressure monitoring. *J Neurotrauma* 2000; 17:479–491
18. Feldman Z, Robertson CS: Monitoring of cerebral hemodynamics with jugular bulb catheters. *Crit Care Clin* 1997; 13:51–77
19. Latronico N, Beindorf AE, Rasulo FA, et al: Limits of intermittent jugular bulb saturation monitoring in the management of severe head trauma patients. *Neurosurgery* 2000; 46:1131–1138
20. Jordan KG: Neurophysiologic monitoring in the neuroscience intensive care unit. *Neurol Clin* 1995; 13:579–626
21. Manno EM: Transcranial Doppler ultrasonography in the neurocritical care unit. *Crit Care Clin* 1997; 13:79–104
22. Suarez JI, Qureshi AI, Yahia AB, et al: Symptomatic vasospasm diagnosis after subarachnoid hemorrhage: Evaluation of transcranial Doppler ultrasound and cerebral angiography as related to compromised vascular distribution. *Crit Care Med* 2002; 30:1348–1355
23. Kirkpatrick PJ, Smielewski P, Czosnyka M, et al: Near-infrared spectroscopy use in patients with head injury. *J Neurosurg* 1995; 83:963–970
24. Nemoto EM, Yonas H, Kassam A: Clinical experience with cerebral oxymetry in stroke and cardiac arrest. *Crit Care Med* 2000; 28:1052–1054
25. Anderson RE: Cerebral blood flow xenon-133. *Neurosurg Clin North Am* 1996; 7:703–708
26. Martin NA, Doberstein C: Cerebral blood flow measurement in neurosurgical intensive care. *Neurosurg Clin North Am* 1994; 5:607–618
27. Haberl PL, Villringer A, Dirnagl U: Applicability of laser-Doppler flowmetry for cerebral blood flow monitoring in neurological intensive care. *Acta Neurochir* (*Suppl*) 1993; 59:64–68
28. Carter LP: Thermal diffusion flowmetry. *Neurosurg Clin North Am* 1996; 7:749–754
29. Schulz MK, Wang LP, Tange M, et al: Cerebral microdialysis: Determination of normal and ischemic cerebral metabolism in patients with aneurysmal subarachnoid hemorrhage. *J Neurosurg* 2000; 93:808–814
30. Vespa P, Prins M, Ronne-Engstrom E, et al: Increase in extracellular glutamate caused by a reduced cerebral perfusion and seizures after human traumatic brain injury: A microdialysis study. *J Neurosurg* 1998; 89:971–982
31. van den Brink WA, van Santbrink H, Steyerberg EW, et al: Brain oxygen tension in severe head injury. *Neurosurgery* 2000; 46:868–878
32. Valadka AB, Shankar SP, Contant CF, et al: Relationship of brain tissue Po_2 to outcome after severe head injury. *Crit Care Med* 1998; 26:1576–1581
33. Kirkpatrick PJ, Czosnyka M, Pickard JD: Multimodal monitoring in neurointensive care. *J Neurol Neurosurg Psychiatry* 1996; 60:131–139
34. Kett-White R, Hutchinson PJ, Czosnyka M, et al: Multimodal monitoring of acute brain injury. *Adv Tech Stand Neurosurg* 2002; 27:87–134
35. Tissue plasminogen activator for acute ischemic stroke: The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *N Engl J Med* 1995; 333:1581–1587
36. Suarez JI, Sunshine JL, Tarr R, et al: Predictors of clinical improvement, angiographic recanalization, and intracranial hemorrhage after intra-arterial thrombolysis for acute ischemic stroke. *Stroke* 1999; 30:2094–2100
37. IMS Study Investigators: Combined intravenous and intra-arterial recanalization for acute ischemic stroke: The Interventional Management of Stroke Study. *Stroke* 2004; 35:904–911
38. Alexandrov AV, Molina CA, Grotta JC, et al: Ultrasound-enhanced systemic thrombolysis for acute ischemic stroke. *N Engl J Med* 2004; 351:2170–2178
39. Mayer SA, Brun NC, Broderick J, et al: Safety and feasibility of recombinant factor VIIa for acute intracerebral hemorrhage. *Stroke* 2005; 36:74–79
40. Mayer SA, Brun NC, Begtrup K, et al: Recombinant activated factor VII for acute intracerebral hemorrhage. *N Engl J Med* 2005; 352:777–785
41. Mendelow AD, Gregson BA, Fernandes HM, et al: Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral hematomas in the International Surgical Trial in Intracerebral haemorrhage (STITCH): A randomised trial. *Lancet* 2005; 365:387–397
42. Qureshi AI, Mohammad YM, Yahia AM, et al: A prospective multicenter study to evaluate the feasibility and safety of aggressive antihypertensive treatment in patients with acute intracerebral hemorrhage. *J Intensive Care Med* 2005; 20:34–34
43. Rinkel GJ, Feigin VL, Algra A, et al: Calcium antagonists for aneurysmal subarachnoid hemorrhage. *Cochrane Database Syst Rev* 2005; 1:CD000277
44. Rinkel GJ, Feigin VL, Algra A, et al: Circulatory volume expansion therapy for aneurysmal subarachnoid hemorrhage. *Cochrane Database Syst Rev* 2004; 4:CD000483
45. Todd MM, Hindman BJ, Clarke WR, et al: Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med* 2005; 352:135–145
46. Molyneux A, Kerr R, Stratton I, et al: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: A randomised trial. *Lancet* 2002; 360:1267–1274
47. Sterz F, Holzer M, Roine R, et al: Hypothermia after cardiac arrest: A treatment that works. *Curr Opin Crit Care* 2003; 9:205–210
48. Bernard SA, Gray TW, Buist MD, et al: Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med* 2002; 346:557–563
49. Holzer M, Bernard SA, Hachimi-Idrissi S, et al: Hypothermia for neuroprotection after cardiac arrest: Systematic review and individual patient data meta-analysis. *Crit Care Med* 2005; 33:414–418
50. Fakhry SM, Trask AL, Waller MA, et al: Management of brain-injured patients by an evidence-based medicine protocol improves outcomes and decreases hospital charges: IRTC Neurotrauma Task Force. *J Trauma* 2004; 56:492–499
51. Bulger EM, Nathens AB, Rivara FP, et al: Management of severe head injury: Institu

tional variations in care and effect on outcome. *Crit Care Med* 2002; 30:1870–1876
52. Cooper JD, Myles PS, McDermott FT, et al: Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: A randomized controlled trial. *JAMA* 2004; 291:1350–1357
53. McIntyre LA, Fergusson DA, Hebert PC, et al: Prolonged therapeutic hypothermia after traumatic brain injury in adults: A systematic review. *JAMA* 2003; 289:2992–2999
54. Marion DW: Controlled normothermia in neurologic intensive care. *Crit Care Med* 2004; 32(2 Suppl):S43–S45
55. Mayer SA, Kowalski RG, Presciutti M, et al: Clinical trial of a novel surface cooling system for fever control in neurocritical care patients. *Crit Care Med* 2004; 32:2508–2515
56. Diringer MN: Treatment of fever in the neurologic intensive care unit with a catheter-based heat exchange system: Neurocritical Care Fever Reduction Trial Group. *Crit Care Med* 2004; 32:559–564
57. Pronovost PJ, Angus DC, Dorman T, et al: Physician staffing patterns and clinical outcomes in critically ill patients: A systematic review. *JAMA* 2002; 288:2151–2162
58. Randolph AG: Reorganizing the delivery of intensive care may improve patient outcomes. *JAMA* 1999; 281:1330–1331
59. Dimick JB, Pronovost PJ, Heitmiller RF, et al: Intensive care unit physician staffing is associated with decreased length of stay, hospital cost, and complications after esophageal resection. *Crit Care Med* 2001; 29:753–758
60. Pronovost PJ, Jenckes MW, Dorman T, et al: Organizational characteristics of intensive care units related to outcomes of abdominal aortic surgery. *JAMA* 1999; 281:1310–1317
61. Gore DC, Prough DS: Impact of intensivists on outcome of critically ill neurologic and neurosurgical patients. *Crit Care Med* 2004; 32:2363–2364
62. Diringer MN: Bringing order to chaos. *Crit Care Med* 2004; 32:2346