

ANESTHESIOLOGY

■ Does Use of Volatile Anesthetic Shorten Time in the Intensive Care Unit after Elective Coronary Surgery? De Hert *et al.* (page 9)

To test whether use of a volatile anesthetic agent in a fast track protocol would result in better postoperative cardiac function than the total intravenous anesthetic regimen, De Hert *et al.* randomly assigned 320 patients to one of four anesthetic protocols. All patients were scheduled for elective coronary surgery with cardiopulmonary bypass and all received sublingual lorazepam and intravenous fentanyl before surgery.

In the propofol group, anesthesia was induced with a continuous infusion of remifentanyl at $0.4 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and a target controlled infusion of propofol set at a target plasma concentration of $2 \mu\text{g}/\text{ml}$. Patients in the midazolam group received a continuous infusion of remifentanyl at the same dosage as the propofol group, combined with midazolam $0.1 \text{ mg}/\text{kg}$, and then $0.5\text{--}1.5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. In the sevoflurane group, anesthesia was also induced with remifentanyl and midazolam, but maintained with remifentanyl and sevoflurane. Finally, in the desflurane group, anesthesia was also induced with remifentanyl and midazolam, and maintained with remifentanyl and sevoflurane.

Global hemodynamic data were registered before the start of surgery, before and after cardiopulmonary bypass, at the end of the operation, and at 6, 12, and 24 h after transfer to the intensive care unit (ICU). When in the ICU, patients were kept sedated for 2 h according to local protocol and extubated when they demonstrated adequate response to command, had oxygen saturation measured by pulse oximetry 95% or greater at a fraction of inspired oxygen of 0.5 or less, pH 7.3 or greater, arterial carbon dioxide tension 55 mmHg or less, and adequate respiratory effort. Filling pressures were kept constant throughout the entire observation period by administering intravenous fluids. Administration of inotropes and vasoactive drugs was done according to specific protocols. Specific criteria were also used for transfer out of the ICU and for hospital discharge.

Patients in the sevoflurane and desflurane groups had shorter stays in the ICU than did those in the propofol and midazolam groups. Hospital length of stay was also shorter for patients receiving volatile anesthetics. The authors found that atrial fibrillation, a postoperative troponin I level of $> 4 \text{ mg}/\text{ml}$, and the need for prolonged inotropic support ($> 12 \text{ h}$) were significant risk factors for prolonged ICU and hospital length of stay. The use of

sevoflurane and desflurane resulted in lower postoperative troponin I levels and less need for inotropic support. The volatile anesthetics appear related to better preservation of early postoperative myocardial function.

■ Predicting Recovery of Consciousness in Acute Brain-injured Patients. Fàbregas *et al.* (page 43)

The Bispectral Index (BIS) of the electroencephalogram is a weighted sum of electroencephalographic subparameters containing time domain, frequency domain, and higher order spectral information, and was approved by the federal Food and Drug Administration in 1996 for monitoring hypnotic effect of anesthetics and sedatives. Fàbregas *et al.* sought to establish a relationship between the BIS and other variables derived from the analysis of the electroencephalographic signal, to measure whether BIS has value as a predictor of return to consciousness.

The researchers withdrew sedative drugs from 25 critically ill unconscious brain-injured patients at least 24 h before the BIS recording. Their brain injuries were due to isolated brain trauma ($n = 8$), multiple trauma ($n = 7$), subarachnoid hemorrhage ($n = 8$), and stroke ($n = 2$). None were able to respond to verbal commands, and most were intubated and receiving mechanical ventilatory support. Patients were assessed for their Glasgow Coma Score on the day of the study. The BIS[®] three-electrode sensor (Aspect Medical Systems, Inc., Newton, MA) was placed on the forehead of the healthiest brain hemisphere (identified by computed tomography scan). For each individual 20-min recording, an estimate of maximal value, minimal value, average, and range of BIS values were calculated. Each patient's neurologic status was defined using the Glasgow Outcome Score (GOS) at the time of ICU discharge, at the time of hospital discharge, and at the end of the follow-up period. Patients were followed for a period of 6 months after their injury, or until they recovered consciousness or died. Only two patients were discharged from the hospital. Seventeen others were transferred to rehabilitation facilities and there were 7 deaths, all but one due directly to brain damage.

Patients were divided into two groups according to their final outcome: those who recovered consciousness (rated from good recovery, GOS of 1; to moderate disability, GOS of 2; or severe disability, GOS of 3) and those who had a bad neurologic outcome, resulting in either persistent vegetative state (GOS of 4) or death (GOS of 5). Investigators found statistically significant differences between the

group of patients who recovered consciousness and those who did not with respect to BIS_{max} , BIS_{min} , BIS_{mean} , BIS_{range} , frontal electromyography, Signal Quality Index values, and also initial Glasgow Coma Score_{BIS}. All patients with an electromyographic score above 1.5 regained consciousness. And although the study did not include plasma levels of sedative drugs during the study day, the results of the study suggest that patients whose BIS_{max} is higher than 52.25 have a probability of recovering consciousness higher than 0.5, and those with BIS_{max} higher than 69 have a probability higher than 0.9. Although BIS® (Aspect Medical Systems, Inc.) was not designed for this particular application in neurologically impaired patients, its availability in the intensive care unit and these results may warrant further study of its contributions to predicting return to consciousness of these severely injured patients.

■ Neuroprotection in a Rat Model of Focal Cerebral Ischemia. Inoue *et al.* (page 75)

To investigate whether adding a caspase inhibitor to isoflurane might provide neuroprotection in rats subjected to focal ischemia, Inoue *et al.* allocated rats to four different protocols. Awake rats received either z-VAD-fmk (a nonspecific caspase inhibitor) or vehicle drug; two other groups of rats received either a combination of isoflurane-zVAD or isoflurane-vehicle.

Animals were subjected to focal ischemia for 60 min by filament occlusion of the middle cerebral artery. In the awake groups, isoflurane was discontinued after occlusion of the middle cerebral artery. In the isoflurane groups, the anesthetic was maintained at 1.5 minimum alveolar concentration during the ischemic procedure. Both before and after ischemia, rats were given daily injections of z-VAD-fmk or vehicle for 14 days. At that point, neurologic assessments were performed and each rat was assigned a score according to an eight-point behavioral rating scale (0 = no neurologic deficit; 7 = dead). The animals were killed and decapitated, and their brains were removed for sectioning and histologic examination.

Out of a total of 64 animals, 4 were excluded from analysis, and 5 more died before histologic analysis could be conducted. Researchers found that infarct volume was less in rats receiving isoflurane-zVAD than in all other groups. Those rats had also demonstrated better neurologic function than the ones in the awake-vehicle group. Upon histologic analysis, the brains from the awake-vehicle group had fewer intact neurons in comparison to all three other experimental groups. When administered alone, isoflurane did not confer a reduction in cerebral injury after ischemia. It appears that a combination therapy such as

isoflurane and zVAD may target different aspects of the pathophysiology of cerebral ischemia (excitotoxicity and apoptosis) and thus may be more effective than administering a single agent to reduce ischemic cerebral injury.

■ Does Central Neuraxial Analgesia Improve Outcomes in Coronary Artery Bypass Patients? Liu *et al.* (page 153)

To shed light on the role of various anesthetic methods in coronary artery bypass graft patients, Liu *et al.* conducted a meta-analysis of existing randomized controlled trials comparing general anesthesia to either general anesthesia-thoracic epidural analgesia or general anesthesia with intrathecal analgesia. The investigators initially identified 58 abstracts for possible inclusion from a scan of five databases including the National Library of Medicine's MEDLINE and the Cochrane Database of Systematic Reviews. Of these potential studies, conducted from 1966 to January 2004, the authors included in their final review 15 epidural anesthesia trials and 17 spinal anesthesia trials, with totals of 1,178 and 668 patients, respectively.

The team recorded each study's methodology and patient outcomes, including incidence of death, myocardial infarction, dysrhythmias, and pulmonary complications, during the postoperative study periods. Times to extubation, visual or verbal analogue pain scales, troponin I levels, and opioid consumption in the postoperative period were also included in the analysis. The authors found that thoracic epidural analgesia significantly reduced risk of dysrhythmias, pulmonary complications, time to extubation, and pain scores at rest and with activity compared to general anesthesia alone. Intrathecal analgesia modestly decreased systemic morphine use and decreased pain scores by 16 mm. Neither thoracic epidural analgesia nor intrathecal analgesia had a significant effect on incidences of mortality or myocardial infarction after coronary artery bypass graft. The risk of spinal hematoma in patients undergoing full anticoagulation for coronary artery bypass graft was 1 in 1,528 for thoracic epidural analgesia and 1 in 3,610 for intrathecal analgesia. Due to the small numbers of patients included in the selected trials, however, the conclusions of this meta-analysis may not be applicable to many cardiac surgical patients. In addition, the mortality rates in the original trials were low, suggesting a low-risk study population that may not be applicable to the population at large. A large randomized controlled trial is needed to further assess the best anesthetic regimen during coronary artery bypass graft.

Gretchen Henkel