

ON THE COVER:

The 2014 American College of Cardiology Perioperative Guideline recommends risk stratifying patients scheduled to undergo noncardiac surgery using either the Revised Cardiac Index, the American College of Surgeons National Surgical Quality Improvement Program Surgical Risk Calculator, or the Myocardial Infarction or Cardiac Arrest calculator. In this issue of ANESTHESIOLOGY, Glance *et al.* used a retrospective cohort of 10,000 patient records to determine how often these three risk-prediction tools agree on the classification of patients as low risk of major adverse cardiac event. They demonstrated wide variability in the predicted risk of cardiac complications using different risk-prediction tools. In an accompanying Editorial View, Fleisher, who served as chair of the Perioperative Guideline Committee, discusses the practical implications of using risk-prediction tools and the current lack of evidence that use of any one tool leads to superior patient outcomes.

- Glance *et al.*: Impact of the Choice of Risk Model for Identifying Low-risk Patients Using the 2014 American College of Cardiology/American Heart Association Perioperative Guidelines, p. 889
- Fleisher: Preoperative Cardiac Evaluation before Noncardiac Surgery Reverend Bayes's Risk Indices and Optimal Variables, p. 867

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- ◆ ◆ **Recommendations for the Nomenclature of Cognitive Change Associated with Anaesthesia and Surgery—2018** 872

L. Evered, B. Silbert, D. S. Knopman, D. A. Scott, S. T. DeKosky, L. S. Rasmussen, E. S. Oh, G. Crosby, M. Berger, R. G. Eckenhoff, and The Nomenclature Consensus Working Group

Suggestions are made regarding definitions and criteria for cognitive disorders associated with anesthesia and surgery, to align with those in other disciplines including psychiatry, gerontology, and neurology.

PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

- ◆ ◆ **Comparison of the TOFscan and the TOF-Watch SX during Recovery of Neuromuscular Function** 880



G. S. Murphy, J. W. Szokol, M. J. Avram, S. B. Greenberg, T. D. Shear, M. Deshur, J. Benson, R. L. Newmark, and C. E. Maher

A new generation of quantitative monitoring using three-dimensional acceleromyographic technology, the TOFscan (Drager Technologies, Canada), has been developed that requires minimal setup for intraoperative use. TOFscan measures the recovery of neuromuscular function with good agreement to an existing device, the TOF-Watch SX (Organon, Ireland), which requires preload application, calibration, and normalization.

- ◆ ◆ **Impact of the Choice of Risk Model for Identifying Low-risk Patients Using the 2014 American College of Cardiology/American Heart Association Perioperative Guidelines** 889



L. G. Glance, E. Faden, R. P. Dutton, S. J. Lustik, Y. Li, M. P. Eaton, and A. W. Dick

Thirty percent of predictions regarding high *versus* low risk are discordant across the risk calculators. The choice of risk-prediction tool could have an impact on the calculated risk and subsequent clinical decisions. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- Differences of Recovery from Rocuronium-induced Deep Paralysis in Response to Small Doses of Sugammadex between Elderly and Nonelderly Patients** 901

T. Muramatsu, S. Isono, T. Ishikawa, N. Nozaki-Taguchi, J. Okazaki, Y. Kitamura, N. Murakami, and Y. Sato

The train-of-four ratio recovery rate after low-dose sugammadex administration was slower in elderly patients than it was in nonelderly patients. Recurarization after low-dose sugammadex administration occurred more frequently in elderly patients than in nonelderly patients. Slower spontaneous train-of-four ratio recovery and impaired renal function were most closely associated with the decreased train-of-four ratio change rate in response to low-dose sugammadex in multiple linear regression analysis.

- ◆ **Caffeine Accelerates Emergence from Isoflurane Anesthesia in Humans: A Randomized, Double-blind, Crossover Study** 912



R. Fong, L. Wang, J. P. Zacny, S. Khokhar, J. L. Apfelbaum, A. P. Fox, and Z. Xie

The authors tested the hypothesis that caffeine speeds anesthetic emergence. Volunteers anesthetized with isoflurane were given caffeine (equivalent to 7.5 mg base) or placebo in a blinded crossover trial. When given caffeine, the volunteers emerged more quickly and at a higher isoflurane concentration.

- Effect of Equipotent Doses of Propofol *versus* Sevoflurane Anesthesia on Regulatory T Cells after Breast Cancer Surgery** 921

C.-S. Oh, J. Lee, T.-G. Yoon, E.-H. Seo, H.-J. Park, L. Piao, S.-H. Lee, and S.-H. Kim

A total of 201 women having breast cancer surgery were randomly assigned to propofol or sevoflurane anesthesia. Cluster of differentiation 39 and 73 expression did not differ nor did any other evaluated immune functions. These results do not support the putative protective effect of propofol on cancer recurrence.

Propofol-based Total Intravenous Anesthesia Is Associated with Better Survival Than Desflurane Anesthesia in Colon Cancer Surgery 932

Z.-F. Wu, M.-S. Lee, C.-S. Wong, C.-H. Lu, Y.-S. Huang, K.-T. Lin, Y.-S. Lou, C. Lin, Y.-C. Chang, and H.-C. Lai

The authors conducted a propensity-matched retrospective analysis of 1,158 patients who had colon cancer surgery. Patients anesthetized with propofol had better overall survival.

BASIC SCIENCE

Resting-state Dynamics as a Cortical Signature of Anesthesia in Monkeys 942

L. Uhrig, J. D. Sitt, A. Jacob, J. Tasserie, P. Bartfeld, M. Dupont, S. Dehaene, and B. Jarraya

When moving from wakefulness to anesthesia, the anatomical structure of connections between brain areas becomes the main driver of the repertoire of functional states. Subjects given anesthesia lose the ability to generate flexible functional brain states that transcend brain anatomy. High similarity between brain structure and function is a new general signature of anesthesia-induced loss of consciousness. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Etomidate and Etomidate Analog Binding and Positive Modulation of γ -Aminobutyric Acid Type A Receptors: Evidence for a State-dependent Cutoff Effect 959

M. McGrath, Z. Yu, S. S. Jayakar, C. Ma, M. Tolia, X. Zhou, K. W. Miller, J. B. Cohen, and D. E. Raines

γ -Aminobutyric acid type A (GABA_A) receptor positive modulatory activities of phenyl ring-substituted etomidate analogs decreased with increasing substituent group volume, reflecting decreases in both potencies and efficacies of the analogs. Their GABA_A receptor positive modulatory activities were strongly correlated with their affinities for the two β^+ – α^- transmembrane anesthetic binding sites of the GABA_A receptor. Open-state binding affinity decreased progressively with increasing substituent group volume.

Preclinical Pharmacology in the Rhesus Monkey of CW 1759-50, a New Ultra-short Acting Nondepolarizing Neuromuscular Blocking Agent, Degraded and Antagonized by L-Cysteine 970

J. J. Savarese, H. Sunaga, J. D. McGilvra, M. R. Belmont, M. T. Murrell, E. Jeannotte, F. E. Cooke, W. B. Wastila, and P. M. Heerd

CW 1759-50 is a new nondepolarizing neuromuscular blocking agent that may have a clinical profile that is superior to that of gantacurium. Studies in rhesus monkeys comparing CW 1759-50 with gantacurium found both of them to be ultra-short acting because of their rapid degradation by L-cysteine adduction. The effects of CW 1759-50 on mean arterial pressure and heart rate were substantially less than those of gantacurium.

Ultrasound Elastography for Rapid, Real-time Detection of Localized Muscular Reaction in Malignant Hyperthermia-susceptible Pigs 989

S. Johannsen, I. Türkmeneli, S. Isbary, N. Roewer, and F. Schuster

In vivo ultrasound (shear-wave) elastography detected a temporary increase in local tissue stiffness soon after intramuscular injection of halothane and caffeine in malignant hyperthermia-susceptible pigs. Quantitative shear-wave elastography allowed earlier detection of reactions to halothane and caffeine than did measurement of local lactate concentrations in microdialysis fluids, although the responses were analogous.

Midazolam and Dexmedetomidine Affect Neuroglioma and Lung Carcinoma Cell Biology *In Vitro* and *In Vivo* 1000


C. Wang, T. Dato, H. Zhao, L. Wu, A. Date, C. Jiang, R. D. Sanders, G. Wang, C. Bevan, and D. Ma

As expected, dexmedetomidine enhanced cancer cell proliferation and migration, primarily by the upregulation of antiapoptotic proteins. By contrast, midazolam suppressed cancer cell proliferation and migration, induced mitochondria mediated apoptosis, and enhanced free radical production. These anticancer effects of midazolam, mediated by its activity at the peripheral benzodiazepine receptor, were achieved at high concentrations only. The data suggest that commonly used agents in the perioperative period may impact tumor cell growth; these effects have been demonstrated in preclinical studies, and therefore their relevance to clinical management of patients undergoing cancer surgery remains to be determined. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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- The infusion of ketamine resulted in meaningful pain relief in about 50% of patients with chronic neuropathic pain. The magnitude of temporal summation of pain and the dynamic engagement of the descending pain modulatory circuit predicted treatment efficacy and point to mechanisms by which ketamine can relieve pain.

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