



## ON THE COVER:

Diagnostic codes listed in health administrative (HA) databases are now commonly used to identify surgical patients with obstructive sleep apnea (OSA) for research purposes, yet the ability of this approach to accurately identify patients has not been validated. In this issue of ANESTHESIOLOGY, McIsaac *et al.* determined the presence of any diagnostic codes, diagnostic procedures, or therapeutic interventions consistent with OSA in an HA database and demonstrated that their presence correlated poorly with an actual diagnosis of OSA made by a sleep physician or the apnea hypopnea index. In an accompanying Editorial View, Neuman emphasizes the critical need for this type of well-done validation study in perioperative database research for guiding the questions that we choose to investigate with retrospective data and for making sense of the insights we can gain through HA database research.

- McIsaac *et al.*: Identifying Obstructive Sleep Apnea in Administrative Data: A Study of Diagnostic Accuracy, p. 253
- Neuman: The Importance of Validation Studies in Perioperative Database Research, p. 243

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## ■ PERIOPERATIVE MEDICINE

### CLINICAL SCIENCE

- ◆◆ **Identifying Obstructive Sleep Apnea in Administrative Data: A Study of Diagnostic Accuracy** 253  
*D. I. McIsaac, A. Gershon, D. Wijesundera, G. L. Bryson, N. Badner, and C. van Walraven*

In approximately 5,000 patients who underwent preoperative polysomnography, 56% met criteria for a diagnosis of obstructive sleep apnea (OSA). In these patients with known or excluded OSA, none of the health administrative diagnostic codes, diagnostic procedures, or therapeutic interventions by themselves or in combination identified OSA with adequately high sensitivity and specificity. Existing studies using administrative codes to identify OSA should be interpreted with caution.

- ◆ Refers to This Month in Anesthesiology
- ◆◆ Refers to Editorial Views

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◆ ***N*-terminal pro-B-type Natriuretic Peptides' Prognostic Utility Is Overestimated in Meta-analyses Using Study-specific Optimal Diagnostic Thresholds** 264

*D. Potgieter, D. Simmers, L. Ryan, B. M. Biccard, G. A. Lurati-Buse, D. M. Cardinale, C. P. W. Chong, M. Cnotliwy, S. I. Farzi, R. J. Jankovic, W. Kwang Lim, E. Mahla, R. Manikandan, A. Oscarsson, M. P. Phy, S. Rajagopalan, W. J. Van Gaal, M. Waliszek, and R. N. Rodseth*

Meta-analysis of studies that made use of a study-specific optimal *N*-terminal fragment B-type natriuretic peptide threshold resulted in a larger risk point estimate for the prediction of the composite outcome of postoperative mortality and nonfatal myocardial infarction at 30 days after noncardiac surgery compared with using a single threshold across all studies. These data suggest that future biomarker studies should be evaluated as continuous variables rather than making use of *post hoc* study-specific optimal thresholds, and care should be taken when conducting meta-analysis on studies that have used study-specific optimal thresholds to evaluate biomarker prognostic ability, as it is likely that this methodology will overestimate biomarker predictive performance.

◆◆🌐 **Hyperinsulinemic Normoglycemia Does Not Meaningfully Improve Myocardial Performance during Cardiac Surgery: A Randomized Trial** 272

*A. E. Duncan, B. Kateby Kashy, S. Sarwar, A. Singh, O. Stenina-Adognravi, S. Christoffersen, A. Alfirovic, S. Sale, D. Yang, J. D. Thomas, M. Gillinov, and D. I. Sessler*

Administration of glucose and insulin while targeting normoglycemia during aortic valve replacement did not meaningfully improve myocardial function. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

◆🌐 **Association between Withholding Angiotensin Receptor Blockers in the Early Postoperative Period and 30-day Mortality: A Cohort Study of the Veterans Affairs Healthcare System** 288

*S. M. Lee, S. Takemoto, and A. W. Wallace*

In a review of over 30,000 inpatient surgical admissions of patients taking angiotensin receptor blockers (ARBs) in the Veterans Affairs Healthcare system between 1991 and 2011, ARBs were not resumed by day 2 after surgery in one third of subjects. Thirty-day mortality was increased approximately 50% in those without resumption of ARBs, and this effect was even greater in patients younger than 60 yr. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

◆ **Association between Intraoperative Hypotension and Hypertension and 30-day Postoperative Mortality in Noncardiac Surgery** 307

*T. G. Monk, M. R. Bronsert, W. G. Henderson, M. P. Mangione, S. T. J. Sum-Ping, D. R. Bentt, J. D. Nguyen, J. S. Richman, R. A. Meguid, and K. E. Hammermeister*

In a review of more than 18,000 patients undergoing noncardiac surgery within the Veterans Administration Hospital system, application of three definitions of blood pressure deviation based on the population and individual patient level data showed that hypotension but not hypertension was associated with increased 30-day mortality.

**A Perioperative Course of Gabapentin Does Not Produce a Clinically Meaningful Improvement in Analgesia after Cesarean Delivery: A Randomized Controlled Trial** 320

*D. T. Monks, D. W. Hoppe, K. Downey, V. Shah, P. Bernstein, and J. C. A. Carvalho*

In 197 women randomized to receive gabapentin, 600 mg before cesarean delivery and 200 mg every 8 h for 2 days postoperatively or placebo, there was a statistically significant but clinically unimportant difference in pain with movement 24 h after surgery. Sedation was greater in women treated with gabapentin.

**Assessment of Cerebral Autoregulation Patterns with Near-infrared Spectroscopy during Pharmacological-induced Pressure Changes** 327

*A. T. Moerman, V. M. Vanbiervliet, A. Van Wesemael, S. M. Bouchez, P. F. Wouters, and S. G. De Hert*

Paradoxical reactions might be part of a normal physiological autoregulatory response, thereby challenging the conventional paradigm. Intact cerebral autoregulation comprises additional patterns of normal cerebrovascular responses that might be obscured if the existence of different mechanisms is ignored, and analysis is based on the mean response of a group.

## Pulse Photoplethysmographic Analysis Estimates the Sympathetic Activity Directed to Heart and Vessels

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R. Colombo, A. Marchi, B. Borghi, T. Fossali, R. Rech, A. Castelli, A. Corona, S. Guzzetti, and F. Raimondi

In controlled experimental conditions, novel pulse plethysmographic indices estimated changes of the sympathetic outflow directed to vessels and the sympathovagal balance modulating heart rate.



## Resting-state Functional Magnetic Resonance Imaging Correlates of Sevoflurane-induced Unconsciousness

346

B. J. A. Palanca, A. Mitra, L. Larson-Prior, A. Z. Snyder, M. S. Avidan, and M. E. Raichle

Sevoflurane-induced unconsciousness leads to a widespread reduction in brain activity. Functional connectivity is selectively reduced within the default mode and ventral attention networks. Motion artifact, a prevalent confounding variable in functional magnetic resonance imaging studies involving anesthetic agents, leads to spurious results if not addressed. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

## Development of an Optimized Pharmacokinetic Model of Dexmedetomidine Using Target-controlled Infusion in Healthy Volunteers

357

L. N. Hannivoort, D. J. Eleveld, J. H. Proost, K. M. E. M. Reijntjens, A. R. Absalom, H. E. M. Vereecke, and M. M. R. F. Struys

A pharmacokinetic model for dexmedetomidine was developed using a target-controlled infusion targeting a wide range of concentrations in healthy volunteers of both sexes with a wide range of ages and weights. The pharmacokinetics of dexmedetomidine was described by a three-compartmental model with only weight as a covariate. A small initial distribution volume allows better estimates of high peak concentrations after rapid infusion.

## BASIC SCIENCE

### Cyclopropyl-methoxycarbonyl Metomidate: Studies in a Lipopolysaccharide Inflammatory Model of Sepsis

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P. Santer, E. Pejo, Y. Feng, W. Chao, and D. E. Raines

A 1-h cyclopropyl-methoxycarbonyl metomidate infusion produced less suppression of adrenocortical steroid synthesis, less elevated plasma inflammatory cytokine concentrations, and lower mortality than did an etomidate infusion in an *Escherichia coli* lipopolysaccharide rat model of sepsis.

## ■ CRITICAL CARE MEDICINE

## BASIC SCIENCE



### Isoflurane Ameliorates Acute Lung Injury by Preserving Epithelial Tight Junction Integrity

377

J. A. Englert, A. A. Macias, D. Amador-Munoz, M. Pinilla Vera, C. Isabelle, J. Guan, B. Magaoay, M. Suarez Velandia, A. Coronata, A. Lee, L. E. Fredenburgh, D. J. Culley, G. Crosby, and R. M. Baron


In a murine two-hit model of endotoxin-induced inflammation followed by ventilator-induced lung injury, isoflurane exposure before mechanical ventilation ameliorated the ventilator-induced lung injury by improving both lung mechanics and vascular leakage without changing inflammatory responses. In mouse lung tissue and in lung epithelial cells injured similarly to the *in vivo* model, decrease of a key tight junction protein (zona occludens 1) was prevented with isoflurane preconditioning. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

### Association between Maturation and Aging and Pulmonary Responses in Animal Models of Lung Injury: A Systematic Review



389

L. R. A. Schouten, M. J. Schultz, A. H. van Kaam, N. P. Juffermans, A. P. Bos, and R. M. Wösten-van Asperen

An investigation of the literature documents that the inflammatory response to injury is exaggerated in aged animals, and there is more edema and alveolar damage and a higher mortality.

- 
**Sphingosine 1-phosphate Receptor 2 Signaling Suppresses Macrophage Phagocytosis and Impairs Host Defense against Sepsis** 409  
*J. Hou, Q. Chen, K. Zhang, B. Cheng, G. Xie, X. Wu, C. Luo, L. Chen, H. Liu, B. Zhao, K. Dai, and X. Fang*

Deficiency in sphingosine 1-phosphate receptor 2 (S1PR2) enhanced bacterial clearance and improved survival in the mouse model of sepsis. These beneficial effects are attributed to an increase in the phagocytic activity of S1PR2-deficient macrophages. Interventions targeting S1PR2 signaling may thus offer a promising therapeutic approach for the prevention and/or treatment of sepsis. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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**Biological Impact of Transpulmonary Driving Pressure in Experimental Acute Respiratory Distress Syndrome** 423  
*C. S. Samary, R. S. Santos, C. L. Santos, N. S. Felix, M. Bentes, T. Barboza, V. L. Capelozzi, M. M. Morales, C. S. N. B. Garcia, S. A. L. Souza, J. J. Marini, M. Gama de Abreu, P. L. Silva, P. Pelosi, and P. R. M. Rocco*


Different combinations of tidal volume and positive end-expiratory pressure (PEEP) were used to create a range of driving pressures in a rat model of acute respiratory distress syndrome due to tracheal instillation of endotoxin for 24 h. Low transpulmonary driving pressure was associated with alveolar collapse and high driving pressure was associated with hyperinflation. The combination of a tidal volume of 6 ml/kg predicted body weight and the lowest PEEP and driving pressure to maintain oxygenation in a normal range minimized ventilator-induced lung injury even in the presence of alveolar collapse. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

## ■ PAIN MEDICINE

### CLINICAL SCIENCE

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**Sufentanil Sublingual Tablet System for the Management of Postoperative Pain after Knee or Hip Arthroplasty: A Randomized, Placebo-controlled Study** 434  
*M. Jove, D. W. Griffin, H. S. Minkowitz, B. Ben-David, M. A. Evashenk, and P. P. Palmer*

In this phase 3 trial, 426 patients were randomized to receive the sufentanil sublingual tablet system or a placebo, with IV opioid rescue after major lower extremity orthopedic surgery. The primary outcome measure of summed pain intensity difference in the first 48 h compared with baseline was better with sufentanil than placebo although nausea and pruritus were also increased with sufentanil.

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**Discharge Readiness after Tricompartment Knee Arthroplasty: Adductor Canal *versus* Femoral Continuous Nerve Blocks—A Dual-center, Randomized Trial** 444  
*A. T. Machi, J. F. Sztain, N. J. Kormylo, S. J. Madison, W. B. Abramson, A. M. Monahan, B. Khatibi, S. T. Ball, F. B. Gonzales, D. I. Sessler, E. J. Mascha, J. You, K. A. Nakanote, and B. M. Ilfeld*

Continuous adductor canal block did not appreciably decrease the time to overall discharge readiness when compared with continuous femoral nerve block even though it did decrease the time until adequate mobilization because both groups often required intravenous opioids beyond the time to mobilization.



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*A. C. Krediet, N. Moayeri, G.-J. van Geffen, J. Bruhn, S. Renes, P. E. Bigeleisen, and G. J. Groen*
- Using digitized anatomical cross-sectional images, this article reviews the necessary anatomical background to successfully interpret ultrasound images of the thoracic paravertebral space, and provides an overview on currently published approaches to ultrasound-guided thoracic paravertebral blockade. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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