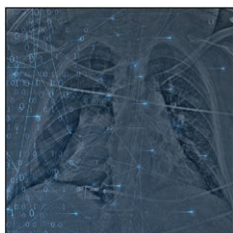




673 Risk Stratification Index 3.0, a Broad Set of Models for Predicting Adverse Events during and after Hospital Admission

Risk stratification helps guide clinical care. Earlier versions of the Risk Stratification Index were based on information not available at the time of hospital admission. The present study developed and validated analytic tools based on International Classification of Diseases, Tenth Revision diagnostic and procedural code histories for predicting care utilization outcomes and adverse events for both surgical and medical inpatient admissions. Logistic regression models were trained on 80% of 18,899,224 qualifying Medicare admissions from 2017 and 2018 and the models were applied to the remaining 20% of the development dataset to document modeling robustness. The final models were evaluated on 9,205,835 admissions from 2019 to document model validation.

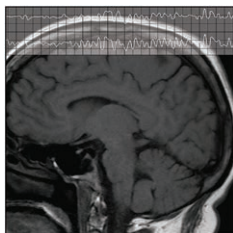
The incidence of endpoints ranged from 2.8% for in-hospital mortality to 35.9% for discharge to a care facility. There was satisfactory discrimination power over the range of operating thresholds and strong correlation between observed and predicted values along the full continuum of risk. Prediction characteristics of models developed using five commonly used machine learning methods were similar to those of the logistic regression models. The models can be implemented at admission to inform clinical decision-making. *See the accompanying Editorial on page 661.* (Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals Studio.)



704 Validation of a Deep Learning–based Automatic Detection Algorithm for Measurement of Endotracheal Tube–to–Carina Distance on Chest Radiographs

Improper endotracheal tube (ETT) positioning may be hazardous if not promptly recognized and managed. It is recommended that the ETT position be evaluated using a portable chest radiograph immediately after tracheal intubation, but radiologists are not always available to read portable radiographs. This study tested the hypothesis that a deep learning–based automatic detection algorithm to measure the ETT–carina distance on portable supine chest radiographs might be more accurate than frontline critical care clinicians in ETT tip detection, carina detection, and ETT–carina distance measurement. The deep learning–based

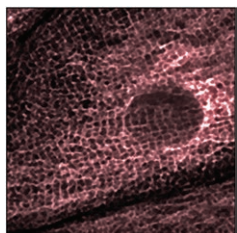
algorithm, trained using the bounding boxes denoting the ETT tip and carina locations and pixel-level segmentation of the distal ETT end and tracheal bifurcation, exhibited robustness in ETT–carina distance measurement during fourfold cross-validation (1,842 radiographs) and external validation (216 radiographs). When performance of the deep learning–based algorithm was compared with that of a diverse group of 11 critical care clinicians (462 radiographs), it was found to be comparable or even superior to them in detecting the ETT tip and carina and measuring the ETT–carina distance. *See the accompanying Editorial on page 664.* (Summary: M. J. Avram. Image: J. P. Rathmell.)



716 Post–cardiac arrest Sedation Promotes Electroencephalographic Slow-wave Activity and Improves Survival in a Mouse Model of Cardiac Arrest

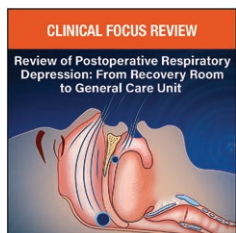
Targeted temperature management has been part of postresuscitation care of patients who achieved return of spontaneous circulation after cardiac arrest to minimize hypoxic-ischemic brain damage. Patients undergoing targeted temperature management are routinely sedated, but the effects of sedation on cerebral physiology and outcomes after cardiac arrest are unknown. The hypothesis that sedation would improve survival and neurologic outcomes after cardiac arrest was tested using continuous electroencephalography (EEG) monitoring and cerebral blood flow measurement to characterize the effects of sedation in mice

resuscitated from experimental cardiac arrest managed with therapeutic hypothermia. Compared with unsedated mice, those sedated with propofol at $40 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ or dexmedetomidine at $1 \text{ } \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ starting at return of spontaneous circulation had improved survival and neurological outcomes. Early administration of sedation ameliorated histologic brain injury, attenuated early cerebral hyperemia, and enhanced EEG slow-wave activity during and soon after sedation. Enhanced EEG slow-wave activity was not observed in mice sedated with propofol at $10 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ starting at return of spontaneous circulation or at $40 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ starting at 60 min after its return. (Summary: M. J. Avram. Image: J. P. Rathmell.)



687 Local Anesthetic Cardiac Toxicity Is Mediated by Cardiomyocyte Calcium Dynamics

Local anesthetics provide regional anesthesia within a nerve distribution through peripheral neuron sodium channel (*e.g.*, Nav1.7) blockade. Many local anesthetics can cause cardiotoxicity, the putative mechanism of which is Nav1.5 cardiac sodium channel blockade. However, *in vitro* human Nav1.5 binding studies report modest channel affinity differences between bupivacaine and ropivacaine despite differences in toxicity. The hypothesis that in addition to Nav1.5 blockade, bupivacaine and ropivacaine divergently perturb other key cardiomyocyte processes consistent with observed *in vivo* cardiotoxicity differences was tested using human induced pluripotent stem cell–derived cardiomyocytes and *in vivo*. Above the toxic threshold *in vitro*, bupivacaine perturbed contractility, was more arrhythmogenic, and adversely affected calcium dynamics more than ropivacaine. Calcium cotreatment mitigated bupivacaine-induced changes but exacerbated the negative effects of ropivacaine. In rats, the L-type calcium channel blocker nifedipine potentiated bupivacaine-mediated contractile depression, beating irregularity, and sarcolemmal calcium dysfunction, while producing no adverse effects with ropivacaine. These results support the role of altered calcium flux in the different cardiotoxicity mechanisms of the two local anesthetics. (Summary: M. J. Avram. Image: Adapted from original article.)



735 Review of Postoperative Respiratory Depression: From Recovery Room to General Care Unit (Clinical Focus Review)

Postoperative respiratory failure secondary to opioid-induced respiratory depression can result in morbidity or death. It often seems to develop acutely and without warning. Administration of opioids blunts the ventilatory response to differing concentrations of arterial carbon dioxide and/or oxygen, which results in slowing of the respiratory rate. Intermittent vital sign checks are insensitive for identifying respiratory depression, but it is recognized promptly in patients who are monitored continuously. Respiratory depression often occurs early in the postoperative period because pain treatment with opioids is more intense when there are residual effects of anesthesia. The perioperative course can influence postoperative respiratory depression risk, with shorter-acting anesthetics being associated with a decreased risk. When assessing the risk of respiratory depression, anesthesiologists should consider not only obstructive sleep apnea but also the overall health of the patient, with the understanding that risk increases with age, disease burden, cognitive decline, and debility. These and other advances in the understanding of postoperative respiratory depression can allow anesthesiologists to better appreciate and take action to reduce the risk of acute postoperative respiratory depression. (Summary: M. J. Avram. Image: S. Jarret.)