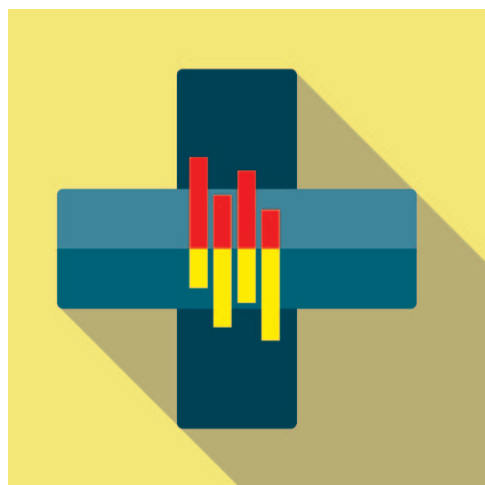


Journal-related Activities and Other Special Activities at the 2015 American Society of Anesthesiologists Annual Meeting

J. David Clark, M.D., Ph.D., Brian P. Kavanagh, M.B., F.R.C.P.C., Piyush M. Patel, M.D., F.R.C.P.C., James P. Rathmell, M.D., Warren S. Sandberg, M.D., Ph.D.



Initial Results of Clinical Trials

Sunday, October 25, 1:10 PM to 3:10 PM, San Diego Convention Center, Upper 20A

Moderators

James C. Eisenach, M.D., Wake Forest University School of Medicine, Winston-Salem, North Carolina.

ANESTHESIOLOGY is sponsoring a Major Trials Session at the 2015 Annual Meeting of the ASA. It will provide a high-profile, large audience forum for initial presentation of major randomized clinical trial results. The session is designed for substantial trials, usually randomized and blinded, with a clinically important primary outcome. Articles selected for the Trials Session will be simultaneously published in the journal as well as have a press release.



24th Annual Journal Symposium: The Anesthesiologist and Healthcare Redesign

Sunday, October 25, 2015, 9:00 AM to 12:00 PM, San Diego Convention Center, Room Upper 4

This year ANESTHESIOLOGY will sponsor four sessions at the Annual Meeting of the American Society of Anesthesiologists (ASA). The 2015 Journal Symposium addresses the changes in healthcare design and delivery in a session titled, "The Anesthesiologist and Healthcare Redesign." It will feature the following moderators and speakers.

Moderators

James P. Rathmell, M.D., Brigham and Women's Hospital, Boston, Massachusetts; and Warren S. Sandberg, M.D., Ph.D., Vanderbilt University Medical Center, Nashville, Tennessee.

The figures were recreated by Annemarie B. Johnson, C.M.I., Medical Illustrator, Vivo Visuals, Winston-Salem, North Carolina.

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Speakers

1. **Using Data to Improve Operating Room Throughput**
Peter F. Dunn, M.D., Massachusetts General Hospital, Boston, Massachusetts; Retsef Levi, Ph.D., Sloan School of Management, MIT, Boston, Massachusetts
2. **Redesigning Surgical Patient Care from Decision to Discharge**
Jonathan P. Wanderer, M.D., Vanderbilt University, Nashville, Tennessee
3. **Designing a New Hospital for Surgical Care**
Brett Simon, M.D., Ph.D., Memorial Sloan Kettering Josie Robertson Surgery Center, New York, New York

Description

A common axiom in architecture reads: “If you want to change the way people work, change the building they work in.” The 2015 Journal Symposium addresses the changes in healthcare design and delivery head on, with this axiom setting the context. Physician anesthesiologists and others involved in the world of perioperative and procedural medicine are facing intense pressure to alter systems of care to improve the value delivered to patients. Such pressures are not new, but the intensity of the pressure has risen dramatically. The advent of the Affordable Care Act and payer initiatives such as bundling and value-based purchasing provide new impetus for healthcare delivery redesign. Recent descriptive publications have detailed elements of a nascent Perioperative Surgical Home (PSH) model of care. Does this construct represent a true reconsideration of perioperative healthcare delivery? How much redesign is required to truly affect the value a perioperative system brings to patients? Does the value accrue to patients or does the value of redesigning perioperative systems actually benefit healthcare systems and payers?

Four experts will introduce these topics for the first 90 min of the symposium, with 20-min presentations and 10-min discussions. The speakers will discuss three different approaches, of increasing scope, for redesigning healthcare delivery systems to meet specific goals. Where available, empirical tests of the redesign efforts’ success at meeting their goals will be presented.

These lectures will be followed by oral presentations of 12 abstracts, summarized below, that were selected for their relevance to the Symposium topic. The full text for each abstract can be found at the ASA abstract Web site.

JS01

“**Effect of Ongoing Process Improvement on an Enhanced Recovery after Surgery Pathway for Colorectal Surgery Patients**” by Adam B. King, M.D., Jonathan P. Wanderer, M.D., Timothy Geiger, M.D., Vikram Tiwari, Ph.D., Warren S. Sandberg, M.D., Ph.D., Matthew D. McEvoy, M.D., Vanderbilt University Medical Center, Nashville, Tennessee. The authors conducted a quality improvement exercise, with the goal of reducing hospital resource length

of stay (rLOS) through systematic application of enhanced recovery after surgery (ERAS) principles in colorectal surgery patients. They created a formal perioperative consult service to oversee the application of pertinent and appropriate ERAS elements for each patient after project initiation. Preimplementation baseline data for 181 consecutive elective colorectal surgery patients (with no exclusions) revealed a median rLOS of 4.2 days (which is in the best-performing quintile of the National Surgical Quality Improvement Project consortium). After implementation, rLOS for the subsequent 284 patients, without exclusions, was 3.3 days. In addition, costs declined by 17.5% after implementation. Both reductions were statistically significant using nonparametric tests. Emergency department visits and 7- and 30-day readmission rates were not measurably affected. The authors demonstrated that already excellent rLOS performance can be improved, that the improvement can be sustained for at least 1 yr, and that substantial LOS reductions can be achieved. Considering only colorectal surgery patients, access (and throughput) could be increased by one third, more than offsetting the cost of the intervention.

JS02

“**Impact on Cost and Cost Variation of a Surgical Home for Nephrectomy Cases**” by Shermeen B. Vakharia, M.D., M.B.A., John Patton, Jr., Ross Moskowitz, M.D., Kwang Pak, B.S., Zeev N. Kain, M.D., M.B.A., Joseph B. Rinehart, M.D., University of California, Irvine, Orange, California. The authors extended an already-developed PSH model to a new service line (urology) and a new case type (nephrectomy). Using a before–after design, the authors studied the impact of a complete perioperative process redesign on length of stay (LOS) and cost of care. Process redesign included comprehensive nutritional, respiratory, and medical optimization, patient education, and risk identification for renal and pulmonary complications and delirium, and complete standardization of case carts across surgeons. There were 148 cases in the control group and 22 cases studied after process change implementation. Mean LOS declined from 3.2 ± 2.7 days to 2.3 ± 0.8 days, mostly attributed by the authors to reduction in complications. Costs declined by approximately 50%. Both comparisons were statistically significant. Although the postintervention sample was small, the variation in costs appeared to be reduced, suggesting that the postintervention process was in better control. Reliability is a key goal of the PSH.

JS03

“**Preoperative Evaluation Clinic Visit Decreases Risk of In-hospital Postoperative Mortality**” by Jeanna D. Blitz, M.D., Samir N. Kendale, M.D., Germain Cuff, D.Phil., Andrew D. Rosenberg, M.D., New York University School of Medicine, New York, New York. In a retrospective exploratory study of 75,763 surgical encounters, the authors compared in-hospital postoperative mortality

between patients who had visited the anesthesiology preoperative clinic for risk stratification, optimization, and care coordination, *versus* those who had not. Propensity scoring (matching) and logistic regression methods were used to compare the in-hospital mortality rate between surgical patients exposed ($n = 39,840$) and not exposed ($n = 35,923$) to the preoperative clinic. After matching, patients who had been seen in preoperative clinic were less likely to die during their surgical admission (odds ratio [OR], 0.55; 95% CI, 0.34 to 0.88). Similar results were obtained after logistic regression analysis (OR, 0.54; 95% CI, 0.36 to 0.82).

JS04

“Effect of Implementing an Enhanced Recovery after Surgery Pathway *via* Perioperative Consult Service for Bariatric Surgical Patients” by Matthew D. McEvoy, M.D., Adam B. King, M.D., Matthew D. Spann, M.D., Vikram Tiwari, Ph.D., Warren S. Sandberg, M.D., Ph.D., Jonathan P. Wanderer, M.D., Vanderbilt University Medical Center, Nashville, Tennessee. Application of ERAS interventions *via* an anesthesia perioperative consult service was undertaken for bariatric surgical patients. This was a formal process improvement exercise including the surgeons and was conducted as a before–after design with 393 control cases, 68 postintervention cases, and no exclusions. After intervention, rLOS declined from 1.6 to 1.4 days, the proportion of patients ready for discharge in less than 2 days increased from 81 to 94% and total hospital costs declined by 37% (all comparisons were statistically significant). Readmission to emergency room or hospital was not measurably increased. Changing the distribution of rLOS so that more patients are discharged in under 48 h means that a patient admitted to preoperative holding in the morning will vacate their postoperative bed the morning of postoperative day 2 at the latest, in time to turn the bed for a new first-case patient leaving the postanesthesia care unit.

JS05

“Medical Follow-up in the Year after Surgery and Subsequent Survival among a National Cohort of Surgical Patients” by Robert B. Schonberger, M.D., Feng Dai, Ph.D., Cynthia A. Brandt, M.D., M.P.H., Matthew M. Burg, Ph.D., Yale University School of Medicine, New Haven, Connecticut. The authors investigated healthcare redesign by attempting to integrate surgical care episodes with efforts to improve longitudinal postoperative preventive medical care. In this retrospective analysis, the association between nonsurgical medical follow-up during the first postoperative year and subsequent all-cause mortality during postoperative year 2 was examined. The postoperative course of U.S. Veterans presenting for surgery from 2006 to 2011 was examined to measure the association between exposure to medical follow-up in the year after surgery and subsequent survival in postoperative year 2. Of 385,790 patients, 113 (0.03%) were removed due to an invalid

date of death. Of the remaining 385,677 patients, 342,563 (88.8%) survived the 365-day postsurgical exposure period and were included. In unadjusted analysis, 5.9% of patients with medical follow-up died during postsurgical year 2. This compares with 9.5% mortality among those lacking medical follow-up. Medical follow-up during the first postoperative year was associated with a reduction in all-cause mortality in postoperative year 2. Care coordination to improve medical follow-up is unlikely to impede long-term postoperative survival.

JS06

“Total Joint Replacement Perioperative Surgical Home Program: Impact of Patient Characteristics and Comorbidities on Postoperative Length of Stay” by Kyle S. Ahn, M.D., Ran Schwarzkopf, M.D., Joseph B. Rinehart, M.D., Maxime Cannesson, M.D., Ph.D., Zeev N. Kain, M.D., M.B.A., University of California, Irvine, Orange, California. Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are two of the most common surgical procedures in the United States. The authors implemented a total joint PSH program, hypothesizing that patients enrolled in the PSH program undergoing primary TKA and THA would have similar postoperative outcomes regardless of patient characteristics, comorbidities, and ASA score. This was a retrospective review of elective primary total hip and knee arthroplasty patients under the total joint replacement PSH. Primary outcome was LOS, and secondary outcomes included readmission rate, postoperative complications, discharge disposition, and postanesthesia care unit stay duration. Age, gender, body mass index, and THA *versus* TKA were not significant predictors of LOS. ASA score remained strongly predictive ($P = 0.0011$). Previously reported predictors of postoperative complications are not independently predictive in joint arthroplasty patients in a PSH care model. This may be due to standardized, early preoperative optimization of all patients in a PSH program. The PSH model has been shown to reduce postoperative outcomes variability among total joint arthroplasty patients regardless of their characteristics and medical comorbidities. Yet, even in a PSH care model, ASA score and body mass index plays a significant role in postoperative outcomes in joint arthroplasty patients.

JS07

“The Impact of Perioperative Systems Design on Diabetic Patient Outcomes” by Jesse M. Ehrenfeld, M.D., M.P.H., Jonathan P. Wanderer, M.D., Maxim Terekhov, M.S., Brian S. Rothman, M.D., Warren S. Sandberg, M.D., Ph.D., Vanderbilt University Medical Center, Nashville, Tennessee. The authors conducted a focused perioperative system redesign intervention to increase the proportion of diabetic patients who received intraoperative glucose monitoring. This comprised an automatic system to detect diabetic patients (from the electronic problem list), detect insulin

administration (from the electronic medical flowsheet), check for recent glucose measurement (lab system), and to remind anesthesia providers to perform intraoperative glucose testing. Assessment of impact was a before (n = 3,994) *versus* after (n = 11,901) design with propensity score matching. The main outcome was the surgical site infection rate. The rate of monitoring increased from 62 to 87% ($P = 0.0001$) and hyperglycemia (glucose >250 mg/dl) on postanesthesia care unit entry decreased (11 to 7%, $P = 0.0019$). Hypoglycemia (glucose <75 mg/dl) on postanesthesia care unit entry was unchanged. The unadjusted surgical site infection rate decreased from 1.5% (n = 61) to 1.0% (n = 117; $P = 0.0061$); after propensity matching, the before and after surgical site infection rates were 1.3 *versus* 0.6%. A targeted intervention using automated systems to “lock in” a reminder improves process performance and health outcomes.

JS08

“Compliance with Surgical Care Improvement Project for Body Temperature Management (SCIP Inf-10) Is Associated with Improved Clinical Outcomes” by Andrew V. Scott, B.S., Jerry Stonemetz, M.D., Jack O. Wasey, B.M., B.Ch., Daniel J. Johnson, B.S., Richard J. Rivers, M.D., Colleen Koch, M.D., Steven M. Frank, M.D., Johns Hopkins Medicine, Baltimore, Maryland. The authors used the Surgical Care Improvement Project (SCIP) guidelines to determine whether SCIP measure compliance is associated with improved outcomes by testing the hypothesis that SCIP Inf-10 compliance is associated with a decreased incidence of hospital-acquired infections and a reduced incidence of ischemic cardiovascular events. Electronic medical record data from 45,304 inpatients was analyzed to assess whether compliance with SCIP Inf-10 (body temperature management) was associated with a reduced incidence of morbidity and mortality. The primary outcomes were hospital-acquired infection and ischemic cardiovascular events. Secondary outcomes were mortality and hospital LOS. Body temperature upon admission to the postoperative care unit was higher in the SCIP-compliant group ($36.6^\circ \pm 0.5^\circ\text{C}$; n = 44,064) compared with the SCIP-noncompliant group ($35.5^\circ \pm 0.5^\circ\text{C}$; n = 1,240) ($P < 0.0001$). SCIP compliance was associated with improved outcomes in both nonadjusted and risk-adjusted analyses. SCIP compliance was associated with a reduced incidence of hospital-acquired infection (3,312 [7.5%] *vs.* 160 [12.9%] events; risk-adjusted OR, 0.68; 95% CI, 0.54 to 0.85), ischemic cardiovascular events (602 [1.4%] *vs.* 38 [3.1%] events; risk-adjusted OR, 0.60; 95% CI, 0.41 to 0.92), and mortality (617 [1.4%] *vs.* 60 [4.8%] events; risk-adjusted OR, 0.41; 95% CI, 0.29 to 0.58). SCIP Inf-10 compliance was associated with a reduced risk for hospital-acquired infections, ischemic cardiovascular events, and mortality, as well as a decreased LOS.

JS09

“Hospital Variability in the Postoperative Management of Patients with Obstructive Sleep Apnea” by Sanjana A.

Malviya, B.S., Sanjay Menon, B.S., Angela Lyden, M.S., Satya-Krishna Ramachandran, M.D., University of Michigan, Ann Arbor, Michigan. The authors performed a retrospective analysis, using data from the Nationwide Inpatient Sample. They studied patients with obstructive sleep apnea, hypothesizing that use of continuous positive airway pressure (CPAP) in these patients during hospitalization would be associated with fewer reintubations, reduced long-term mechanical ventilation, LOS, cost, and mortality. Data were divided into quartiles based on CPAP use and subjected to Kruskal–Wallis analysis. No differences were found between quartiles in postoperative reintubation, median total charges, or median LOS. Use of CPAP was associated with reduction in long-term ventilation and in-hospital mortality (both statistically significant); pair-wise comparisons showed that the differences were between low- and high-CPAP use quartiles.

JS10

“Care Redesign and Non-OR Anesthesia (NORA): A Strategic Imperative—The Data Speaks” by Wendy L. Gross, M.D., Evan J. Blaney, M.D., David Preiss, M.D., Jason D. Stewart, M.D., Christopher Chen, M.D., Dennis McNicholl, D.O., Richard D. Urman, M.D., Joshua C. Vacanti, M.D., Andrew R. Bond, M.D., Robert N. Pilon, M.D., Brigham and Women’s Hospital, Boston, Massachusetts. The authors compared operational performance metrics—utilization, cancellation rates, procedural anesthesiologist hours spent on preprocedure history and physical examinations, and idle time spent waiting for proceduralists between OR cases and nonoperating room anesthesia (NORA) sites. Utilization of scheduled anesthesia hours was 51% for NORA sites *versus* 83% in the OR. The NORA cancellation rate due to unrecognized comorbidities was 5% *versus* 0.5% for OR cases. The opportunity cost of nonbillable time was greater than \$600K per quarter (nonbillable hours \times mean NORA collections per hour), including the opportunity cost of executing histories and physical examinations, which exceeded \$150K per quarter. Thus, in the studied institution, NORA is an activity where establishing process consistency and reliability through perioperative systems design could substantially improve clinician, patient, and financial experiences.

JS11

“U.S. Navy’s First Functional Restoration Pain Program: Improving Readiness, Restoring Function, and Relieving Pain” by Steven Hanling, M.D., Sheila Medina-Torne, M.P.H., Parisa Nahavandi, B.S., Kathleen McChesney, Psy.D., Meredith Schumacher, D.P.T., Tara Sheridan, M.D., Ana Texidor, R.N., Ivan K. Lesnik, M.D., Naval Medical Center, San Diego, California. Functional restoration pain programs (FRPP) demonstrate substantial improvements in patient outcomes. Chronic pain is a substantial impairment to military personnel. This is the first interdisciplinary pain treatment program offered

by the U.S. Navy. FRPP is an intensive, multidisciplinary, medically supervised program, consisting of 5 half days a week, for 8 weeks. Disease management techniques include patient- and family-focused pain education and quantitatively directed progressive exercise rehabilitation. Self-reported and objective measures are collected as part of a process improvement initiative. Enlisted service members in FRPP ranged from 19 to 43 yr of age. There were significant treatment gains after the completion of the FRPP program. Improved psychosocial measures were noted in pain self-efficacy questionnaire and chronic pain acceptance questionnaire-8 total scores, which are indicative of increased beliefs about the patient's ability to accomplish a range of activities despite pain. Significant improvements among active duty participants were seen in both psychosocial and physical function measures immediately after FRPP relative to their pretreatment functioning levels. Initial findings from this functional restoration program highlight its therapeutic potential to support the service member's ability to return to full duty.

JS12

“The Use of Transthoracic Echocardiography Performed Preoperatively by Anesthesiologists in Perioperative Medical and Surgical Planning” by Daniel P. Walsh, M.D., Julie Hoffman, R.N., Sasha K. Shillcutt, M.D., University of Nebraska Medical Center, Omaha, Nebraska. The use of perioperative echocardiography by anesthesiologists has expanded in recent years. The authors examine the impact of echocardiography *via* a Perioperative Echocardiography Consult Service (PECS). The purpose was to evaluate the use of on-site preoperative transthoracic echocardiography (TTE) performed by anesthesiologists on perioperative medical and surgical management. Retrospective data from the PECS Quality Assurance Database on all patients over the age of 19 yr old who had a TTE examination performed during their Preanesthesia Screening Clinic was included. Evaluation for change in preoperative medical and surgical planning was recorded, and the impact on clinical perioperative management was analyzed. Seventy-nine patients were identified as receiving a preoperative TTE *via* PECS through December 31, 2014. Preliminary data of the first 50 patients indicate that 39 patients (74%) had changes of care based on their TTE examination. Twenty-five (64%) of these changes were based on positive TTE examination findings. Changes in perioperative anesthesia management included adding invasive monitoring, changing anesthetic type, changing induction plan, delaying case for medical optimization, or further testing or consult before surgery for further information. Appropriate preoperative echocardiographic testing by anesthesiologists can change surgical and medical management in anywhere from 44 to 84% of examinations. The most common indication for preoperative TTE examination was murmur or known valve disease.

Best Abstracts: Clinical Sciences and Basic Sciences

ANESTHESIOLOGY will sponsor two Best Abstract Sessions this year, one in basic science and another in clinical science. These abstracts were chosen by a panel of editors, who examined the highest scoring abstracts from the ASA subcommittees, choosing those with important scientific and clinical application and novelty. Subsequently, a combination of these editors and appointees from the ASA will choose one abstract in each category to receive the Best Abstract award for basic and clinical science at the meeting in San Diego.

Following are summaries of the superlative abstracts that will be presented.

Best Abstracts: Clinical Sciences

Saturday, October 24, 1:10 PM to 3:10 PM, San Diego Convention Center, Upper 4

Moderators

Brian P. Kavanagh, M.B., F.R.C.P.C., Hospital for Sick Children, University of Toronto, Toronto, Canada; and Piyush M. Patel, M.D., F.R.C.P.C., University of California, San Diego, San Diego, California.

BOC01

“Resting-state Brain Functional Connectivity Changes Associated with Cognitive Outcomes following Cardiac Surgery” by Jeffrey N. Browndyke, Ph.D., Todd Harshbarger, Ph.D., Tiffany Bisanar, R.N., John H. Alexander, M.D., Yanne Toulgoat-Dubois, B.A., Miles Berger, M.D., Ph.D., William D. White, M.P.H., Mark F. Newman, M.D., Joseph P. Mathew, M.D., Department of Psychiatry and Behavioral Sciences, Duke University, Durham, North Carolina. Postoperative cognitive dysfunction occurs in a subset of patients after anesthesia and surgery, but the connectivity between functional neuroanatomical substrates in the brain is not known. To evaluate functional connectivity, patients undergoing cardiac surgery and control nonsurgical patients were subjected to a battery of neuropsychological tests and magnetic resonance imaging at baseline and 6 weeks postsurgery. Statistically significant positive relationships were found between regions of postoperative change in intrinsic functional connectivity and cognitive outcomes in the posterior cingulate cortex and right superior frontal gyrus in the patients who underwent surgery. The data suggest that posterior cingulate cortex and right superior frontal gyrus are important neuroanatomical regions of the brain that merit further investigation of postoperative cognitive decline.

BOC02

“Neuroimaging Suggests That Stellate Ganglion Block Improves Posttraumatic Stress Disorder (PTSD) through an Amygdala-mediated Mechanism” by Michael T. Alkire, M.D., Michael Hollifield, M.D., Rostam Khosh-sar, M.D., Linda Nguyen, M.P.H., Stephanie R. Alley,

M.A., Christopher Reist, M.D., Long Beach VA Healthcare System and University of California, Irvine, California. Stellate ganglion block (SGB) has recently been shown to provide rapid and sustained relief of PTSD symptoms. To evaluate the mechanisms that underlie the efficacy of SGB, functional brain metabolic activity with positron emission tomography was performed in male patients with PTSD. Positron emission tomography was performed 1 week before and 1 week after SGB under fluoroscopic guidance. SGB was effective in three of five patients. The orbital frontal cortex was more active in the pre-SGB scan in comparison with post-SGB scan. Less active regions included left insula, right frontal cortex, left dorsolateral prefrontal cortex, and posterior hippocampus. Importantly, improvement in symptoms correlated with brain regions that centered on the amygdala and hippocampus primarily in the right hemisphere. The data suggest that there might be a dysregulation of orbital frontal cortex to amygdala inhibition that likely exists when symptoms of PTSD are severe.

BOC03

“Perioperative Duloxetine to Improve Postoperative Quality of Recovery after Abdominal Hysterectomy: A Prospective, Randomized, Double-blinded, Placebo-controlled Study” by Gildasio S. De Oliveira, Jr., M.D., M.S., Northwestern University, Chicago, Illinois. Females may have a poorer quality of recovery from surgery. This randomized controlled study assessed the ability of duloxetine, an antidepressant, to improve the quality of recovery after hysterectomy. The use of duloxetine 60 mg both before and 24 h after surgery was associated with improved quality of recovery and lower opioid use. Serotonin–norepinephrine reuptake inhibitors may improve the quality of recovery after surgery in female patients.

BOC04

“Does a Visit to the Preoperative Evaluation Clinic Affect Observed-to-expected In-hospital Length of Stay” by Ghislaine C. Echevarria, M.D., Jeanna D. Blitz, M.D., Samir M. Kendale, M.D., Germaine Cuff, Ph.D., Andrew D. Rosenberg, M.D., New York University School of Medicine, New York, New York. The effect of a Preoperative Evaluation Clinic (PEC) visit on 30-day readmission rate has been studied, but the relationship with postoperative in-hospital LOS, which is directly related with cost of care, has not been established. Propensity scoring methods (matching and inverse weighting) were used to compare observed/expected LOS ratio (O/E) between patients exposed ($n = 17,593$) and not exposed ($n = 11,235$) to PEC, after controlling for selection bias. The O/E ratio was lower in patients visiting the PEC. This suggests a beneficial effect for PEC visits.

BOC05

“Enhanced Recovery after Surgery Clinical Pathway for Patients Undergoing Pancreatic Surgery Decreases

Hospital Length of Stay” by Hayden P. Kirby, M.D., Timothy P. Rohman, M.D., Robert S. Isaak, D.O., Lyla Hance, M.P.H., Hong J. Kim, M.D., Lavinia M. Kolarczyk, M.D., University of North Carolina at Chapel Hill, Chapel Hill, North Carolina. ERAS clinical pathways facilitate early postoperative recovery. This study measured the effect of implementing an ERAS pathway on LOS after pancreatic surgery. Pre-, intra- and postoperative considerations were included in designing the ERAS pathway. Use of the ERAS pathway was associated with 2.6 and 2.8 day reductions in LOS for Whipple and distal pancreatectomy patients, respectively. Use of ERAS pathways may accelerate recovery and optimize the use of healthcare resources.

BOC06

“Banked Blood Is Deficient in 2,3-DPG Compared to Autologous-salvaged Blood, and This ‘Storage Lesion’ Is Incompletely Reversible at 72 h” by Andrew V. Scott, B.S., Erika Nagababu, Ph.D., Daniel Johnson, B.S., Joshua Lipsitz, B.S., Viachaslau Barodka, M.D., Dan E. Berkowitz, M.D., Khaled M. Kebaish, M.D., Steven M. Frank, M.D., Johns Hopkins School of Medicine, Baltimore, Maryland. Key questions remain about the concept of a “storage lesion” in transfused blood. Levels of 2,3-diphosphoglycerate (2,3-DPG) (increases the ability of hemoglobin to release oxygen in tissues) were measured, and the P-50 (lower values reflect left-shifted hemoglobin–oxygen dissociation curve) calculated, before and after surgery, on postoperative days 1, 2, and 3, as well as from blood bank and from cell-saver blood. The 2,3-DPG (and P-50) in stored blood (mean storage 25 days) was approximately 10% of the values in cell-saver or in preoperative patient blood. 2,3-DPG (and P-50) was unchanged after surgery in patients who received cell-saver blood and/or no stored blood; by contrast, patients who received any stored blood had values of 2,3-DPG (and P-50) approximately 30% of preoperative levels, and this had not normalized by the third postoperative day. Additional understanding of the pathophysiology of red-cell storage might impact on approaches to transfusion and monitoring.

BOC07

“Randomized Control Trial Analyzing the Pulmonary and Systemic Inflammatory Response Secondary to Lung Resection Surgery Using Propofol versus Sevoflurane. Final results” by Francisco De La Gala, Sr., M.D., Ph.D., Patricia Pinero, M.D., Almudena Reyes Fierro, M.D., Ignacio Garutti, M.D., Luis Olmedilla, M.D., Ph.D., Elena Vara, M.D., Ph.D., Javier Casanova, M.D., Ph.D., Patricia Cruz, M.D., Ph.D., Duque Patricia, M.D., Ph.D., Carlos Simon, M.D., Ph.D., Hospital Gregorio Maranon, Madrid, Spain. Several studies have pointed to potential impacts of anesthetic agents on systemic inflammation and organ injury. In thoracic surgery requiring one-lung anesthesia, the potential for post-anesthetic lung injury is high, and the consequences of such injury (acute respiratory distress syndrome) are serious. A total

of 180 patients undergoing one-lung anesthesia were randomized to receive, as the primary anesthetic agent, propofol or isoflurane, each titrated to a common target bispectral index, and with otherwise common anesthetic management protocols. All patients demonstrated increases in proinflammatory mediators in the bronchoalveolar fluid after (vs. before) surgery; such increases were greater after propofol *versus* sevoflurane. Postoperative circulating levels of proinflammatory mediators were higher after propofol *versus* sevoflurane. Although propofol was associated with a higher incidence of postoperative pulmonary complications, this was not reflected in LOS in the acute care unit or in the hospital. The study power was insufficient to confirm an impact on mortality. Choice of anesthetic agent may impact the inflammatory perioperative milieu; additional research is required to determine if and how this may impact upon patient outcome.

BOC08

“A Thermodynamic Breathing Sensor—A New, Noninvasive Method of Monitoring Ventilation” by David Preiss, M.D., Ph.D., Benjamin Drew, Student, James Gosnell, R.N., Bhavani S. Kodali, M.D., James H. Philip, M.D., Perioperative Pain Medicine, Brigham and Women’s Hospital, Boston, Massachusetts. Capnography is commonly used to assess respiratory rate. Feasibility of capnography in the awake, spontaneously ventilating patient is often limited by entrainment of air and dislodgement of equipment. A new thermodynamic sensor, Linshom Respiratory Monitoring Device (LRMD), was developed to obviate this concern. The accuracy and precision of LRMD was compared with standard capnography in 26 young healthy volunteers. There was a high degree of correlation between the two modalities with a bias of -0.8 ± 0.9 breaths/min. These preliminary results, which need corroboration in patients with significant comorbidity, indicate that LRMD is a promising device for monitoring of respiratory rate that merits further development.

BOC09

“Molecular Modeling Leads to a New Class of Intravenous Anesthetics” by Edward J. Bertaccini, M.D., Margaret Frances Davies, Ph.D., Noelle Cayla, M.S., Melis Sunay, B.S., Boris Heifets, M.D., Ph.D., James R. Trudell, Ph.D., Bruce M. MacIver, Ph.D., Stanford University and Palo Alto VA Hospitals, Palo Alto, California. Several anesthetic agents have activity at the GABA-A receptor. Molecular modeling predicted the binding affinity of a new class of agents that might serve as chemical scaffolds for iterative drug discovery. High-throughput *in silico* docking screens identified 12 structures. By computational docking, those with high binding were testing *in vivo* in tadpoles, and their electrophysiologic effects were evaluated in hippocampal brain slices. The most potent agent (compound B) produced a loss of righting reflex in tadpoles with an effective concentration of approximately 500 nM. Whole cell patch

clamp analyses demonstrated enhanced GABA-A receptor-mediated IPSC amplitude and prolongation of the open state. Molecular modeling predicted binding affinity of a new class of agents that will serve as chemical scaffolds for iterative drug discovery.

BOC10

“Exercise Improves Postoperative Cognitive Decline in Rats with Metabolic Syndrome by Rectifying Inflammation Resolution and the Microbiome” by Mervyn Maze, M.B., Ch.B., Xiaomei Feng, M.D., Ph.D., Susana Vacas, M.D. Lauren G. Koch, Ph.D., Steven L. Britton, Ph.D., University of California, San Francisco, San Francisco, California. Anesthesia and surgery cause inflammation in the brain and cognitive dysfunction in the postoperative period (POCD), and this memory dysfunction is exaggerated and persistent in experimental models of metabolic syndrome. Exercise can modulate inflammation. The effect of exercise in high-capacity and low-capacity runner rats on POCD, hippocampal inflammation, and the gut microbiome was evaluated. In the low-runner rats, inflammation and POCD were greater; these abnormalities were rectified by preoperative exercise. Interestingly, exercise also rectified the abnormal microbiome in the lower-runner rats. Preoperative exercise improves postoperative function, and it may provide an opportunity to improve surgical outcomes in high-risk patients.

Best Abstracts: Basic Sciences

Sunday, October 25, 1 PM to 3 PM, San Diego Convention Center, Upper 4

Moderators

J. David Clark, M.D., Ph.D., Stanford University, Palo Alto, California; Piyush M. Patel, M.D., F.R.C.P.C., University of California, San Diego, San Diego, California.

BOS01

“Selective Pharmacologic Targeting of the γ -aminobutyric Acid Type A (GABA-A) Receptor $\alpha 4$ Subunit in Airway Smooth Muscle to Alleviate Bronchoconstriction” by Gene T. Yocum, M.D., George Gallos, M.D., Margot Ernst, Ph.D., James M. Cook, Ph.D., Charles W. Emala, M.D., Columbia University, New York, New York. GABA-A agonists relax airway smooth muscle cells; among the six α -subunits expressed in GABA-A receptors, human airway smooth muscle expresses only $\alpha 4$ and $\alpha 5$; this raises the possibility for selective bronchodilation without central nervous system impact (mediated mostly by $\alpha 1$, $\alpha 2$, and $\alpha 3$). Two agonists (CMD-45 and XHe-III-74) with $\alpha 4$ - and $\alpha 6$ -selectivity have been synthesized by computational design. In oocytes that were engineered to selectively express one of the six GABA-A subunits ($\alpha 1$, $\alpha 2$, $\alpha 3$, $\alpha 4$, $\alpha 5$, or $\alpha 6$), the selective agonists (CMD-45 and XHe-III-74) produced greater accentuation of GABA-A current where $\alpha 4$ or $\alpha 6$

were expressed. CMD-45 and XHe-III-74 produced greater airway relaxation in isolated tracheal rings from wild-type *versus* $\alpha 4$ knockout mice, and low doses of each compound increased the potency of albuterol-induced relaxation of human airway smooth muscle strips. Inhaled XHe-III-74 reduced bronchoconstriction in sensitized mice (*in vivo*), and human airway smooth muscle cells (*in vitro*) demonstrated less calcium flux in response to histamine when pretreated with either CMD-45 or XHe-III-74. Selective GABA-A agonists might preferentially cause bronchodilation with minimal central nervous system effects.

BOS02

“Y Chromosome Plays a Protective Role against Hypoxia-induced Pulmonary Hypertension in Gonadectomized Mice” by Soban Umar, M.D., Ph.D., Alex Centala, B.S., Mariam Barseghyan, B.S., Maureen Ruiz-Sundstrom, B.S., Arthur P. Arnold, Ph.D., Mansoureh Eghbali, Ph.D., UCLA Medical Center, Los Angeles, California. Pulmonary hypertension is four times as common in women than men, but in experimental models of pulmonary hypertension, female (*vs.* male) animals are relatively protected. The “four core genotypes” mouse model renders the complement of sex chromosomes (XX, XY) unrelated to the gonadal sex and produces XX gonadal males, XX gonadal females, XY gonadal males, and XY gonadal females. In addition, the XY* (XY-Star) mouse allows identification of the role of the Y chromosome or the number of X chromosomes. Gonadectomized mice were exposed to hypoxia for 3 weeks, and in these mice, the presence of a Y chromosome protected against development of pulmonary hypertension (in terms of echocardiography, right heart catheter study, histology). In addition, the presence of a Y chromosome was more important than the number of X chromosomes. Because the Y chromosome is small (*i.e.*, contains relatively few genes), screening and evaluation of Y chromosome genes that are expressed in the lung may rapidly provide insights into potential therapy.

BOS03

“Reversal of Burn Injury-induced Muscle Wasting by Antiproteolytic Effects of Specific $\alpha 7$ ACHRS Agonist, GTS-21” by Shikuza Kashiwagi, M.D., Mohammed A. Khan, Ph.D., Shingo Yasuhara, M.D., Ph.D., Jeevendra Martyn, M.D., Massachusetts General Hospital, Shriners Hospital for Children, Boston, Massachusetts. Muscle wasting (increased breakdown and/or diminished synthesis) is an important adverse component of critical illness. However, $\alpha 7$ acetyl choline receptors ($\alpha 7$ ARs) are up-regulated in many tissues during inflammation and muscle wasting; although $\alpha 7$ AR stimulation can reduce inflammation, its impact on muscle wasting is not known. Anesthetized mice were subjected to 30% full-thickness burn. Compared with sham-operated animals, burn injury resulted in increased expression of Atrogin-1 and MuRF-1, two ubiquitin ligases

known to mediate muscle degradation. Treatment with GTS-21, a specific $\alpha 7$ AR agonist, reduced the expression of Atrogin-1 and the relative skeletal muscle loss (relative to total body mass). Selective stimulation of acetyl choline receptors might help prevent muscle loss in critical illness.

BOS04

“Isoflurane Differentially Effects Firing Correlations among Parvalbumin Interneurons *versus* Pyramidal Neurons in Mouse Frontal Cortex” by Andrew Hudson, M.D., Ph.D., UCLA Department of Anesthesiology and Perioperative Medicine, Los Angeles, California. The increase in electroencephalogram low-frequency power with increasing depth of anesthesia has been thought to be due to increasing synchronization of pyramidal neurons of the cortex; however, the relative contribution of inhibitory interneurons is not clear. A red fluorescent dye was targeted to parvalbumin expressing interneurons that also expressed Cre recombinase and isoflurane was administered in a graded manner. Activity of pyramidal and interneurons was evaluated in cortical layers 2 to 3. With increasing depth of anesthesia, correlation of activity was greater in interneurons than in pyramidal cells. The data are consistent with the premise that increasing synchronization of the electroencephalogram is in part due to synchronization of inhibitory interneurons.

BOS05

“Recovery of Sensory Processing from Propofol Anesthesia in Somatosensory *versus* Higher-order Cortices in Primates” by Yumiko Ishizawa, M.D., Ph.D., Shaun Patel, Ph.D., Omar J. Ahmed, Ph.D., Emery N. Brown, M.D., Ph.D., Emad N. Eskandar, M.D., Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts. To better understand how information is processed in the cortex before, during, and after propofol anesthesia, single-neuron recordings from premotor and sensory (S1 and S2) cortex in response to tactile and sensory stimuli were obtained from monkeys in whom microelectrode arrays were implanted. As expected, under propofol anesthesia, responses to stimulation were abolished. Recovery of S1 and S2 neurons was complete 60-min postanesthesia. By contrast, recovery of bimodal neurons in the premotor was incomplete even 120-min postanesthesia. These results indicate that there is differential recovery of neuronal function during awakening from anesthesia and that restoration of function is delayed in neurons in the premotor cortex in comparison with neurons in the sensory cortex.

BOS06

“Depletion of Microglia Is Neuroprotective after Cardiac Arrest” by Mizuko Ikeda, M.D., Ph.D., Ines P. Koerner, M.D., Ph.D., Oregon Health and Science University, Portland, Oregon. Although microglial activation is thought to contribute to delayed neuronal death in experimental models of global ischemia, their relative contribution to ongoing

neuronal loss remains to be defined. Mice expressing tamoxifen-inducible Cre recombinase were utilized to drive diphtheria toxin receptor expression in microglia and peripheral macrophages. Administration of diphtheria toxin ablated the slow turnover brain microglia, whereas the rapid turnover peripheral macrophages recovered. Neuronal loss in the hippocampus after global ischemia was significantly reduced with brain microglial depletion. These data are consistent with the premise that microglial activation plays an important role in global ischemia-induced delayed neuronal death.

BOS07

“Xenon Affects the Thalamic Input in Cortical Layer IV and Attenuates Cortical Processing in Layer II/III: A VSDI [Voltage Sensitive Dye Imaging] *In Vitro* Study” by Matthias Kreuzer, Ph.D., Stephan Kratzer, M.D., Gerhard Rammes, Ph.D., Eberhard F. Kochs, M.D., Paul S. Garcia, M.D., Rainer Haseneder, M.D., Emory University School of Medicine, Decatur, Georgia. The relative contribution of suppression of thalamocortical and cortical-cortical connectivity in xenon-induced unconsciousness is not known. Thalamocortical slices from mice were prepared and were loaded with a voltage-sensitive dye. The changes in fluorescence in various cortical layers were recorded in response to stimulation of the thalamus. Xenon did not affect stimulus propagation, but it significantly reduced the responses in layer II/III of the cortex. The distribution of the responses within the cortex was not affected. The data show that xenon reduces thalamocortical connectivity but does not appear to influence functional connectivity in the cortex.

BOS08

“Inhibition of RhoA Activity with TAT-C3 Attenuates Propofol-mediated Neurotoxicity” by Minyu Jian, M.D., Matthew Pearn, M.D., Junji Egawa, M.D., Brian Head, Ph.D., Piyush M. Patel, M.D., Ruquan Han, M.D., University of California, San Diego, San Diego, California. Anesthetic exposure during the neonatal period leads to a substantial loss in synapses that persists into adulthood. The mechanism underlying synaptic loss is not known but RhoA activation, actin depolymerization, and neurite loss contribute to this loss. The effect of RhoA inhibition on neuronal death and neurite loss were determined in human and rodent neurons *in vitro* and in the hippocampus of mice exposed to propofol. Propofol increased RhoA activation and decreased dendritic arborization in both human and rodent neurons *in vitro*. *In vivo*, propofol decreased mossy

fibers in the infrapyramidal bundle of the hippocampus 4 weeks after exposure. The data indicate that propofol toxicity is mediated in part by RhoA activation and that propofol alters the development of hippocampal neuronal networks.

BOS09

“Analysis of Malignant Hyperthermia Using Patient-derived Induced Pluripotent Stem Cells (iPSCs) and Skeletal Muscle Cells Differentiated from These iPSCs” by Hidemi Harima, M.D., Mitsuru Ishikawa, Ph.D., Wado Akamatsu, M.D., Ph.D., Kenjiro Kosaki, M.D., Ph.D., Manabu Ohyama, M.D., Ph.D., Hideyuki Oakno, M.D., Ph.D., Hiroshi Morisaki, M.D., Ph.D., Keio University School of Medicine, Tokyo, Japan. Mutations in the ryanodine receptor 1 (RyR1) gene convey susceptibility to malignant hyperthermia (MH). To determine how MH is triggered *via* RyR1, iPSCs were generated from lymphocytes and fibroblasts from patients with known susceptibility to MH, and the iPSC were differentiated into skeletal muscle cells. MH patient-specific iPSC generated more lactate upon exposure to sevoflurane than control iPSC. The MH patient-specific iPSCs were also successfully differentiated into skeletal muscle cells that expressed myotubes and RyR1. iPSCs and myocytes generated from these iPSC can serve as a useful model for the study of the pathophysiology of MH.

BOS10

“Multidirectional Assessment of Pain-related Behavior in Bone Cancer Pain Model in Mice” by Hideaki Mori, M.D., Tetsuro Nikai, M.D., Ph.D., Shimane University Hospital, Izumo, Japan. The assessment of pain and its consequences in animals is a difficult challenge, but a critical one for preclinical pain research. In these studies, measures of mobility, anxiety, and sociability were assessed in a mouse cancer pain model. Evidence for effects in each of these domains was found. These results will facilitate translational cancer pain studies.

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Competing Interests

The authors declare no competing interests.