Poster Presentations

(Note: Bold name represents poster presenter)

#1 **Incidence and Etiology of Early and Late Onset Ventilator-Associated Pneumonia in a University Hospital**
Ozan Akca M.D., M. Gnoni, M.D.; M. Saad, M.D.; G. Franklin, M.D.; J. Ramirez, M.D.

#2 **Age and Gender Adversely Affect Adequacy of Transthoracic Echocardiography in Post-Operative Cardiac Intensive Care Unit Patients**
Brigid C. Flynn, M.D.; Jessica Spellman, M.D.; Vivek Moitra, M.D.; Carol Bodian, Dr.Ph.

#3 **SWIFT: Nudging Providers Towards Alternative Patient Discharge Strategies**
Brian W. Pickering, M.D., FFARCSI, DICM; Mark T. Keegan, M.D.; Bekele Afessa, M.D.; Ogie Gajic, M.D.

#4 *Honorable Mention*
Expression of Fetal and Adult Acetylcholine Receptor Isoforms Following Acute Denervation
Christopher Kramer, M.D.; Manfred Blobner, M.D.; Saida Zoubaa, M.D.; Alexander Kretschmer, Christiane Frick, M.D.; Gerhard Rammes, Ph.D.; Heidrun Fink, M.D.

#5 **Consequence of Intraoperative Resuscitation Strategy on Post-operative Lung Function**
Ashima Dhamija, M.D., Anne Boyd, B.A.; Leonard J. Lind, M.D.; Judith Strong, Ph.D.; Steven J. Lisco, M.D.

#6 **Predictors of Acute Kidney Injury in Patients Undergoing Extrapleural Pneumonectomy**
Annette Mizuguchi, M.D., Ph.D.; Aya Mitani, MPH; Joseph V. Bonventre, M.D. Ph.D.; David S. Sugarbaker, M.D.; Gyorgy Frendl, M.D., Ph.D.

#7 *Young Investigators Award*
Early Postoperative Statin Therapy is Associated with a Lower Incidence of Acute Kidney Injury Following Cardiac Surgery
Frederic T. Billings, IV, M.D.; Chang Yu, Ph.D.; Mias Pretorius, M.D.; Nancy J. Brown, M.D.

#8 **New Cell Proliferation in the Dentate Gyrus is Selectively Altered by Propofol in Young Rats**
Diana M. Erasso, M.S.; Rafael E Chaparro, M.D.; Carolina Quiroga, M.D.; Devanand Mangar, M.D.; Samuel Saporta, Ph.D.; Enrico M Camporesi, M.D.

#9 **Antibiotic Impregnated Cement Spacer Associated Acute Renal Failure as a Cause of Patient Mortality Following a Complicated Total Knee Arthroplasty**
Sarah B. Kane, M.D.; Deven S. Kothari, M.D.; Marc J. Popovich, M.D.

#10 **Isoflurane or A Caspase -3- Inhibitor, Limit Memory and Behavioral Deficits After Hypotension Plus Hypoxia Insult**
Rafael E. Chaparro, M.D., Ph.D.; Carolina Quiroga, M.D., MBA; Diana Erasso, M.S., Ph.D.; Rachel Karnoski, Ph.D.; Devanad Mangar, M.D.; Enrico Camporesi, M.D.

#11 **Anesthetics and Analgesics Effects on Amyloid Precursor Protein (APP) Alzheimer's Mouse Model.**
Carolina E. Quiroga, M.D., MBA; Rafael Eduardo Chaparro, M.D., Ph.D.; Diana Erasso, M.S.; Rachel Karlnoski, Ph.D.; Marcia Gordon, Ph.D.; Dave Morgan, Ph.D.; Enrico Camporesi, M.D.

#12 **Survival After Inpatient Cardiac Arrest: A Retrospective Review of Associated Factors**
Louanne M. Carabini, M.D.; M. Ault, M.D.; A. M. Naidech, M.D., MSPH; L. Rochlen, M.D.; S. Afifi, M.D.

#13 **Effect of Dexmedetomidine on Physiologic Parameters in Acute Lung Injury**
Jewel D. Montgomery, M.D.; M. Castellon, M.S.; R.D. Minshall, Ph.D.; D.E. Schwartz, M.D.

#14 **Pulse Oximetry Saturation to Inspired Oxygen Ratio as a Measure of Hypoxia Under General Anesthesia**
Ravi S. Tripathi, M.D.; James M. Blum, M.D.; Andrew L. Rosenberg, M.D.; Kevin Tremper, M.D.

#15 **Biological Markers of Acute Inflammation After Complex Spine Surgery**
Michael K. Urban, M.D., Ph.D.; Shane Reid, B.A.; Michael Ho, M.D.; Ketty M. Jules-Elysee, M.D.; Thomas King, M.D.; Oheneba Boachie-Adjei, M.D.

#16 **Utility of I.V. Nitroglycerine for Dampened Arterial Wave**
Richard B. Silverman, M.D.; Bruce Saltzman, M.D.; Roger Marks, M.D.

#17 **Retrospective Study of Acute Lung Injury following Thoracotomy for Major Spine Surgery**
Marie-Hélène Tremblay, M.D., FRCPC; Jens Lohser, M.D., MSc, FRCPC; Marcel Dvorak, M.D., FRCSC; Donald EG Griesdale, M.D., MPH, FRCPC; Craig R. Ries; M.D., FRCPC, Ph.D.

#18 **Intraoperative Anesthetic Characteristics and the Development of ARDS: A Pilot Study**
Christopher G. Hughes, M.D.; Liza Weavind, M.D.; Arna Banerjee, M.D.; Nathaniel Mercaldo, M.S; Schildcrout Jonathan, Ph.D.; Pratik Pandharipande, M.D., MSCI

#19 **Low-pressure Microcuff Adult Endotracheal Tube reduces the Incidence of Ventilator-Associated Pneumonia**
Rachel A. Karlnoski, Ph.D.; Jaya Kolla, M.D.; Gerardo Munoz, M.D.; Katheryne Downes, M.S.; Peggy Thompson, Sherri Klacsan, Lynne Kelley, M.D.; Devanand Mangar, M.D.; Enrico Camporesi, M.D.; John Schweiger, M.D.

#20 **The Delivery of Critical Care Education within American Anesthesiology Residency Training Programs**
Kevin W. Hatton, M.D.; Amy DiLorenzo, Brenda G. Fahy, M.D.; Randall M. Schell, M.D.

#21 **Palliative Care in the Cancer ICU**
Jay P. Roby, M.D.; Kim, Peter, M.D.; Yang, Susie, M.D.; Mogos, Mariana, M.D.; Roffey, Peter, M.D.; Thangathurai, Duraiyah, M.D.

#22 **Preoperative Pulmonary Hypertension is a Risk Factor for the Development of ALI after High-Risk Surgery**
Arun Subramanian, M.B.B.S, Gajic O, M.D.; Schroeder D.; Joyner MJ, M.D.; Kor DJ, M.D

#23 **Estrogen Protects Glomerular Endothelial Cells from Ischemia: Role for GPR30?**
Michael P. Hutchens, M.D., M.A.; Yasuharu Kosaka, M.D.; Daniel F Lotspeich, M.D.; Radko Komers, M.D., Ph.D.; Paco Herson, Ph.D.; Patricia D. Hurn, Ph.D.; Sharon Anderson, M.D.

#24 **Critical Care Issues in Face Transplantation**
Amanda M. Russell, M.D.; Deven S. Kothari, M.D.; Marc J. Popovich, M.D.

#25 **A Case of Posterior Reversible Encephalopathy Syndrome (PRES) in the Intensive Care Patient**
Christopher S. Eddy, M.D.; Oscar J. Viegas, M.D.

#26 **CVP/PAD Ratio Predicts Length of ICU Stay after Cardiac Surgery**
Daniel S. Rubin, M.D.; Avery Tung, M.D.

#27 **The Relationship Between CVP and Right Ventricular Function in Cardiac Surgery Patients**
Daniel S. Rubin, M.D.; Avery Tung, M.D.

#28 **A Survey of Current Anesthesiology Resident Perceptions of a Career in Critical Care Medicine**
Mark H. Enker, M.D.; Stephen Badger, M.D.; Robert Pousman, D.O.; C. Lee Parmley, M.D., J.D.

#29 **Impact of HIV-infection on Short-Term Outcomes of Critically Ill Patients with Acute Lung Injury**
Pedro A. Mendez-Tellez, M.D.; Damluji, A.; Ammerman, D.; Fan, E.; Sevransky, J.; Colantuoni, E.; Pronovost, P.J.; Needham, D.M.

#30 *Honorable Mention*
Anti-Apoptotic Effects Of Nitrite On Liver Ischemia Reperfusion Injury
John D. Lang, M.D.; Zihiu Meng, M.D.; Yuliang Liu, M.D.; Rakesh P. Patel, Ph.D.; Wei Li, M.D.,Ph.D.

#31 **Intra-Operative Use of Lung Protective Strategies by Anesthesia Providers**
Jason K. Klopotowski, M.D.; James Bloom, M.D.; Andrew L. Rosenberg, M.D.; Pauline Park, M.D.

Poster 1

Incidence and Etiology of Early and Late Onset Ventilator-Associated Pneumonia in a University Hospital

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Departments of Internal Medicine, and Surgery

Background: Ventilator-associated pneumonia (VAP) is defined as pneumonia occurring more than 48 hours after initiation of mechanical ventilation. It is the most common nosocomial infection in the ICU, and increases mortality. Guidelines for therapy of VAP suggest the use of narrow spectrum antibiotics in patients for early-onset VAP, because multi-drug resistant bacteria are unlikely in these patients. However, data is limited to support such recommendations. The objective of this study was to define the incidence and etiology of early-VAP versus late-VAP.

Methods: With the IRB approval of University of Louisville, we reviewed the medical records of 168 patients who were mechanically ventilated for more than 48 hours. VAP was diagnosed by the CDC criteria. Early-VAP was defined as development of VAP during the initial 6 days of intubation, and late-VAP was considered >6 days of intubation and mechanical ventilation. VAP incidence was calculated using 1,000 ventilator-days and compared using Z-statistics. Incidence of multi-drug resistsant bacteria was calculated for patients with early-VAP and late-VAP,

Results: The incidence of early-VAP was 40/1,000 vent-days, and late-VAP incidence was 14/1,000 vent-days (P=0.002). Multi-drug resistant organisms were identified in 46% of early-VAP and 77% of late-VAP.

Conclusion: The risk for the development of VAP is significantly higher during the initial days of mechanical ventilation. Interestingly, multi-drug resistant organisms caused early-VAP very frequently. Therefore, the presence of early-VAP by itself cannot support the use of narrow-spectrum empiric antibiotherapy.

Age and Gender Adversely Affect Adequacy of Transthoracic Echocardiography in Post-Operative Cardiac Intensive Care Unit Patients.

Brigid C. Flynn, M.D.; Jessica Spellman, M.D.; Vivek Moitra, M.D.; Carol Bodian, Ph.D.
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Background: Previous studies have attempted to elucidate factors contributing to inadequate transthoracic echocardiography (TTE) imaging in intensive care unit (ICU) patients. Various patient characteristics have been proposed as risk factors for inadequate TTE in ICU patients(1,2,3). We sought to determine which patient characteristics in post-surgical cardiac ICU patients were associated with inadequate TTE imaging.

Objective: We conducted a retrospective review of 1038 patients consecutively admitted to a tertiary care cardiac intensive care unit. The first 300 patients who received a TTE within the first seven days postoperatively were included for analysis. An attending cardiologist interpreted all echocardiograms. Results were recorded as adequate, inadequate, or partially adequate for the left ventricle, the right ventricle and combined left and right ventricles. Multivariate logistic regression analysis was used to determine the significance of the mentioned risk factors for an inadequate TTE.

Results: We found that increasing age and male gender were significant risk factors for an inadequate TTE visualization. Inadequate visualization is defined as the inability to assess left ventricular function. See Table 1.

Discussion: Previous studies have reported different risk factors for an inadequate TTE in the intensive care unit(1,4,5). To our knowledge this is the largest study examining age and gender as possible risk factors for an inadequate TTE. This is also the first investigation examining risk factors for an inadequate TTE in post-operative cardiac patients; a population in which echocardiography may provide data for care altering decisions.

Age: Increasing age adversely affected image quality possibly due to age-related changes such as calcification of the thoracic skeleton, kyphosis, scoliosis, and decreased flexibility limiting patient positioning. With age, the lungs become hyperinflated (increased residual volume) resulting in slowing of the ultrasound waves due to the low acoustic impedance of air. The body may also have a higher fat content, which causes an acoustic impedance mismatch creating reflection of ultrasound waves and decreasing acoustic penetrance.

Gender: Male gender was associated with inadequate TTE's possibly because males generally have larger thoracic cavities than women, with decreased transmission of ultrasound waves through air. Also possible is that males in our population had more complex heart conditions that precluded accurate assessment due to the nature of the disease processes. In summary, these data suggest that patient factors can be used to stratify which patients will have an inadequate TTE.

References:

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2. Price S, Nicol E, Gibson DG, Evan TW. Intensive Care Med 32:48-59.
3. Zema MJ, Caccavano M. Br Heart J 48:428-33.
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Table 1. Independent risk factors by multivariate analysis associated with inadequate visualization by transthoracic echocardiogram.

	Adequate visualization	
Factor	OR (95% CI)	P
Increasing age	1.03/year (1.01, 1.06)	0.01
Male	2.2 (1.1, 4.6)	0.03

SWIFT: Nudging Providers Towards Alternative Patient Discharge Strategies

Brian W. Pickering, M.D., FFARCSI, DICM; Mark T. Keegan, M.D.; Bekele Afessa, M.D.; Ogie Gajic, M.D.
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Introduction: The care of patients in the ICU is expensive and potentially hazardous. Readmission to the ICU is associated with worse outcome and increased cost. Providers are poor judges of the risk of patient readmission. The Stability and Workload Index For Transfer (SWIFT) score is a previously developed tool (1) which predicts unplanned ICU patient readmission. A score >15 is associated with a 6-15% risk of return to the ICU within 24 hours of discharge. We describe the implementation of this scoring tool in a medical ICU and present an analysis of first quarter data which demonstrate the impact on provider discharge planning and judgments.

Methods: Calculation and assessment of the SWIFT score has been routine in our Medical ICU since December 2008. Prior to introduction of the SWIFT score eduction of both physician and nursing staff took place. The SWIFT score and associated percentage risk for readmission have been incorporated into a daily rounds tool for the purpose of discharge planning. Bedside providers are encouraged, through prior education and regular information sessions, to discuss the SWIFT score when it is >15. A record of whether the SWIFT score was discussed and subsequent decision making regarding ICU dismissal is made by the bedside nurse. Predefined changes to the discharge plan are recorded by the bedside nurse and include: no changes made; enhanced communication with receiving team; change in receiving team/destination; reversal of decision to discharge the patient from the ICU. Regular updates regarding compliance with SWIFT score discussion and readmission rates are provided to physicians and nurses via email and scheduled information sessions.

Results: Over a 5 month period, of the 734 patients discharged alive from the medical ICU, 228 (31%) had the SWIFT score discussed. In that group 71 (31%) had some change in discharge plan recorded; enhanced communication n= 45; changed discharge service or location=21; remained in the ICU n= 10. In the group who had SWIFT discussed, 3/228 (1.3%) were readmitted within 24 hours compared to 18/506 (3.6%) in the group who did not have the score discussed, 2 tailed Fisher's Exact Test= 0.1. Median ICU length of stay (days) remained unchanged, (2.3) compared to the same period in 2008 (2.4),

Conclusion: In the time period analyzed, the discussion of the patient's SWIFT score was associated with significant changes in provider discharge behaviors, resulting in more conservative discharge strategies without a significant increase in overall ICU LOS. At this point the observed differences in readmission rates are not statistically significant.

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Honorable Mention

Expression of Fetal and Adult Acetylcholine Receptor Isoforms Following Acute Denervation

Christopher Kramer, M.D.; Manfred Blobner, M.D.; Saida Zoubaa, M.D.; Alexander Kretschmer; Christiane Frick, M.D.; Gerhard Rammes, Ph.D.; Heidrun Fink, M.D.
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Introduction: In innervated skeletal muscle, acetylcholine receptors (AChRs) are restricted to the neuromuscular junction where the adult isoform (α1β1δε) is expressed. Denervation increases expression of AChRs. Previous studies investigated total expression of AChRs or subtypes on the mRNA-level. Little is known about differential isoform regulation on a protein level in the junctional and extrajunctional areas. We, therefore, investigated the qualitative and quantitative expression patterns of adult and fetal (α1β1δγ) AChR subtypes as well as histological changes in the diaphragm muscle after 1, 3, and 9 days of denervation.

Material and Methods: 40 male Sprague-Dawley rats were either unilaterally cervically phrenicotomized or sham-operated. After 1, 3, or 9 days, respectively, both hemidiaphragms were excised. Adult and fetal AChR isoforms were determined by Western Blot (WB). Isoform expression was localized by immunohistochemistry (IHC). Fiber type composition, cross-sectional area (CSA) and histomorphological changes were evaluated on ATPase (pH 9,4 and pH 4,6) and HE stains. Data were statistically analyzed by t-test ($p<0.05$).

Results: Denervation for up to 9 days did not change expression of adult AChR compared to sham-operation (WB: 0.8 ± 0.8 vs. 0.9 ± 0.9; IHC-score junctional: 0.5 ± 0.5 vs. 0.4 ± 0.5; IHC-score extrajunctional: 0.0 ± 0.0 vs. 0.0 ± 0.0). 1 day after denervation, fetal AChRs are up-regulated at the junctional site. [IHC score: 1.1 ± 1.2 (denervated) vs. 0.3 ± 0.7 (non-denervated)]. After 3 days of denervation fetal AChRs were not only seen at the junctional site [IHC-score: 2.4 ± 0.7 (denervated) vs. 0.3 ± 0.7 non-denervated)], but also extrajunctionally throughout the muscle membrane [IHC score: 1.5 ± 0.5(denervated) vs. 0.1 ± 0.3 (non-denervated)]. Maximum up-regulation of fetal AChRs was at day 9 [WB: 145 ± 179 (denervation) vs. 0.6 ± 0.8 (sham operation)], where they are expressed at the junctional site [IHC score: 2.6 ± 0.5 (denervation) vs. 0.4 ± 0.5 (vs. sham operation)] as well as on the muscle membranes of all fibers [IHC-score: 3.0 ± 0.0 (denervation) vs. 0.1 ± 0.3 (sham operation)]. After 3 days of denervation extrajunctional expression of fetal AChRs was predominantly restricted to muscle membranes of type1 and type2a fibers, while on day 9 they were evenly expressed on type1, type2a and type2b/x muscle fibers. Over the course of denervation there was a selective atrophy of type 2b/x fibers whereas CSA of type1 and 2a fibers remained unchanged or slightly hypertrophied. Accordingly, total numbers of atrophic and necrotic fibers, sarcolemmal nuclei and connective tissue width increased significantly following denervation.

Conclusion: Typical histomorphological changes following denervation were displayed in our model. Moreover, we could demonstrate for the first time that denervation selectively up-regulates junctional and extrajunctional fetal AChRs without changing the expression of adult AChRs. Interestingly, 3 days after denervation fetal AChR distribution is fiber type-dependant, whereas after 9 days this type restriction is not observed any longer. Thus, it is likely that the transcriptional program for the fetal AChR gene expression is differently controlled in the muscle fiber types.

Consequence of Intraoperative Resuscitation Strategy on Post-operative Lung Function

Ashima Dhamija, M.D.; Anne Boyd, B.A., Leonard J. Lind, M.D.; Judith Strong, Ph.D.; Steven J. Lisco, M.D.
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Background: Recent trauma literature advocates balanced component therapy for resuscitation of injured and bleeding patients. Massive transfusion protocols recommend a 1:1 ratio of packed red blood cells and fresh frozen plasma. Several papers have shown in non-bleeding patients undergoing elective intraabdominal surgery, a restrictive fluid management strategy may be best in reducing postoperative morbidity. Despite absence of data, many surgeons now merge these two concepts and advocate a paradigm of blood and fluid management that adheres to both a trauma-style resuscitation strategy and a restriction of nonblood containing fluids for any surgical patient sustaining perioperative hemorrhage.

Methods: After Internal Review Board approval, a database of patients transfused during surgery for years 2003-08 at a University trauma center was reviewed. All patients studied were transfused intraoperatively and then admitted intubated to the Intensive Care Unit. The amount of blood products, crystalloid solutions, colloid solutions, and cell saver were recorded; the lowest PaO2/fraction of inspired oxygen ratio (P/F ratio) within the first post operative day (surrogate for lung injury), as well as, condition at discharge (alive or dead) were also collected. One unit of blood product was defined as 1 unit of packed red blood cells (pRBC), 1 unit of fresh frozen plasma (FFP), 10 units of cryoprecipitate (CRYO) or 1 bag of pooled platelets (PLT). Data was analyzed using the Spearman's Rank Correlation Test, Mann-Whitney rank sum test and ANOVA on ranks.

Results: 630 patients qualified for this study of these 357 patients underwent emergent surgery. Patients undergoing emergent surgery received more blood products than did patients undergoing non-emergent surgery (Mann-Whitney rank sum test, $p<0.001$). Crystalloid and colloid infused was similar in both groups ($p=0.549$ and $p=0.296$, respectively). P/F ratio did not differ significantly between emergent and non-emergent surgery ($p=0.204$). . None of the blood products transfused or the amount of colloid administered correlated significantly either positively or negatively with P/F ratio. Only the amount of crystalloid infused had a significant correlation with the P/F ratio (Spearman $r = 0.137$, $p = 0.00$). Patients who did not survive to discharge had both the lowest P/F ratios (Death=192 10, Alive=271 8; $p<0.001$) and received the least amount of crystalloid (Death= 2947 257 ml, Alive=5101 247 ml; $p<0.001$).

Discussion: For bleeding surgical patients, intraoperative transfusion strategies and resuscitation goals continues controversial for both anesthesiologists and surgeons. This study looked at a general population of surgical patients coming to the operating room under both emergent and non-emergent conditions. We could not demonstrate either the amount or type of blood products administered correlated with post-operative pulmonary dysfunction. More interestingly and contrary to prevailing belief was that patients receiving relatively more crystalloid did not have a higher incidence of postoperative pulmonary dysfunction. In fact, those patients receiving more crystalloid actually had significantly better lung function and better in-hospital survival. This topic requires further investigation.

Predictors of Acute Kidney Injury in Patients Undergoing Extrapleural Pneumonectomy

Annette Mizuguchi, M.D., Ph.D.; Aya Mitani, MPH; Joseph V. Bonventre, M.D., Ph.D.;
David S. Sugarbaker, M.D.; Gyorgy Frendl, M.D., Ph.D.
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Introduction: Predictors of Acute Kidney Injury in Patients Undergoing Extrapleural Pneumonectomy
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Background: Extrapleural pneumonectomy with intraoperative intracavitary heated cisplatin therapy has improved survival of malignant mesothelioma patients. However, it is associated with a high incidence of renal failure. Our objective was to identify the perioperative predictors of acute kidney injury in this population.

Methods: Using a retrospective cohort of patients who underwent extrapleural pneumonectomy, we hypothesized that various perioperative variables may contribute to the development of acute kidney injury. We defined acute kidney injury (our outcome variable) as the increase in creatinine of 150% over the preoperative baseline value. Univariate associations between the predictors and outcome were assessed by chi-square or Fisher exact test. A prediction model was created using multiple stepwise logistic regression.

Results: The incidence of acute kidney injury was 38.6% (n=108/280). The incidence of acute kidney injury among the cohort receiving intraoperative intracavitary heated chemotherapy was 47.4% (n=64/135) and 30.3% (n=44/145) among those who did not receive intraoperative intracavitary heated chemotherapy. The multivariate stepwise logistic regression model indicated that intraoperative heated cisplatin therapy was a strong predictor of acute kidney injury (OR 2.36 [CI 95% 1.1, 5.1]). Additionally, the need for increased number of postoperative vasopressor requirement (OR 2.4 [CI 95% 1.5, 3.7]) and the need for fresh plasma transfusion in the ICU (OR 2.36 [CI 95% 1.1, 5.0]) were statistically significant.

Conclusions: Our preliminary analysis indicates that intraoperative intracavitary heated chemotherapy, postoperative vasopressor use and postoperative need for fresh plasma transfusions are strong predictors of acute kidney injury in patients undergoing extrapleural pneumonectomy. Further analysis is planned to identify other modifiable risk factors.

Summary: We identified perioperative predictors of acute kidney injury in patients undergoing extrapleural pneumonectomy with intraoperative intracavitary cisplatin therapy for malignant mesothelioma.

Young Investigator Award

Early Postoperative Statin Therapy is aAssociated with a Lower Incidence of Acute Kidney Injury Following Cardiac Surgery

Frederic T. Billings, IV., M.D.; Chang Yu, Ph.D.; Mias Pretorius, M.D.; Nancy J. Brown, M.D.
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Introduction: Acute Kidney Injury (AKI) complicates 8-14% of cardiac surgeries and predicts dialysis, length of stay, and death. Renal and systemic inflammation, impaired vasodilation, and oxidative stress promote cardiac surgery AKI. In contrast, statins reduce inflammtion, improve endothelial function, and limit oxidant production. In ischemia-reperfusion animal models, single-dose statin treatment reduces renal dysfunction and markers of inflammtation. This study tests the hypothesis that statin use reduces AKI following cardiac surgery.

Methods and Results: We assessed the association of preoperative statin use or early postoperative statin use on the incidence of AKI in patients undergoing elective cardiac surgery. Early postoperative statin use was defined as statin treatment within the first postoperative day. Sixty-eight of 324 (21.0%) patients developed AKI, defined using AKIN consensus criteria, following elective cardiac surgery. Patients with AKI stayed in the hospital longer (P=0.03) and were more likely to develop pneumonia (P=0.002) or die (P=0.001). Lower body mass index (P=0.003) and early postoperative statin use (P=0.03) were associated with a lower incidence of AKI. Preoperative statin use did not associate with AKI. In multivariate logistic regression, age (P=0.03), male gender (P=0.02), body mass index (P<0.001), and early postoperative statin use (P=0.006) independently predicted AKI (Figure 1). Early postoperative statin use reduced the odds of AKI by 68%. Propensity score adjusted risk assessment, including preoperative risk factors for AKI, intraoperative markers of severity of surgical intervention, and postoperative markers of prolonged recovery, confirmed the association between early postoperative statin use and reduced AKI (P=0.007). This association between early postoperatve statin use and AKI was consistent between preoperative statin users and non-users (Figure 2).

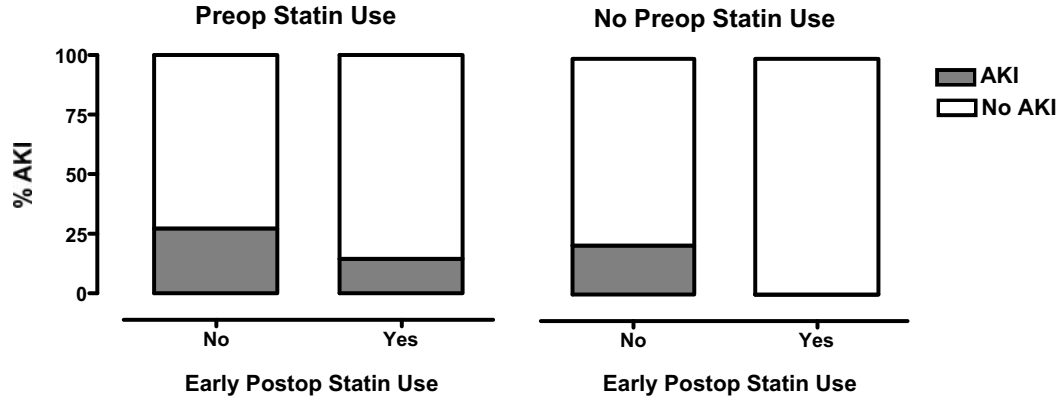
Conclusions & Future Directions:
Early postoperative statin use is associated with less AKI following cardiac surgery, before and after adjustment for differences in AKI risk factors among early postoperative statin users and non-users. Placebo-controlled randomized trials are necessary to validate this observation and to better evaluate the effect of early postoperative statin use on AKI. Postoperative statin treatment is easy to implement and may protect cardiac surgery patients from AKI and the subsequent morbidity and death.

Figure 1.
Multivariate Logistic Regression Model for Acute Kidney Injury

Variable	Odds Ratio	P value	95% CI	
Preoperative Statin Use	1.24	0.50	0.66	2.32
Early Postop Statin Use	0.32	0.006	0.14	0.72
Age, years	1.03	0.03	1.004	1.06
Gender, Male vs. Female	2.41	0.02	1.19	4.89
Baseline creatinine, mg/dl	0.35	0.16	0.08	1.49
Body mass index, kg/m2	1.08	<0.001	1.04	1.13
CPB time, minutes	1.002	0.20	1.00	1.01

CI, confidence interval; BMI, body mass index; CPB, cardiopulmonary bypass.

Figure 2.
Acute kidney injury (AKI) in early postoperative statin users versus non-users, stratified by preoperative statin use.



New Cell Proliferation in the Dentate Gyrus is Selectively Altered by Propofol in Young Rats

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Introduction: General anesthetics are used frequently in young children every year during surgical procedures, imaging studies and sedation in the ICU. The possibility of anesthesia-induced alterations during an uneventful anesthetic in neonates or infants has led to serious questions about the safety of pediatric anesthesia. Adult new cell proliferation occurs in predominantly two regions of the brain, the dentate gyrus (DG) and the olfactory bulb (OB), and although the function is not certain, there is evidence that hippocampal adult new cell proliferation is important for learning and memory (1). Thus, alteration of new cell proliferation in the DG by anesthesia might explain postoperative learning impairments in young children (2). In this study we assessed new cell proliferation in the DG and OB of young rats and new memory formation after propofol exposure attempting to investigate if propofol affects new cell proliferation in a generalized or specific manner.

Methods: 4 month and 21 month old rats were anesthetized for 3 hours with propofol at a dose of 35mg/kg/hr. Additional rats exposed to propofol vehicle served as controls. Body temperature was maintained at 37 °C during the procedure with a thermostatically controlled heating pad. Perioperiative parameters such as body temperature, oxygen saturation and heart rate were measure throughout the anesthesia period. After propofol anesthesia all rats were injected with BrdU (50mg/kg IP) 10 minutes and 18 hours following anesthesia to label nascent neurons. A novel appetitive olfactory learning test was used to assess learning and memory two days after anesthesia. After 7 days, rats were euthanized; the brains removed. Serial sagittal frozen sections (30µm) of one hemisphere were collected for BrdU immunohistochemistry. BrdU-positive cells were counted in the dentate gyrus of the hippocampus and in the granule and glomerular cell layer of the olfactory bulb using unbiased stereology methods.

Results: The number of BrdU+ cells in the dentate gyrus of propofol exposed rats was significantly less (2125 ± 175.3)as compared to controls (1542 ± 163.6) (p= 0.0128) [figure A]. However, this difference was not demonstrated in the number of BrdU+ cells in the olfactory bulb of propofol exposed rats (2843 ± 502.6) compared to control [figure B]. Moreover, Learning in young rats exposed to propofol was also significant impaired as compared to control (p=0.0157).

Conclusions: New cell proliferation in the dentate gyrus was selectively affected by propofol in young rats but no in old rats.

Summary: This is a study of the effect of Propofol on new cell proliferation in the dentate gyrus vs. olfactory bulb of young and old rats.

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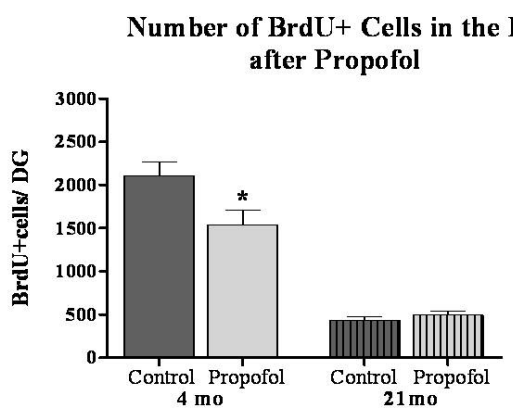
Additional File #1:

A.



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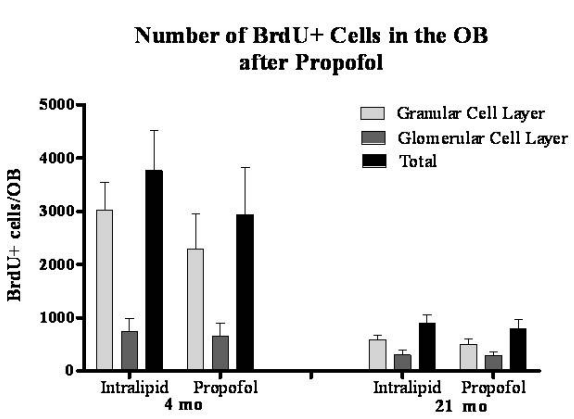

Antibiotic Impregnated Cement Spacer Associated Acute Renal Failure as a Cause of Patient Mortality Following a Complicated Total Knee Arthroplasty

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Anesthesiology Institute, Cleveland Clinic

Introduction: We report a case of acute renal failure (ARF) in a 69 year old male treated with an aminoglycoside impregnated cement spacer for septic arthritis from an infected total knee arthroplasty (TKA). To our knowledge, this is the first case of antibiotic impregnated cement spacer induced ARF leading to patient mortality.

A 69 year old male with a complicated past medical history (Table 1) including TKA complicated by infection requiring multiple reoperations presented with methicillin resistant staphylococcus aureus septic arthritis. He subsequently underwent removal of the infected hardware with placement of antibiotic spacers containing 4 grams of vancomycin and 14.2 grams of tobramycin.

Post operatively, home medications were continued along with IV vancomycin. Despite an adequate hemodynamic profile, post operative renal function continued to decline (Figure 1). This prompted a search for nephrotoxic etiologies and tobramycin toxicity was discovered. Between post operative days #3-20 his clinical course continued to decline as he became increasingly fluid overloaded, dyspneic, hypoxemic, encephalopathic and malnourished. He then underwent therapeutic thoracentesis for pleural effusion and was admitted to the intensive care unit (ICU) on POD #8 where he responded well to steroids, inhalers and diuresis.

Despite improvement in renal indices, tobramycin levels declined but remained above the nephrotoxic level of 2 mcg/mL (Figure 1). However, explantation of the spacers was considered an unacceptable surgical risk in the setting of improved renal indices. He was able to maintain reasonable solute control, but volume control remained challenging. He was non-oliguric but continued to display ineffective diuresis in the setting of high dose furosemide (as high as 320 mg per day). By POD #20 intermittent hemodialysis was instituted for an 8 liter positive fluid balance.

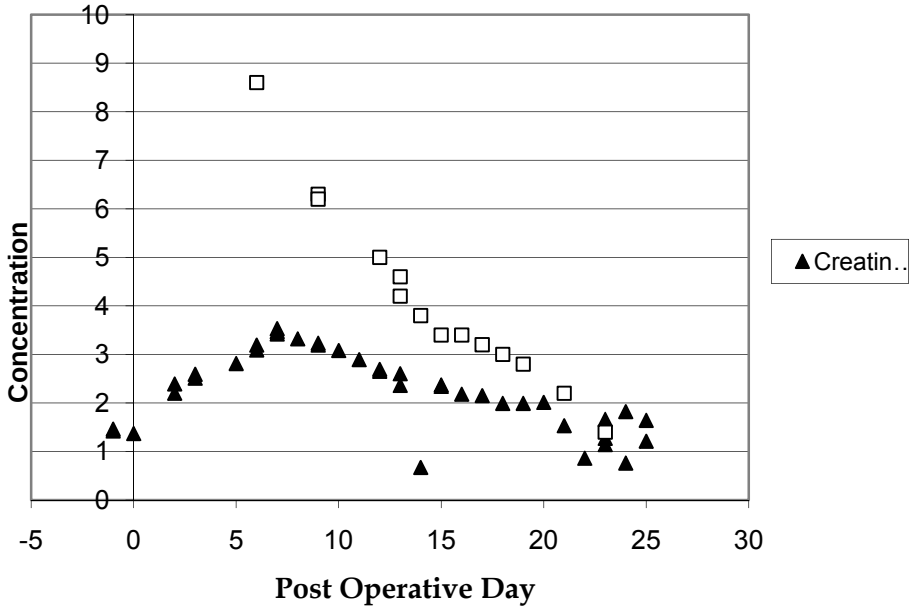
On POD #23 the patient suffered a PEA cardiopulmonary arrest with return of spontaneous circulation after 20 minutes. Hypoxia from fluid overload, ongoing sepsis and possible aspiration were likely explanations. He was readmitted to the ICU where mechanical ventilation, broad spectrum antibiotic coverage and vasopressor support were initiated. By POD #26 the patient met the criteria for brain death, the family withdrew artificial life support, and the patient expired soon after.

Several reports describe antibiotic spacer induced ARF. To our knowledge, however, none have led to patient mortality. Ischemic ATN likely occurred in the perioperative period, but renal recovery did not follow the expected post operative course in a stable patient suggesting ongoing insult. Septic/uremic encephalopathy leading to aspiration in a patient who was fluid overloaded and hypoxemic from acute renal failure contributed to the PEA arrest and ensuing anoxic brain injury. Leaching of nephrotoxic agents from impregnated spacers should be considered in all patients with similar presentation.

Table 1

Past Medical History	Home Medications
Diabetes Mellitus Type 2	Insulin
Hypertension	Amlodipine, Lisinopril, Metoprolol
Congestive Heart Failure	Furosemide
Atrial Fibrillation	Warfarin
Myocardial Infarction	Aspirin
Hemochromatosis	
Hyperlipidemia	Ezetimibe, Zocor
Hypothyroidism	Levothyroxine
Chronic Renal Insufficiency (diabetic/hypertensive nephropathy)	Baseline Serum Creatinine = 1.6 mg/dL Baseline BUN = 34 mg/dL Procrit
s/p Left Total Knee Replacement x 2 s/p Bilateral Total Hip Replacement	Doxycycline
COPD	Albuterol, Ipratropium
Seizure disorder	Dilantin
GERD	Nexium

Figure 1



Isoflurane or A Caspase -3- Inhibitor, Limit Memory and Behavioral Deficits After Hypotension Plus Hypoxia Insult

Rafael E. Chaparro, M.D., Ph.D.; Carolina Quiroga, M.D. MBA 1-3; Diana Erasso, MS, Ph.D. candidate 1-3; Rachel Karnoski, Ph.D. 1-2; Devanad Mangar, M.D. 1-2-4; Enrico Camporesi, M.D.1-2-3
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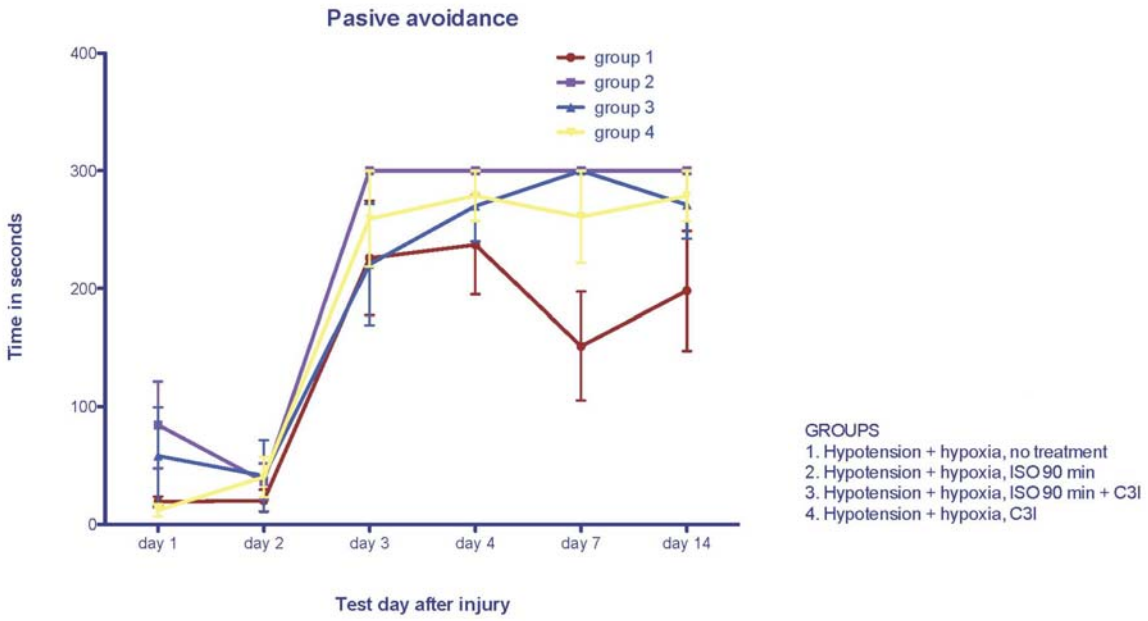
Introduction: We have previously demonstrated that short periods of hypotension cause histological changes in the hippocampus, these changes are not reflected in memory or motor behavior. We used a more intense rat hemorrhagic shock model plus hypoxia to assess functional outcome at different time points post-injury.

Methods: Sprague-Dawley rats were subjected to severe hypotension induced by withdrawal of arterial blood from the right femoral artery. The mean arterial blood pressure was maintained between 20-30 mm Hg with isoelectric EEG for three consecutive minutes, while at the same time the animal was breathing 12% O2 in N2 for 8 min and Hb sat was maintained at 72%. Shed blood was immediately returned to venous circulation, returning systemic pressure to normal. At the end of the hypotensive period the animals were returned to breath air. Animals were evaluated at different time points before there brains were harvested for quantitative neurohistology. All rats received hypotension + hypoxia and were subsequently separated into four groups of 8 animals each as follow. Group 1, Control, no treatment, Group 2 received 90 minutes of Isoflurane 1%. Group 3 was treated with Isoflurane for 90 min 1% plus an IP injection of a caspase -3 inhibitor (Z-DEV 50 micrograms) 3 times (immediately after the injury and at days 1 and 7), Group 4 was treated only with caspase 3 inhibitor, at the same times. A neurological assessment was performed before the study and at 1, 4 and 14 days post-hypotensive insult. We used a 48 point evaluation scale, the higher the number the worse the deficit. We also tested memory by using Passive Avoidance at day 3, 4, 7 and 14. Statistical evaluation was done with ANOVA followed by paired and unpaired t-test.

Results: Neurological assessment showed that hypotentension plus hypoxia caused only minor abnormalities, albeit statistically significant in some cases. Isoflurane per 90 min is protective at day 4 after the insult; the caspase inhibitor was protective at all times during the study but the combination of caspase 3 inhibitor plus Isoflurane did not improved the neurological score. Passive Avoidance testing showed that new memories were created but exposure to Isoflurane improved the performance in comparison with the animals with no treatment. Animals treated with the caspase inhibitor or with Isoflurane plus caspase inhibitor only showed improvement at day 7.

Discussion: These observations suggest that in this hemorrhagic model plus hypoxia there is a mild cerebral damage that is reflected by motor and memory changes. Isoflurane showed to be protective in the motor evaluation as well as the memory test. The caspase 3 inhibitor also showed to be beneficial. In agreement with previous similar results, this neural lesion is not improved by the combination of Isoflurane + caspase 3 inhibitor.



Poster 11

Anesthetics and Analgesics Effects on Amyloid Precursor Protein (APP) Alzheimer's Mouse Model

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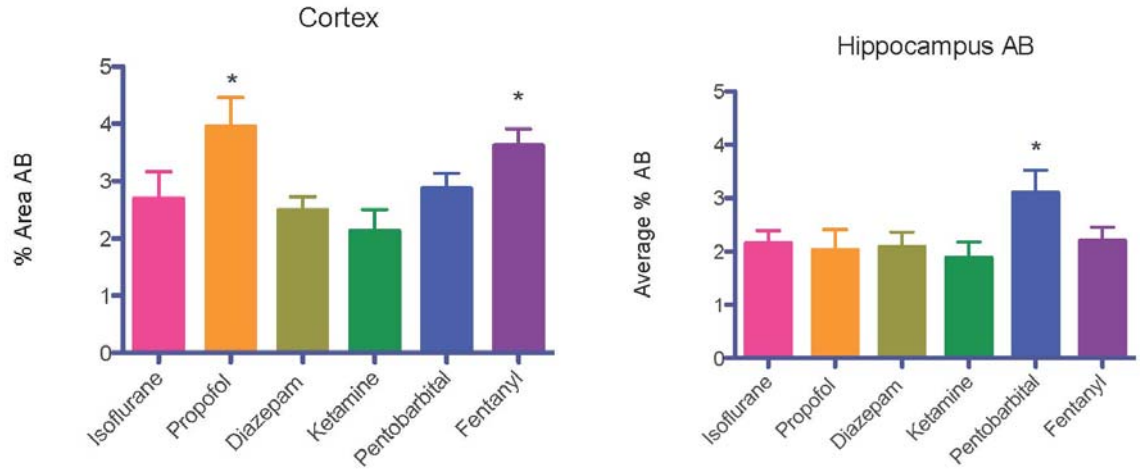
Introduction: Anesthetics and analgesics are widely used in maintenance of the critical care patients. Mostly inhaled anesthetics have been suggested as contributors to the development Alzheimer's disease. Isoflurane has previously been reported to induce apoptosis, and to increase levels and aggregation of Alzheimer's disease–associated amyloid -protein in vitro. In clinical setting however, anesthetics are not used alone but in general patients are exposed to a combination of anesthetics, analgesics and sedatives. We wanted to address the relevance in vivo of the use of those substances in the Tg2576 APP Alzheimer's mouse model.

Methods: 14-15 month-old Tg7526 mice were anesthetized-sedated for 90 minutes once a week for 4 weeks. Temperature was maintained at 37°C± 0.5°C, heart rate, respiratory rate and O2 saturation were monitored. Sedation was assessed with the loss of pedal withdrawal reflex and an adapted Ramsey scale of 5 or 6/6 (1: anxious, agitated; 2: tranquil; 3: respond to stimulus only; 4: Brisk response to pain and/or loud noise; 5: Sluggish response to pain and/or loud noise; 6: No response). All animals recovered from the exposure in room air. Mice were divided into six groups as follows; group 1: Isoflurane 1% vapor; Group 2: Propofol Via IV; Group 3: Diazepam; Group 4: Ketamine ; Group 5: Pentobarbital and Group 6: Fentanyl (all the last 4 products were administered via IP). In addition there was also a group of nontransgenic mice as controls. Navigation Behavior was evaluated through a Y maze twice: one day before starting the exposures and 6 days after the fourth exposure. Brains were harvested one day after the last Y maze: one half saved for immunohistochemistry and the other half sliced and stained for Congo Red and A-Beta.

Results: Preliminary data showed a significant improvement in the navigation behavior evaluation in the group of mice exposed to ketamine ($p<0.05$). These mice indeed recorded better scores post-exposure average 65% alternations vs 52% average initially. We did not find any other significant change in the behavioral.
A-Beta deposition was considerably greater in the groups treated with Propofol, Fentanyl and Pentobarbital. Predominance of location in the cortical area observed with Propofol and in the Hippocampal area for Pentobarbital. Fentanyl had the second highest deposition in the cortical area and also presented the highest deposition observed in the CA1 hippocampus area. Congo Red results did not offer additional significant information.

Discussion: Our results suggest that exposure to the anesthetics and analgesics did not cause a significant detriment in the navigation behavior of the transgenic mice.
Histologically Propofol, Pentobarbital and Fentanyl presented an increment of Amyloid Beta deposition.



Survival After Inpatient Cardiac Arrest: A Retrospective Review of Associated Factors

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Introduction: In 2005, the American Heart Association revised the CPR guidelines with a new focus on efficient basic life support and immediate defibrillation.1 Despite these updates, there is little evidence of improved outcomes after inpatient sudden cardiac arrest (SCA).2 This study aimed to uncover factors associated with survival after SCA on a university healthcare campus. Our hypothesis was that survival from inpatient SCA would be associated with patient age, time, date, rhythm and location (hospital ward) of the arrest.

Methods: We conducted a retrospective analysis of the cardiac arrest event database at a tertiary care medical center. Inclusion criteria required documentation of SCA in accordance with the Utstein Style definitions.3 We excluded duplicate and canceled calls, false arrests and events with incomplete documentation. Primary outcome variable was immediate survival from SCA; secondary outcome was survival to hospital discharge. Variables analyzed were age, gender, date, time, location and rhythm. Categorical data were compared with Chi-squared and continuous data with Student's t-test where appropriate; $P<=0.05$ was considered significant. We had 89% power to detect a 10% change in a categorical outcome.

Results: There were 1317 cardiac arrest calls from August 2003 to August 2008 with 494 meeting the criteria for inclusion. Overall, 251(51%) patients survived the immediate arrest event and 91(18%) survived to hospital discharge. Rhythm was the only factor associated with survival of the event and to hospital discharge ($P<0.001$ for both). PEA (38%) and asystole (24%) were more prevalent than ventricular arrhythmias (11% VT/VF) and carried 18% and 20% survival to hospital discharge respectively compared to the 30% of patients with VT/VF who survived to discharge. Pulseless arrests without a documented rhythm (24%) carried the worst prognosis with only 8% survival to hospital discharge.[figure1]

Discussion: This study shows a high rate of immediate survival from in-hospital cardiac arrest. Survival to discharge is within range of that quoted in the literature.2 Given the fact that VT/VF are known to deteriorate to PEA and asystole, the poor survival rate for PEA and asystole may be related to delayed rhythm analysis. Notably, time of day (after-hours arrest) and month of arrest ("July effect") were not associated with survival; this may demonstrate efficacy of training and supervision. Patient location was used as a marker of acute illness and response time; and surprisingly was not associated with survival. Future studies should focus on improved documentation of arrest event variables such as time to rhythm analysis and defibrillation as they may directly correlate with survival from inpatient SCA.

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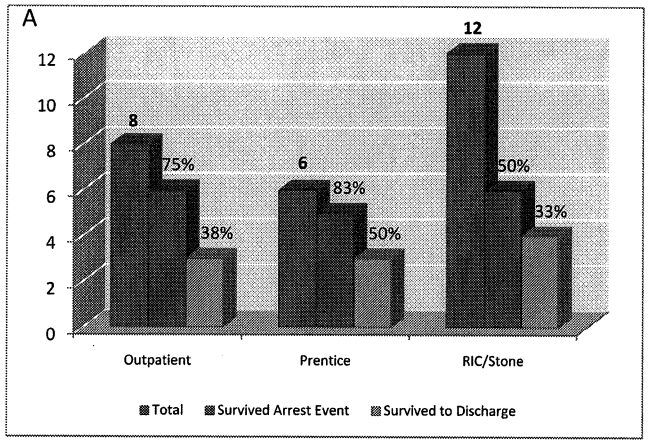

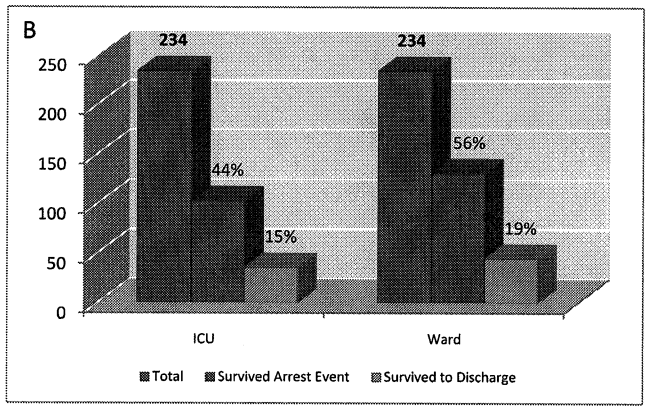

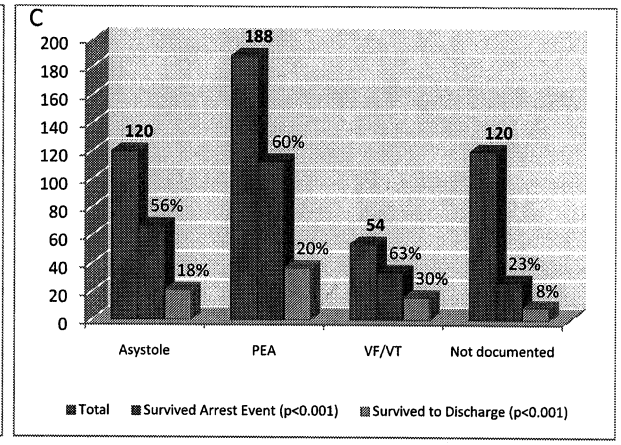

Figure 1: *A and B:* Survival percentages versus patient location (marker of acuity and response time). Prentice and RIC/Stone are separate inpatient buildings within the University campus. There was no statistically significant association between patient location and immediate survival or survival to hospital discharge . *C:* Survival versus documented rhythm during cardiac arrest. Results were statistically significant for both immediate survival and survival to hospital discharge. (**N**) is total events; n(%) is a proportion of the total.

Poster 13

Effect of Dexmedetomidine on Physiologic Parameters in Acute Lung Injury

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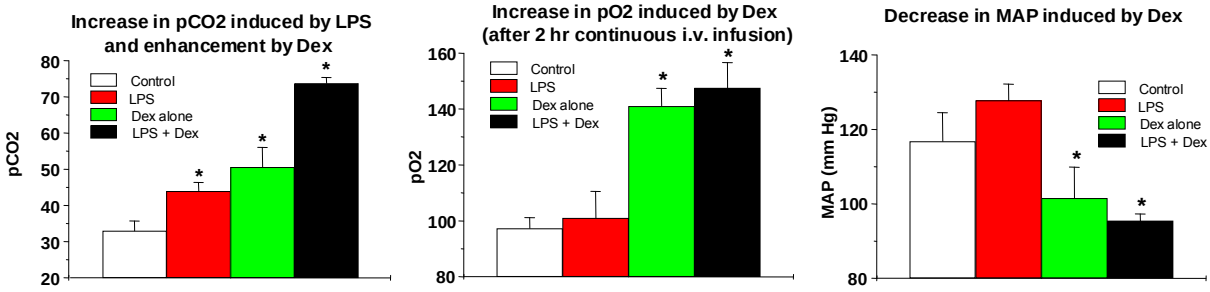
Introduction: Acute lung injury (ALI) and the more severe acute respiratory distress syndrome (ARDS) are life threatening conditions characterized by inflammation of lung parenchyma and vascular leakage leading to impaired gas exchange and hypoxemia. The triggering mechanisms for ARDS/ALI are not completely understood, and current treatments provide supportive care rather than target specific mechanisms that have a definitive effect upon outcome. As Dexmedetomidine (DEX) was demonstrated to decrease inflammation and mortality in septic mice, we, in a preliminary study, investigated the effect of DEX on albumin permeability and lung edema formation in an endotoxin mouse model of ALI. This study showed that DEX decreased albumin permeability and lung edema formation, suggesting DEX has a protective effect against Acute Lung Injury. In an effort to elucidate the mechanism by which DEX confers lung protection, we studied the effects of DEX on arterial blood gases and blood pressure in the same endotoxin mouse model of ALI.

Methods: Mice were divided into four groups: no lung injury/no treatment (control); lung injury/no treatment (LPS/saline), no lung injury/ dexmedetomidine treatment (saline/DEX), and lung injury/dexmedetomidine treatment (LPS/DEX). After exposure for 60 min to nebulized normal saline or 10 mg of LPS in saline solution to induce an inflammatory response, mice were given an i.v. bolus injection of saline or DEX (100 μg/kg) followed by a constant infusion (10 μg/kg/hr) for 2 hrs. Blood pressure and arterial blood gases were measured prior to nebulization, prior to bolus and infusion, and post-infusion (at time 0h, 2h and 4h). Mice were euthanized, and lung tissue was collected for determination of myeloperoxidase activity (a measure of neutrophil infiltration). All data collected between groups was compared using ANOVA.

Results: Treatment with DEX after induction of lung injury by LPS attenuated the inflammatory response (specifically decreasing neutrophil infiltration-MPO activity in the lung) and decreased MAP while increasing both PaCO2 and PaO2.



Discussion: DEX increased PaO2 and PaCO2 in combination with a decrease in MAP which suggests that the mechanism of lung protection could be related to hypoventilation and improved perfusion at the level of the alveoli. Because of the vasoactive nature of Dex, this improved perfusion may be related to modulation of hypoxic pulmonary vasoconstriction. DEX partially blocked neutrophil infiltration in LPS challenged lungs which may be related to improving the integrity of lung capillary endothelium and/or alveolar epithelium. DEX blocked LPS-induced acute lung injury in mice and thus may be the sedative of choice for patients with ALI or ARDS.

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Pulse Oximetry Saturation to Inspired Oxygen Ratio as a Measure of Hypoxia Under General Anesthesia

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Introduction: As a surrogate to arterial oxygen (PaO2) and the fraction of inspired oxygen (P/F) ratio, the pulse oximetry saturation (SpO2) to FiO2 ratio (S/F) has been studied in adult and pediatric medical intensive care units in patients with known lung injury (1,2). The purpose of this study was to examine the S/F ratio as a noninvasive marker in patients under general anesthesia.

Methods: This is a retrospective study including all adult general anesthetics performed with an ABG analysis at our institution from January 2005 to September 2008 excluding cardiac and thoracic procedures. Intraoperative data included arterial blood gas results (PaO2), corresponding median ventilator FiO2, and monitored SpO2 within 15 minutes of the ABG with the exclusion of SpO2 values greater than 97% and less than 70%. S/F ratios that corresponded with P/F ratios of 300 were determined.

Results: The data set included a total of 2564 ABG's. P/F ratios ranged from 49 to 600 with a mean 256.26 (SD=128.16), and S/F ratios ranged from 71 to 462 with a mean of 187.43 (SD=70.55).
There was a correlation between S/F and P/F ratios ($r=0.454$, $p<0.01$). Using linear regression analysis, the equation was developed S/F=(0.226 x P/F) + 129 with P/F ratios of 300 and 200 corresponding to S/F ratios of 197 and 174, respectively. In subgroup analysis, a linear relationship was maintained in each ASA class.
We also compared the impact of positive end-expiratory pressure (PEEP) on the correlation between the S/F and the P/F ratios. We defined moderate PEEP as 5-9 cm H2O and then high PEEP as >9 cm H2O. With this subgroup analysis, the correlation remained significant in both subgroups and stronger than in the general populations (moderate PEEP $r=0.536$, $p<0.01$; high PEEP $r=0.627$, $p<0.01$).
With subgroup analysis of patients divided by their mean P/F (P/F>300, P/F<300), the correlations remained for the <300 group ($r=0.606$, $p<0.01$) with no significant correlation in patients with a mean P/F ratio>300. By using only cases with PEEP (>=5cm H2O) in patients with a mean P/F< 300, the correlation is the strongest ($r=0.641$, $p<0.01$) and an P/F of 300 correlates with an S/F of 223 using the equations S/F = (0.466 x P/F) + 83.

Conclusion: In patients under general anesthesia, P/F and S/F ratios are linearly related. The S/F ratio could screen for when more aggressive interventions are necessary and for early diagnosis of acute lung injury. We feel this is a reliable aid to clinicians concerned about hypoxia and lung injury. As a noninvasive measure, the S/F ratio could trend patients at risk for lung injury. The calculation is simple and could help early lung protective ventilation. In conclusion, the S/F ratio correlates with the P/F ratio in our cohort of patients undergoing general anesthesia.

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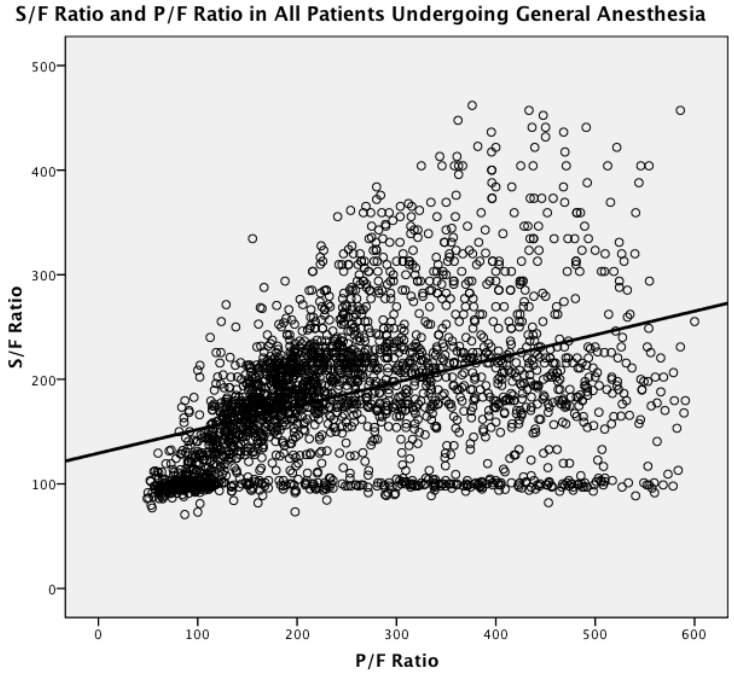

Biological Markers of Acute Inflammation After Complex Spine Surgery

Michael K. Urban, M.D., Ph.D.; Shane Reid, B.A.; Michael Ho, M.D.; Ketty M. Jules-Elysee, M.D.;
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Hospital for Special Surgery

Introduction: There is significant morbidity in adult patients who undergo complex corrective procedures for spinal deformities. We have shown that about 15% of these patients demonstrate evidence of acute lung injury and levels of broncho-alveolar lavage fluid (BAL) cytokines (IL-6, TNF-a) and inflammatory cells correlated positively with postoperative respiratory complications. In this report we assessed systemic cytokine levels with perioperative events in complex spine procedures.

Methods: 14 adult patients scheduled for elective sequential anterior then posterior corrective spinal deformity surgery were enrolled. All patients received the same general anesthetic. All patients were monitored in an ICU for at least the first 24 hours and sedated and ventilated for at least the first 12 postoperative hours.All patients were evaluated by a pulmonologist preoperatively and followed by the same pulmonologist postoperatively, who made the decision regarding the length of time for postoperative ventilation. Serum cytokine levels IL-6, IL-8, TNF-a were drawn at Baseline(Bas) after the induction of general anesthesia but prior to surgery, after the anterior fusion (Ant), after the posterior fusion (Post) and on the morning of postoperative day one (POD1). Samples were collected on ice, centrifuged and supernatant frozen at -70 until analyzed. Chest XRays were taken on each postoperative day for 5 days; fluids and hemodynamic data collected intraoperatively and until the patient was discharged from the ICU. Data stored and analyzed using SPSS.

Results: The mean IL-6 and IL-8 levels increased about 10X from baseline to POD-1, with the greatest increase after surgery; while TNF levels were initially high and except for one patient remained stable (Fig). Five patients had significantly higher levels than the remaining 10; for IL-6 1016 vs 302 pg/ml and for IL-8 55 vs 18 pg/ml. These two groups were similar for patient demographics and length of surgery. They differed in estimated blood loss 3750 vs 2325ml, lenght of postoperative ventilation 51 vs 14 hours and number of spinal levels fused.

Discussion: Several studies have demonstrated that acute lung injury associated with trauma or sepsis is the result of damage produced by inflammatory cells and cytokines. In our previous study elevated BAL cytokines were associated with postoperative lung injury. In this study systemic IL-6 and IL-8 levels were elevated in those patients with postoperative respiratory complications. These patients had the most extensive spinal surgical procedures and experienced the greaatest blood loss. Future goals would be the amelioration of the inflammatory response in order to reduce postoperative acute lung injury.

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Utility of I.V. Nitroglycerine for Dampened Arterial Wave

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University of Miami

Introduction: Dampening of the arterial wave form is a common phenomenon. There are several causes of this including, leaning on the extremity, bubbles in the arterial line, flexing of the wrist (in the radial artery) and vasospasm. There does not seem to be much data on the overall occurrence or specific etiologies. In the operating room we trouble shoot and try to remedy by repositioning the hand, aspirating and flushing the catheter to clear away any obstruction or clot as we no longer use harparinized flush. The one etiology that is rarely considered or addressed is primary vasospasm just distal to the
catheter orifice.

Methods: In 5 patients that had radial artery catheters placed and proceeded to dampen we repositioned. If that did not result in a better wave form we imaged the artery with ultrasound and recorded a arterial diameter. We gave a 3 second saline flush and re-imaged the artery. In each case the artery wave form dampened within 20 minutes. Subsequently we injected 100mcg (1cc) of nitroglycerin in the arterial line and re-imaged the artery and again measured the caliber.

Results: In each of the 5 patients that received the intra-arterial nitroglycerin there was a marked change in arterial caliber. In the ultrasound images presented we can see a pre-NTG diameter of .72 cm2 while the post-injection the caliber dilated to .84cm2. There was sustained vasodilation and no further dampening of the wave form for the remaining 2-4 hours of surgery. In addition the cuff blood pressures correlated well with the arterial

Discussion: Dampening of arterial wave form from a radial arterial line is a common phenomena. The incidence of this being caused by vasospasm is unknown but conventional flushing with saline appears to have only a modest effect. Certainly other substances (i.e. papaverine1) can dilate the artery and subcutaneous nitroglycerine have been investigated for initial canalization2. However, flushing with a very modest amount of nitroglycerin not only relieved the spasmed artery but gave a true blood pressure reading with no apparent adverse local or systemic effects.

Retrospective Study of Acute Lung Injury Following Thoracotomy for Major Spine Surgery

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Purpose: Acute lung injury (ALI) is a well defined syndrome of impaired oxygenation and diffuse pulmonary edema, which may occur after lung cancer surgery that requires one-lung ventilation (OLV).(1) The etiology is multifactorial, but volu- and barotrauma of the non-operative lung and ischemia/reperfusion injury of the operative lung may be important mechanisms.(2,3) As OLV is also sometimes used in thoracotomy for major spine surgery, we hypothesized that it might lead to ALI. Our objective was to determine the incidence of ALI and its risk factors after spine surgery with thoracotomy approach.

Methods: With approval from the institutional ethics committee, we performed a retrospective cohort study of all patients undergoing thoracotomy for thoracolumbar surgery between January 2001 and December 2008 at VGH. ALI was defined as: 1) diffuse pulmonary infiltrates on the chest radiograph; 2) impaired oxygenation with a PaO2/FiO2 ratio ≤300; and 3) absence of clinical evidence of left atrial hypertension. We have expressed normal data as mean±standard deviation and skewed data as median (interquartile range [IQR]).

Results: 33 patients underwent major thoracolumbar surgery with anterior release and thoracotomy. The majority were male (73%), with a mean age of 41±16 years and a median ASA classification of 3 (IQR 2-3). ALI occurred postoperatively in 17 patients (52%) with 3 requiring ICU admission. In comparing intraoperative risk factors in ALI patients (n=17) vs. nonALI patients (n= 16), there was no statistically significant difference between estimated blood loss volume (2.0[IQR 1.5-3.0] vs. 3.0[IQR 1.1-5.5] liters), crystalloid volume (6.0[IQR 5.5-8.0] vs. 5.0[IQR 4.1-7.5] liters), number of patients transfused (9 vs. 11) or number of patients receiving OLV (9 vs. 6). However, ALI was associated with an intraoperative maximum peak inspiratory pressure (PIPmax) ≥30 cm H2O, although this was not statistically significant (p=0.06, Fischer's exact test).

Conclusion: Patients undergoing thoracolumbar surgery with thoracotomy approach exhibited a high incidence of postoperative ALI (52%) – a rate that is 10-20 times the reported ALI incidence following lung resection surgery for cancer. Since high intraoperative ventilatory pressure has previously been shown to be a risk factor for ALI in lung cancer surgery, we predict that a high incidence of ALI in spine-thoracotomy, with or without OLV, will be of significant interest to spine surgeons and anesthesiologists.

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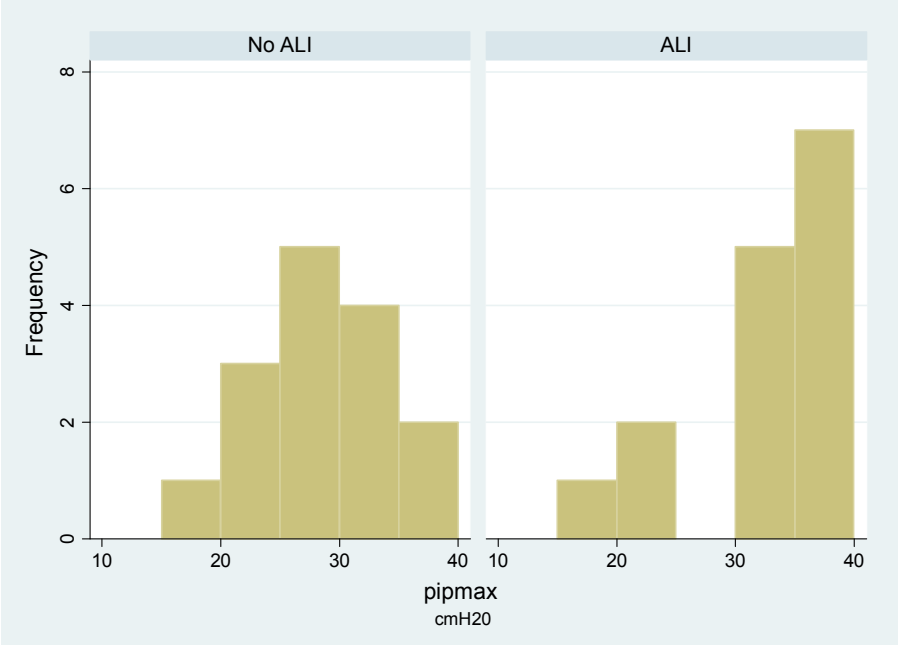

Intraoperative Anesthetic Characteristics and the Development of ARDS: A Pilot Study

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Introduction: Excessive fluid administration, high tidal volume and airway pressure, and blood transfusion have been implicated as risk factors for acute respiratory distress syndrome (ARDS). Sparse research has examined intraoperative exposure to these factors on the development of ARDS. This pilot study aims to identify intraoperative risk factors for the development of postoperative ARDS.

Methods: After IRB approval, a database was queried for patients admitted to the ICU who had undergone surgery under GETA within 24 hours of ICU admission, had acute respiratory failure requiring mechanical ventilation, and had a PaO2/FiO2 ratio ≤ 200. Patients were excluded if they had traumatic chest injuries, were post liver transplant, or diagnosed with pneumonia or acute lung injury prior to surgery. ARDS cases were then identified by the presence of non-cardiogenic respiratory failure with radiographic evidence of bilateral diffuse alveolar opacities. Patients who met initial criteria but did not have diagnostic features of ARDS served as controls. For each independent variable (fluid resuscitation, tidal volume per ideal body weight (TV/IBW), and blood products administered), the other two and the following were considered confounders: peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), Acute Physiology and Chronic Health Evaluation (Apache) II score, and postoperative sepsis or pneumonia. All confounders were aggregated into a propensity score to conserve power. Pearson chi-square tests and Wilcoxon rank-sum tests were used to compare variables.

Results: A total of 89 patients met inclusion criteria, and 25 developed ARDS. Demographic data of patients with and without ARDS, including details of their intraoperative management, are shown in Table 1. [table1] A significant association was observed between intraoperative fluid resuscitation and the development of postoperative ARDS. Among subjects with the same propensity, the odds of a subject developing ARDS when receiving 20+ mL/kg/hr was 3.8 times that of subjects receiving 0-10 mL/kg/hr (p=0.04). The odds of developing ARDS in subjects receiving 11-20 mL/kg/hr versus 0-10 mL/kg/hr was 2.4 (p=0.14). No association between TV/IBW or blood transfused and the development of ARDS was found.

Conclusion: This pilot study presents evidence to suggest a relationship between intraoperative fluid resuscitation and the development of postoperative ARDS and provides a foundation for the design of a larger prospective study.

Table 1: Demographics and Intraoperative Course of Patients

	ARDS Status		
	No N=64	Yes N=25	P-Value
Age (yrs)	44 (29,59)	55 (46,59)	0.13
Sex (Male)	70%	56%	0.20
APACHE II Score	15.5 (12,19.2)	16 (13,18)	0.33
TV/IBW (mL/kg)	9.3 (8.3,10.1)	9.0 (8.3,10.0)	0.60
PIP (cm H2O)	27.0 (23.0,32.0)	31.0 (24.0,40.0)	0.11
PEEP (cm H2O)	0.0 (0.0,0.0)	0.0 (0.0,4.0)	0.35
Blood units transfused	1.0 (0.0,5.0)	0.0 (0.0,4.0)	0.77
Resuscitation rate (mL/kg/hr)	10.5 (6.8,19.9)	16.4 (9.3,29.4)	0.08
Postoperative pneumonia or sepsis (Yes)	47%	68%	0.073

Low-pressure Microcuff Adult Endotracheal Tube Reduces the Incidence of Ventilator-Associated Pneumonia

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Background: Ventilator associated pneumonia (VAP) is a leading cause of morbidity and mortality in ICU patients with rates of up to 15% of all hospital acquired infections1,2. A new endotracheal (ET) tube Microcuff* (Kimberly-Clark) combats VAP with its design to reduce micro-aspirations in the intubated patient.

Methods: A retrospective review with historical control patient cohort was performed after a year long facility wide conversion to the Kimberly-Clark Microcuff Adult ET tube, which included all of the adult medical ICUs, operating rooms, and crash carts. Data was obtained from patients admitted to the adult ICUs from July 2006 to July 2008 who received mechanical ventilation for >24 hours with hospital-acquired pneumonia diagnoses occurring ≥ 24 hours following intubation. From July 2006 to June 2007, the Mallinckrodt Intermediate Hi-Lo ET Tube was the standard ET tube and was considered the control group in our study. In July 2007, the Microcuff tube was implemented hospital-wide. During the two year study period 4022 patients were ventilated for greater than 24 hours without an initial diagnosis of pneumonia. Ninety two adult patients developed VAP and all were included in our study analysis. Of the 4022 patients that were mechanically ventilated for >24 hours, a computer generated randomized selection at a ratio of 4:1 (mechanical ventilated patients without VAP: mechanically ventilated VAP patients) was used to randomly select the study cohort. Patient demographics, comorbidities, total number of ICU days, length of mechanical ventilation, length of hospital stay, and mortality were examined.

Results: Among the adult patients intubated for 24 hours or longer, the rate of microbiologically confirmed VAP was reduced by 61% per vent day. During the first year of the Microcuff implementation there were 28 episodes of VAP in 14830 vent days, compared to 64 episodes of VAP in 13229 vent days the year prior. When normalized, this equates to a VAP rate of 1.9 episodes per 1000 vent days versus 4.8 episodes per 1000 vent days the year prior. The Microcuff tube was associated with a significantly lower incidence of VAP (Chi-Square Test, p-value < 0.05) and number of ICU days (Mann-Whitney U Test, p-value < 0.05). No significant differences were observed in length of hospital stay, length of mechanical ventilation, or mortality.

Conclusions: After the implementation of the Kimberly-Clark Microcuff ET tube, we have observed a clinically and statistically significant reduction in the incidence of VAP.

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The Delivery of Critical Care Education within American Anesthesiology Residency Training Programs

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Background: A required component of American anesthesiology residency programs is training in the care of critically ill patients. Currently, the ACGME requires anesthesiology residents to complete a minimum of 4 months of critical care training during their residency, of which up to 2 rotations can occur during the clinical base year. The primary objective of this study was to evaluate the critical care training provided to anesthesiology residents.

Methods: An anonymous online survey was developed, and following IRB approval, invitations to complete this survey were sent to all American anesthesiology residency program directors (PD) via electronic mail. Invitation reminders were sent to all PD approximately 3 and 6 weeks after the initial invitation. All anonymous survey data were then evaluated by the researchers.

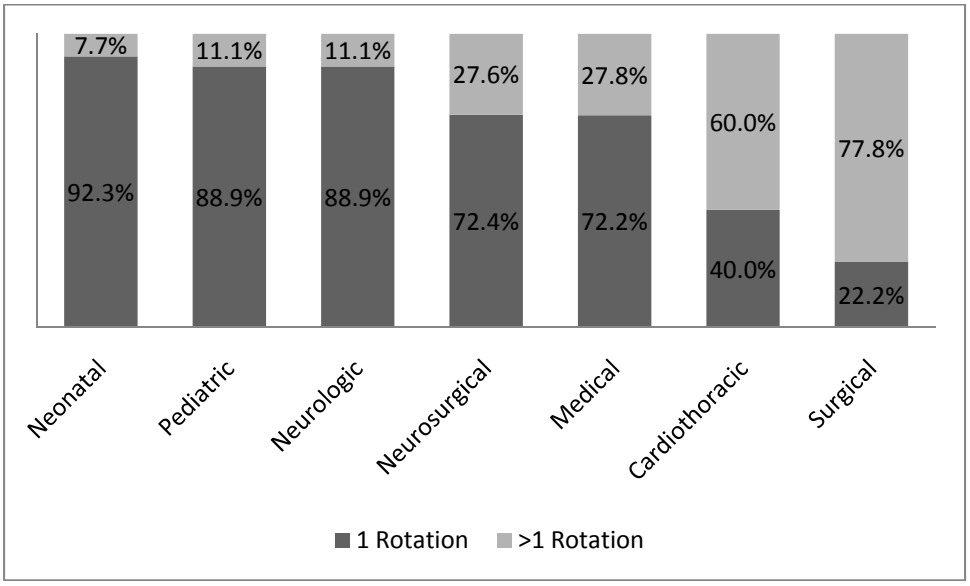
Results: Data was collected from 85 (64.9%) American anesthesiology residency programs. Of these programs, 78 (91.8%) completed the survey questions related to the specific ICU environments where critical care training was provided during their anesthesiology residency programs. This data is summarized in Table 1. Additionally, with the exception of the surgical ICU and cardiothoracic ICU, the majority of residency programs do not require more than one rotation in each institutionally-defined ICU environment during resident training (Figure 1).

Discussion: The results of this anonymous survey of American anesthesiology residency PD demonstrate that anesthesiology residents are commonly exposed to a breadth of critical care environments throughout their training. However, a much smaller emphasis seems to be placed on the depth of exposure to critical care as most rotations provide only a single month-long experience in each ICU. Additionally, exposure to the medical ICU, the neonatal ICU and the pediatric ICU typically occurs only early in residency training (PGY-1 and PGY-2) when residents may not be able to gain maximum experience from the rotation. Further investigation may be warranted to discover the best practices and potential educational benefits of graded critical care experiences as they relate to critical care training within an anesthesiology residency program.

Table 1: Rotations provided during residency training for each ICU environment for each year of residency training. Data is provided as number of residency programs with calculated percentage of total programs.

	PGY-1 (%)	PGY-2 (%)	PGY-3 (%)	PGY-4 (%)
Cardiothoracic ICU	11 (14.1%)	17 (21.8%)	27 (34.6%)	21 (26.9%)
Medicine ICU	47 (60.3%)	15 (19.2%)	12 (15.4%)	9 (11.5%)
Neonatal ICU	11 (14.1%)	2 (2.6%)	1 (1.3%)	0 (0%)
Neurologic ICU	2 (2.6%)	2 (2.6%)	6 (7.7%)	3 (3.8%)
Neurosurgical ICU	11 (14.1%)	10 (12.8%)	17 (21.8%)	15 (19.2%)
Other ICU	5 (6.4%)	4 (5.1%)	3 (3.8%)	1 (1.3%)
Pediatric ICU	11 (14.1%)	5 (6.4%)	4 (5.1%)	3 (3.8%)
Surgical ICU	39 (50.0%)	51 (65.4%)	55 (70.5%)	38 (48.7%)

Figure 1: Programs that provide single or multiple rotations during entire residency training for each ICU environment. Data is expressed as percentage of total number of programs providing each specific ICU experience.



Palliative Care in the Cancer ICU

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Introduction: In cancer ICU settings, it is not uncommon for patient care to be changed from curative to palliative. Dying patients are often depressed, especially if they are young. Intensivists and ICU residents must have an understanding of palliative care issues, which include management of depression and pain control. We are reporting a case of acute, severe depression in a patient with terminal testicular cancer.

Case report: A 21 year old male with testicular cancer with questionable pulmonary metastases was admitted to the ICU for respiratory distress. Initially he was intubated, managed on a mechanical ventilator and in a period of one week successfully extubated. A few days later, he developed dyspnea and further testing revealed pulmonary metastases. After discussion with the patient, family members and oncology team the patient's status was changed to DNR (do not resuscitate).
The patient's pain was initially controlled with moderate doses of morphine, but soon became resistant despite increasing doses. He continued to be dyspneic and severely depressed. He was then started on a supplemental ketamine/fentanyl infusion and low dose (25mg) desipramine (Tricyclic). Despite worsening respiratory conditions, his mood improved within 24 hours and he was also able to sleep through the night. In spite of continued tachypnea, he denied anxiety secondary to respiratory distress. He continued to be comfortable, and his mood improved until he died two weeks later.

Discussion: It is not uncommon to see patients suffer from depression and severe insomnia in the terminal stages of illness. Most antidepressant medications require two to four weeks to relieve symptoms of depression. Ketamine is a phencyclidine derivative that has analgesic and sedative effects without depressing respiration. It has NM.D.A blocking activity that provides pain relief while minimizing narcotic requirements. Furthermore, it is useful in preventing the hyperalgesia produced by narcotics such as morphine and fentanyl. Recently, it has been shown to work as a rapid antidepressant1 when administered in small doses. Ketamine has other beneficial effects including a decrease in TNF levels, and bronchodilation.
Desipramine is a tricyclic antidepressant with minimal anticholinergic side effects compared to other antidepressants. We have found that small doses are adequate for optimal effect and that symptoms begin to improve in two to three days.2 It also has analgesic effects (neuropathic pain).
The combination of desipramine and ketamine facilitated the rapid relief of depressive symptoms in this patient.

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Preoperative Pulmonary Hypertension is a Risk Factor for the Development of ALI After High-Risk Surgery

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Introduction: Acute elevations in pulmonary arterial pressure may play a role in the development and progression of acute lung injury (ALI).[1-3] Little is known regarding the effects of chronic pulmonary hypertension. Recent pre-clinical data suggests the potential for a protective effect resulting from vascular remodeling.[4] This effect has not been confirmed in humans. This investigation evaluates the association between pre-operative elevations in pulmonary arterial pressure and the development of postoperative ALI in patients undergoing high-risk elective surgery.

Methods: After obtaining institutional review board approval, we identified all patients with a preoperative transthoracic echocardiogram evaluating right ventricular systolic pressure (RVSP) from a pre-existing 1:2 matched case-control study in which patients who developed ALI in the postoperative period (cases) were each matched with patients who did not develop ALI (controls)[5]. Univariate analyses were performed on multiple pertinent baseline risk factors and intraoperative exposures, including RVSP. As the original database was matched by surgical procedure, age, gender, and ASA class, we performed an initial conditional logistic regression analysis (stratified by type of surgery) and included the additional matched variables as covariates. Since a number of potential risk factors were identified in univariate analyses, a second multivariable analysis was performed to assess the potential association of RVSP with ALI after adjusting for age, ASA class, duration of anesthesia and volume of red blood cells (RBC) administered.

Results: Forty-seven patients who developed postoperative ALI (cases) and 86 matched controls had a documented preoperative RVSP. Univariate analysis identified preoperative RVSP as a statistically significant predictor of postoperative ALI (OR=1.03; 95% C.I. 1.01 to 1.05; p=0.010; Table 1). Subsequent multivariable evaluation including the covariates age, ASA class, duration of anesthesia, and volume of RBCs administered also noted a statistically significant association between preoperative RVSP and postoperative ALI (OR=1.02; 95% C.I. 1.00 to 1.04; p=0.049).

Discussion: In this case-control evaluation of patients undergoing elective high-risk surgery, preoperative elevations in RVSP were associated with the development of postoperative ALI. These results contradict the limited available pre-clinical data. Additional clinical data are needed to confirm the effect of chronic pulmonary hypertension on the development of postoperative ALI and to better define the underlying mechanisms.

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3. West JB., Am J Physiol Lung Cell Mol Physiol 2003;285:L501-513
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Table 1. Univariate analysis of baseline risk factors and intraoperative predictor variables of matched ALI case controls.

	Controls (n=86)		Cases (n=47)		OR	p-value
RVSP (mm Hg)#	41.1	(17.3)	50.2	(20.4)	1.027	0.010
Diabetes Mellitus+	16.0	(18.6%)	17.0	(36.2%)	2.998	0.015
Congestive heart failure+	42.0	(48.8%)	19.0	(40.4%)	0.801	0.577
COPD+	10.0	(11.6%)	9.0	(19.1%)	2.130	0.181
Smoking Status+	38.0	(44.2%)	34.0	(75.6%)	6.004	<.001
Alcohol Use+	18.0	(20.9%)	17.0	(38.6%)	2.069	0.106
Duration of Anesthesia (min)#	318.3	(117.1)	430.9	(154.1)	1.007	<.001
Volume or RBC (ml)#	942.5	(1088.7)	1734.6	(1860.9)	1.001	0.003
Mean MAP (mm Hg)#	69.3	(6.9)	66.9	(8.4)	0.924	0.017

RVSP = right ventricular systolic pressure,

COPD = chronic obstructive pulmonary disease,

RBC = red blood cell,

MAP = mean arterial blood pressure.

= mean (standard deviation), + = No (%).

Estrogen Protects Glomerular Endothelial Cells from Ischemia: Role for GPR30?

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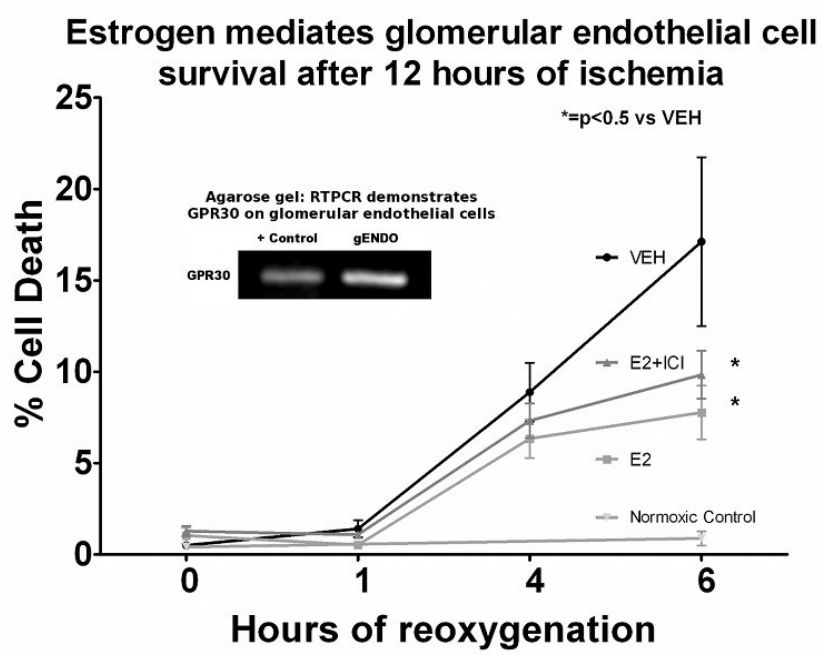
Rationale: Renal endothelium may contribute to renal injury from ischemia. Estrogen has been shown to protect the kidney from ischemia(1). Estrogen is known to have salutary effects in ischemic endothelium.
We hypothesized that estrogen protects renal endothelium from ischemia via an estrogen receptor (ER) α/β independent mechanism, possibly through the novel ER GPR30.

Methods: Immortalized glomerular endothelial cells were raised in culture to 80% confluence and exposed to 1% oxygen for 12 hours and 6 hours reoxygenation in medium containing 1 μM EST, 1 μM EST+0.5μM .ICI, or VEH. Cell death was assessed by propidium iodide staining and phase contrast microscopy. RNA was extracted from cells using a commercial kit and RT-PCR performed. PCR was then performed using 20 bp primers designed with NIH Primer-Blast for GPR30 (NM_029771.2). Renal homogenate was used for control. Data analysis employed 2 way ANOVA for multiple group comparisons, significance set at $p<0.05$.

Results: Estrogen protected endothelial cells, an effect not reversed by ICI (% death, 6hr VEH 17±8, EST 4±4, EST-ICI 5±4,,$P<0.05$ EST/EST ICI vs VEH, fig 1). GPR30 is present in glomerular endothelial cells (fig1, inset).

Conclusion: Estrogen protects glomerular endothelial cells and this effect is not reversed by antagonism of ERα/β. GPR30 is present in these cells. Estrogen's protective effect may not be mediated by classical receptors, and it is possible that it is mediated through GPR30.



Critical Care Issues in Face Transplantation

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Introduction: There has been a growing interest in allographic transplantation of nonvital structures, particularly limbs. Recently our institution embarked on an allographic face transplant. We hypothesized that such a procedure would have substantial post surgical critical care issues. We present our experience with immediate perioperative concerns in facial transplantation as they apply to the intensivist.

Methods: A 45 year old female with a history of a shotgun wound to the face with nearly thirty reconstructive surgeries presented for partial facial allograft transplantation. Past medical history included only those issues related to her injury, including Bell's palsy, anxiety disorder, depression and chronic pain with opiate dependency. Intraoperative course was 23 hours and 39 minutes with minimal blood loss and no hemodynamic perturbations.

Results: In the ICU several key issues emerged requiring careful balance amongst competing interests. These concerns included:
• Providing adequate analgesia and sedation for pain control and minimizing threats to the graft that may be inflicted by patient movement while simultaneously awakening and weaning mechanical ventilation.
o Control of erratic movement was of vital importance to preserve the delicate graft. Delirium and agitation in a patient with extensive psychological history including post traumatic stress disorder and anxiety disorder required judicious use of medication and a multidisciplinary team approach. Careful titration of opioids was needed to provide comfort yet facilitate weaning and awakening in an opiate tolerant patient.
• Ensuring adequate oxygen carrying capacity to maximize tissue/flap oxygenation while minimizing the risk of "hyperviscosity" induced ischemia.
o Hyperviscosity can have untoward effects on blood flow; however, oxygen carrying capacity must also be maintained to assure graft and tissue oxygenation. Use of the Vioptix tissue oxygen analyzer guided transfusion of only 2 units of PRBC for a hematocrit <25%.
• Providing adequate prophylaxis for opportunistic infections in an immunocompromised patient naïve to sulfa medications where hypersensitivity reactions could mimic acute rejection.
o Because our patient was historically naïve to sulfa drugs, trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis for pneumocystis carinii pneumonia (PCP) was not ideal due to the difficulty of clinically differentiating a hypersensitivity reaction to sulfa drugs from acute rejection. Aerosolized pentamidine was used with success, however, a complete history of drug reactions and possible allergy testing could have proved useful.

Conclusions: Though facial transplantation is in its infancy, there are substantial issues that are relevant to critical care. As more of these procedures are performed it is essential that intensivists become familiar and comfortable with their management.

A Case of Posterior Reversible Encephalopathy Syndrome (PRES) in the Intensive Care Patient

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Case Report: 56 year-old female with history of chronic constipation presents to the emergency department after the onset of abdominal pain, nausea, and bilious vomiting over 24 hours. Initial evaluation revealed hypotension (68/palp); acute abdomen; anuria; elevated serum potassium, creatinine, and lactate levels; and a colon distended with stool. The patient received 6 liters of crystalloid in the ER, but remained hypotensive and anuric. Following surgical consultation, the patient was taken to the operating room for a sub-total colectomy. During the case, the patient was noted to be acidotic (pH 7.1) and exhibited EKG changes (QRS widening, peaked T-waves) that improved with sodium bicarbonate and calcium chloride. At the end of the procedure, the patient developed pulseless ventricular tachycardia and was successfully resuscitated with “code” drugs, chest compressions, and five rounds of defibrillation.

The patient presented to the surgical ICU intubated, sedated, and requiring a low-dose norepinephrine infusion. The patient’s course in the ICU included management of shock, renal replacement therapy, multiple surgical revisions, and eventual extubation on post-op day #10. On post-op day #18, the patient was noted to have three episodes of generalized seizures. The following day, the patient manifested an additional protracted episode of seizure activity, during which she became hypoxemic (SpO2 ~ 80%) and bradycardic to 40 bpm, and she required intubation for respiratory insufficiency. Per the nursing notes, the patient’s non-invasive blood pressure measurements prior to this last seizure episode had ranged from 160-180/90-110.

Subsequently, the Neurology service began seizure prophylaxis with levetiracetam and recommended aggressive control of patient’s hypertension with a nicardipine infusion. A non-contrasted MRI of the head revealed numerous regions of parenchymal T2 prolongation, most prominent in the right parietal-occipital region. These radiographic findings, along with the patient’s clinical picture, were consistent with a diagnosis of Posterior Reversible Encephalopathy Syndrome (PRES). The patient was weaned from the ventilator and extubated on post-op day #20. She was noted to be disoriented, and she had a right gaze preference. Over the next four days, the patient’s blood pressure was controlled, and she was noted to have full neurological recovery with return to her baseline mental status and resolution of visual disturbances.

PRES is a fairly novel clinicoradiologic condition characterized by altered mental status, seizures, visual disturbances, and radiographic findings of posterior cerebral edema. It has been described in cases of hypertensive crisis, renal failure, eclampsia, immunosuppressive therapy, and electrolyte imbalance(1). It is thought to occur due to elevated blood pressure exceeding the autoregulatory capacity of the posterior cerebral vasculature. The hallmark of this condition is the prompt resolution of symptoms with adequate blood pressure control.

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CVP/PAD Ratio Predicts Length of ICU Stay after Cardiac Surgery

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Introduction: Recent studies suggest that right ventricular (RV) failure is a risk factor for prolonged ICU stay in patients undergoing cardiac surgery.[1] Although RV function is difficult to measure, one possible assessment tool is the ratio of central venous pressure to pulmonary capillary wedge pressure (CVP/PCWP), which has been shown to predict outcomes after right ventricular infarction.[2] We hypothesized that, a related measure, an elevated CVP/PAD ratio, would predict a prolonged ICU course in patients undergoing cardiac surgery. To test our hypothesis, we prospectively examined patients undergoing complex cardiac surgery at a tertiary care medical center and compared the CVP/PAD ratio obtained preoperatively and postoperatively with ICU length of stay.

Methods: After informed consent and institutional review board approval, patients undergoing all types of cardiac surgery were prospectively enrolled. Measurements from the PA catheter were taken after induction and before incision, 10 minutes after full reversal of heparinization, and on the morning of postoperative day one (POD1). Patients were then followed daily until their discharge from the ICU. Data analysis was performed using Microsoft excel, with statistical significance taken at $p<0.05$.

Results: We enrolled 31 patients with an average of 66 11 years. 19 were men and the average BMI was 28 5.2 kg/m^2. Fifteen underwent CABG alone, 7 underwent CABG with a valve repair or replacement, 2 underwent robotic CABG, and 9 underwent valve replacement or repair including 2 tricuspid valve repairs. CVP/PAD ratios ranged from 0.08 to 1.13 and the average ICU stay for all patients was 3.1 3.7days. All CVP/PAD ratios correlated positively with ICU length of stay with increasingly strong correlation on POD1.

CVP/PAD correlation with ICU length of stay CVP/PAD Average Correlation
Pre-op 0.46 0.18 0.32 ($p<0.05$)
Post-op 0.56 0.25 0.35 ($p<0.05$)
POD #1 0.55 0.17 0.48 ($p<0.005$)

Conclusions: We found that CVP/PAD ratio correlated strongly with length of postoperative ICU stay. Our findings suggest that RV dysfunction, as measured by CVP/PAD ratio, likely plays a significant role in recovery from complex cardiac surgery. Possible mechanisms for this relationship include improved diuresis and/or a more rapid wean of inotropic support with better RV function. Further research is required to better quantitate right ventricular function and understand its relationship to postoperative outcome.

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The Relationship Between CVP and Right Ventricular Function in Cardiac Surgery Patients

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Introduction: Central venous pressure (CVP) is commonly used to assess right ventricular (RV) function and guide fluid therapy in critically ill patients. Although recent data suggests that the relationship between CVP and volume responsiveness is poor, the relationship between CVP and RV function remains unclear.[1] We hypothesized that CVP values for patients undergoing cardiac surgery would correlate with RV function assessed echocardiographically and by cardiac output (CO). To test our hypothesis, we simultaneously measured CVP, echocardiographic estimates of RV function and CO in patients undergoing complex cardiac surgery at a tertiary care medical center.

Methods: Patients undergoing cardiac surgery were prospectively enrolled after informed consent and internal review board approval. All measurements were performed after induction of anesthesia and placement of invasive monitors. Ventilator settings were standardized as follows: TV: 8mL/kg, RR 10, 0 PEEP from initiation of ventilation until the measurements were taken. Prior to incision CVP and thermodilution cardiac output was measured by pulmonary artery catheter. A complete transesophageal echo exam was then performed by a physician certified in perioperative transesophageal echocardiography and RV function was graded using the following scale: normal (1), mildly depressed (2), moderately depressed (3) and severely depressed (4). Patients with moderate and severe tricuspid regurgitation (TR) were excluded from the study. Statistical analysis was performed using Microsoft excel with statistical significance taken at $p<0.05$

Results: 31 patients were enrolled in the study. 15 underwent CABG alone, 7 underwent CABG with a valve repair or replacement, 2 underwent robotic CABG, and 9 underwent valve replacement or repair including 2 tricuspid valve repairs. The transesophageal echo examination revealed 19 patients with normal function, 8 with mildly depressed function, 3 with moderately depressed function and 1 with severely depressed function. 3 patients were excluded due to moderate or severe TR. CVP correlated poorly with both RV function when assessed by ECHO ($r=0.18$, $p=<0.2$) and CO ($r=-0.05$, $p<0.25$).

Conclusion: We found that CVP correlated poorly with RV function as measured by transesophageal echo and cardiac output. Our findings suggest that an elevated CVP does not identify RV dysfunction. One possibility is that over time the RV may accommodate to chronically high filling pressures. Another is that other factors besides RV function may affect CVP. Further research is required to better define the meaning and relevance of CVP monitoring.

[1] Marik PE, et al. Does Central Venous Pressure Predict Fluid Responsiveness? Chest,2008, Jul;134(1):172-8

A Survey of Current Anesthesiology Resident Perceptions of a Career in Critical Care Medicine

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Introduction: Based on recent trainee information, the Committee on Manpower for Pulmonary and Critical Care Societies (COMPACCS) estimated intensivist supply would meet demand until the year 2007.After this, a shortage will begin to occur, reaching approximately 20 percent by 2020 and 35 percent by 2030. The Patient-Focused Critical Care Enhancement Act attempts to expand the critical care workforce and establish best practices to maximize the efficiency of existing critical care personnel. This prompted an investigation to assess views and opinions of anesthesiology residents regarding a career in critical care anesthesia. This most recent survey serves as a follow-up to a survey that was circulated to second- and third-year residents in 2002, since their recent experience in critical care medicine has most likely enabled them to formulate strong opinions on the subject.

Methods: We created a 15-question survey that was distributed via e-mail to all program directors of ACGME-accredited U.S. anesthesiology training programs with instructions to dispense to all anesthesiology residents in each level of training. Analysis includes answers from all respondents who took the survey in the 145 day period from September 2008 to February 2009.Three hundred and eighty four residents out of 5,218 residents completed responses, all of which were submitted anonymously.

Results: Procedure-related-nature of the practice and lifestyle were the two most important factors as to why residents chose anesthesiology as a specialty. The majority of respondents plan to pursue private practice careers as opposed to a career in academics. Of those individuals who will be engaging in subspecialty training, more than 40% plan on working in obstetrical anesthesia and critical care medicine.More than 50% of respondents require greater than three months of critical care medicine during residency. More than 40% stated that the majority of the critical care faculty was from anesthesiology, followed by surgery and then medicine. The majority of individuals ranked the importance of critical care training as either very or somewhat important in their ability to function as an anesthesiologist. More than 50% of residents recognized the importance of a dedicated intensivist as very important. Almost 25% of residents stated that the amount of hours worked was a very important factor in influencing their decision to pursue a career as a critical care anesthesiologist. More than 40% of respondents perceive a career in critical care anesthesia to be in great demand. Less than 30% still felt there is little demand for a critical care anesthesiologist in private practice and more than 30% said they were uncertain, up from 25% in the previous survey.

Conclusions: Although residents recognize the importance and demand of CCM; they still don't choose to specialize because of lifestyle and hours. These results are similar to the survey from 2002.

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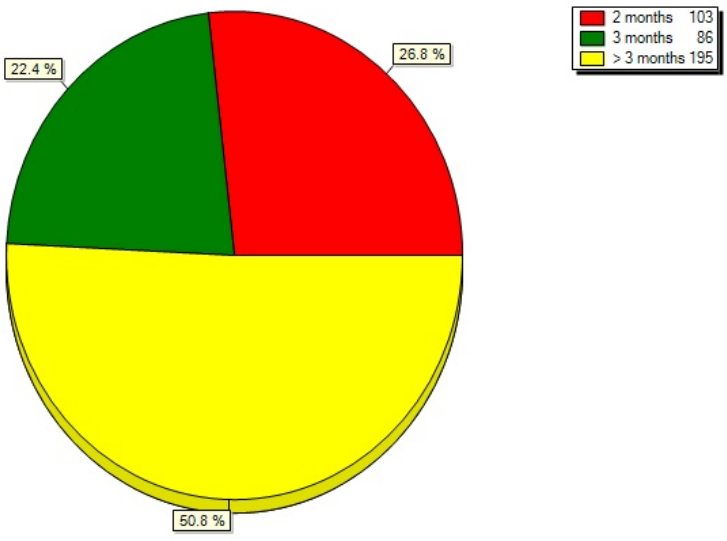
How Many Months in Critical Care are Required by Your Program?



Impact of HIV-infection on Short-Term Outcomes of Critically Ill Patients with Acute Lung Injury

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Introduction: Acute respiratory failure (ARF) is the most common reason for ICU admission among HIV-infected individuals. In the subset of ARF patients who are severely ill with Acute Lung Injury (ALI), it is unclear whether short-term outcomes of HIV-infected patients are similar to non-HIV-infected patients.

Hypothesis: In-hospital mortality, and ICU and hospital length of stay (LOS) for HIV-positive versus HIV-negative ALI patients are similar.

Methods: Data was obtained from the ongoing, IRB-approved Improving Care of Acute Lung Injury Patients (ICAP) prospective cohort study (1). Results are reported as proportions and medians, and compared using chi-square, Fisher exact, or Wilcoxon rank-sum tests, as appropriate. The independent effect of HIV status on in-hospital mortality was evaluated using multivariable logistic regression.

Results: Of 520 consecutive ALI patients enrolled in the study, 66 (13%) were HIV-positive. The median (IQR) age was lower in HIV-positive versus HIV-negative patients [43 (38, 49) vs. 54 (44, 65), p <0.001]. In the HIV-positive group, there was a lower prevalence of chronic lung disease [11 (18%) vs. 123 (27%), p = 0.07] and diabetes [6 (9%) vs. 108 (24%), p = 0.007], and higher prevalence of drug abuse [41 (62%) vs. 84 (19%), p <0.001] and liver disease [38 (58%) vs. 90 (20%), p <0.001].

In HIV-positive patients, pneumonia was the most common ALI risk factor [43 (65%) vs. 184 (41%), p = 0.001], and the median APACHE II score was higher [27 (22, 33) vs. 26 (20, 33), p = 0.06]. The maximum daily SOFA score was similar between groups [12 (8, 15) vs.11 (8, 15), p = 0.79].

There were no differences in patients' short-term outcomes. HIV-positive vs. HIV-negative ALI patients had similar mortality in ICU [27 (41%) vs. 178 (39%), p = 0.79] and hospital [29 (44%) vs. 208 (46%), p = 0.78]. There was no difference in median ICU LOS [survivors: 12 (8, 26) vs. 15 (10, 25), p = 0.53, and non-survivors: 10 (7, 14) vs. 10 (5, 18), p = 0.98] and median hospital LOS [survivors: 29 (15, 44) vs. 25 (16, 39), p = 0.74, and non-survivors: 13 (10, 20) vs. 15 (8, 26), p = 0.51]. After adjustment for potential confounders using multivariable logistic regression, HIV infection was not an independent predictor of in-hospital mortality (OR 1.39, 95% CI 0.69 – 2.78).

Conclusions: In ALI patients, HIV infection was not associated with worse short-term outcomes. HIV status may not be an important factor to consider when evaluating the potential benefit of critical care therapies on short-term outcomes for patients with ALI.

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Honorable Mention

Anti-Apoptotic Effects of Nitrite on Liver Ischemia Reperfusion Injury

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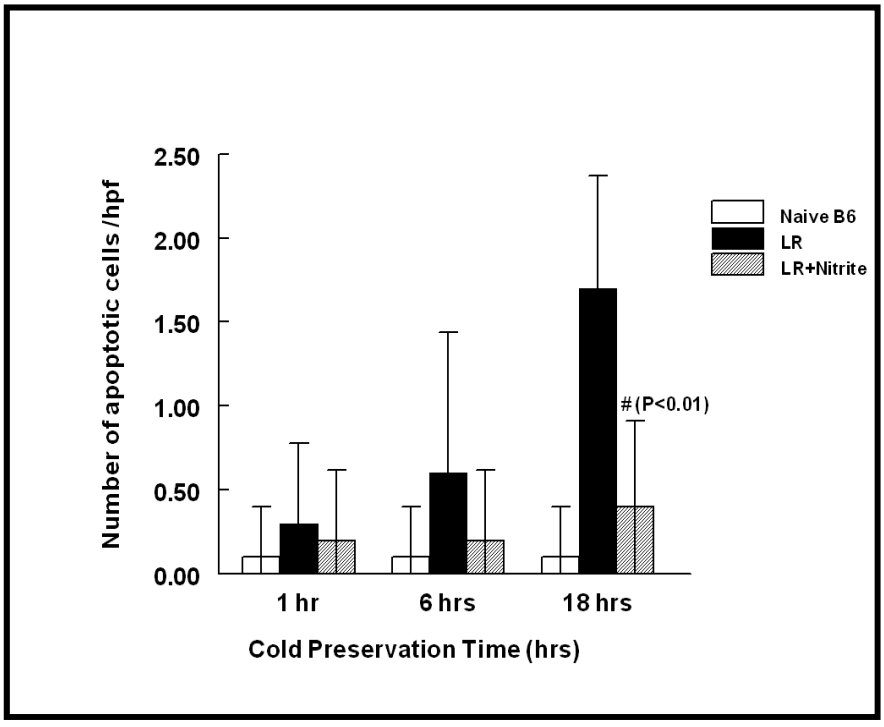
Introduction: Liver ischemia/reperfusion injury (IRI) is a major cause of primary graft non-function or initial function failure post-transplantation, and leads to frequent episodes of both acute and chronic rejection. Moreover, increased susceptibility of marginal donor livers to IRI limits the number of livers available for transplantation. Effective therapies for the prevention and treatment of liver IRI remain elusive. Nitric oxide (NO) is a highly reactive free radical produced from L-arginine and is involved in a multitude of critical cellular events. It is produced by macrophages and dendritic cells (DCs) and plays a role in immune regulation and host innate and adaptive immunity. NO has been found to attenuate liver IRI through various mechanisms, including preventing hepatocellular apoptosis and reducing macrophage infiltration. In this study, we examined the therapeutic effect of the NO product, nitrite, as a means of protecting the liver, with a particular focus on hepatocellular apoptosis following liver transplantation.

Methods: B6 mice livers were preserved for an extended period of time in either Lactate Ringer's (LR) solution or University of Wisconsin (UW) solution with or without the addition of nitrite at 25 uM. The syngeneic recipients of liver grafts were also treated with or without nitrite by intraperitoneal injection. Liver function and hepatocellular apoptosis were evaluated by ALT, AST, and LDH assays, tissue H&E and TUNEL staining before or post-transplantation.

Results: Liver ALT, AST, and LDH release were significantly reduced in both nitrite supplemented LR and UW preservation solution compared to the LR and UW only controls. The protective effect of nitrite was correlated with cold preservation time, the longer the more significant. In parallel with the reduction of enzyme release in the nitrite treated preservants, the histological examination revealed better preserved hepatic morphology and architecture. Hepatocellular apoptosis was markedly reduced in the nitrite treated liver compared to the LR and UW only control groups. Moreover, liver grafts with extended cold preservation times of 12 to 24 hours showed improved liver tissue histology and graft function at 2 hours post-reperfusion in either the nitrite supplemented preservation or nitrite treated recipients or combined treatments compared to the UW only control.

Conclusion: Nitrite treatment affords protection to the liver donor and improves acute graft function post-transplantation.



Intra-Operative Use of Lung Protective Strategies by Anesthesia Providers

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Background: The critically ill patient with Acute Respiratory Distress Syndrome or Acute Lung Injury (ARDS/ALI) is frequently seen in the in the operating room. While there are a variety of methods to address hypoxia, previous studies have identified lung protective ventilation strategies (LPVS) that have beneficial effects in both oxygenation and mortality in ARDS.1.2 We sought to examine the use of various oxygenation strategies in the OR including LPVS in patients undergoing anesthetics with a known history of ARDS.

Methods: Between January 1, 2005 and January 1, 2009 we used a general anesthetic records to assess the ventilation parameters in patients over 17 years of age and an average preoperative P/F ratio of <= 300. This dataset was then merged with a known research dataset of patients screened for ALI/ARDS. Using the standard predicted body weight (pbw) equation we calculated the milliliters pre kilogram (ml/kg pbw) with which the patient was being ventilated. Positive end expiratory pressure (PEEP), peak airway pressures (PIP), FiO2, oxygen saturation (SaO2) and tidal volume in ml/kg were compared between groups.

Results: We found 972 operative cases that met criteria for inclusion. 269 cases were found to have a diagnosis of ALI/ARDS prior to the OR case. Patients were divided into two groups based on if they did have ALI/ARDS. Comparison of patients groups found statistically insignificant differences between the ventilation strategies between the groups in PIP, but no other category. The tidal volumes in cc/kg pbw was 8.6 and PEEP was 4.4 cmH2O. PIP were found to be 29.5 cmH2O on average in the non ALI group and 27.5 in the ALI group. Mortality at 90 days was found to be considerably higher in the ALI group (29 vs 17 percent). Univariate analysis of ventilatory parameters significant for death at 90 days were examined for both groups. No intraoperative ventialtory parameter was found to be significant for death in the ARDS group, however, PIP was found to be significant in the non ALI/ARDS group.

Conclusion: Similar ventilation strategies in cc/kg pbw and PEEP were utilized between ALI/ARDS and non ALI/ARDS patients. The average tidal volume was 8.6 cc/kg pbw and the average PEEP was 4.4 cmH2O in all patients. This suggests that anesthesiologists are not using LPVS when ventilating patients with low P/F ratios. This data does not suggest a mortality difference at 90 days in known ARDS patients, however, there is some suggestion that higher PIP may be suggestive of mortality at 90 days in non-ARDS patients.

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