

## **01. Fibrinolysis Resistance Following Injury is a Risk Factor for Subsequent Intensive Care Unit Pneumonia**

Ivan Rodriguez; Ernest Moore; Hunter Moore; Peggy Knudson; Peter Moore; Trevor Nydam; Hunter Moore; Elizabeth Pomfret; Russel Tracy; Steven Wisniewski; Fredric Pieracci; James Morrissey; Angela Sauaia

**Background:** Pneumonia (PNA) is associated with high morbidity and costs in the intensive care unit (ICU) and its early identification is key for optimal outcomes, but early biomarkers are lacking. Recent studies suggest that fibrinolysis resistance (FR) after major abdominal surgery is linked to a 3-fold increased risk of infection, consistent with animal models in which plasmin (driver of fibrinolysis) modulates immune response.

**Hypothesis:** FR within 48 hours postinjury is associated with an increased risk of PNA.

**Methods:** Patients enrolled in a randomized controlled trial for hemorrhagic shock were evaluated for FR. FR was quantified by thrombelastography with exogenous tissue plasminogen activator (tPA-TEG) at 24 and 48 hours post injury and measuring LY30 (%). A receiver-operating characteristics curve (ROC) analysis was used to identify an inflection point (Youden Index) for increased risk of PNA. PNA was based on a clinical diagnosis requiring treatment >48 hours postinjury. The cutoff was then validated in a cohort of ICU patients at risk for venous thromboembolism (VTE). Multivariable logistic regression was used to control for confounders. Proteomics was used to assess for altered immune response between groups.

**Results:** In the bleeding cohort, 125 patients were enrolled in which 49 had tPA-TEGs at 24 and 48 hours (median ISS= 27, 7% PNA). A composite tPA-TEG LY30  $\leq$  4% at 24 and 48 hours was found to be the optimal cutoff for increased risk of PNA. This cohort with persistent tPA resistance had a 7-fold increased rate of PNA (4% vs 28%  $p=0.048$ , Figure 1: A). In the ICU cohort, 88 had tPA-TEG at 24 and 48 hours post ICU admission (median ISS=28, 6% PNA). The tPA-TEG LY30  $\leq$  4% was associated with a 10-fold increased rate of PNA (19 vs 1.5%  $p=0.002$ , Figure 1: B). In patients with traumatic brain injury, the same association was found (33% vs 3.2%  $p=0.006$ ). Adjusting for confounders, the tPA-TEG persisted as a significant risk factor for PNA (adjusted OR=35.7, 95%CI 1.9-682,  $p=0.018$ ). Proteomics identified increased MHC class I polypeptide A ( $P=0.006$ ) and SERPINA3 ( $P=0.018$ ) in the tPA resistant cohort, with decreased expression of mannose binding lectin protein C ( $P=0.018$ ).

**Conclusions:** FR quantified by tPA-TEG within 48 hours of ICU admission is associated with an increased risk of PNA in bleeding patients and those at risk for VTE. Prospective validation of the tPA-TEG LY30 optimal cutoff for PNA and further investigation into whether endogenous FR is a cause of an altered immune response related to MHC I and complement or an epiphenomenon for postinjury PNA are needed.

## **02. Postoperative antibiotic practices and surgical site infections in twenty low- and middle-income country hospitals**

Alex Zhuang; Maia Nofal; Natnael Gebeyehu; Nichole Starr; Sara Taye Haile; Habtamu Woldeamanuel; Assefa Tesfaye; Senait Bitew; Abebe Bekele; Thomas Weiser; Tihitena Negussie Mammo

**Background:** Worldwide, 1 in 6 inpatient antibiotic prescriptions are for surgical prophylaxis, including postoperative prophylaxis.<sup>1</sup> The World Health Organization recommends against prophylactic antibiotics for preventing surgical site infection (SSI).<sup>1</sup> In Sub-Saharan Africa,

postoperative antibiotic use is common due to perceptions that it reduces SSI rates, but data informing recommendations against postoperative antibiotics are largely derived from high-income countries.<sup>1–4</sup>

**Hypothesis:** Postoperative antibiotic use does not reduce SSI risk in patients undergoing clean and clean-contaminated operations in low- and middle-income hospitals.

**Methods:** Prospective data was collected from 2019-2022 on patients enrolled in Clean Cut, an SSI reduction quality improvement program currently being implemented in Ethiopia, Liberia, Madagascar, India, and Bolivia.<sup>5</sup> We included patients from 20 hospitals with wound class I or II operations without clinical sign of infection for 48 hours postoperatively (Figure 1). We assessed the association between postoperative antibiotic prophylaxis and SSI via logistic regression, controlling for patient and case factors, and degree of adherence to perioperative infection prevention practices.

**Results:** Of 6,945 patients included, 6,529 (94.0%) received antibiotics postoperatively, of which 6,319 (91.0%) were for prophylaxis. Ceftriaxone was most frequently prescribed (2,486, 35.8%) for an average of 1.5 days. There was no difference in the risk of SSI between patients who received postoperative prophylactic antibiotics and those who did not (RR 1.21, 95% CI 0.95-1.54,  $p=0.143$ ) (Table 1). Length of stay (LOS) was 1.4 days longer for those receiving postoperative prophylaxis.

**Conclusions:** In this large prospective observational cohort, postoperative antibiotics did not reduce SSI rates for clean and clean-contaminated cases but was associated with longer LOS in resource-limited healthcare systems. With the growing threat of antimicrobial resistance, surgical initiatives to implement antimicrobial stewardship programs are critical.

### **O3. Area Deprivation Index (ADI) Predicts Increased 90-day Mortality in Critically Ill Patients with Sepsis**

Whitney Kellett; Anahita Jalilvand; Holly Baselice; Megan Ireland; Wendy Wahl; Jon Wisler

**Background:** Measures of community distress show mixed results regarding their association with health outcomes in critically ill patients. Area Deprivation Index (ADI) has emerged as a more clinically-relevant socioeconomic metric. While the ADI has been shown to improve surgical risk adjustment, its association with mortality, particularly in septic patients, remains unclear. The primary objective of this study was to evaluate the association between ADI and mortality in patients admitted to the surgical ICU (SICU) with sepsis.

**Hypothesis:** We hypothesized that higher area deprivation would be associated with higher cumulative 90-day mortality in surgical patients with sepsis.

**Methods:** All admissions (N=1401) for sepsis (SOFA  $\geq 2$ ) between 2014-2019 were reviewed. Clinical, demographic characteristics, and ADI scores were obtained for each patient and classified into “high distress” (ADI  $\geq 85$ th percentile,  $n=400$ ) and “control distress” (ADI  $< 85$ th percentile,  $n=976$ ). The primary outcomes were in-hospital and 90-day mortality.

**Results:** The high ADI cohort was younger ( $58.5 \pm 15.4$  vs  $60.8 \pm 15.2$ ,  $p=0.01$ ) and more likely to be African American (24% vs 10%,  $p < 0.005$ ), transferred from an outside facility (52.0% vs 44.8%,  $p=0.015$ ), and have COPD (26.5% vs 19.0%,  $p=0.002$ ). While admission SOFA scores were comparable between groups, the high ADI cohort presented with higher rates of NSTIs (17.5% vs 10.9%,  $p = 0.006$ ) and were more likely to suffer renal failure (20.3% vs 15.3%,  $p = 0.02$ ). Compared to the control cohort, high ADI patients had increased in-house (27.3% vs 21.6%,  $p=0.025$ ) and 90-day mortality (35% vs 28.9%,  $p=0.03$ ). After adjusting for baseline characteristics and sepsis presentation, high ADI was associated with increased odds of 90-day mortality (OR  $1.39 \pm 0.24$ , 95th CI: 1.09-2.07).

**Conclusions:** High ADI was an independent predictor of 90-day mortality in critically ill surgical patients with sepsis. This is one of the first studies to demonstrate an association between area deprivation and mortality in septic patients. Future studies should focus on identifying mitigating interventions to improve outcomes in the high ADI population.

#### **O4. Risk of Adverse Surgical Outcomes in Patients with Recent Covid-19 Infection: An Emulated Target Trial**

William O'Brien; Kalpana Gupta; Kamal Itani

**Background:** The American Society of Anesthesiologists published recommendations in December, 2020 on the timing of surgery in recently recovered Covid-19 patients. There are several recent studies about vaccination, infection, and timing of surgery, with conflicting findings. In this study we emulated a trial within a large national Veteran population. Our goal was to assess whether Covid-19 infection before surgery is associated with risk of adverse postoperative outcomes.

**Hypothesis:** Patients with recent infection in the 30 or 60 days before surgery face increased risk compared with those without infection.

**Methods:** Study design was a target trial emulation with pseudo-randomization to control (without recent infection), vs 2 mutually exclusive exposures (1st chronological infection in preoperative days 1-30 or 31-60). Eligibility was major surgery during January 1, 2021 – September 30, 2021 reviewed by the Veterans Affairs Surgical Quality Improvement Program. Time zero for pseudo-randomization was day 60 before surgery. A propensity score model with inverse weighting balanced characteristics across exposure groups. Propensity score covariates were factors known at time zero that would be predictive of exposure, including Covid-19 vaccination status. The endpoint was any of the following within 30 days after surgery: death, cardiac events, central nervous system outcomes, respiratory outcomes, surgical infection, or thromboembolic events. Weighted logistic regression estimated the odds ratio (OR) of any outcome as a function of exposure group, perioperative factors (since they were not known at time zero), and any covariates with standardized mean difference > 0.2 after weighting.

**Results:** The overall study population was 29,072 surgeries, and characteristics across exposure groups were well-balanced and typical of VA population studies. Outcomes occurred in 1,337 (4.7%) within the no-infection group, 18 (7.6%) within the preoperative day 1-30 infection group, and 7 (3.2%) within the 31-60d infection group. The OR (95% confidence interval) for postoperative outcomes was 1.49 (0.84-2.46) for patients with infection in preoperative days 1-30 and 0.70 (0.28-1.43) for infection in preoperative days 31-60.

**Conclusions:** In this large population of Veterans undergoing surgery during the initial 9 months of vaccine availability, we found that recent Covid-19 infection was not associated with a significantly higher risk of adverse outcomes, compared with those not recently infected.

#### **O5. A Self-Sustaining Antibiotic Prophylaxis Program to Reduce Surgical Site Infections**

Jessie Codner; Elissa Falconer; Eli Mlaver; Jyotirmay Sharma; Grant Lynde

**Background:** Our multi-institutional healthcare system was observed to have a higher-than-expected surgical site infection rate. A gap analysis identified three opportunities to improve preoperative prophylactic antibiotic administration: standardized antibiotic selection, standardized antibiotic administration, and feedback regarding antibiotic administration compliance.

**Hypothesis:** Implementation of a multifaceted quality improvement initiative including a near-real-time preoperative antibiotic compliance feedback tool will improve compliance with antibiotic administration protocols and surgical site infection rate.

**Methods:** A compliance feedback tool designed to provide monthly reports to all anesthesia and surgical personnel was implemented at two facilities, in 09/2017 and 12/2018. Internal case data was tracked for antibiotic compliance, and these data were merged with ACS NSQIP data at the case level to provide process and outcome measures for surgical site infections. Implementation success was evaluated by comparing protocol compliance and risk-adjusted rates of superficial and deep SSI before and after the quality improvement implementation.

**Results:** A total of 20,385 patients were included in this study; 11,548 patients in the pre-implementation and 8,837 in the post-implementation groups. Baseline patient and operative characteristics were similar between groups, except the post-implementation group had a higher median expected SSI rate (2.2% vs 1.6%). Post-implementation, antibiotic protocol compliance increased from 86.3% to 97.6%, and superficial and deep SSIs decreased from 2.8% to 1.9% ( $p < 0.001$ ). The odds of superficial and deep SSI in patients in the implementation group was 0.69 (0.57, 0.83) times the odds of superficial and deep SSI in pre-implementation patients while adjusting for age, sex, diabetes mellitus, ASA class, wound class, smoking, and COPD. Observed-to-expected ratios of superficial and deep SSI decreased from 0.82 to 0.48 after the intervention.

**Conclusions:** Surgical antibiotic prophylaxis standardization and providing near-real-time individualized feedback resulted in sustained improvement in antibiotic compliance rates and reduced superficial and deep surgical site infections.

## **O6. ER to OR Pathway for Patients with Acute Appendicitis and Acute Cholecystitis: Outpatient Emergency General Surgery**

Husayn Ladhani; Morgan Pinkston; Barry Platnick; Eric Campion; Ernest Moore; Daniel VanDerPloeg; Renaldo Williams; Fredric Pieracci; D. Yeh, MD

**Background:** The current healthcare workforce crisis has caused unique bed capacity issues. An Emergency Department to Operating Room (EDOR) pathway was implemented at our institution to eliminate inpatient admission for patients presenting with these two low acuity emergency general surgical conditions.

**Hypothesis:** EDOR pathway can avoid inpatient admission without excessive readmissions.

**Methods:** Over a 2-month period, patients presenting to our ED with acute appendicitis (AA) or acute cholecystitis (AC) with planned operative intervention were managed via the EDOR pathway: they were taken from the ER to OR if an OR was immediately available, or to the ED Clinical Decision Unit (CDU) while awaiting OR. Prior to this, patients for whom an OR was not immediately available were admitted to the ward and returned to their inpatient bed postoperatively prior to discharge. Following an uncomplicated operative course, EDOR pathway patients were discharged from the PACU.

**Results:** A total of 56 patients were entered in the EDOR pathway: 30 (54%) with AA and 26 (46%) with AC (Table 1). Median [IQR] ED LOS was 8.6 [5.1-13.2] h. Thirty (54%) patients were transferred to CDU prior to OR; four were admitted postop and the remaining 26 were considered averted preop admissions. Of the 26 patients who bypassed the CDU (ED straight to OR), 6 were admitted postop and the remaining 20 were considered averted postop admissions. Therefore, a total of 46 (82%) out of 56 pathway patients were able to avoid admission. ED length of stay (LOS) was greater for patients with AC vs AA (12.7 h vs 5.4 h,  $p < .001$ ), and more patients with AC were transferred to CDU prior to OR (85% vs 27%,  $p < .001$ ). Postop, 46 (82%) were successfully discharged from PACU. The most common reason for admission

postop was clinical judgment (more difficult than expected operative course, or high suspicion for complication). For the 23 patients with 30-day postoperative data, 6 (26%) presented to ED within 30 days for a suspected complication, of which only 2 (9%) were readmitted.

**Conclusions:** An EDOR pathway was successful in avoiding hospital admission for >80% of acute appendicitis and acute cholecystitis patients with a 9% readmission rate.

## **O7. Disparities in Complicated and Uncomplicated Diverticulitis Management**

Maria Barahona; Andrew Tran; Allison Gasnick; Justin Dvorak; Justin Brady; Vanessa Ho; Esther Tseng

**Background:** Historically, systemic racism has contributed to disparate outcomes in surgical patients. In operatively managed diverticulitis, patients from minority racial groups are more likely to experience worse outcomes, including morbidity and mortality. The aim of our study was to examine a propensity matched cohort of complicated and uncomplicated diverticulitis to quantify whether there is a racial disparity in the provision of operative management.

**Hypothesis:** After propensity matching, patients from racial minorities would be less likely to receive surgery.

**Methods:** We utilized TriNetX, a global federated network providing access to de-identified statistics on electronic health record data from approximately 103 million patients in 70 healthcare organizations. We studied two cohorts: uncomplicated and complicated diverticulitis. The main outcome of interest was whether an operation was performed within 30 days of diagnosis. We performed a propensity score match between operative and non-operative patients, adjusting for the following confounders: age at diagnosis, ethnicity, gender, diabetes, hypertensive disease, ischemic heart disease, cerebrovascular disease, and chronic lower respiratory disease. We compared the distribution of race among these matched cohorts using chi-squared tests.

**Results:** We matched 28,846 pairs of patients with uncomplicated diverticulitis and 10,585 pairs of patients with complicated diverticulitis. Within the cohort of uncomplicated diverticulitis patients, white patients made up a larger proportion of the operatively managed group (78.5% vs 74.2%,  $p<0.001$ ), whereas patients who were Black or Asian had more representation in the nonoperative group (9.2% vs 13.7%,  $p<0.001$ ; 0.58% vs 1.2%,  $p<0.001$ , respectively). This was also true in complicated diverticulitis, where white patients made up a larger proportion of the operatively managed group (80.3% vs 76.7%,  $p<0.001$ ) and Black patients were skewed towards the nonoperative group (8.5% vs 10.9%,  $p<0.001$ ).

**Conclusions:** We demonstrated racial disparities in the surgical management of complicated and uncomplicated diverticulitis, suggesting that patients of minority race are less likely to be treated with operations. If only the most severe cases of diverticulitis in minority patients are being treated with operations, this may explain a higher rate of poor outcomes in these cohorts.

## **O8. Does Oral Health a Day Keep the Infection Away?**

Chelsea Guy-Frank; Kayli Quinton; Sophia Syed; James Klugh; Shawn Adibi; Lillian Kao

**Background:** Oral hygiene care is routine in surgical intensive care units (ICUs) and is associated with reduced ventilator-associated pneumonias. Other evidence suggests that perioperative oral care can reduce surgical site infections after abdominal surgery. However, little is known regarding whether baseline oral health status is associated with hospital-acquired infections (HAIs), which is further limited by a lack of a standardized oral health score.

**Hypothesis:** We hypothesize that poor oral health, as graded by the Oral Health Risk Assessment Value Index (OHRAVI), is associated with more HAIs in critically injured trauma patients.

**Methods:** A prospective observational study was performed of dentulous adult trauma ICU patients without severe orofacial trauma at a level 1 trauma center. Patients were seen within 72 hours of admission and scored 0-3 (best to worst) in 8 OHRAVI categories to obtain an index (average) score. The primary outcome was a composite of HAIs: ventilator-associated pneumonia, central line-associated bloodstream infection, catheter-associated urinary tract infection and surgical site infection. Univariate and multiple logistic regression analyses were performed to evaluate associations between Index score, periodontal disease, and HAIs.

**Results:** Of the 62 patients, most were male (74%), white (40%), bluntly injured (77%) with a median injury severity score of 22. Fifty percent went for an emergency operation and overall, 82% required an operation. Half were intubated when scored. Twenty patients (32%) had an HAI and over half had more than one (31 HAIs total). Univariate analysis found increasing age and lack of daily brushing/dental visits associated with increasing index score. Patients with any periodontal disease had a higher frequency of HAIs (35%) versus no disease (18%). On logistic regression analysis worsening periodontal disease had a higher odds of a HAI (OR 1.93 95% CI [0.77,4.82]), but a higher index score did not (OR 0.31 [0.06,1.74]).

**Conclusions:** The presence of periodontal disease on trauma ICU admission appears to be associated with a higher odds of HAI. Surprisingly, no association was demonstrated between index OHRAVI score and HAI. This may be due to OHRAVI being designed in the dental outpatient rather than ICU setting. Development of a validated assessment tool for oral health evaluation in the ICU may be useful in determining the effectiveness of oral care interventions in patients at high risk for HAIs.

## **O9. The hyperinflammatory state: increasing proclivity to develop necrotizing enterocolitis**

Katherine Snyder; Heather Liebe; Alena Golubkova; Tyler Leiva; Heather Liebe; Camille Schlegel; Catherine Hunter

**Background:** Necrotizing enterocolitis (NEC) is a devastating disease of premature neonates with significant morbidity and mortality. NEC is associated with prematurity, a hyperinflammatory response, and dysregulation of intestinal barrier function.

**Hypothesis:** We hypothesize that NEC patients with a greater degree of prematurity will have an increased hyperinflammatory intestinal response compared to those without NEC.

**Methods:** Enteroids were generated from intestinal tissue from varying degrees of premature neonates undergoing resection. They were treated in triplicate with 100ug/mL lipopolysaccharide (LPS), subjected to 24 hours of hypoxia inducing experimental NEC, then compared with untreated controls. Gene and protein expression of Tumor Necrosis Factor (TNF- $\alpha$ ) and interleukin 8 (IL-8) were evaluated via RT-qPCR and ELISA to measure inflammatory response. ANOVA determined statistical significance ( $p < 0.05$ ).

**Results:** Enteroids from NEC tissue that were treated with LPS + hypoxia expressed significantly higher levels of IL-8 (RTqPCR ( $p = 0.003$ ), ELISA ( $p = 0.0002$ )) when compared to untreated NEC-derived enteroids with an increase in inflammatory marker concentration in those with a greater degree of prematurity (ELISA ( $p = 0.0015$ )). A significantly higher level of IL-8 was seen in NEC-derived enteroids compared to control enteroids after treatment (RT-qPCR ( $p = 0.024$ )) with a positive trend seen on ELISA. TNF- $\alpha$  levels were significantly elevated in NEC-derived enteroids following treatment compared to untreated NEC-derived enteroids (RTqPCR ( $p = 0.006$ ) and ELISA ( $p = 0.002$ )) and compared to non-NEC-derived enteroids that underwent treatment on RTqPCR ( $p = 0.025$ ) and ELISA ( $p < 0.0001$ ).

**Conclusions:** Enteroids generated from neonates with NEC have an elevated hyperinflammatory response in response to NEC-inducing stimuli compared with controls. Enteroids generated from neonates with NEC with a greater degree or prematurity have a larger increase in inflammatory markers.

This tendency towards a hyperinflammatory state may be correlated with an infant's proclivity to develop NEC and further demonstrates the hyperinflammatory state of prematurity. Further research could lead to strategies to identify and treat at-risk infants.

## **O10. Reported Practice Patterns Vary for the Management of Suspected Incisional Surgical Site Infection**

Patrick Delaplain; Jeffrey Santos; Justin Dvorak; Tina Mele; Rondi Gelbard; Christopher Guidry; Philip Barie; Sebastian Schubl

**Background:** Surveillance of surgical site infections (SSI) has become mandatory secondary to the associated morbidity, mortality, and cost. However, wound management and use of antibiotics (abx) vary widely among surgeons. There is little guidance, or even established consensus, regarding when empiric therapy for superficial SSIs should be initiated and what that therapy entails.

**Hypothesis:** Management of incisions with signs of SSI lacks consensus and management is variable among individual surgeons.

**Methods:** The Surgical Infection Society was surveyed regarding management of incisional SSI. Cases were provided with varying wound appearance, initial wound class, postoperative day (POD), and presence of a prosthesis. Responses were multiple choice format. Reported p-values are Chi-squared tests.

**Results:** 78 SIS members responded. Respondents believed that both mild erythema (55%) and clear drainage (64%) could be observed, whereas substantial erythema or purulence should be treated with complete (22% and 50%) or partial (55% and 40%) opening of the incision. Degree of erythema did not influence administration of abx, but purulence was more likely to be treated with abx than clear drainage (38% vs. 6%,  $p < 0.001$ ). There were no differences based on wound class, except that clean cases were more likely to be treated with gram + coverage alone (wound class 1 [26%] vs. 2 [10%] vs. 3 [13%] vs. 4 [4%],  $p < 0.001$ ). POD 3 was an inflection point for more aggressive treatment, with fewer reporting observation alone (Table). Respondents were more likely to obtain imaging, start broad-spectrum abx, and return to the OR for purulent drainage in the presence of mesh. Table. Responses for POD Scenarios\* Count (%) p-value

	POD 0	POD 3	POD 5
Observation	67(86)	42(54)	35(45)
Abx (gram + only)	2(3)	8(10)	7(9)
Abx (gram - only)	1(1)	0(0)	0(0)
Broad-spectrum abx	5(6)	18(23)	21(27)
Imaging	1(1)	0(0)	6(8)
Partially open incision, wet-to-dry	1(1)	16(21)	25(32)
Completely open incision, wet-to-dry	2(3)	2(3)	2(3)
Completely open incision, topical antiseptic	0(0)	1(1)	1(1)
Completely open incision, negative pressure wound therapy	3(4)	1(1)	2(3)

\*Open adhesiolysis with enterotomy, minimal (<10 mL) spillage, primary repair, mild erythema.

**Conclusions:** Presented with scenarios with escalating concern for SSI, respondents reported lower rates of observation, increased use of abx, and increased surgical drainage. However, many scenarios lack consensus regarding appropriate therapy (e.g., imaging, extent of incision opening, abx.)

## **O11. Provider Perceptions of Antibiotic Initiation Strategies for Hospital Acquired Pneumonia**

Christopher Guidry; Aubrey Swilling; Jacob O'Dell; Robel Beyene; Christopher Watson; Robert Sawyer

**Background:** The practice of rapidly initiating antibiotics for patients with suspected infection has recently been criticized yet remains commonplace. Provider comfort level has been an understudied aspect of this practice.

**Hypothesis:** We hypothesized that there would be no significant differences in provider comfort level between the two treatment groups.

**Methods:** We prospectively surveyed critical care intensivists who provided care for patients enrolled in the Trial of Antibiotic Restraint in Presumed Pneumonia (TARPP), which was a multicenter cluster-randomized crossover trial that evaluated an immediate antibiotic initiation protocol compared with a protocol of specimen-initiated antibiotic initiation in ventilated patients with suspected new-onset pneumonia. In the specimen-initiated arm, for patients without shock, antibiotics were withheld until there was objective evidence of infection, usually a positive Gram stain. At the end of each enrollment arm, physicians at each center were surveyed regarding their overall comfort level with the recently completed treatment arm, and perception of adherence. Providers completing the specimen-initiated arm were further queried regarding clinical changes that would urge them to initiate antibiotics without waiting for objective evidence.

**Results:** We collected 51 survey responses from 31 unique participants. Most respondents had been in practice for 10 years or less (0-5 years: 38.7%, 6-10 years: 25.8%). Providers perceived a higher rate of adherence to the immediate initiation arm than the specimen-initiated arm (Always Adherent: 37.5% vs. 11.1%;  $p=0.045$ ). Providers were less comfortable waiting for objective evidence of infection in the specimen-initiated arm than with starting antibiotics immediately (Very Comfortable: 83.3% vs. 40.7%;  $p=0.004$ ). Providers listed a worsening PaO<sub>2</sub>/FiO<sub>2</sub> ratio (63%), Bronchoscopy findings (40.7%) and a rising WBC (29.3%) as the most common reasons why antibiotics might be started before return of microbiological evidence of pneumonia. 100% of respondents stated they would participate in a similar study in the future.

**Conclusions:** There are significant differences in provider comfort levels and perceptions of adherence when considering two different antibiotic initiation strategies for suspected pneumonia in ventilated patients. These findings should be considered when planning future studies.

## **O12. Impact of a Multiplex PCR Assay for Rapid Diagnosis of Pneumonia on Antibiotic Use in Trauma ICU Patients**

Danielle Detelich; Jim Beardsley; Joshua Chait; Alexandra Monetti; Andrew Nunn

**Background:** Ventilator-associated pneumonia is a frequent complication in injured patients. The BioFire FilmArray Pneumonia Panel (PNA Panel) is a multiplex PCR that facilitates timely identification of certain respiratory pathogens prior to culture results. The PNA Panel was implemented in November 2021. All ICU respiratory cultures had a PNA Panel sent immediately at the time culture specimen was obtained.

**Hypothesis:** Use of PNA Panel decreases time to antibiotic de-escalation for suspected VAP in injured patients.

**Methods:** Adult Trauma ICU patients with quantitative respiratory cultures were included sequentially either before (PRE) or after (POST) implementation of the PNA Panel. Only the first respiratory culture from a patient was included, and patients were excluded if there was any documented infection other than a respiratory source.

**Results:** 60 total patients were analyzed, 30 PRE and 30 POST. The median time to first antibiotic change was significantly shorter in the POST group (61 vs 22.6 hours,  $p<0.001$ ). In the POST cohort, 25/30 of empiric antibiotic regimens were eligible for change (de-escalation or escalation) based on PNA Panel. Of these, 88% were actually changed with a median time of 15.4 hours from sample collection. Median total days of antibiotic therapy (DOT) were not different overall (9 vs 10,  $p=0.207$ ),



but median vancomycin DOT were decreased in the POST group (3 vs 2,  $p < 0.001$ ). Diagnosis of pneumonia was confirmed in 13/30 PRE and 15/30 POST. In patients with pneumonia confirmed on culture, median total antibiotic, vancomycin, and cefepime DOT were significantly less in the POST group (12 vs 10 days  $p = 0.008$ ; 3 vs 2 days  $p = 0.003$ , 4 vs 3 days 0.029, respectively).

**Conclusions:** Utilization of BioFire PNA Panel in addition to bacterial culture significantly reduced time to achieve targeted antibiotic therapy in suspected pneumonia and reduced the number of days of vancomycin therapy. In patients who have pneumonia based on culture, PNA panel use was associated with reduced total antibiotic DOT.

### **O13. Neonatal SOFA Scores Predict Mortality in Infants with Necrotizing Enterocolitis and Spontaneous Intestinal Perforation**

Irving Zamora; Marshall Wallace; Jamie R. Robinson; Mhd Wael Alrifai; Joern-Hendrik Weitkamp; Stephanie Moore; Jon Schoenecker; Shilin Zhao; Ashley E. Markowski; Jeffrey Upperman; Martin Blakely

**Background:** Necrotizing enterocolitis (NEC) and spontaneous intestinal perforation (SIP) are common conditions affecting premature infants, which typically lead to sepsis, very unpredictable clinical courses, and high rates of infectious morbidity and mortality. In adults the Sequential Organ Failure Assessment (SOFA) predicts mortality. Similarly, neonatal SOFA (nSOFA) scores have been shown to predict mortality in infants with sepsis. Investigators have not evaluated whether nSOFA scores predict mortality in infants with NEC and SIP.

**Hypothesis:** We hypothesized that repeated nSOFA scores, automatically embedded within the electronic medical record, would predict mortality in neonates with medical or surgical NEC and SIP.

**Methods:** A retrospective, single-center study of preterm neonates admitted between 2019 and 2022. The nSOFA scores were analyzed for patients with NEC and SIP for the 72 hours surrounding surgical consultation and surgical intervention.

**Results:** In the 80 infants who met inclusion criteria, 60 (75%) had NEC, and 20 (25%) had SIP. Of the NEC patients, 53 (88%) had medical NEC and 7 (12%) had surgical NEC. Overall mortality was 20% ( $n = 16$ ). Mortality rates were: 85% (6/7) in surgical NEC, 17% (9/53) with medical NEC, and 5% (1/20) with SIP. Surgical intervention was performed in 36 (45%) patients; 21 had peritoneal drain placement and 15 had laparotomy. Receiver operating characteristics area under the curve for mortality (Figure 1) was 0.87 (95% CI: 0.76–0.97) for NEC and 0.89 for SIP patients around the time of surgical consultation, demonstrating a strong association of nSOFA score and mortality. Independent of diagnosis, nSOFA scores prior to intervention were also different between survivors and non-survivors (Figure 2).

**Conclusions:** Neonatal SOFA scores, continuously available within the electronic medical record, predicted mortality in premature infants with NEC and SIP. These scores can likely help providers counsel families of these infants and inform treatment decisions.

### **O14. Open versus Laparoscopic Appendectomy: A post hoc analysis of the EAST Appendicitis MUSTANG Study**

Lauren Thompson; Brianna Cohen; Gerd Daniel Pust; D. Yeh, MD; Walter Ramsey; Patricia Byers; Nicholas Namias; Jonathan Meizoso

**Background:** We sought to understand which factors are predictive of open appendectomy as final operative approach.

**Hypothesis:** We hypothesize that higher American Association for the Surgery of Trauma (AAST)

Emergency General Surgery (EGS) grade is associated with open appendectomy.

**Methods:** Post hoc analysis of the EAST MUSTANG prospective appendicitis database. All adults undergoing appendectomy were stratified by final operative approach: laparoscopic or open appendectomy (including conversion from laparoscopic). Univariate analysis was performed to compare group characteristics and outcomes, and multivariate logistic regression was performed to identify demographic, clinical, or radiologic predictors of open appendectomy.

**Results:** 3024 cases were analyzed. 174 (5.8%) patients underwent open appendectomy, including 116 converted from laparoscopic to open. Mean age was  $41 \pm 16$  y and 53% were male. Compared to the laparoscopic group, open surgery was associated with more comorbidities; higher proportion of symptoms greater than 96 hours; higher AAST EGS grade; and higher incidence of perforated and gangrenous appendicitis with purulent contamination, abscess/phlegmon, and purulent abdominal/pelvic fluid on intraoperative findings (Table 1). On multivariate analysis controlling for comorbidities, clinical and imaging AAST grade, duration of symptoms, and intraoperative findings, only AAST Clinical Grade 5 appendicitis predicted open appendectomy (OR 6.12, 95% CI 1.32-28.34,  $p=0.02$ ).

**Conclusions:** In the setting of appendicitis, only generalized peritonitis (AAST Clinical Grade 5) on presentation was associated with increased odds of open appendectomy.

### **O15. Characterizing the crosstalk between programmed cell death pathways in cytokine storm with an agent-based model**

Solomon Feuerwerker; Gary An

**Background:** Programmed cell death pathways (PCDPs), such as apoptosis, pyroptosis, and necroptosis, are critical components of host defense against infection. Though initially studied individually, there is an increasing recognition of extensive crosstalk between PCDPs, resulting in a highly redundant system responsive to a breadth of potential pathogens. However, since pyroptosis and necroptosis propagate inflammation, these redundancies also present challenges for therapeutic control of dysregulated hyperinflammation seen in cytokine storm generated organ dysfunction.

**Hypothesis:** We hypothesize that the conversion of static diagrams that embody existing knowledge regarding apoptosis, pyroptosis, and necroptosis into simulation models can enhance our understanding of the dynamics of the crosstalk between PCDPs.

**Methods:** Literature regarding apoptosis, pyroptosis, and necroptosis was reviewed and transposed into an agent-based model, the Programmed Cell Death Agent Based Model (PCDABM). Computational experiments were performed to simulate the activation of various PCDPs as seen by differing microbes, specifically: *Salmonella enterica*, Enteropathic *Escherichia coli* (EPEC), and Influenza A virus (IAV). The potential protective value of PCDP crosstalk was evaluated by silencing either pyroptosis, necroptosis, or both. Computational experiments were also performed simulating the effect of potential therapies blocking Tumor Necrosis Factor (TNF) and Interleukin-1 (IL-1).

**Results:** The PCDABM was implemented in the agent-based modeling toolkit NetLogo. Computational experiments of infection with *S enterica*, EPEC and IAV reproduced cross-activation of PCDPs with effective microbial clearance. Silencing inflammation-propagating PCDPs (pyroptosis and necroptosis) reduced the ability to effectively clear infection. Simulations of anti-TNF and anti-IL-1 did not significantly reduce the aggregated amount of inflammation-generated system damage, the surrogate for cytokine storm-generated tissue damage.

**Conclusions:** Significant redundancies have evolved in host PCDPs in order to maintain protection

against a wide range of pathogens. However, these redundancies also challenge attempts at dampening the pathogenic hyperinflammatory state of cytokine storm using therapeutic immunomodulation. Integrative simulation models such as the PCDABM can aid in identifying potentially targetable inflection points that can mitigate cytokine storm while maintaining effective host defense.

## **O16. Choice of Machine Learning Models is critical to detecting subconscious racial bias in surgical infections.**

Addison Heffernan; Reetam Ganguli; Isaac Sears; Robert Parker; Daithi Heffernan

**Background:** Surgical quality datasets are critical to decision making tools including surgical infection (SI). Machine learning models ((MLMs), a branch of artificial intelligence, have gained traction in surgical algorithms. Given their non-human mathematical basis, MLMs could detect unseen subconscious biases within surgical datasets.

### **Hypothesis:**

**Methods:** 5 years of NSQIP data was imported into Python, pre-processed and split into 80 % training and 20% testing to generate MLMs. We tested hierarchy of validity of four MLMs (XGBoost(XGB), K-Next Nearest Neighbor(KNN), Random Forest(RanFor) and Logistic Regression(LR)) to predict post-op SI. ROC Area Under Curves(AUC) were generated. To assess built-in racial bias by merely “knowing a patient’s race”, MLMs were tested with vs without vs random allocation of “race”. Finally, to test adaptability of MLMs to low data processing, low resource environments, we adapted and tested MLMs to a database from a rural academic, hospital in Kenya.

**Results:** Overall, 3,416,094 NSQIP patients, ave. age 57.4 yrs, 57% were male, and 11% non-elective. SI rate was 3.3% in elective in 8.6% for emergency cases. First, a hierarchy of MLMs predictive demonstrated that XGB and RanFor had superior predictability (AUC 0.90) compared with KNN (AUC=0.67), LR worst performance ( $p<0.01$  XGB vs KNN and vs LR), Further XGB, RandFor and KNN performed best when applied to emergency compared to elective cases ( $p<0.05$  for paired groups). Non-White patients had an increased risk for infection (OR=1.19; $p<0.05$ ). Concerningly, merely “telling” XGB or RanFor MLMs the race of the patient significantly affected whether a non-White patient would be predicted to develop a post-operative SI [XGB (0.96 vs 0.90;  $p<0.05$ ) and RanFor (0.97 vs 0.91;  $p<0.05$ )]. Manipulating “race” within the dataset did not affect either KNN (0.67 vs 0.65) or LR (0.52 vs 0.51). Next, we translated Python-based MLMs to a prospectively gathered dataset of critically ill patients from Kenya (442 patients, ave age 36 years, 64% male, 26% infection rate). KNN remained the lowest performing model (76.1% predictability). This time RanFor proved superior to all other models with 83% predictability.

**Conclusions:** We identified a hierarchy of MLMs- XGBoost proving superior in emergency cases. This is critical since MLMs and AI are increasingly used in surgical decision algorithms. MLMs can detect, and potentially correct, subconscious inherent bias built into human generated datasets. MLMs can also be tools used in low resource countries.

## **O17. Influence of Insurance Status on Disease Severity and Risk Measures in Acute Care Surgery**

Isaac Sears; Chibueze Nwaiwu; Andrew Stephen; Daithi Heffernan

**Background:** Quantitative measures such as the Charlson Comorbidity Index (CCI) and All Patient Refined Data Reference Groups (APR-DRGs) are commonly used to stratify patients according to the severity of their disease for the purpose of determining risk of serious complications based on

documented comorbidities. However, it is more likely that increasing numbers of comorbidities may imply better access to healthcare to be able to have diagnoses made rather than merely degrees of illness. We hypothesized that among patients requiring acute care surgery, insurance status, as a proxy for healthcare access, would be associated with CCI score and APR-DRGs independent of the actual risk of complications

### **Hypothesis:**

**Methods:** Patients 18–65 years with acute appendicitis, cholecystitis, or perforated diverticulitis from 2010-2019 were identified in the National Inpatient Sample. We identified two subgroups based on insurance status: a “private insurance” (insured) group and a “self-pay” (uninsured) group. We compared the CCI score, APR-DRG severity, and APR-DRG risk of mortality between groups after adjusting for confounders. We computed adjusted odds ratios (ORs) for the following complications: in-hospital surgical site infection, in-hospital mortality, prolonged length of stay (hospital stay >90th percentile for each condition), and need for re-operation.

**Results:** Overall, 232,410 admissions were included; 189,037 were insured, and 43,373 were uninsured. Compared to the uninsured group, the insured group had higher demographic-adjusted average CCI score (0.31 vs. 0.19,  $p < 0.001$ ) and APR-DRG severity (1.52 vs. 1.47,  $p < 0.001$ ). APR-DRG risk of mortality was higher in the insured group though not significantly different (1.11 vs. 1.09,  $p = 0.57$ ). Conversely, the insured group had lower adjusted odds of in-hospital surgical site infections (OR 0.80, 95% CI 0.68-0.95,  $p = 0.012$ ), in-hospital mortality (OR 0.56, 95% CI 0.36-0.88,  $p = 0.012$ ) and prolonged length of stay (OR 0.79, 95% CI 0.76-0.82,  $p < 0.001$ ). The adjusted OR for reoperation was not significant (OR 1.00, 95% CI 0.97-1.02,  $p = 0.72$ ).

**Conclusions:** Although the CCI scores and APR-DRGs implied that the insured group was sicker, the uninsured group suffered more complications. This phenomenon likely reflects better healthcare access with comorbidity identification and documentation among insured patients. Uninsured patients may harbor hidden, undocumented comorbidities that impact care of patients with surgical emergencies.

## **O18. A Novel Scavenging Peptide, MOP3, Attenuates Inflammation in Sepsis**

Colleen Nofi; Monowar Aziz; Gaifeng Ma; Ping Wang

**Background:** Sepsis is characterized by a dysregulated host immune response to infection. Milk fat globule-EGF factor VIII (MFG-E8) is an opsonin that promotes the clearance of apoptotic cells by macrophages to control hyperinflammation in sepsis. By contrast, extracellular cold-inducible RNA-binding protein (eCIRP), a novel alarmin, is elevated in serum and exaggerates inflammation in sepsis. Given the scavenging function of MFG-E8 and the lack of effective therapeutics in sepsis, this study aimed to determine the therapeutic potential of a novel, MFG-E8-derived oligopeptide 3 (MOP3) designed to bind and link eCIRP to the integrin receptor for clearance.

**Hypothesis:** We hypothesize that through clearance of eCIRP, MOP3 protects against inflammation in sepsis.

**Methods:** MOP3 was designed by screening for effective 15-amino acid (AA) long sequences from MFG-E8's interaction site with eCIRP. These AAs were tagged with three additional AAs, “RGD”, known to interact with the integrin receptor and promote phagocytosis. Binding of MOP3 to recombinant murine (rm) CIRP and to the  $\alpha\beta_3$ -integrin receptor was quantified by Biacore analysis. Sepsis was induced in wild type mice through cecal ligation and puncture (CLP). Mice were treated with either MOP3 (10  $\mu\text{g/g}$  BW) or vehicle through retro-orbital injection. After 20 hours, serum was

collected and analyzed for inflammatory parameters by ELISA and calorimetric assays.

**Results:** MOP3 demonstrated strong binding to rmCIRP and to the  $\alpha\beta3$ -integrin receptor, with a  $KD$   $1.3 \times 10^{-8}$  M and a  $KD$  of  $7.76 \times 10^{-7}$  M, respectively. MOP3 treatment protected septic mice from systemic inflammation by significantly reducing serum IL-6 by 72% and TNF- $\alpha$  by 58%. MOP3 treatment also significantly reduced markers of tissue injury, including LDH by 54%, AST by 30%, and ALT by 22%. (Table) Sham CLP+Vehicle CLP+MOP3 Serum IL-6 (pg/mL)  $10.8 \pm 6.7$   $2435 \pm 596.6^*$   $688.3 \pm 327\#$  Serum TNF- $\alpha$  (pg/mL)  $2.3 \pm 0.8$   $42.6 \pm 12.8^*$   $17.7 \pm 4.7\#$  Serum LDH (IU/L)  $38.2 \pm 5.7$   $322.7 \pm 49.8^*$   $147.9 \pm 30.9\#$  Serum AST (IU/L)  $35.9 \pm 4.7$   $97.5 \pm 8.3^*$   $68.2 \pm 3.7^*\#$  Serum ALT (IU/L)  $28.8 \pm 3.3$   $54.7 \pm 2.2^*$   $42.6 \pm 2.5^*\#$  \* $p < 0.05$  vs. Sham, # $p < 0.05$  vs. CLP+Vehicle by one-way ANOVA and SNK method, N=8-12 mice per group.

**Conclusions:** By clearing eCIRP from circulation, MOP3 protects against systemic inflammation and tissue injury in sepsis. Given the advantages of synthetic peptides as therapeutics, MOP3 provides an exciting new treatment to attenuate inflammation and improve outcomes in sepsis.

### O19. Hot Patient? Stay Cool.

Mikayla Moody; Robert Sawyer; Saad Shebrain

**Background:** Prolonged fever or leukocytosis in patients treated for infection concerns clinicians because of a possible missed source of infection, a secondary infection, or inadequate antimicrobial therapy.

**Hypothesis:** We hypothesized that these patients suffer worse outcomes, including higher mortality and longer antimicrobial treatment.

**Methods:** From 2017 to 2022, data were prospectively collected on patients treated for infection in the SICUs of two university-affiliated hospitals. Demographics, microbiological data, severity of illness (APACHE-II score), and outcomes were recorded. Patients with white blood cell count (WBC)  $\geq 15.0 \times 10^9/L$  or a maximum temperature (TMAX)  $\geq 38.5^\circ C$  were divided into quartiles based on days until reduction of WBC to  $\leq 15.0 \times 10^9/L$  and days until normalization of temperature to  $\leq 38^\circ C$  for a full calendar day. Univariate analysis followed by logistic regression (LR) analyses were performed to predict factors associated with prolonged fever or leukocytosis, subsequent/secondary infections, and in-hospital mortality. Model performance was assessed using the Hosmer and Lemeshow test and ROC curve analysis.

**Results:** 697 patients were identified: 343 with WBC  $\geq 15.0 \times 10^9/L$  and 238 with TMAX  $\geq 38.5^\circ C$ . Mean time to normalizing WBC was  $5.5 \pm 0.4$  days with the highest quartile  $\geq 7$  days (prolonged leukocytosis-PL). The mean time to resolution of fever was  $4.1 \pm 0.3$  days with the highest quartile  $\geq 4$  days (prolonged fever-PF). By LR analysis, younger age, initial WBC, hospital days until diagnosis, and splenectomy were independently associated with PL; younger age and prior transfusion were associated with PF. Mortality in patients with leukocytosis was 21.9% and in patients with fever, 14.7%. By LR, only increasing age and APACHE-II score (but not PL or PF) were associated with increased mortality. Patients with PL received more days of antibiotics compared to patients without PL ( $18.5 \pm 3.0$  vs.  $9.5 \pm 0.5$ ,  $p < 0.0001$ ). Neither PL nor PF was associated with the development of a subsequent infection.

**Conclusions:** While patients at risk for prolonged fever or leukocytosis could be identified, neither of these events was associated with worse outcomes. This may reflect inter-individual variations in the host inflammatory response rather than a marker of infection severity or inadequate treatment. When faced with a patient with prolonged fevers or leukocytosis, the best course of action is to treat these

patients based on established evidence-based guidelines.

## **O20. Still Using the P-value, Stop It! A Bayesian Analysis of the STOP-IT Trial**

James Klugh; Chelsea Guy-Frank; Claudia Pedroza; Robert Sawyer; Jeffrey Claridge; Lillian Kao

**Background:** Bayesian statistics is an alternative to traditional frequentist methods and produces a probability (i.e., likelihood) of treatment benefit or harm rather than the commonly misused p-value. The Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection (STOP-IT) trial demonstrated a four-day course of antibiotics to be similar to liberal antibiotic administration. However, equivalence was not claimed due to inability to reach the full sample size.

**Hypothesis:** We hypothesized that a post hoc Bayesian analysis would demonstrate a high probability of no clinically significant difference in outcomes.

**Methods:** The primary outcome in the trial was a composite of surgical-site infection (SSI), recurrent intrabdominal infection (rIAI), or death within 30 days after the index source-control procedure. Secondary outcomes included the components of the primary composite and an SSI or rIAI with a resistant pathogen. Bayesian analyses were used to calculate risk ratios (RR) and 95% credible intervals (CrI) under a neutral prior. Probabilities were calculated for any benefit of a four-day course of antibiotics ( $RR < 1$ ) and for risk differences (RD) of less than 5% or 10%. Equivalence in the landmark STOP-IT trial was defined as less than a 10% margin of difference.

**Results:** The probability of benefit of a four-day antibiotic course was 55% (Table). The probability was 83% for a RD of 5% or less and 99% for a RD of 10% or less. The probability was 80% that a four-day course reduced the risk of SSI and 72% that it reduced the risk of SSI or rIAI with a resistant pathogen. The probabilities that the four-day course decreased mortality or rIAI were 40% and 30% respectively. There was a >87% probability of a RD of 5% or less and >99% of a RD of 10% or less for all secondary outcomes.

**Conclusions:** On Bayesian analysis, a four-day treatment of antibiotics after source control had over a 99% probability of being equivalent to liberal antibiotic administration when using the STOP-IT margin of 10%. Bayesian analysis provides useful information for outcomes with low event rates or limited sample sizes and provides more easily interpretable and applicable information to clinicians and patients.

## **O21. Oxidative injury leads to lipid radical accumulation in a human necrotizing enterocolitis enteroid model**

Alena Golubkova; Tyler Leiva; Katherine Snyder; Heather Liebe; Camille Schlegel; Jason Hansen; Peter Vitiello; Catherine Hunter

**Background:** Necrotizing enterocolitis (NEC) is an infectious and inflammatory intestinal disease that affects premature infants. Oxidative stress has a role in dysregulated cellular responses that follow onset of NEC. Specific targets of peroxidation are yet to be defined in NEC, but intracellular radical accumulation is a potential consequence if cellular detoxification mechanisms are immature, overwhelmed, or dysfunctional. The ability of intestinal epithelial cells to mitigate toxic radicals can push cellular fate towards death versus proliferation, playing a role in its capacity to overcome injury and proceed to intestinal repair.

**Hypothesis:** We hypothesized that oxidative injury in a human NEC enteroid model targets fatty acids that are abundant in the cell, leading to lipid peroxidation, and overwhelming cellular antioxidant mechanisms with accumulation of toxic lipid radicals.

**Methods:** Human intestinal samples were collected from premature infants undergoing resection for surgical NEC or other clinically indicated reason. Samples underwent processing to propagate primary enteroid lines. Enteroid cultures were grown to maturity and experimental NEC was induced by incubation with LPS (lipopolysaccharide) in hypoxic conditions for 48 hours. Lipid peroxidation was measured in live cultures at the end of the experiment by application of a BODIPY® 581/591 C11-based fluorescent reporter (Invitrogen TM) and analyzed with flow cytometry (Stratedigm-3).

**Results:** Experimental NEC conditions lead to a significant increase in lipid radicals in treated enteroid cultures (Figure 1). Moreover, human intestinal snap frozen tissue resected for active NEC, reveals significantly decreased protein levels of glutathione peroxidase 4 (Gpx4), a key enzyme in intracellular glutathione (GSH) antioxidant machinery responsible for neutralizing lipid radicals and fighting toxic accumulation.

**Conclusions:** Cellular targets of oxidative injury in NEC can play a vital role in influencing cellular fate and ability to fight injury. Accumulation of lipid radicals is a result of exposure to NEC in an enteroid model. If the level of lipid peroxidation overwhelms the ability of intracellular antioxidant machinery to neutralize lipid radicals, there are consequences that favor cellular death. Decreased Gpx4 expression likely contributes to the affected cell's inability to effectively detoxify.

## **O22. Sirt3 Deletion Promotes Inflammation and Mortality in Polymicrobial Sepsis**

Hanna Labiner; Kelli Sas; Joseph Baur; Carrie Sims

**Background:** Sirtuin 3 (Sirt3) is a NAD-dependent deacetylase that confers resilience to cellular stress by promoting mitochondrial activity. Mitochondrial dysfunction is a major driver of inflammation during sepsis.

**Hypothesis:** We hypothesize that Sirt3 expression improves survival in polymicrobial sepsis by mitigating the inflammatory response.

**Methods:** C57BL/6J mice and constitutive Sirt3 KO (S3KO) mice underwent cecal ligation and puncture (CLP) or sham surgery. Intracellular mRNA expression was quantified using RT-PCR. Serum IL6 protein expression was quantified using ELISA. Spectrophotometric assays were used to quantify serum AST and ALT. For in vitro studies, bone marrow derived macrophages (BMDMs) were harvested from S3KO and WT mice and treated with LPS.

**Results:** Following CLP, hepatic Sirt3 levels decrease significantly from baseline by 9hr (77% decrease,  $p < 0.01$ ) and remain depressed 24hr post-insult. Serum IL6 protein levels 6hr post-CLP were higher in S3KO mice (169.5 ng/mL vs 84.0 ng/mL,  $p = 0.03$ ), but by 12hr levels in both groups were comparable. In LPS treated BMDMs IL6 mRNA levels peaked earlier in S3KO cells than WT (4hr vs 8hr), although peak levels were not significantly different. While S3KO mice had decreased survival during the first 48hr following CLP compared to WT (55% vs 94.1%,  $p = 0.01$ ), there was no difference in 5d survival (50% vs 65%,  $p = 0.092$ ). AST and ALT were elevated in both groups at 36hr and 5d, but there was no difference between S3KO and WT mice.

**Conclusions:** Although S3KO mice initially had increased inflammation and mortality, this difference abated later on, and overall survival and organ dysfunction were comparable between the two groups. This pattern is consistent with the timeline of sepsis-induced Sirt3 downregulation in the WT mice. This suggests that Sirt3 downregulation occurring in sepsis is at least partially responsible for the initial hyper-inflammatory response and subsequent mortality. Our data supports upregulation of Sirt3 as a promising therapeutic strategy for further research in sepsis.

## **O23. Evaluation of Antibiotic Stewardship Programs in India Through a Pilot Needs Assessment Model**

Abhinay Tumati;; Harjot K Singh; Manjari Joshi; Philip S Barie; Mayur Narayan

**Background:** Surgical Site Infections (SSI) are common yet preventable complications. Antibiotic stewardship programs (ASP) can mitigate SSI. While there are recent U.S. Centers for Disease Control (CDC), World Health Organization (WHO), and Indian Council of Medical Research (ICMR) guidelines on ASP for resource-limited settings, implementation globally has lagged. In India, there are few data on SSI and even less is known about ASP and its potential role.

**Hypothesis:** In this survey, we aim to understand the current state of ASP and SSI surveillance at 5 Indian hospitals.

**Methods:** A prospective survey of 5 Indian academic medical centers, selected for geographic dispersion, was conducted. We collected descriptive variables about the hospitals' existing ASP programs/infrastructure, surgical volume, SSI counts, and percentage of multidrug-resistant organisms (MDRO) by specialty (obstetrics, pediatrics, adult) between 2017-2021. Data were collected in REDCap and analyzed in Microsoft Excel.

**Results:** Three of the five (60%) centers completed the survey. Inpatient surgical bed capacity ranged from 392 to 1269. All 3 institutes performed SSI surveillance, with varying frequency (i.e., daily to monthly). Two centers had formal patient safety monitoring and infection prevention committees; however, none had an ASP committee. Only one had formal education on patient preparation for surgery, skin antisepsis, or antimicrobial resistance/ASP. All 3 centers had an accessible microbiology lab but only one institution had a pharmacy system to provide data on antimicrobial utilization. SSIs were reported at all centers, but the majority were superficial incisional SSI (range 72-100%). During the 5-y period, the mean frequency of MDRO were, specifically MRSA, ESBL, and CRE 3.9% (range 1.5%-11.5%), 32.7% (range 15.1%-57.4%), and 16.0% (range 3.7-30.0%), respectively.

**Conclusions:** In surveyed academic medical centers in India, there is wide variation in SSI prevention and surveillance practices, including data collection/dissemination, as well as differences in availability of education/guidelines for providers. SSI were prevalent in adults, but data were limited for obstetrics and pediatric services (data not shown). In general, high frequency of MDRO were seen but with wide variation. Multiple opportunities exist to standardize ASP toward reducing SSI in India, but lack of infrastructure poses substantial barriers.

## **O24. Impact of disability on postoperative infectious complications**

Wardah Rafaqat; Emanuele Lagazzi; Jefferson Proaño-Zamudio; Dias Argandykov; May Abiad; Angela Renne; Anne-Sophie C. Romijn; Elaine van Ee; Casey Luckhurst; Jonathan Parks; John Hwabejire; George Velmahos; Michael P. DeWane

**Background:** Despite over 61 million people in the U.S. suffering from a disability, the impact on postoperative outcomes remains understudied, which may contribute to disparities observed in the healthcare of people living with disability. This study aimed to examine postoperative infectious complications in patients having healthcare conditions associated with disability.

**Hypothesis:** Disability is associated with a higher risk of postoperative infectious complications.

**Methods:** This was a retrospective review of the prospectively gathered National Readmission Database (2019) among patients undergoing common general surgery procedures. As per the CDC, disability was defined as severe hearing, visual, intellectual, or motor impairment/caregiver dependency. A propensity-matched analysis comparing patients with and without a disability was performed to compare outcomes, including 30-day readmission, postoperative septic shock, sepsis,



bacteremia, pneumonia, catheter-associated urinary tract infection (CAUTI), UTI, catheter-associated bloodstream infection, Clostridium difficile infection, and superficial, deep and organ-space surgical site infections. Patients were matched using age, gender, comorbidities, illness severity, income, neighborhood, insurance, elective procedure, and the hospital's bed size and type.

**Results:** A total of 710,548 patients were analyzed, of which 9,451 (1.3%) had at least one disability condition. Motor disability was the most common (3,762 (40.5%)), followed by visual (2,909 (31.3%)), intellectual (1,468 (15.8%)), and hearing impairment (1,400 (15.1%)). Patients with disability were older (64 vs 57 years;  $p<0.001$ ), insured under Medicare (65.2% vs 37.3%  $p<0.001$ ), and had an Elixhauser Comorbidity score  $\geq 3$  (69.2% vs 41.9%;  $p<0.001$ ). After matching, 9,292 pairs were formed. Patients with a disability had a significantly higher incidence of 30-day readmission, pneumonia, CAUTI, UTI. [See Figure]

**Conclusions:** Severe intellectual, hearing, visual, or motor impairments were associated with a higher incidence of 30-day readmission and infectious complications. Further investigation is needed to uncover any gaps in care that may drive these disparities.

## **O25. Frailty and Operative versus Nonoperative Mortality in Common Emergency General Surgery Conditions**

Caleb W. Curry; Marisa R. Imbroane; Andrew Tran; Christopher Towe; Esther Tseng; Christopher Towe; Jeffrey Claridge; Vanessa Ho

**Background:** In the older adult, development of abdominal sepsis may be catastrophic. Frailty increases perioperative risk, but it is unknown if there is a frailty level for which nonoperative management would be favored over operative management for common emergency general surgery conditions.

**Hypothesis:** The effect of frailty on operative and nonoperative mortality will differ by disease.

**Methods:** We identified patients aged 65 and older with appendicitis, diverticulitis, cholecystitis, peptic ulcer, or ischemic bowel in January to September 2017 using the National Readmissions Database. Operative and nonoperative management were identified based on presence or absence of a major abdominal surgery on index admission. Time to death up to 90 days post-discharge was the primary outcome. Frailty quintiles (1-5; 5 indicating most frailty) were calculated using a deficit accumulation score derived from 38 possible diagnoses. Cox proportional hazards analysis, stratified by disease type, estimated how frailty affected time to death after operative and nonoperative management (reference=nonoperative quintile 1), adjusted for age, sex, and shock.

**Results:** We included 304,573 patients (56% female, median age 77 years [IQR 71-84]). Mortality was highest for ischemic bowel (24%) and lowest for appendicitis (1%) (Figure 1). Mortality hazard tended to increase over frailty quintiles for each disease except ischemic bowel. The effect of frailty on mortality for operative and nonoperative patients differed by disease. In appendicitis and cholecystitis, operatively managed patients had a lower mortality hazard at all frailty levels. For diverticulitis, peptic ulcer disease, and ischemic bowel, nonoperatively managed patients had a lower mortality hazard over most frailty levels.

**Conclusions:** Frailty is an important prognosticator, but its magnitude of impact on survival for operatively and nonoperatively managed patients differed by disease. In particular, operative management favored survival over all frailty quintiles in appendicitis and cholecystitis, suggesting frailty alone may not be a strong enough indicator to decline surgical intervention in those disease processes.

## O26. Variations in Incision Management Based on Surgical Scenarios

Jeffrey Santos; Patrick Delaplain; Jeffrey Santos; Justin Dvorak; Tina Mele; Rondi Gelbard; Christopher Guidry; Philip Barie; Sebastian Schubl

**Background:** Wound classification (WC) can guide management of incisions to decrease rates of surgical site infection and post-op complications. There is variability in assigning WC by surgeons and a lack of consensus regarding incision management at the conclusion of surgery (CoS).

**Hypothesis:** Management of incisions at CoS lacks consensus and varies among individual surgeons.

**Methods:** Surgical Infection Society member survey on the management of incisions at CoS. Several general surgery (GS) and trauma laparotomy (TL) case scenarios tested influence of operation type, intra-operative contamination (spillage), and hemodynamic (HD) stability on incision management (e.g., close fascia or skin, use of incision or wound vacuum-assisted closure [VAC]). 66% of respondents was considered consensus. Chi-square test,  $\alpha=0.05$ . Response heterogeneity was quantified by Shannon index (SI).

**Results:** Among 78 respondents, the only consensus GS scenario was elective splenectomy (91% close skin/dry dressing). Open appendectomy and left colectomy/end-colostomy had the greatest heterogeneity (SI 1.68 and 1.63, respectively) with a split (20%-30%) among close skin/dry dressing, incisional VAC, skin open/wet->dry dressing, or another tactic. In TL scenarios, the majority used damage control for HD instability (53%-67%) but not for HD stable patients (pts) (0-1.3%,  $p<0.001$ ). Two TL scenarios reached consensus: close skin/dry dressing for HD stable splenectomy pts (87%) and fascia open/wound VAC for HD unstable colon resection/anastomosis (67%). Fecal diversion for rectal injury and colon resection/anastomosis (both HD stable) had high heterogeneity (SI 1.56 and 1.48, respectively). In penetrating T, the trend was for more use of wet->dry dressings and incision/wound VAC with increased spillage in HD stable pts (Figure). Figure. Comparison of intra-operative wound management tactics for penetrating T in HD stable patients by anatomic location and degree of spillage.

**Conclusions:** Damage control was favored in HD unstable TL pts, with use of wet->dry dressings and incision/wound VAC with spillage in penetrating T. However, most scenarios did not achieve consensus. High variability of practices regarding incision management at CoS was confirmed.

## O27. Narrowing the Gap: Preclinical Trauma/Sepsis model with Increased Clinical Relevance

Jennifer Munley; Lauren Kelly; Gwendolyn Gillies; Preston Coldwell; Erick Pons; Kolenkode Kannan; Letitia Bible; Philip Efron; Alicia Mohr

**Background:** Overall outcomes for trauma patients have improved over time. However, 10% of severely injured patients develop sepsis, which is associated with worse outcomes and increased mortality. The use of relevant preclinical studies remains necessary to understand mechanistic changes following injury and sepsis at the cellular and molecular level.

**Hypothesis:** We hypothesized that a preclinical rodent model of multicompartamental injury with postinjury pneumonia and chronic stress would replicate inflammation and organ injury similar to trauma patients in the intensive care unit (ICU).

**Methods:** Male and proestrus female Sprague-Dawley rats ( $n=8$ /group) aged 9-11 weeks were

subjected to either polytrauma (PT) (lung contusion, hemorrhagic shock, cecectomy, and bifemoral pseudofracture), PT with daily chronic restraint stress (PT/CS), PT with postinjury day 1 pseudomonas pneumonia (PT+PNA), PT/CS with pneumonia (PT/CS+PNA) or naïve controls. Weight, hemoglobin, white blood cell count (WBC), serum creatinine, plasma toll-like receptor 4 (TLR4), and urine norepinephrine (NE) were evaluated on day 2. ANOVA with pairwise comparisons were performed with significance defined as  $*p < 0.05$ .

**Results:** Rats who underwent PT+PNA and PT/CS+PNA lost more weight compared to their those without sepsis (PT, PT/CS) and naïve rats ( $*p < 0.03$ ). PT/CS+PNA exhibited worse acute kidney injury with elevated serum creatinine compared to PT, PT/CS ( $*p < 0.01$ ). Both pneumonia groups had a leukocytosis greater than uninfected (PT, PT/CS) ( $*p < 0.004$ ). Each experimental group exhibited severe anemia compared to naïve rats ( $*p < 0.0001$ ). Plasma TLR4 was elevated in PT+PNA compared to uninfected counterparts ( $*p = 0.01$ ). Urine NE was elevated in PT+PNA and PT/CS+PNA compared to naïve ( $*p < 0.02$ ), with PT/CS+PNA exhibiting the highest levels.

**Conclusions:** Sepsis, with postinjury pneumonia, induced significant systemic inflammation, acute kidney injury, leukocytosis, and anemia following polytrauma and chronic stress. Advanced animal models that replicate the critically ill human condition will help overcome the classic limitations of previous experimental models and enhance their translational value.

## **O28. The Burden of Income Disparity and Behavioral Factors on Infectious Complications in Emergency General Surgery**

Emanuele Lagazzi; Jefferson Proaño-Zamudio; Dias Argandykov; Wardah Rafaqat; May Abiad; Anne-Sophie Romijn ; Elaine van Ee; Angela Renne; George Velmahos; Haytham Kaafarani; John Hwabjire

**Background:** Compared to elective surgery, emergency general surgery (EGS) is associated with several folds higher risk of complications, including postoperative infections. The impact of social and behavioral determinants of health on infections following EGS remains unclear.

**Hypothesis:** We hypothesized that socioeconomic disparity, mental health, and behavioral determinants of health are associated with postoperative infectious complications after EGS.

**Methods:** All patients undergoing EGS in the 2019 National Readmission Database were included. We defined EGS as all non-elective general surgery procedures. The primary outcome was any 30-day infectious complication. Secondary outcomes included infectious complication type (e.g. pneumonia, urinary tract infection, sepsis, surgical site infection) and mortality. Multivariable regression analyses were used to study the impact of patient characteristics, social characteristics (e.g. annual income, insurance type), and behavioral characteristics (e.g. substance use disorder, psychiatric illness, neurodevelopmental disorders) on postoperative infection. Substance use disorders were divided into opioid, cocaine, and other substance use disorder. Psychiatric illness was categorized as depression, bipolar disorder, and schizophrenia.

**Results:** Of 367,348 patients included in this study, 75,522 (20.53%) had infectious complications during the index hospitalization or within 30 days from discharge. Medicare (OR, 1.3; 95% CI, 1.26-1.34), Medicaid (OR, 1.24; 95% CI, 1.19-1.29), lowest income by quartile (OR, 1.17; 95% CI, 1.13-1.22), opioid use disorder (OR, 1.18; 95% CI, 1.10-1.29), other substance use disorder (OR, 1.14; 95% CI, 1.02-1.26), schizophrenia (OR, 1.23; 95% CI, 1.13-1.34) and neurodevelopmental disorders (OR, 2.16; 95% CI, 1.90-2.45) were associated with higher rates of 30-day infectious complication. Similar findings were seen in the specific infectious complication types, such as pneumonia and UTI (Figure 1).

**Conclusions:** In EGS patients, socioeconomic status, substance use disorder, psychiatric comorbidities, and neurodevelopmental disorders were associated with a higher risk of infectious complications at 30

days. These findings warrant targeted infection prevention programs and standardized interventions that postoperatively address social and behavioral determinants of health.

## **O29. Intraabdominal Polymicrobial Sepsis Suppresses Interferon Responses in Immune Cells**

Haotong Zhang; Da Tang; Jennifer Darby; Alyssa Gregory; Thomas Walko; Timothy Billiar

**Background:** Interferon (IFN) responses in immune cells are suppressed after bacterial sepsis, burns, and trauma. There have been multiple clinical trials, but the IFN applications didn't appear efficient in improving septic patients' outcomes. While it has been assumed that this is due to impaired IFN release, recent transcriptomic studies from our group and others suggest that IFN signaling may be suppressed during sepsis.

**Hypothesis:** We tested the hypothesis that bacterial sepsis leads to impaired IFN responsiveness in immune cells.

**Methods:** C57/Bl6 mice were treated with LPS (iv 5mg/kg, n=4/group) or subjected to cecal ligation and puncture (CLP, n=4/group). Peripheral Blood Mononuclear Cells (PBMC) and Bone Marrow Mononuclear Cells (BMMC) were isolated at 6 or 30hr and subjected to single-cell RNAseq. Other cells were placed in culture and exposed to Type I or Type II IFN ex vivo for 18 hours. These cells were then isolated and subjected to transcriptomic analysis.

**Results:** Consistent with previous reports, LPS treatment resulted in the up-regulated IFN-responsive genes based on RNAseq analysis. Leukocytes isolated from mice subjected to CLP exhibited suppressed IFN transcriptomic responses. Cultured BMMC from CLP-treated mice exhibited suppressed responses to IFNs compared to controls ( $p < 0.05$  vs. cell from control mice).

**Conclusions:** The results of these experiments demonstrate that IFN responses are insult-specific and that IFN responses in immune cells are suppressed during CLP sepsis. Therefore, the mechanisms leading to alterations in IFN signaling during bacterial sepsis are likely to be multi-factorial and include changes in the responsiveness of immune cells to exogenous IFN.

## **O30. Ludwig's Angina: Higher Incidence and Worse Outcomes Associated with the Onset of the COVID-19 Pandemic**

Melissa Canas; Ricardo Fonseca; Alejandro De Filippis; Leonardo Diaz; Hussain Afzal; Aaron Day; Jennifer Leonard; Kelly Bochicchio; Grant Bochicchio; Mark Hoofnagle

**Background:** Ludwig's Angina (LA) is a diffuse cellulitis of the submandibular space and adjacent tissues, usually originating from dental infections. Early recognition and treatment are of utmost importance to avoid complications. During the COVID-19 pandemic, odontogenic treatments were often delayed due to the implementation of mask mandates, lockdown, and uncertainty of the novel coronavirus.

**Hypothesis:** We hypothesized that delayed odontogenic treatments associated with the onset of the COVID-19 pandemic would increase incidence of Ludwig's Angina and worse outcomes related to these infections.

**Methods:** Our prospectively maintained Acute and Critical Care Surgery database spanning Jun-2018 to Jun-2022 was queried for patients admitted with CT images suggestive of Ludwig's Angina and a diagnosis confirmed by ENT consult. We abstracted demographics, outcomes, clinical care management details, and microbiology results. Patients were stratified into two groups: pre-COVID

(Jun-2018 to Dec-2019) and COVID-onset (Jan-2021 to Jun-2022). The incidence of LA for each period was defined as: (new LA cases) ÷ (ED evaluations of oral and/or dental infections x 1.5 years). We subsequently analyzed the groups using chi-squared and student T-test.

**Results:** During the pre-COVID timelapse, a total of 1,301 patients were admitted to the ED with oral and/or dental infections. In the COVID-onset group, only 641 patients were admitted with these diagnoses. In the pre-COVID group, we identified 32 patients with the diagnosis of LA for an incidence of 0.02 per year. The COVID-onset group consisted of 41 patients, with an incidence of 0.04 per year. There was no difference in demographics or antibiotic treatment between the two groups. Development of necrotizing fasciitis was significantly more likely in the COVID-onset group (0% vs 15%;  $p < 0.024$ ), and they were also more likely to return to the OR for repeated debridement (3% vs 22%;  $p < 0.020$ ). Hospital length of stay, ICU length of stay, and ventilator days were also increased in this group ( $4.3 \pm 3.5$  vs  $9.5 \pm 11.3$ ;  $1.1 \pm 1.2$  vs  $9.5 \pm 7.1$ ;  $0.3 \pm 1$  vs  $3.6 \pm 7.1$  respectively;  $p < 0.001$ ). The most common isolated microbe pre-COVID was *S. viridans* (55.5%) vs polymicrobial with mixed upper respiratory microorganisms (69.2%) with COVID-onset.

**Conclusions:** During the onset of the COVID-19 pandemic, non-emergent dental procedures were often deferred because they were considered high risk for the spread of COVID-19. Although most dental infections diagnosed early have an excellent prognosis and low complication rate, delayed treatment was associated with a higher incidence of Ludwig's Angina and overall worse outcomes in our study population.

### **031. Open or closed? Management of skin incisions after emergent general surgery laparotomies**

Brett Tracy; Julia Coleman; Holly Baselice; Shruthi Srinivas; Sara Scarlet; Rondi Gelbard

**Background:** The management of midline abdominal skin incisions following an emergent laparotomy varies. We sought to determine if there was a relationship between incisional management and postoperative wound complications among patients undergoing emergent laparotomy for general surgery.

**Hypothesis:** We hypothesize that skin closure technique is not associated with adverse wound outcomes.

**Methods:** We performed a retrospective review of emergency general surgery patients (>18 years) who underwent an exploratory laparotomy within 6 hours of surgical consultation. Patients whose fascia was not closed during the index operation were excluded. Patients were divided into groups: open skin (OS) and closed skin (CS). Open skin included negative pressure wound therapy or wet-to-dry gauze; closed skin included closure with staples or sutures. We collected data on demographics, hemodynamics, laboratory values, hollow viscus perforation (HVP), and drain placement. Our primary outcome was rate of postoperative intra-abdominal abscess (IAA), superficial surgical site infection (SSSI), and incision dehiscence.

**Results:** The cohort comprised 388 patients: 42.3% OS (n=164) and 57.7% CS (n=224). There was no difference in age, BMI, or sex between groups, but there were more HVPs in the OS group (71.3% vs 20.5%,  $p < .0001$ ). OS compared to CS patients had greater heart rates (95.9 vs 88.2,  $p < .0001$ ), WBC (15.3 vs 11.7,  $p = 0.0001$ ) but lower albumin (3.3 vs 3.7,  $p < .0001$ ). There was no difference in complications, IAA, SSSIs, or dehiscence between groups; however, OS patients had a greater rate of drain placement (51.2% vs 17.9%,  $p < .0001$ ). In a subgroup analysis of patients with HVP (n=163), there was no difference in complications but a greater rate of drain placement in the OS group (43.5% vs 60.7%,  $p = 0.04$ ). For the overall cohort and subgroup of HVP, there was no difference in overall complications, IAA, SSSI, or dehiscence between patients with or without drains. On multivariable logistic regression, temperature (OR 1.5, 95% CI 1.1-2,  $p = 0.005$ ), white blood cell count (OR 1.04, 95% CI 1.01-

1.08,  $p=0.02$ ), HVP (OR 6.7, 95% CI 3.7-12,  $p<.0001$ ) and drain placement (OR 2.1, 95% CI 1.2-4,  $p=0.02$ ) were significant predictors of OS (AUC 0.829).

**Conclusions:** Open skin management occurs often after emergency general surgery laparotomies and is more common among patients with HVP, leukocytosis, and drain placement. However, rates of SSIs and wound dehiscence are similar between OS and CS patients. Our results suggest that skin closure is not contraindicated in the presence of sepsis and HVP.

### **O32. ROCK Inhibition attenuates pro-apoptotic factors associated with Necrotizing Enterocolitis**

Tyler Leiva; Katherine Snyder; Alena Golubkova; Camille Schlegel; Catherine Hunter

**Background:** Necrotizing Enterocolitis (NEC) is a devastating disease of neonates. Although the pathogenesis is incompletely understood, it consists of an altered intestinal microbiome and dysregulation of cellular pathways, such as proliferation/apoptosis. The Rho-associated protein kinase (ROCK) pathway is a key regulator of differentiation and proliferation. The mitogen activated protein kinase's (MAPK) are a family of proteins that integrate both intracellular and extracellular factors resulting in various responses involved in cellular processes, such as apoptosis. Two downstream proteins activated by MAPK's include NF- $\kappa$ B and Caspase 9.

**Hypothesis:** We hypothesize that inhibition of the ROCK pathway may attenuate the pro-apoptotic effects of NEC.

**Methods:** The intestinal epithelial-derived cell line, Caco-2 BBe cells were grown to maturity and used for experimentation. These cell lines were then divided into 4 groups: a control group, an experimental NEC group, a ROCK Inhibitor (RI) treated group, and an experimental NEC group treated with RI. Experimental NEC was achieved by adding 100 $\mu$ g/mL of lipopolysaccharide (LPS) to the media for 24 hours. Treatment with 10 $\mu$ M of RI, Y-27632 was administered to both experimental NEC and control cell lines. Cell pellets were then harvested and western blot analysis for NF- $\kappa$ B and Caspase 9 was performed. ANOVA was performed and significance was defined as a  $p$ -value  $< 0.05$ .

**Results:** Induction of experimental NEC resulted in a statistically significant increase in both NF- $\kappa$ B and Caspase 9 proteins ( $p$ -value 0.011 and 0.003 respectively) (Figure 1). The addition of RI alone, resulted in a decrease in both proteins when compared to untreated cells. RI administration in cells exposed to experimental NEC resulted in no significant increase in both NF- $\kappa$ B and Caspase 9.

**Conclusions:** NEC has been shown to increase the apoptosis-related factors NF- $\kappa$ B and Caspase 9 in vivo. RI administration attenuates this increase even in the presence of experimental NEC and preserves similar expression of both proteins. This signifies that ROCK inhibition may be protective against one of the key pathogenic processes involved in NEC.

### **O33. The Impact of Surgical Infections on Readmission After Trauma in Geriatric Patients**

Manuel Castillo-Angeles ; Barbara Okafor; Christine Wu; Ali Salim; Reza Askari

**Background:** Surgical infections have been found to be more prevalent in geriatric surgical patients, leading to an increased mortality and readmission rates. However, little is known about the impact of these complications in geriatric patients after traumatic injury. The purpose of this study was to determine the impact of surgical infections on readmission rates after trauma in geriatric patients.

**Hypothesis:** We hypothesize that surgical infections would represent a moderate proportion of patients being readmitted within 30 days after discharge.

**Methods:** We performed a retrospective analysis of Medicare inpatient claims from 2014 to 2015. All

patients 65 years or older with a diagnosis of traumatic injury were included. Surgical infections as a reason for readmission were determined by the primary ICD-9 diagnosis codes. The readmission rate was determined as the proportion of patients with an unplanned readmission within 30 days after their discharge. As a subgroup analysis, we then separated readmitted patients into those who returned to the same hospital and those who went to other hospitals. Demographic and clinical characteristics were collected. Multivariate logistic regression analysis was performed to identify the association between surgical infections and readmission.

**Results:** 754,313 geriatric trauma patients were included. Mean age was 82.13 (SD 0.50), 68% were female and 91% were white. 21,615 (2.87%) were readmitted within 30 days of discharge. 1,856 (8.59%) patients were readmitted due to surgical infections. Of all readmitted patients, 34% were readmitted to a hospital different than the original one. In unadjusted analysis, patients with surgical infections were more likely to be readmitted to their index admission hospital (10.46% vs. 4.96%,  $p < 0.001$ ). After adjusting for clinical and demographic variables, patients with surgical infections had lower rates of readmission to a different hospital (Odds Ratio [OR] 0.38, 95% Confidence Interval [CI] 0.33 – 0.43,  $p < 0.001$ ).

**Conclusions:** The readmission rate in geriatric trauma patients is relatively low and surgical infections do not account for a high proportion of these patients. However, surgical infections represent a reason for readmission to the index hospital, which discourages fragmentation of care. Further work is needed to keep decreasing readmissions due to surgical infections in this trauma subpopulation.

### **O34. Occurrence of Clostridium Difficile Enterocolitis in Burn Victims Relative to Total Body Surface Area of Injury**

Deepak Ozthail; Caroline Corley; Savannah Skidmore; Heather Evans

**Background:** Burn patients are at high risk of infection. Among hospitalized patients Clostridium difficile enterocolitis (CdE) is relatively common due to the routine use of antibiotics and immunomodulation of critical illness. We have observed that CdE occurs at a lower rate than expected in burn victims relative to other at risk population. In order to assess this assertion, we queried a large commercially available multi-center data network to determine if the risk of CdE was influenced by burn injury and how it was affected by total body surface area (TBSA) of burn injury.

**Hypothesis:** We believe that burn patients will have a lower risk of CdE than all other at-risk populations and that it will be aggregated by degree of injury.

**Methods:** We queried a national data-network across 71 institutions from 2002 to 2022. Patients were divided into cohorts based on the extent of total body surface area (TBSA) injured. CdE was the primary outcome. In addition, the risk of CdE was compared between burn victims and other at-risk populations.

**Results:** Cohort size and risk of CdE relative to TBSA injured: <10% (95,127; 0.212%), 10-19% (14,685; 0.429%), 20-29% (4,674; 0.535%), 30-39% (2,271; 1.318%), 40-49% (1,323; 0.756%), 50-59% (884; 1.810%), 60-69% (681; 1.468%), 70-79% (516; 1.938%), 80-89% (486; 2.058%) and >90% (541; 1.848%). Risk of CdE was increased relative to TBSA injured (slope = 0.0021). Overall risk of CdE for all burn victims was 0.265%. The risk of CdE for all other cohorts: all hospitalized (5,328,190; 0.889%), outpatients & antibiotics (9,327,416; 1.050%), inpatient & antibiotics (3,039,238; 2.659%), immunocompromised (2,431,130; 0.777%), gastric acid suppression (8,143,381; 0.505%) and sepsis (1,209,609; 3.196). The relative risk of CdE was lower in burn victims than all other at-risk groups, most notably, hospitalized patients (RR = 0.373) and sepsis (RR = 0.087).

**Conclusions:** Overall burn trauma appears to incur a lower risk of CdE with risk increased relative to TBSA size. Critical illness and antibiotic exposure are significant risk factors however, this is in sharp contrast with burn victims that are typically septic and receiving broad spectrum antimicrobial suppression. When compared with other relatively lower risk groups, burn injury remains significantly protective against

CdE occurrence. Further investigation is required to determine the mechanisms that contribute to these observations.

### **O35. Surgical Site Infections after Cholecystectomy in the Acute Care Surgery Era**

Abigail Raiter; Krista Wilhelmson; Melissa Harry

**Background:** In the era of acute care surgery (ACS) urgent cholecystectomies (UC) performed by ACS specialists has led to higher rates of successful laparoscopic operations and improved outcomes, even with increased case complexity. However data on surgical infection risk following UC is lacking.

**Hypothesis:** We hypothesize that patient and case complexity will be associated with higher rates of SSI.

**Methods:** A prospective observational study was performed including all UC by the ACS team at a rural level 1 trauma center between April 2021 and March 2022. Patient demographics, comorbidities, hospital data, operative data and pathology were collected. The severity of cholecystitis was graded using the Parkland grading scale (PGS) for cholecystitis.

**Results:** 213 patients underwent UC. Patients ages ranged between 18-95, and approximately half were female (table below). Most patients had pre-existing comorbidities. Laparoscopic cholecystectomy was successful in 93% of cases, 4% converted to open, 2% underwent laparoscopic subtotal cholecystectomy and 0.5% underwent planned open procedure. SSI occurred in 17 patients (6 patients had superficial SSI, 10 organ space SSI and one patient both superficial and organ space SSI). Many pre-operative patient factors were associated with increased risk of infection; however none were modifiable. Antibiotic dosing and duration varied; similar number of patients received perioperative, both peri- and postoperative, and pre-, peri- and postoperative antibiotics. However, antibiotics pre- or postoperatively did not decrease infections. The SSI rate was similar or lower for patients receiving only peri-operative antibiotics compared to longer duration. Intra-operative factors associated with increased risk of SSI were severe cholecystitis (higher PCG scores), longer case duration, bile spillage, and surgical drains. Patients with SSI had significantly longer hospital stays and readmissions.

**Conclusions:** SSIs occurred in 8% of UCs. Pre and intraoperative factors were associated with increased risk of SSI and those with SSI had worse postoperative outcomes. Most factors were not modifiable prior to surgery but avoidance of bile spillage may decrease SSI. Appropriate antibiotic timing is still unclear, however more antibiotics did not decrease SSIs.

### **O36. Social determinants of health associated with urgent versus elective cholecystectomy**

Sara Myers; Crisanto Torres; Sabrina Sanchez; Lisa Allee; Crisanto Torres; Tracey Dechert; Lisa Allee; Tejal Brahmhatt; Tracey Dechert; Tejal Brahmhatt;

**Background:** Benign gallbladder disease being (BGD) is the most frequent indication for cholecystectomy in the United States. However, many patients present with complicated disease requiring urgent interventions with increasing morbidity and mortality. We sought to investigate the association of individual and population-based social determinants of health on acute versus elective presentation of BGD.

**Hypothesis:** We hypothesized that acute presentation of BGD requiring urgent surgery would be associated with individual and census tract SDH including race/ethnicity, language, employment,



education, income, insurance status, and supermarket access.

**Methods:** All patients undergoing elective (EC), urgent (UC), and delayed (DC) cholecystectomy at our urban, safety-net hospital (2014-2021) for BGD were included (N=3197). Patient demographic and clinical data from the EMR was linked to population-level socioeconomic characteristics using census tracts. Descriptive and inferential statistics were used to analyze the data.

**Results:** The demographic, clinical, and population-level socioeconomic characteristics of our cohort are summarized in Table 1. In multinomial logistic regression we found that patients who were older (RRR=1.01, p=0.040), male (RRR=0.64, p<0.001), Black (RRR=1.6, p=0.008), and Hispanic (RRR=1.58, p=0.022) had a higher relative risk of presenting with UC. Patients who primarily spoke Spanish (RRR=0.48, p<0.001) or Portuguese (RRR=0.23, p<0.001), had a primary care provider (PCP) (RRR=0.73, p=0.007), and lived in census tracts with a higher percentage of internet access (RRR=0.97, p=0.002) had a lower relative risk of presenting with UC.

**Conclusions:** Of the multiple variables we evaluated, race/ethnicity, primary language spoken, and having a designated PCP were most significantly associated with presentation with UC vs EC. This highlights the important role of PCPs in early identification and management of BGD.

### **037. Short versus Long Antibiotic Duration for Necrotizing Soft Tissue Infection: A Systematic Review and Meta-Analysis**

Nicole Lyons; Brianna Cohen; Christopher O'Neil; Walter Ramsey; Kenneth Proctor; Nicholas Namias; Jonathan Meizoso

**Background:** Necrotizing soft tissue infections (NSTI) are rapidly spreading and life-threatening infections that require emergent and aggressive surgical intervention with immediate antibiotic initiation. However, there are wide variations in clinical practice and no expert consensus on duration of antibiotic therapy after source control.

**Hypothesis:** We hypothesized that a short course of antibiotics would be as effective as a longer course.

**Methods:** A systematic review of the literature was performed using PubMed, Embase, and Cochrane Library from inception to November 2022 following the PRISMA guidelines. Observational studies comparing short (<7 days) versus long (≥7 days) antibiotic duration for NSTI were included. Primary outcome was mortality and secondary outcomes included limb amputation and Clostridium difficile infection (CDI). Cumulative analysis was performed with Fisher's exact test. Meta-analysis was performed using a fixed effects model and heterogeneity was assessed using Higgins I-square.

**Results:** A total of 622 titles were screened and four observational studies evaluating 532 patients met inclusion criteria (Table). Kenneally et al defined long course as >2 days, so these patients were excluded. The average age of patients was 52 years, 67% were male, 61% had Fournier's gangrene, and 40% had diabetes mellitus. There was no difference in mortality when comparing short to long duration antibiotics on both cumulative analysis (5.6% vs 4.0%, p=0.51) and meta-analysis (relative risk= 0.9, 95% confidence interval= 0.8 to 1.0, I-square=0, p=0.19)(Figure). There was no significant difference in rates of limb amputation (11% vs 8.5%, p=0.50) or CDI (20.8% vs 13.3%, p=0.14). Meta-analysis for secondary outcomes could not be performed as these were only reported in two studies.

**Conclusions:** Short duration antibiotics may be as effective as longer duration antibiotics for NSTI after source control. Further high-quality data such as randomized clinical trials are required to create evidence-based guidelines.

### **O38. Gastric Perforation in Temporary Abdominal Closure as a Predictor of Fungal Intra-abdominal Infection in Trauma Patients**

Leonardo Diaz; Alejandro De Filippis; Melissa Canas; Ricardo Fonseca; Hussain Afzal; Jennifer Leonard; Mark Hoofnagle; Kelly Bochicchio; Grant Bochicchio

**Background:** Gastric perforation has been linked to intra-abdominal Candida infections. The use of temporary abdominal closure (TAC) has also been shown to increase the rate of fungal intra-abdominal infection (FIAI). We analyzed the association between gastric injuries in trauma patients who underwent TAC and their risk of FIAI.

**Hypothesis:** We hypothesized that patients with gastric perforations in the setting of TAC have a higher incidence of FIAI than bacterial intra-abdominal infection (BIAI).

**Methods:** Our prospectively maintained Trauma Registry was queried for all level 1 trauma patients who underwent an emergency laparotomy and TAC between August 2019 and August 2022. Patients were stratified by FIAI vs BIAI. Demographics, intra-operative findings, culture data, antimicrobials, and clinical outcomes were collected. The diagnosis of FIAI and BIAI was confirmed by Infection Disease consultation. Data were analyzed using Student's t-test, Chi-square, and multi-variable logistic regression.

**Results:** 1,030 level one trauma patients were admitted during the study period. Of these, 87 patients required emergency laparotomy with TAC. Most patients were male (85.1%) and admitted for penetrating trauma (71.3%). There were a total of 14 intra-abdominal infections (16.1%) with an equal number of FIAIs (n= 7) and BIAIs (n=7). Five of the 7 patients with FIAI (71.4%) had gastric perforation as compared to 14.3% in the BIAI group (p=0.045). There were no statistically significant differences in demographics or comorbidities. The FIAI group had a significantly higher rate of ICU readmission (42.8% vs 14.3% p 0.024) compared to the BIAI group. When analyzed by multivariable logistic regression in patients with TAC, controlling for gastric injuries vs non-gastric injuries; BMI, mechanisms of injury, number of laparotomies, APACHE and IV drug use, the combination of gastric injuries and TAC was found to have 17-fold increase in FIAI (OR 17.042, P 0.018).

**Conclusions:** Gastric perforation in the setting of TAC is more predictive of FIAI than BIAI in critically injured trauma patients. FIAI patients also had a significantly higher rate of ICU readmission. Surgeons should be aware of the high rate of FIAI in this high-risk patient population and consider early empiric antifungal treatment.

### **O39. The impact of preoperative chlorhexidine baths on outcomes in pediatric patients undergoing adnexal surgery**

Javier Valdes; Monique Motta; Azalia Avila; Shenae Samuels; Tamar Levene

**Background:** Surgical site infections (SSIs) increase the risk of mortality, length of hospital stay and health care costs. Pre-operative bathing protocols with antiseptic agents such as chlorhexidine 4% (CHG) have been implemented in many institutions. Although there is data supporting this practice for select cases, its efficacy in adnexal surgery among pediatric patients is unknown.

**Hypothesis:** Pre-operative bathing with CHG does not lead to improved outcomes for pediatric patients undergoing adnexal surgery.

**Methods:** We conducted a retrospective chart review of 115 non-neonatal, pediatric patients who

underwent adnexal surgery from November 2017 to November 2022. Rates of SSIs, returns to emergency room (ER) and readmissions were compared for patients who did or did not receive a pre-operative antiseptic bath using CHG. Statistical analysis was conducted using Pearson's chi-square test or Fisher's exact test for categorical variables and independent t-tests for continuous variables with statistical significance at  $p < 0.05$ .

**Results:** The mean age at time of surgery was 13.3 years (range 0.75-20 years) with most patients identified as white (67.8%) followed by black (25.2%) and nearly half being Hispanic (54.8%). Patients underwent detorsion of adnexal structures and/or resection of adnexal masses or cysts. Nearly one quarter of our study population (26.1%) received a pre-operative bath with CHG. All patients underwent preparation of skin in the operating room just prior to incision with CHG and isopropyl alcohol skin preparation solution. Overall, the rate of SSIs was 1.7% ( $n=2$ ) and there were no ER visits or readmissions due to SSIs. There was no statistically significant difference in outcomes between pediatric patients undergoing pre-operative CHG bath with those not undergoing CHG bath prior to adnexal surgery.

**Conclusions:** Our data suggest that pre-operative bathing with CHG does not alter the rates of SSIs, ER visits or readmission rates for pediatric patients undergoing adnexal surgery. A larger multicenter prospective study would be required to determine a study sufficiently powered to make clinical recommendations.

#### **O40. Identification of Risk Factors for Intra-Abdominal Candidiasis**

Kelsey Habighorst; James Sanders; Sara Hennessy; Kristina Goff; Bingchun Wan; Meagan Johns

**Background:** Intra-abdominal candidiasis (IAC) is associated with significant morbidity and mortality in hospitalized patients. Identifying high-risk populations may facilitate early and selective directed therapy in appropriate patients and avoid unwarranted treatment and any associated adverse effects in those who are low risk.

**Hypothesis:** Unique risk factors exist for the development of IAC compared to other forms of invasive candidiasis.

**Methods:** This retrospective, case-control study included patients greater than 18 years of age admitted from July 1, 2010 to July 1, 2021 who had a microbiologically confirmed intra-abdominal infection (gastrointestinal culture positive for either a *Candida* spp. [cases] or bacterial isolate [controls] collected intraoperatively or from a drain placed within 24 hours). Patients receiving peritoneal dialysis treatment or with a peritoneal dialysis catheter in place or treated at an outside hospital were excluded. Multivariable regression was utilized to identify independent risk factors for the development of IAC.

**Results:** Five hundred and twenty-three patients were screened, and 250 met inclusion criteria (125 per cohort). Univariate analysis revealed the following were statistically different between cases and controls: acute kidney injury, absolute neutrophil count  $< 500$  cells/mm<sup>3</sup>, preexisting hemodialysis, gastric acid lowering agent exposure, immunosuppression, diabetes mellitus, admission to the intensive care unit (ICU), ICU length of stay, mechanical ventilation for  $> 48$  hours prior to culture collection, presence of a central venous catheter, upper gastrointestinal tract procedure prior to culture collection, parenteral nutrition utilization, prior hospitalization within 90 days, exposure to corticosteroids, diagnosis of sepsis or septic shock,  $>1$  abdominal drain in place prior to culture collection,  $>1$  trip to the operating room for any major surgery prior to culture collection, or presence of an anastomotic leak at the time of culture collection. Multivariable analysis identified exposure to corticosteroids (Odds Ratio (OR) 5.79; 95% CI 2.52-13.32,  $p < 0.0001$ ), upper gastrointestinal tract surgery (OR 3.51; 95% CI 1.25-9.87,  $p = 0.017$ ), and mechanical ventilation (OR 3.09; 95% CI 1.5-

6.37,  $p = 0.002$ ) were independently associated with IAC. The AUROC and goodness of fit were 0.7813 and  $P=0.5024$ , respectively.

**Conclusions:** Exposure to corticosteroids, upper gastrointestinal tract surgery, and mechanical ventilation are independent risk factors for the development of IAC suggesting these factors may help identify high-risk individuals requiring antifungal therapy.

#### **O41. Breathomics and the Use of Exhaled Volatile Organic Compounds to Detect COVID-19**

Kristiana Sather; Gregory Sherwood; Raia Finc; Gregory Beilman; Philippe Buhlmann; Steven Koester; Elizabeth Luszczek

**Background:** The COVID-19 pandemic presented many challenges to the global healthcare system. A major challenge early in the pandemic was to rapidly detect the presence of COVID-19 to allow appropriate precautions and to apply specific therapies. Volatile Organic Compounds (VOC) have been identified as potential distinguishing features in patients with a variety of underlying disorders, with the panel of compounds detected in exhaled breath serving as a chemical fingerprint.

**Hypothesis:** Patients with COVID-19 would exhibit unique features in exhaled breath distinguishing them from normal controls.

**Methods:** We performed a prospective observational pilot study on hospitalized, non-ventilated COVID-19 patients and healthy controls. All patients were adults and had a COVID-19 diagnosis made with molecular testing within 72 hours of the study. Patients and controls exhaled into a mask directing flow across a graphene-based sensor designed to detect the presence of disease-related VOC, resulting in real-time conversion of chemical content to electronic data. Outputs were analyzed based on detected changes in voltage and capacitance features. Linear discriminant analysis was used to compare COVID-19 patients to normal controls.

**Results:** Eight patients and 10 healthy subjects completed testing with the VOC device in June-August 2020. Clinical characteristics of COVID-19 patients and volunteers are listed in the Table. Linear discriminant analysis demonstrated significant discrimination between COVID-19 patients and normal controls with area under the curve of 0.85. When control and COVID-19 patients were compared based on distinguishing characteristics, there was a significant difference in signal ( $p=0.0005$ , Figure).

**Conclusions:** In this pilot study, electronic signals from VOCs in exhaled breath distinguished patients with COVID-19 infection from healthy controls. This technology has significant potential to rapidly detect infection or other pathology in patients with acute illness. Further testing is required to evaluate clinical utility.

#### **O42. Meta-analysis of hemodynamic goal directed fluid therapy during surgery on the prevention of surgical-site infection**

Hasti Jalalzadeh; Rick Hulskes; Markus Hollmann; Marja Boermeester

**Background:** Surgical site infection (SSI) is the most common postoperative complication and substantially increases health-care costs. Perioperative fluid management has been proposed to reduce SSI and other postoperative complications. We aim to investigate the influence of intra-operative goal directed fluid therapy (GDFT) on SSI and other postoperative outcomes.

**Hypothesis:** We hypothesize that a goal directed fluid therapy during surgery will reduce the number of patients with an SSI.

**Methods:** This systematic review and meta-analysis compared any GDFT management with no specific

fluid management in the prevention of SSI in adult patients undergoing any type of surgery. We searched for randomized controlled trials (RCTs) in MEDLINE, Embase, and Cochrane CENTRAL, published up to Nov 22, 2022. Studies comparing different GDFT regimens, or only pre- or postoperative GDFT were excluded. Summary relative risks with corresponding 95% CIs were calculated using a random effects model. Sensitivity analysis based on risk of bias, and subgroup analysis based on studies with high versus low risk patients (high risk:  $\geq 50\%$  of patients ASA  $\geq 3$ ) were carried out. Trial sequential analysis (TSA) was performed to assess the risk of random error. The Cochrane Risk of Bias-2 tool and GRADE approach were used to evaluate the certainty of evidence. This study is registered with PROSPERO, CRD42022277535.

**Results:** The search resulted in 1319 articles, of which 64 studies were included in this systematic review and meta-analysis. The overall incidence of SSI was 11.7% (1261 of 10,745 patients). The pooled relative risk of SSI was 0.69 (95% CI 0.60–0.80) for GDFT versus control fluid therapy. Sensitivity analysis of only studies with low risk of bias did not change the overall effect (RR 0.74, 95%CI 0.60-0.91 in favor of GDFT). In studies including high-risk patients, the effect of GDFT was greater (RR 0.61, 95%CI 0.49-0.77) than for low risk patient studies (RR 0.77, 95%CI 0.63-0.94). In the TSA the cumulative z-line crossed the boundary for effect but did not reach the required sample size, indicating that new RCTs are unlikely to modify the effect estimate.

**Conclusions:** Goal directed fluid therapy in adult patients undergoing surgery is effective for the prevention of surgical site infections, and new RCTs are unlikely to change this outcome.