O1. Gut microbial metabolites improve survival to bacterial peritonitis via the Aryl hydrocarbon receptor

Robert Keskey; Adam Lam; Jason Xiao; Alexander Zaborin; Olga Zaborina; John Alverdy

Background: The gut microbiota play an important role in shaping the immune response to pathogens. We have previously demonstrated that mice treated with a fecal microbiota transplant (FMT) were rescued from bacterial peritonitis. FMT-induced survival correlated with gut microbiota production of butyrate, but the exact mechanism of FMT protection remains unknown.

Hypothesis: We hypothesized that changes in gut microbiota metabolites alter macrophage phenotype and dictate survival from bacterial peritonitis.

Methods: C57/B6 wild-type mice were injected intraperitoneally (i.p.) with Serratia marcescens (S.m.) at an LD50. Body temperatures were monitored hourly to delineate survivors(S) from non-survivors (NS). Cecal contents and peritoneal fluid were isolated for metabolomics via mass spectrometry. Peritoneal macrophages (pMacs) were isolated using magnetic bead isolation. Experimental conditions included: FMT via enema at time of S.m. injection, depletion of macrophages with i.p clodronate 24 hours prior to S.m. injection, and i.p. Aryl hydrocarbon receptor (AhR) inhibitor (StemRegginin) at the time of S.m. injection. Microbial metabolites and pMac phenotype were compared between S and NS. Gene expression of pMacs was determined using qRT-PCR.

Results: Body temperature delineated survivors from non-survivors starting at 8 hours post injection (p.i) with S.m (S: -0.3°C vs NS: -1.0°C, p=0.03). Survivor pMacs had a significantly higher expression of Arginase-1 at both 8h and 15h p.i. and a significant reduction of Nos2 ($p < 0.01$) at 15h p.i. FMT was able to rescue mice from S.m. peritonitis (FMT: 100% (10/10) survival vs. No FMT: 50% (5/10) survival). Macrophage depletion reduced FMT's ability to rescue (FMT+ control: 100% (5/5) survival vs. FMT + clodronate 2/5 (40%) survival). There was a significant increase in tryptophan metabolites (Indole-3-lactic acid, indole-3-acetic acid, Tryptamine) in the cecum and peritoneal cavity of surviving mice at both 8 and 15h post injection. Tryptophan metabolites have previously been shown to signal via the AhR. When AhR was inhibited, survival from S.m. was significantly reduced (AhRi 0% (0/10) survival vs. Control 50% (5/10) survival). Additionally, FMT was unable to rescue mice in the presence of AhR inhibition (100% (10/10) survival FMT + control vs. 0% (0/10) survival FMT+AhRi).

Conclusions: Survival from bacterial peritonitis is dependent on both macrophages and AhR signaling via tryptophan metabolites produced by the gut microbiota.

O2. Fecal IgA levels are inversely correlated with gut microbial alpha diversity in the perioperative setting

Harika Nalluri; Harika Nalluri; Julia Nugent; Matthew Bobel; Sonja Boatman; Wolfgang Gaertner; Christopher Staley; Cyrus Jahansouz

Background: One of the greatest challenges in colorectal surgery is life-threatening infection from anastomotic leak. Surgical bowel preparation (SBP), consisting of mechanical bowel preparation (MBP) and oral antibiotics (OA), can reduce infection-related complications and is thought to alter gut microbiota, but there is little mechanistic understanding of the intestinal response to this intervention. Fecal secretory IgA plays a critical role in mucosal immunity and is the first line of defense in protecting intestinal epithelium from pathogenic microorganisms. We aimed to investigate how fecal IgA may be affected by perioperative changes in gut microbiota by comparing patients before and after colorectal surgery or screening colonoscopy.

Hypothesis: We hypothesized that MBP alone would result in reduced microbial diversity associated with increased fecal IgA, and that these changes would be further amplified by addition of OA.

Methods: We performed a prospective observational study comparing fecal samples from 14 adult patients undergoing colorectal surgery (n=5) or screening colonoscopy (n=9). Surgical patients underwent pre-operative SBP, while colonoscopy patients underwent MBP alone. Patients provided pre-operative and two-week post-operative fecal samples. Microbial characterization was performed by 16S rRNA amplicon sequencing with alpha diversity measured by Shannon index. Fecal IgA was quantified by ELISA.

Results: Microbial alpha diversity was unchanged by MBP alone in colonoscopy patients (Kruskal-Wallis P=0.30), while microbial diversity was significantly lowered with addition of OA to MBP in surgical patients (P=0.03). Fecal IgA was inversely correlated with microbial diversity by Shannon index (Spearman ρ=-0.69, P<0.0001).

Conclusions: SBP leads to a reduction in gut microbial alpha diversity, while MBP alone does not significantly affect microbial composition. Reduced microbial diversity may contribute to increased fecal IgA in the perioperative setting. Future studies will explore involved functional pathways between microbiota, microbially-produced metabolites, and the immune system.

O3. Comparison of Infectious Complications After Surgical Fixation versus Epidural Analgesia For Acute Rib Fractures

Tareq Kheirbek; Thomas Martin; Jessica Cao; Holden Spivak; Andrew Stephen; Charles Adams, Jr.; Stephanie Lueckel

Background: Surgical stabilization of rib fractures (SSRF) has been shown to be associated with improved mortality and respiratory complications. Patients who are not offered SSRF are often treated with epidural analgesia (EA) to improve pulmonary mechanics. We sought to compare infectious complications in patients undergoing either SSRF or EA.

Hypothesis: We hypothesized that infectious complications are equivalent between the two treatment groups.

Methods: Trauma Quality Improvement Program 2017 dataset was queried for adult trauma patients who were admitted with acute rib fractures. ICD10 codes were used to identify patients who underwent SSRF or EA. We excluded patients who did not receive either and those who received both treatment in the same admission. Primary outcome was development of sepsis. Secondary outcomes were specific infections of ventilator associated pneumonia (VAP), catheter associated urinary tract infection (CAUTI), and central line associated blood stream infections (CLABSI). Multiple logistic regression analyses were used to adjust for age, injury severity (ISS), chest AIS, flail chest injury, traumatic brain injury (TBI), and comorbidities.

Results: We identified 3,551 patients, of whom 2,252 underwent SSRF and 1,299 underwent EA. SSRF patients were younger (mean 55 vs 60, 0.0001), had higher ISS (19 vs 14, $p<0.001$) and had longer hospital LOS (median 12 vs 8, $p<0.001$). There was no difference in mortality (2.7 vs 2.6%, NS), however, SSRF had higher rate of sepsis complications (1.6% vs 0.5%, $p=0.001$), VAP (5.1 vs 0.9%, $p<0.001$), CAUTI (1.7 vs 0.5%, $p=0.001$), and CLABSI (0.3% vs 0, $p=0.04$). Adjusted for age, ISS, chest AIS category, TBI, flail injury, and comorbidities, SSRF was associated with higher odds of sepsis (2.72, 1.08-6.83), CAUTI (2.99, 1.13-7.96), and VAP (3.39, 1.82-6.33). For those who developed sepsis, there was no statistical difference between the two groups in mortality or hospital LOS.

Conclusions: Despite no difference in mortality, SSRF was associated with increased risk of septic complications in patients with rib fractures compared to epidural analgesia. Identifying, and addressing, risk factors of sepsis in this patient population is a critical performance improvement process in order to optimize outcomes without increased adverse events.

O4. Different Surgeon, Different Duration: Lack of Consensus on Appropriate Antimicrobial Prophylaxis and Therapy

Patrick Delaplain; Patrick Delaplain; Haytham Kaafarani; Philip Barie; Leo Andrew Benedict; Sebastian Schubl

Background: The principles of antimicrobial stewardship promote the appropriate prescribing of agents with respect to efficacy, safety, duration, and cost. Antibiotic resistance often results from inappropriate use (e.g., indication, selection, duration) of antibiotics. We evaluated possible practice variability in duration of antimicrobial

administration in surgical infection treatment (Rx) or prophylaxis (Px) amongst a group of experts.

Hypothesis: There is lack of consensus regarding the duration of antibiotic Px and Rx for many common indications.

Methods: An anonymous survey was distributed to all members of the Surgical Infection Society (SIS) seeking opinions regarding patterns of use of antimicrobial agents for a variety of scenarios, including pre- and post-procedural antibiotic Px and duration of antibiotic Rx for commonly encountered infections. Standard descriptive statistics were used to compare survey responses.

Results: Sixty-three SIS members responded, most of whom (67%) have held a leadership position within the SIS or contributed as an annual meeting moderator or discussant; 76% have been in practice for >5 years. Regarding perioperative Px, >80% agreed that a single dose is adequate for most indications, with the exception of gangrenous cholecystitis (40% single dose, 38% pre-op + 24 hours) and inguinal hernia repair requiring a bowel resection (70% single dose). There was more variability regarding the use of antibiotic Px for various bedside procedures (e.g. tracheostomy, chest tube, central line) with respondents split between none needed (Range: 27%-66%) vs. a single dose (Range: 31%-67%). Opinions regarding the duration of antimicrobial Rx for hospitalized patients who have undergone a source control operation or procedure varied widely based on indication (Fig.) Only 2/20 indications achieved more than 60% consensus despite available Class I evidence: 7 days for ventilator-associated pneumonia (77%), and 4+1 days for perforated appendicitis (62%).

Conclusions: With the exception of perioperative antibiotic Px, there is little consensus regarding antibiotic duration among surgical infection experts, despite Class I evidence and several available guidelines. This highlights the need for further high-level research and better dissemination of guidelines.

O5. Is Same Day Discharge After Appendicitis Safe? A Post-hoc Analysis of the EAST MUSTANG Study

Eva Urrechaga; Eva Urrechaga; Alessia Cioci; Khaled Abdul Jawad; Rebecca Saberi; Gareth Gilna; Majid Chammas; Daniel Yeh; Nicholas Namias; Rishi Rattan

Background: Most studies supporting the safety of same-day discharge (SDD) after appendectomy are limited to single centers and include only uncomplicated cases. We sought to determine the safety of SDD after appendectomy.

Hypothesis: We hypothesize there will be no difference in a 30-day composite outcome between SDD versus overnight observation.

Methods: The prospective, multicenter EAST Appendicitis Study database was queried for adults undergoing appendectomy who were then stratified into SDD or discharge

after one night of hospitalization (OBS). Subjects with hospitalization >1 night, loss to follow up, or malignant pathology were excluded. Outcome of interest was a composite endpoint of 30-day readmission or emergency department (ED) visit. Propensity score matching (PSM) using standardized mean differences <0.1 was performed with the following variables: age, Charlson comorbidity index (CCI), ED arrival time, operative approach, operative duration, intraoperative findings, and administration of post-operative antibiotics. Chi-square and Fisher-exact tests were used for categorical variables and Wilcoxon test was used for non-normal continuous variables. Variables significant ($p<0.2$) on univariate analysis were used in a multivariate logistic regression to calculate the odds of achieving the composite endpoint (OR [95% CI]).

Results: A total of 1818 subjects were included, of which 422 (23%) were SDD. PSM resulted in 413 pairs. After PSM, there was no difference between OBS and SDD in the composite 30-day outcome (8.2% vs 7.0%, p=.60). OBS was more likely than SDD to have a Clavien-Dindo complication (2.6% vs 0.5%, p=.02) and post-operative antibiotics for >24hrs (7.3% vs 3.6%, p=.05). On logistic regression controlling for covariates, SDD was not associated with higher odds of the 30-day endpoint [OR 0.83 (1.21-5.33)].

Conclusions: Same-day discharge after appendectomy for appendicitis is not associated with increased odds of readmission or emergency room visit at 30 days when compared to overnight observation. However, selection bias for overnight observation is likely. Further study is needed to identify which patients can be safely discharged the same day.

O6. Fermentable fiber mitigates antibiotic-induced disturbances of the gut microbiota and host health

Tiffany Toni; Robert Keskey; Adam Lam; Tiffany Toni; Renee Thewissen; Janani Vigneswaran; Brian Fleischer; Alexander Zaborin; Olga Zaborina; John Alverdy

Background: A Western diet, high in fat and low in fiber, has adverse effects on the composition and function of the gut microbiota resulting in impaired recovery of the host following antibiotic exposure. Here we tested the independent effects of dietary fat and fermentable fiber on the host and gut microbiota to differentiate which dietary component drives this response.

Hypothesis: We hypothesized that dietary fiber, independent of dietary fat, would alter the intestinal microbiota and mitigate the negative effects of antibiotics on the host.

Methods: Mice were fed refined diets varying in fat (high fat-HF or low fat-LF) and fiber (high fiber-HFb or low fiber-LFb) content for six weeks. Mice were then administered antibiotics (PO clindamycin and IP cefoxitin) twice daily for five days and assessed for antibiotic side effects (weight loss and severity of diarrhea on a 2 point scale). Cecum and stool samples were collected to determine the impact of diet on the microbiota pre- and post-antibiotic exposure using 16S rRNA gene amplicon sequencing and mass spectrometry to measure short chain fatty acids.

Results: Fermentable fiber was protective to the murine host exposed to antibiotics, as demonstrated by a reduction in the severity of antibiotic-induced diarrhea in both high fat (diarrhea score 1.85 HF/LFb vs 1.1 HF/HFb, p≤0.01) and low fat (diarrhea score 1.6 LF/LFb vs 0.3 LF/HFb, p ≤ 0.01) diets. Dietary fiber also reduced antibiotic-induced weight loss in the high fat diets (-16.3±3.2% HF/LFb vs -9.1±5.1% HF/HFb). Compositionally, the high fiber groups were found to have greater bacterial density in ng DNA/mg stool (125.2 ± 51.7 LFb vs 463.3 ± 180.9 HFb) with a higher abundance of health-promoting Bacteroidetes along with a lower abundance of Firmicutes and Proteobacteria. Functionally, high fiber was associated with increased short chain fatty acid production (nmol/cecum) in both high fat (butyrate 81.5±8.9 HF/LFb vs 276.2±1 HF/HFb, p≤0.05) and low fat (butyrate 201.4±56.4 LF/LFb vs 567.8±404 LF/HFb) diets. Interestingly, functional prediction from 16S sequencing demonstrated an increased abundance of the luxS/AI-2 quorum-sensing molecule in the high fiber groups, which has been demonstrated to increase the resiliency of the microbiota to antibiotics.

Conclusions: Fermentable fiber, especially in a high fat diet, increases the resiliency of the host to antibiotics and correlates with a higher abundance of health-promoting microbiota that produce butyrate and the quorum sensing molecule AI-2. Dietary supplementation with fermentable fiber may offer an approach for mitigating the negative effects of antibiotics.

O7. Modified Frailty Index-5 predicts infectious complications following cholecystectomy: a retrospective cohort analysis

Osaid Alser; Osaid Alser; Robert Sinyard; Robert Sinyard; Lydia Maurer; Jonathan Parks; John Hwabejire; April Mendoza; Jason Fawley; Noelle Saillant; David King; Haytham Kaafarani; George Velmahos; Peter Fagenholz

Background: Although most surgeons consider patient frailty in pre-operative decision making, few studies have examined the impact of frailty on outcomes after cholecystectomy. We aimed to evaluate the association between frailty as measured by the modified Frailty Index-5 (mFI-5) and infectious complications in patients undergoing cholecystectomy.

Hypothesis: Patients with higher mFI-5 scores are more likely to experience infectious complications following cholecystectomy.

Methods: We queried the ACS-NSQIP 2006-2017 database to include patients who underwent either open or laparoscopic cholecystectomy, with no other concomitant procedures. The outcome of interest was a composite of 30-day infectious complications (surgical site infection [SSI], sepsis, urinary tract infection [UTI], or pneumonia). The 30-day postoperative infectious complications were evaluated based on calculated mFI-5 score (ranging from 0 to 1, 1 being the highest). Univariable and multivariable logistic regression analyses were performed to assess the association between infectious complications and mFI-5.

Results: A total of 364,259 patients underwent a cholecystectomy. The median age (inter-quartile range [IQR]) was 49 (35, 63) years, and most patients were female (n=256,125, 70.3%), obese (n=192,294, 54.1%), and underwent laparoscopic cholecystectomy (n=344,872, 94.7%). The median mFI-5 score was 0, with most patients receiving either a score of zero (224,285, 61.6%) or 0.2 (97,364, 26.7%). In univariate analysis, higher mFI-5 scores were significantly associated with rates of infectious complications (p<0.001) [Figure 1]. After adjusting for relevant covariates such as demographics, comorbidities, and operative details, mFI-5 was independently associated with infectious complications (OR [95% CI]: 2.34 [1.72-2.20], p<0.001, c-statistic: 0.74), particularly sepsis (3.71 [2.09-6.60], p<0.001, 0.84), UTI (3.11 [2.27-4.25], p<0.001, 0.69), and pneumonia (3.57 [2.65-4.81], p<0.001, 0.84). Higher mFI-5 scores were not independently associated with higher rates of SSI (1.25 [0.81-1.95], p=0.318, 0.73).

Conclusions: Frailty, as measured by the mFI-5, is a strong independent predictor of infectious complications following cholecystectomy. The mFI-5 is a valuable tool to adjust for physiologic reserve in multivariable analysis, to potentially aid in risk stratification and decision making for high-risk patients considering cholecystectomy.

O8. FER Gene Delivery Rescues Immune Response in Geriatric Mice after Lung Contusion and Pneumonia

Vladislav Dolgachev; David Machado-Aranda; MV Suresh; Alexis Kralovich; George Yalamanchili; Krishnan Raghavendran; David Machado-Aranda

Background: FEline sarcoma Related protein (FER) is a non-receptor pleiotropic protein that self-phosphorylates and activates other protein kinases. This amplification effect has been associated with oncogenesis and metastatic potential but is essential for immune cell differentiation. Transgenic mice with catalytic-deficient FER (FER-/-) have an exuberant neutrophilic response to lung contusion (LC) and pneumonia (PNA); however, they succumb due to a lack of bacterial clearance. The loss of FER and immunological defects are pronounced in aging cohorts regardless of strain. We asked if electroporation-mediated delivery of FER gene could restore the innate immune response after the combined insult of LC and PNA.

Hypothesis: Loss of FER function creates a defective immune response, especially in elderly subjects.

Methods: Young (< 2-month-old) and Elder (> 4-month-old) C57Bl6 and FER-/- mice were used in combined unilateral LC and Klebsiella PNA (500 CFU) model. FER gene or a saline-sham was delivered into the lung using trans-thoracic electroporation (EP) of naked plasmid DNA solution distributed by gravity after pharyngeal drop. Survival was measured. In a parallel experiment, we collected bronchial-alveolar lavage fluid after 24 h of insult, and cells and their Mitochondrial Membrane Potential (MMP) were characterized by flow cytometry. Aging associated-transcripts (IGF-1, SIRT-1, TERT, N-

ras, HeyL, DDX58 were measured by RT-PCR.

Results: EP of FER plasmid (FER-EP) boosted 5 and 10-fold the number of bronchoalveolar (BAL) macrophages with high MMP in C57Bl6 and FER-/-,geriatric mice, and associated with a significant reduction of mortality ($p < 0.03$). The increase in MMP was less noticeable in younger mice. EP of FER stimulated levels of Myeloperoxidase and improved bacterial clearance in all genotypes. Among age-related transcripts, IGF-1 and DDX58 were significantly increased by the rescue in both genotypes. Amplified - IGF-1 coding for insulin growth factor-1; and DDX58 for mitochondrial upstream regulator of NfKB and interferons - indicates an improved endurance of immune cells to metabolic stress while fighting off infection.

Conclusions: FER-EP therapy enhanced immune response to LC + PNA by recruiting alveolar macrophages with high MMP and correlating respiratory burst. While unknown compensatory mechanisms operate in younger mice, FER-EP treatment provided rescue and restored innate immune response in elderly mice. Thus, FER's loss of function could be an essential step in the appearance of immunosenescence and defective inflammatory responses in the aged lung.

O9. Revisiting the SIS Delphi Analysis of the Research Agenda in Surgical Infections: Advancements and unanswered questions

Patrick Delaplain; Patrick Delaplain; Haytham Kaafarani; Philip Barie; Sebastian Schubl

Background: In 2006, the Surgical Infection Society (SIS) used a modified Delphi process to enlist SIS member-experts to identify 15 research priorities in the field of surgical infectious diseases; it was intended to serve as a research “road map” for the next 1-2 decades. We sought to evaluate the progress made in each of these priority areas.

Hypothesis: We examined the progress achieved with respect to the 15 research areas identified by the Delphi process at that time, hypothesizing that advances in knowledge would be achieved in most domains, if not all.

Methods: SIS members were surveyed to: 1) Determine whether each priority area question had been satisfactorily answered in the last 14 years; 2) assess the quality of evidence answering each question (1-3 scale); and 3) delineate whether there is a current unmet need for continued research in each area. Randomized controlled trials (RCTs) regarding these initiatives were also identified via literature search and their citations in the literature were tabulated.

Results: Sixty-six members of the SIS responded to the survey. Thirteen of 15 research priority areas saw an increase in data perceived to be available as adjudged by experts, as well an increase in the number of RCTs addressing that topic. However, there were only six questions that were deemed by experts to be answered sufficiently—primarily regarding antibiotic duration for certain conditions and the impact of glycemic control on

infection. The questions that remained unanswered related to nosocomial infections, sepsis/septic shock, prevention of SSI, and antimicrobial pharmacokinetics. For a majority of the questions that experts believed were not answered sufficiently (8/9), respondents opined that continued research into these areas was warranted (Table).

Conclusions: Whereas 40% (6/15) of the research questions prioritized by the SIS in 2006 were answered to the satisfaction of member-experts, there are many questions that remain unanswered despite an increase of available data. Revisiting these research priorities highlights advancements made in the field of surgical infections, but also helps identify the areas that would benefit from continued study. That a majority of questions remain unanswered underscores an opportunity for member-experts to collaborate on SIS-managed or -endorsed RCTs.

O10. Modeling the Trojan Horse hypothesis of Surgical Site Infections (SSIs)

Sanjiv Hyoju; Michael Srienc; Alexander Zaborin; Benjamin Shogan; Olga Zaborina; John Alverdy

Background: Despite the prevailing notion that the majority of SSIs are due to some type of intraoperative contamination event, there are more data to refute this claim than support it. We previously demonstrated that GFP-labeled MRSA introduced into the gut can silently travel to a remote surgical wound and cause a clinical SSI.

Hypothesis: We hypothesized that that low abundance pathogens present among the normal gut microbiota can be induced to silently travel and cause a clinical SSI.

Methods: Male C56BL/6 mice 7 weeks old were randomly assigned to consume either a standard chow diet (SD) or a Western diet (WD) for 6 weeks. WD-fed mice were split into two groups with one group receiving 5 days of antibiotics (clindamycin PO/cefoxitin IP) and a second group receiving a single-dose antibiotic. Controls consisted of WD and SD-fed mice without exposure to antibiotics. Surgical wounds were sterilely created in the back muscle using a cautery injury and placement of silk sutures. All mice were sacrificed on postoperative day 10 for direct inspection of the wound and culture. A composite scoring system (CSS) was developed that included the following parameters: "fully closed and healed wound=0, partial wound dehiscence=1, gross full wound dehiscence=2 + no purulent discharge=0, serous discharge=1, purulent discharge=2 + no abscess =0, punctate abscesses=1, gross abscess formation=2 + negative culture=0, monomicrobial culture= 1,polymicrobial culture =2.

Results: The CSS in all groups of mice was statistically higher across all groups of mice consuming a WD (CSS mean ± SE, 3.6± 0.6 WD vs 0.7± 0.1 SD, p=0.0007). Antibiotic treatment did not increase the CSS in WD-fed mice. Wound culture positivity was highest in WD-fed mice with antibiotics treatment groups (75% WD versus 11% SD). Prolonged exposure to antibiotics in WD mice produced polymicrobial wound infections (Enterobacter cloacae complex, E. faecalis, Proteus mirabilis, E coli, Klebsiella oxytoca, and Enterococcus gallinarum) compared to WD-fed mice exposed to

only a single dose of antibiotics (88% vs 10%). Predominant organisms in WD-fed mice included Enterobacter cloacae complex or Methicillin Sensitive Staphylococcus aureus (MSSA) whereas SD-fed mice had a very low incidence of culture positivity consisting mainly of monomicrobial MSSA.

Conclusions: The combination of consumption of a western diet and prolonged antibiotic exposure led to impaired wound healing and the presence of polymicrobial infections with enteric organisms. Genetic sequencing is pending to confirm the suspicion that spontaneous dissemination of enteric pathogens is the causative mechanisms of the SSIs observed in this model

O11. Addressing COVID-19 in the surgical ICU: Incidence of antibodies in healthcare personnel at a quaternary care center

Alexi Bloom; Alexi Bloom; Elizabeth Ulrich; Isabela Romano; Isabela Romano; Abdul Kader Natour; Jeffrey Johnson; Arielle Hodari Gupta; Loay Kabbani

Background: During the initial surge of the pandemic, many hospitals around the country were quickly tasked with transitioning surgical care areas, such as the surgical intensive care unit (ICU), into medical ICUs for patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). This investigation sought to determine the seroprevalence of COVID-19 antibodies in healthcare personnel (HCP) providing care to patients with COVID-19 in different hospital settings at a quaternary care center in a metropolitan area heavily impacted during the initial surge of the pandemic.

Hypothesis: HCP working in the surgical ICU will have a greater rate of seropositivity than those in the medical ICU. Non-ICU personnel will have a lower rate of seropositivity than those primarily working in an ICU.

Methods: Six weeks after the system's first COVID case, serologic testing for COVID-19 using a rapid antibody test was offered to HCP. Participants voluntarily completed a demographics questionnaire. Their location of employment within the hospital, COVID-19 exposures, adherence to personal protective equipment (PPE) usage, and COVID-19 related symptoms were also collected.

Results: A total of 853 HCP participated in the study. Most of the cohort was composed of registered nurses (49.5%, 384) and doctors (17%, 132). The overall incidence of IgG seropositivity was 10.6%. No difference in IgG seropositivity across occupation ($p=0.7$) or gender ($p=0.2$) was observed. The medical and surgical ICUs did not differ in terms of IgG seropositivity ($p=0.621$), but adherence to PPE use was significantly different. The surgical ICU staff were more compliant with frequency of PPE use during patient contact ($p=0.007$), whereas the medical ICU staff more frequently reported always wearing PPE outside patient rooms ($p<0.001$). IgG seropositivity was higher in the non-ICU cohort (13%, 45) compared to the ICU group with (8.8%, 34) but this did not reach

statistical significance (p=0.07). Both ICU and non-ICU personnel similarly reported wearing PPE outside patient rooms (p=0.175). However, more ICU than non-ICU personnel reported always wearing PPE during patient contact (p=0.02).

Conclusions: IgG seropositivity in HCP was not significantly different between those caring for COVID-19 patients in the medical versus the surgical ICU. Adherence to PPE usage does appear to be different between the ICUs. HCP working in an ICU demonstrated a lower rate of seropositivity than the non-ICU personnel. Our study suggests that rapid conversion of other clinical areas into COVID ICUs can be done safely without increased risk of seropositivity to HCP.

O12. Bacterial Co-Infection is Associated with Thrombotic Complications and Immunothrombotic Cellular Clusters in COVID-19

Ander Dorken Gallastegi; Ander Dorken Gallastegi; Leon Naar; Elizabeth M. Van Cott; Ander Dorken Gallastegi; Rachel P. Rosovsky; David J. Gregory; Damodaran Annamalai; Ronald Tompkins; Jarone Lee; Haytham Kaafarani; Haytham Kaafarani; Haytham Kaafarani; George Velmahos; Galit H. Frydman; Galit Frydman

Background: COVID-19 is known to induce a proinflammatory and prothrombotic state. However, the relationship between bacterial co-infections (CoIs) and this immunothrombotic state remains unclear. This study explores circulating immunothrombotic cellular cluster (CICC) phenotypes and their association with CoIs and thrombosis in COVID-19.

Hypothesis: Bacterial CoIs are associated with a higher risk of thrombotic complications and higher levels of CICCs in patients with COVID-19.

Methods: Blood samples were collected from patients with a positive SARS-CoV2 PCR at a tertiary academic referral center. Imaging flow cytometry was used to measure CICCs including platelet (plt)-leukocyte aggregates (PLAs: 1 leukocyte + plt or plt microparticle), circulating leukocyte clusters (CLCs: >2 leukocytes ± any other cell) and platelet-erythrocyte aggregates (PEAs: >1 erythrocyte + plt) (Figure 1). CoIs were diagnosed via culture and/or radiology in the appropriate clinical setting. Thrombotic events were defined as described in Table 1.

Results: Forty-six blood samples were analyzed; 24 patients (52%) had at least one CoI with the most common being urinary tract infection (n:15, 33%) followed by pneumonia (n:13,28%). Eleven patients (24%) experienced thrombotic complications with line or ECMO clotting being the most common (n:7, 16%) followed by DVT (n:4, 9%). Patients with CoIs had a significantly higher incidence of thrombotic complications compared to those without CoI (9% vs. 38%, p=0.024). Patients experiencing a thrombotic complication with and without CoI had significantly higher CLCs compared to patients without thrombotic complications (p=0.033) (Table 1).

Conclusions: Bacterial CoIs are associated with an increased risk of thrombotic

complications in patients with COVID-19. CLC levels appear to be correlated with thrombotic risk in the setting of COVID-19, irrespective of CoI status. We have identified unique CICC phenotypes, which may lead to further mechanistic understanding of thrombosis in the face of infection, along with potential new drug targets.

O13. Gender Disparities in the Operative Management of Complicated Diverticulitis

Laura Godat; Allison Berndtson; Amy E. Liepert; Jay Doucet; Todd Costantini

Background: Effective treatment for complicated diverticulitis requires prompt infectious source control to limit morbidity and mortality. Treatment paradigms for complicated diverticulitis include antibiotics, percutaneous drainage or operative intervention for colon resection including the potential need for colostomy placement. While disparities in care for diverticulitis related to race and insurance status have been identified, the effect of gender on surgical care for complicated diverticulitis is unknown.

Hypothesis: We hypothesized that gender disparities would exist in the operative management of patients with complicated diverticulitis.

Methods: Admissions from the emergency department for complicated diverticulitis; defined as ICD-9 codes for diverticulitis with peritonitis or abscess, were identified in the National Inpatient Sample Database from 2012 – 2015 Q3. Patients age 18 and over were included. Demographics data, Charlson Comorbidity Index (CCI) and mortality were obtained. ICD-9 codes were used to identify operative interventions including open or laparoscopic colectomy, ostomy, or percutaneous abscess drainage.

Results: There were 21,821 patients identified with complicated diverticulitis. 50.4% of patients were male and 49.6% of patients were female. The mean age of males was 53.0 ± SD 13.8 while the mean age of females was 61.7 ± SD 13.7 ($p<0.001$). Female patients with complicated diverticulitis were less likely than males to undergo operative intervention as age increased (see figure), with the largest disparity in operative intervention between genders occurring for patients age ≥ 60. There was no difference in percutaneous drainage procedures related to gender. Compared to males, females ≥ 60 were less likely to have a CCI > 3 suggesting they had fewer medical comorbidities. Females with complicated diverticulitis had increased in-patient mortality compared to males (3.2% vs. 1.8%, $p<0.001$).

Conclusions: Gender disparities exist in the surgical care of patients with complicated diverticulitis. Females were less likely to undergo operative intervention for complicated diverticulitis as age increased compared to males which was associated with increased mortality. Determing factors that lead to disparities in surgical care for female patients with diverticulitis may improve outcomes.

O14. Comorbidities Matter As Distressed Communities Index Fails to Predict Mortality in Necrotizing Soft Tissue Infection

Michael Villarreal; Kathryn Schubauer; Kathia Gonzalez-Gallo; Courtney DiDonato; Zoe Krebs; Jon Wisler

Background: Necrotizing soft tissue infections (NSTI) are life-threatening infections requiring prompt recognition and intervention. The distressed communities index (DCI) is a comprehensive ranking of socioeconomic well-being based on zip code. We sought to identify the role of DCI in predicting mortality in NSTI, as it remains unknown.

Hypothesis: As a community is deemed more distressed, based on their composite DCI, mortality from NSTI will increase.

Methods: A retrospective analysis of institutional data for patients diagnosed with NSTI (2011-2020) requiring surgical intervention was performed. We reviewed all cases to ensure rapidly progressive necrotic infection with microbial growth was present. Patients without these findings, prisoners, and pregnant women were excluded. The DCI is a composite score based on community-level factors: unemployment, education level, poverty rate, median income, business growth, and housing vacancies. DCI scores were matched to the patient's zip code. Stratification of DCI was performed using quintiles. Parametric and non-parametric analyses were performed to evaluate both the demographic and clinical characteristics. Multivariable regression analyses were performed to identify independent variables associated with outcomes.

Results: 629 patients met inclusion criteria. Overall mortality was 10.4% (N=65) of the cohort. Patients who died were more likely to be female (57%), older (median age 59, IQR [56,68]), have a BMI ≥30 (61.5%), have a Charlson index ≥5 (35.4%), and have a DCI within the at-risk or distressed quintiles (61.9%). After regression analysis, neither the composite DCI by quintile, nor the individual component scores, were found to correlate with mortality. Interestingly, underlying heart disease, hepatic dysfunction, and renal disease at baseline were found to significantly correlate with mortality from NSTI with p-values < .05.

Conclusions: Socioeconomic status and insurance payer have been consistently championed for inclusion when constructing risk models, evaluating resource utilization, comparing hospitals, and determining patient management. The severity of community distress measured by DCI did not correlate with mortality for NSTI, despite contrasting evidence in other disease processes. This finding is likely due to a combination of both individual and community-level resources. This is highlighted by the recognition that co-morbidities did correlate with mortality, especially renal dysfunction. The absence of DCI-related associations observed in this study warrants further investigation, as do mechanisms for the prevention of further organ dysfunction.

O15. Does Race Impact Mortality from Infections in the Surgical Intensive Care Unit?

Elizabeth D. Krebs; Taryn Hassinger; Robert Sawyer

Background: Racial differences in patient outcomes continue to come to light throughout medicine. However, it is not yet known if race contributes to outcomes from surgical infections. We sought to investigate the impact of race on outcomes following infections treated in the surgical intensive care unit (ICU).

Hypothesis: We hypothesized that Black patients admitted to a surgical ICU would have higher mortality from surgical infections compared to White patients.

Methods: All patients admitted to a single-center surgical and trauma intensive care unit from October 1996-July 2017 were prospectively evaluated for presence of infections, either present on ICU admission or acquired in the ICU. A retrospective cohort study of a prospectively-collected database compared Black vs. non-Hispanic White patients with the primary outcome of in-hospital mortality. Those with race identified as “other” or “Hispanic” were excluded from the present study. Univariate analysis compared demographic details and outcomes, while a multivariable logistic regression evaluated the risk-adjusted impact of race on in-hospital mortality.

Results: A total of 3,063 patients were evaluated, of whom 425 (13.8%) were classified as Black and 2,638 classified as White. The groups had similar percentages of patients with a prior solid organ transplant (10.4% vs. 11.8%, $p=0.40$) and patients admitted following trauma (31.8% vs. 34.0%, $p=0.36$). Black patients were younger (median age 53 vs. 58, $p<0.01$). Rates of diabetes were higher in Black patients (26.8% vs. 20.1%, $p<0.01$), while rates of chronic pulmonary disease were lower (11.1% vs. 15.2%, $p=0.02$). In-hospital mortality was not statistically different between Black vs. White patients (14.8% vs. 17.0%, $p=0.26$). Though many factors did impact in-hospital mortality on multivariable analysis, race was not associated with a difference in in-hospital mortality ($p>0.05$, Table).

Conclusions: In this 20-year evaluation of intensive care unit patients, race did not impact mortality from surgical infections. Social determinants of health, including race, may have a greater impact on community-acquired infections than in the hospital setting.

O16. The Impact of Elder-friendly Care on Infection and Delirium following Acute Care Surgery

Melissa Shears; Shelly Jun; Jayna Holroyd-Leduc; Diana Rucker; Rachel Khadaroo

Background: Postoperative infections are common and universally expensive complications in surgical patients. Older adults are especially vulnerable to postoperative complications and may be at a higher risk for developing subsequent

neurological complications, such as delirium, secondary to infection. The aim of this analysis was to: (1) examine the association between postoperative infection and delirium among patients >65 years recovering from emergency abdominal surgery; and (2) explore the impact of Elder-friendly Approaches to the Surgical Environment (EASE) interventions on postoperative infection and delirium complications.

Hypothesis: We hypothesize that EASE interventions would decrease post-operative infectious complications and delirium in older patients having emergency surgery.

Methods: We conducted a prospective before-and-after study at a tertiary care hospital in Alberta, Canada. Older patients, ≥ 65 years old, who preoperatively required assistance with less than 3 activities of daily living and were admitted for acute care surgery were eligible. We excluded patients who were transferred from other medical services, underwent elective or trauma surgery cases. In this analysis, we report on patients who received: (i) standard care; or (ii) EASE interventions. Surgical complications were determined using the Clavian-Dindo Classification. Associations were explored with the Chi-square test (two-sided; $p< 0.05$). All analyses were performed using STATA 14.0.

Results: A total of 293 patients (mean age=75.6 years, 49% female; n=153 control) were recruited at the EASE intervention site. Postoperatively, 9.2% of these patients developed a surgical-site infection (SSI) and 19.5% delirium. There was an association between postoperative SSI and delirium complications (OR 1.9; 95% CI 0.90-3.9, p=0.06). Moreover, the EASE intervention, which was a multi-faceted quality improvement initiative that integrated a geriatrician to the surgical team and early mobilization practices, was significantly associated with a decrease in organ/space surgical site infection (p=0.04) and delirium (p=0.006).

Conclusions: Older patients having acute care surgery are highly vulnerable to postoperative complications, and subsequent functional decline or death. Post-operative infections in particular pose a serious threat to older patients who may develop major neurological sequela, such as delirium. Targeted elder-friendly approaches to recovery may reduce postoperative complications among older patients and mitigate its downstream effects.

O17. Mechanism of Bacteroides fragilis modulating lymphocytes in a clinically applicable 3D intestinal organoid sepsis model

Isabella Heffernan; Runping Zhao; Alfred Ayala; Daithi Heffernan; Daithi Heffernan

Background: Abdominal sepsis induces lymphocyte dysfunction, microbiome disruptions and intestinal lumen destruction. Probiotics with homeostasis capabilities, are rarely mechanistically directed. We have previously demonstrated that Bacteroides fragilis probiotics direct a restorative lymphocyte phenotype. Immunomodulation by B.fragilis occurs via polysaccharide A(PSA) – TLR receptor interactions. However, mechanism remain poorly understood in acute sepsis.

Hypothesis: Polysaccharide A - TLR interactions mediate the Bacteroides fragilis immunomodulatory effects upon T-cells within an organoid model of sepsis.

Methods: LPS mimicked gram-neg infection. To test T-cell/probiotic interaction, T-cells were cultured with Bacteroides fragilis(B.frag) or Lactobacillus acidophilus(L.acid). Phenotyping included PD-1, BTLA and TLR-4 expression. Cytokines included IL-6, IL-4, IFN-γ as well as IL-33, an intestinal lumen restorative cytokine. To assess immunomodulatory effects of PSA, culturing was repeated using PSA knockout strain of B.frag(ΔPSA-Bf). To assess TLR-4 in T-cells, TLR-4-siRNA was transfected. Lgr5+ stem cell derived intestinal organoids were grown in a 3-dimensional matrix. T-cells, microbes(B.frag, ΔPSA-Bf or L.acid)+/-LPS and organoids co-cultured. Histology assessed organoid injury. The microbicidal peptide α-defensin assessed organoid function.

Results: After stimulation with LPS, L.acid induced marked increase in IL-4 (453 vs 57 pg/ml) and IL-6 (2,153 vs 277 pg/ml) but only moderate increase in IL-33. B.frag largely suppressed IL-4 and IL-6, but increased restorative IL-33 (57 vs 8 pg/ml;$p<0.01$) and IFN-g. Conversely, ΔPSA-Bf did not increase IL-33 or suppress IL-4 or IL-6. B.frag and L.acid increased TLR-4 and PD-1(84% vs 89% vs 20%) expression. A protective PD-1-high sub-population(17%) emerged in response to B.frag, but not to ΔPSA-Bf. Following TLR-4 siRNA transfection, T-cell responses to L.acid was unchanged. The protective effect of wild type B.frag was not observed. To create a clinically translatable model, intestinal organoids were grown. Following co-culture, LPS-stimulated T-cells influxed towards the organoids, and greatly increased with L.acid. Conversely, B.frag reduced immune cell influx. Histology revealed no overt Organoid damage. α-defensin markedly increased in response to T-cell:L.acid but not T-cell:B.frag. This protective effect was not seen with ΔPSA-Bf, or following with TLR-4-siRNA transfection.

Conclusions: The immuno-restorative mechanism of B. fragilis as a probiotic involve PSA-TLR-4 interaction. Harvesting the unique properties of B.frag derived PSA will offer targeted probiotic-based sepsis recovery strategies.

O18. Violation of Postoperative Antibiotic Guidelines in Acute Appendicitis: A Multicenter, Quality Improvement Study

Khaled Abdul Jawad; Khaled Abdul Jawad; Haytham Kaafarani; Leon Naar; Ryan Lawless; Alexis Cralley; Daniel Cullinane; Chris Dodgion; Ali McCormick; Jeffry Nahmias; Erika Tay; Marie Crandall; Jennifer Mull; Brandon R. Bruns; Chris Knapp; Daniel Yeh

Background: National guidelines for the management of acute, non-perforated appendicitis recommend against routine postoperative antibiotics after appendectomy, but compliance varies across institutions in the United States.

Hypothesis: We sought to study variations in antibiotic protocol violations after a period

of education and feedback within departments of surgery.

Methods: Participating sites from the Eastern Association for the Surgery of Trauma (EAST) multicenter appendicitis study (MUSTANG) were invited to participate in this study. “Baseline” data of postoperative antibiotic protocol violations in subjects with acute, non-perforated and non-gangrenous appendicitis undergoing appendectomy over an 18-month period were analyzed and confidential feedback was provided to each site. After a period of internal education on each site’s antibiotic protocol, “Follow-Up” data was collected over a 3-month period to study variations in violations. Paired sample t-test was used to compare “Baseline” and “Follow-Up” data for each site, and p-values ≤ 0.05 were considered statistically significant.

Results: Eight sites participated and contributed data to this quality improvement project: Baseline data included 736 subjects and Follow-Up data included 202 subjects. Mean % of postoperative protocol violations in Baseline and Follow-Up were 30% ± 22 and 7% ± 10, respectively (p=.002). All sites showed decrease in protocol violations on Follow-Up after the period of education: three sites reported no violations, four reported >50% decrease, and one site reported a decrease of <50% (Figure).

Conclusions: Surgeon education and feedback on national guidelines for adjunctive antibiotic therapy after appendectomy for acute, non-perforated appendicitis is associated with a decrease in rates of violations. This method may be effective in improving quality of care by protecting patients from overexposure to antibiotics and antibiotic-associated adverse effects.

O19. Is Staphylococcal TSST-1 Pathophysiology Mediated by a CD40-Dependent Mechanism in Keratinocytes?

Mary Oliver; Saira Nisar; Bonnie Carney; Lou'ay Hussein; Lauren Moffatt; Jeffrey Shupp

Background: S. aureus infection after burn injury causes significant morbidity and mortality. It produces superantigen (sAg) virulence factors such as Toxic Shock Syndrome Toxin-1 (TSST-1) which may cause a cytokine storm through the bypassing of T-cell activation. Non-Thymocyte-mediated cellular activation is poorly understood. CD40 a costimulatory molecule present on a variety of epithelial cell types has been implicated as a putative mechanism for TSST-1 infection. Here we investigate the interaction between TSST-1 and CD40 on keratinocytes.

Hypothesis: Pathophysiological effects of TSST1 are mediated via binding to CD40 receptor on keratinocytes.

Methods: Normal human epidermal keratinocytes (NHEKs) were grown and exposed to 100 µg/mL TSST-1 for 6 hours. RNA was purified and qRT-PCR was performed for IL-8, TNF, and CCL20 (n=3). Under separate treatment conditions, NHEKs were transfected with scrambled controls or siRNA for 24 hours to knockdown (KD) CD40 and TSST-1 treatment and qRT-PCR was carried out as previously described (n=3). Additionally,

cells were lysed for Western blot analysis of CD40 and STAT3 phosphorylation patterns (n=3).

Results: qRT-PCR analysis showed an increase in cytokine gene expression after 6hr TSST-1 treatment. IL-8 and TNF production increased ~2-fold (1.99±0.12, 2.84±0.91) and CCL20 by ~11-fold (11.44±6.69) when compared to the untreated control. Western blot analysis showed CD40 bands at 45kDA in 6hr TSST-1-treated NHEKs. Moreover, densitometry analysis showed significantly increased ratios of phosphorylated STAT3:STAT3 at 79kDA when compared to the untreated control (p=0.02). After CD40 siRNA transfection, CD40 KD was confirmed with a 5-fold decrease compared to controls and scrambled siRNA. Upregulation of cytokines IL-8 and TNF were observed after CD40 KD and TSST-1 treatment; (12.52±10.33, 19.4±0.61) whereas CCL20 expression was down-regulated (-6.62±0.31).

Conclusions: These initial studies in elucidating NHEK response to TSST-1 show that the CD40 pathway is likely activated in response to exposure to toxin leading to upregulation of key pro-inflammatory cytokines and phosphorylation of STAT3. However, continued upregulation of cytokines after CD40 KD suggest that TSST-1 interactions with NHEKs may not be solely a CD40-dependent mechanism. Further work, involving immunocytochemistry for colocalization of TSST-1 and CD40 post-treatment, and ELISAs is ongoing. By elucidating the mechanism by which sAgs interact with skin cells during infection, pharmacotherapies may be able to be developed to antagonize these pathways resulting in novel treatments for infection.

O20. Evaluating the relationship between shock, physiologic normalcy, and surgical site infection in trauma laparotomy

Shah-Jahan Dodwad; Krislynn Mueck; Kayla Isbell; Charles Wade; John Harvin; Lillian S. Kao; Michael Wandling

Background:
Patients undergoing trauma laparotomy (TL) suffer from high rates of surgical site infection (SSI). Little is known about the relationship between shock, restoration of physiologic normalcy, and SSI.

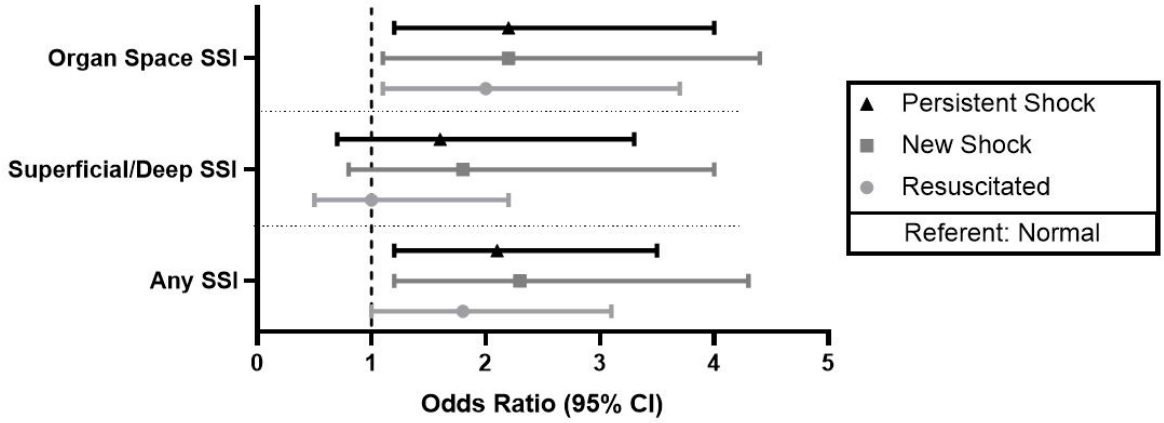
Hypothesis:
We hypothesized that patients who were physiologically normal or resuscitated out of shock would have a lower rate of SSI than those with persistent or new shock by the end of TL.

Methods:
Adult patients who underwent definitive TL at a level 1 trauma center between 2011 and 2019 were included. Shock was defined as having a shock index ≥0.9 or a base excess ≤-6. Patients who were either physiologically normal or in shock throughout TL were classified as “normal” or “persistent shock,” respectively. Patients who were resuscitated from shock were classified as “resuscitated.” Patients who began normal but developed shock by the end of TL were classified as “new shock.” Unadjusted rates

and risk-adjusted odds ratios for organ-space SSI (OS-SSI), superficial/deep SSI (SD-SSI), and any SSI were identified.

Results:
1191 patients were included, 50% “normal,” 20% “persistent shock,” 21% “resuscitated,” and 9% “new shock.” Rates of any SSI were 8.5% for “normal,” 13.6% for “persistent shock,” 11.3% for “resuscitated,” and 24.3% “new shock.” Rates of OS-SSI were 5.8% for “normal,” 11% for “persistent shock,” 8.9% for “resuscitated,” and 17.8% for “new shock.” Rates of SD-SSI were 4.5% for “normal,” 5.5% for “persistent shock,” 4% for “resuscitated,” and 11.2% for “new shock.” After adjusting for covariates selected *a priori*, "resuscitated,” “new shock,” and “persistent shock” were associated with significant increased odds of OS-SSI and any SSI, but no significant increased risk of SD-SSI (see figure).

Relationship between perioperative physiologic status and SSI



Adjusted for age, sex, injury mechanism, injury severity score, and full-thickness small bowel and colon injuries.

Conclusions:
Shock before, during, or after TL, regardless of adequate resuscitation, was associated with an increased odds of OS-SSI and any SSI. These findings highlight the importance of maintenance of peri-operative physiologic normalcy in TL.