PATTERN-BASED ANALYSIS OF GENE EXPRESSION PROFILE BY CANONICAL DISCRIMINANT ANALYSIS COULD IDENTIFY THE PATHOPHYSIOLOGY REGARDLESS OF THE SEVERITY

Goro Tajima MD, PhD, Eri Uemura MD, Ayako Tokunaga PhD, Miyuki Miura, Takahiro Umehara PhD, Kazuya Ikematsu MD, PhD, Osamu Tasaki MD, PhD
Nagasaki University Hospital Acute & Critical Care Center

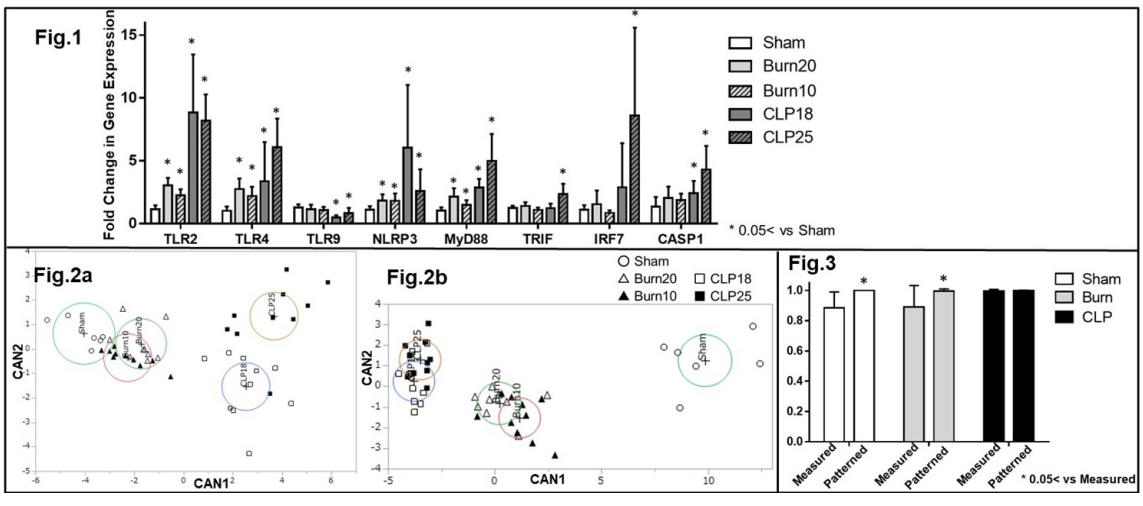
Invited Discussant: Lawrence Diebel, MD

Introduction: Under the severe systemic inflammation, it is difficult to identify the pathophysiology using a single biomarker which varies according to the severity. We reported that there were distinctive patterns of gene expression of the innate immune receptors according to the injury in 76th AAST meeting. We aimed to clarify that the pattern-based analysis of the gene expression profile could determine the pathophysiology regardless of the severity.

Methods: We employed cecal ligation and puncture (CLP) using 18G and 25G needle, and 20% and 10% full thickness burn injury model for the different severity inflammation. C57BL/6 mice underwent sham (n=6), CLP18, 25 (n=10 in each), or Burn20, 10 (n=10 in each). 24 hours after injury, mice were sacrificed, and total RNA was extracted from whole blood. Using quantitative RT-PCR, we investigated gene expression of innate immune receptors and signaling molecules (Fig.1). All the measured data was scaled to the relative value divided by the largest mean value in the parameters for patterning. Canonical discriminant analysis (CDA) was performed using the measured data and the patterned data, and compared the diagnostic rate according to the injury regardless of the severity

Results: Gene expressions of TLR2, TLR4, NLRP3 and MyD88 were significantly increased in all the groups compared to sham ($p < 0.05$). That of TLR9 was significantly decreased in both CLP groups compared to sham ($p < 0.05$) (Fig.1). CDA using measured data could considerably distinguish each groups (Fig.2a). On the other hand, CDA using patterned data showed identification according to the pathophysiology more clearly (Fig.2b). Pattern-based analysis showed higher diagnostic rate in sham (88.5% vs 100%) and Burn (88.2% vs 99.5%) regardless of the severity compared to measured data ($p < 0.05$) (Fig.3).

Conclusion: Pattern-based analysis of the gene expression by CDA could identify the pathophysiology clearly regardless of the severity.



Session XI: Quickshot Session I 1-13
Quickshot 2: 9:06 AM - 9:12 AM

CAN THE USE OF A PUBLICLY-AVAILABLE SAFETY ALERT APP IMPROVE URBAN TRAUMA TEAM PRE-HOSPITAL NOTIFICATION?

Leandra Krowsoski MD, Charles DiMaggio PhD, Rafael Sedaghatzandi, Spiros Frangos MD, Cherisse Berry MD, Marko Bukur MD, Manish Tandon MD, Douglas Isaacs MD, H. Leon Pachter MD, Michael Klein MD
NYU School of Medicine

Invited Discussant: John Porter, MD

Introduction: Pre-hospital notification is a core component of mature trauma systems and is associated with improved survival. Although Emergency Medical Services (EMS) commonly provide pre-notifications, numerous factors, including primarily focusing on patient care, may delay communications. Citizen® is a publicly-available mobile app that monitors emergency radio transmissions to inform users of surrounding urban area safety threats. This app has been used informally by trauma surgeons at our institution to stay apprised of nearby public safety incidents that could potentially lead to trauma team activations. We hypothesized that the app may provide earlier pre-notification than conventional EMS contact. The objective of this study was to assess the ability of this app to provide timelier trauma team pre-notification and to investigate the accuracy of the information provided.

Methods: All trauma activation alerts at an urban Level 1 trauma center over a two-year period (July 2017-June 2019) were retrospectively reviewed. These alerts were compared to public safety alerts broadcast by the Citizen® app within the trauma center's catchment area over the same timeframe and matched by incident using temporal, geographic, mechanistic, and demographic information. Only incidents that were deemed a match were included in the analysis. Our primary outcome was the difference in notification times between EMS-prompted hospital notification and the app notification. Information and timestamps between traditional notifications (i.e. field EMS to central dispatch to hospital) and the app were compared using the Mann-Whitney U test. We estimated agreement and Cohen's kappa for interrater reliability between sources for injury causes and mechanisms, as well as the sensitivity, specificity and predictive value of the app compared to EMS notifications.

Results: One hundred twelve subjects were matched from 107 incidents. Citizen® app notifications preceded EMS 95.5% of the time (107/112). The mean difference between EMS and app notification times was 42 minutes (95% CI 32, 52) with a range of -15 minutes to 329 minutes. Ten patients involved in five multiple-casualty incidents (MCI) were identified; all were categorized as MCIs by the app an average of 36 minutes before the traditional system (95% CI 25, 47), with notification times ranging from 9 minutes to 56 minutes earlier (Figure 1). Under a non-parametric paired Mann-Whitney U test, the time differences for notifications were statistically significant for both MCI ($p=0.006$) and individual incidents ($p < 0.001$). Overall agreement on mechanism of injury for the two sources was 69.6% with a kappa of 0.61 ($p < 0.001$); the app was most accurate in correctly identifying gunshot wounds with a sensitivity, specificity, and predictive value all greater than 90%.

Conclusions: A publicly-available mobile app that informs users about community safety incidents can provide timely trauma team pre-notification with reasonable information accuracy. Further studies are needed to define how to best integrate crime surveillance and safety alert mobile apps into current pre-notification processes to strengthen 21 st-century trauma communication systems.

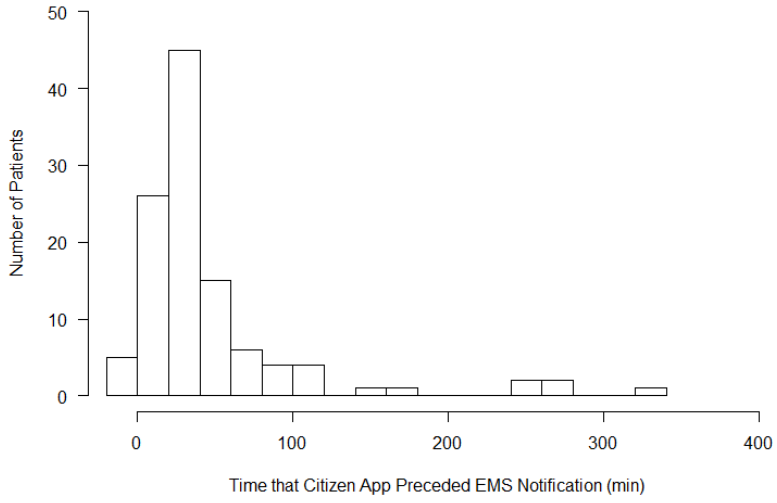


Figure 1: Differences in Notification Times

DAYS THAWED DOES NOT AFFECT SURVIVAL, BLEEDING, OR BIOMARKERS IN PATIENTS RECEIVING PREHOSPITAL FRESH FROZEN PLASMA: PAMER SECONDARY ANALYSIS

Katherine Reitz MD, Daniel Gruen PhD, Francis X. Guyette MD, Joshua B. Brown MD, MSc, Mark Yazer MD, Brian Daley MD, MBA, Richard S. Miller MD, Brian G. Harbrecht MD, Jeffrey A. Claridge MD, MSc, Herbert A. Phelan, III MD, Brian Zuckerbraun MD, Jason Sperry MD
UPMC

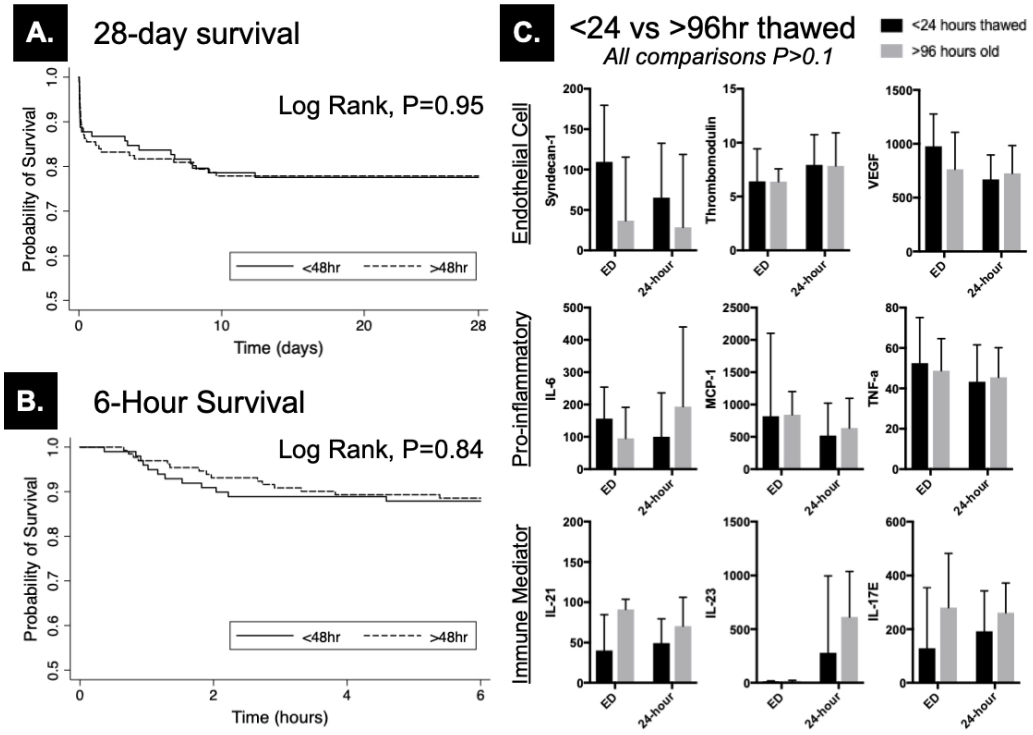
Invited Discussant: Martin Schreiber, MD

Introduction: Prehospital plasma administration during air medical transport reduces the endotheliopathy of trauma, circulating pro-inflammatory cytokines, and 28-day mortality among traumatically injured patients at risk of hemorrhagic shock. To facilitate prehospital plasma administration, each hospital base stored thawed plasma for up to 5 days (120 hours). Animal models suggest longer storage of thawed plasma increases the risk of early death. However, no clinical data currently exists evaluating the age of thawed plasma and its association with post-traumatic mortality.

Methods: We performed a secondary analysis from the prehospital plasma administration randomized controlled trial, PAMPer. Patients at risk for hemorrhagic shock were randomized 1:1 to 2 units of prehospital plasma or standard of care. Among patients randomized to plasma, we dichotomized the days of thawed plasma into < 48 and > 48 hours comparing baseline characteristics and 24-hour transfusion requirements. Survival analysis was performed to determine the survival benefit of plasma by time thawed. Inflammatory cytokines were quantified in those with plasma thawed < 24 and > 96 hours at emergency department (ED) admission and 24 hours later, compared with Kruskal–Wallis.

Results: 230 patients received prehospital plasma, 99 (43%) received plasma thawed for < 48 hours. There were no statistically or clinically significant differences in age (45 years [SD 17]), mechanism of injury (blunt, N=46 [20%]), injury severity score (24 [SD 15]), prehospital interval (47 minutes [SD 21]), or interfacility transfers (N=52 [23%]; all p>0.5). There were also no differences in ED vitals: heart rate (107 [SD 22]), systolic blood pressure (106mmHg [SD 33]), and Glasgow coma scale (8 [SD 6]; all p > 0.2). Kaplan-Meier curve (**FigA, B**) demonstrates no differences in 28-day (p=0.95) or 6-hour (p=0.84) mortality. There were no differences 24-hour packed red blood cell transfusions (< 48, 3 [IQR 1,6] vs > 48, 3 [IQR 0, 7]; p=0.52) or multisystem organ failure (< 48 hours, N=64 [65%] vs > 48 hours, N=81 [62%]; p=0.66) among > 24-hour survivors (N=198 [86%]). There were no differences in endothelial, pro-inflammatory, immune cytokines among plasma thawed for < 24 or > 96 hours (all P > 0.1; **FigC**).

Conclusion: Despite preclinical data, we provide no evidence that longer storage of thawed plasma confers negative outcomes among patients at risk of hemorrhagic shock.



STANDARDIZATION OF OPIOID PRESCRIPTION AFTER TRAUMA (STOP TRAUMA): A PROSPECTIVE INTERVENTION TO REDUCE EXCESSIVE OPIOID PRESCRIPTION.

Eric Walser MD, Amy Makish, Patrick Muprhy MD, MSc, MPH, Luke Hartford MD, MSc, Laura Allen MSc, Collin Clarke MD, Daryl Gray MD, Richard Hilsden MD, Neil Parry MD, Ken Leslie MD, Kelly Vogt MD, MSc
Western University

Invited Discussant: Alexandra Briggs, MD

Introduction: Opioid abuse is one of the major contemporary issues in health care, and trauma patients are at high risk for post-injury opioid use disorders. We undertook this study to determine if the introduction of a standardized pain management pathway was associated with 1) at least equivalent pain control and 2) a reduction in opioid prescription amongst patients admitted to a Canadian Level I trauma centre.

Methods: This was a prospective trial between January 2019 and February 2020, with a standardized pain management pathway introduced in September 2019. Trauma patients admitted for > 24 hours and discharged home were eligible. Those with an ICU stay > 14 days, age > 85 years, or those using opioids at admission were excluded. The intervention included: 1) physician and nursing education; 2) emphasis on multi- modal analgesia; 3) patient and family education. Rational prescribing based on inpatient opioid use was recommended, but discharge prescriptions were at clinician discretion. Patients completed a modified Brief Pain Inventory at their first trauma clinic visit (within 2 weeks of discharge). The primary outcome was patient-reported pain on a 10-point scale, compared using a two-sample *t*-test for non-inferiority (NI). Sample size for NI ($p < 0.025$) was determined *a priori* to be 44 patients in each group. Secondary outcomes were compared using chi-square test, Mann-Whitney U test, and independent samples *t*-test, where appropriate.

Results: A total of 147 patients were included; 100 pre- intervention (Pre-I) and 47 post- intervention (Post-I). The mean pain scores were 4.7 (SD 2.3) in the Pre-I phase and 4.3 (SD 2.6) in the Post-I phase (mean difference -0.4, 97.5% CI -1.4 to 0.5, $p < 0.001$ for NI, $p=0.34$ for superiority). Secondary outcomes are compared in Table 1. The reduction in discharge prescription OME (oral morphine equivalents) corresponds to a 38% reduction in overall opioid prescription.

Variables	Pre-I (n=100)	Post-I (n=47)	*p*
Age, mean (SD)	49.8 (18.4)	48.8 (18.5)	0.76
Gender, n male (%)	77 (77)	32 (68)	0.31
LOS, median days [IQR]	3.5 [2-5]	3.0 [2-6]	0.77
ISS, mean (SD)	15.5 (7.7)	14.9 (8.5)	0.66
Good[a] pain control in hospital, n (%)	76 (76)	32 (68)	0.31
Good[a] pain control post- discharge, n (%)	59 (59)	26 (53)	0.67
Discharge Rx total OME, median [IQR]	**72 [0-144]**	**0 [0-144]**	**0.013***
Patients discharged with opioid Rx, n (%)	67 (67)	22 (47)	0.019*
Patients receiving additional opioid Rx post-discharge, n (%)	22 (22)	9 (19)	0.67

a- Patients rating their pain control Good or Very Good on a 5- point Likert scale, **Rx**- prescription

Table 1. Characteristics and outcomes of patients treated pre- and post- intervention.

Conclusion: A standardized multimodal pain pathway with emphasis on patient and provider education was NI with respect to post-discharge pain and significantly reduced opioid prescription following trauma. We believe implementation of similar protocols will have a significant impact on the opioid crisis.

Session XI: Quickshot Session I 1-13
Quickshot 5: 9:24 AM - 9:30 AM

THE RELATIONSHIP BETWEEN CORTISOL REPONSE AND THE DEVELOPMENT OF CHRONIC PAIN IN TRAUMATICALLY INJURED PATIENTS

Colleen Trevino PhD, Timothy Geier PhD, Rachel S. Morris MD, Terri deRoon-Cassini PhD
Medical College of Wisconsin

Invited Discussant: Preston Miller, MD

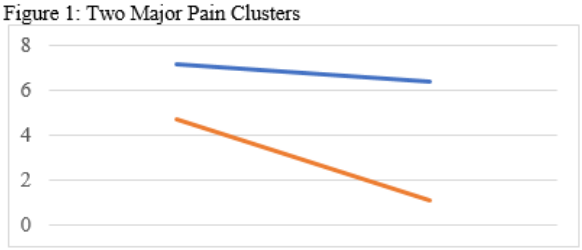
Introduction: The relationship between pain and stress is widely accepted, yet the underlying neuroendocrine mechanisms involved are less understood. Cortisol secretion during a non–pain-related stress response, found during the fight or flight response, may distract attention from a concurrent painful stimulus, thereby inhibiting pain. However, when pain is the stressor, cortisol secretion may intensify its experience and condition a fear-based memory of pain. Although these hypotheses have not been validated, it seems logical cortisol dysfunction contributes to the development of chronic pain. This study attempts to determine the relationship between acute pain, chronic pain, and the stress response in the traumatically injured population.

Methods: Secondary analyses of a prospective observational study with participants admitted to a Midwestern Adult Level I Trauma Center post traumatic injury, with interview and serum cortisol taken at hospitalization (baseline) and 6 months after discharge was completed using Ward's Method hierarchical cluster analysis, Pearson's correlations, and linear regressions.

Results: Two major clusters were identified (Figure 1). The Chronic Pain (CP) group were those participants who had severe pain at discharge and continued to have severe pain. The Resolved Pain (RP) group were those who had moderate pain at discharge and their pain improved or resolved. Pain score at discharge significantly, negatively correlated with baseline cortisol levels (r= -0.142, p=0.02). Minority status, single individuals, low cortisol at baseline, and greater psychological distress at baseline significantly increased the likelihood of developing chronic pain (Figure 2).

Conclusions: Higher baseline pain scores were associated with low cortisol. Low cortisol and greater psychological stress, which also appear to be associated with minority status and single individuals, contribute to the development of chronic pain in the traumatically injured population. Trauma victims who do not have an adequate cortisol response to acute injury and pain are at risk for the development of chronic pain after injury. Further exploration is needed to determine the etiology of a blunted cortisol response and may be associated with pre-injury stressors.

Figure 1: Two Major Pain Clusters



		Mean Baseline Pain Rating (SD)	Mean 6 Month Pain Rating (SD)
Chronic Pain	n=45	7.2 (2.1)	6.4 (1.9)
Resolved Pain	n=123	4.7 (2.5)	1.1 (1.4)

Figure 2: Likelihood of Developing Chronic Pain

	n Chronic Pain	n Resolved Pain		OR (95% CI)
High BL Cortisol	13	72	15.3% of high BL cortisol with CP	0.29 (0.14-0.60)*
Low BL Cortisol	32	51	38.6% of low BL cortisol with CP	1.00 (1.00-1.00)*
Minority	31	57	35.2% of minorities with CP	2.56 (1.24-5.29)*
White	14	66	17.5% of whites with CP	1.00 (1.00-1.00)*
No Relationship	23	40	57.7% of singles with CP	2.12 (1.06-4.25)*
Relationship	22	81	27.2% of relationship with CP	1.00 (1.00-1.00)*

$P < 0.001$

Session XI: Quickshot Session I 1-13
Quickshot 6: 9:30 AM - 9:36 AM

TRAUMA CENTER DESIGNATION CAN NULIFY THE EFFECT OF CARE DISCONTINUITY

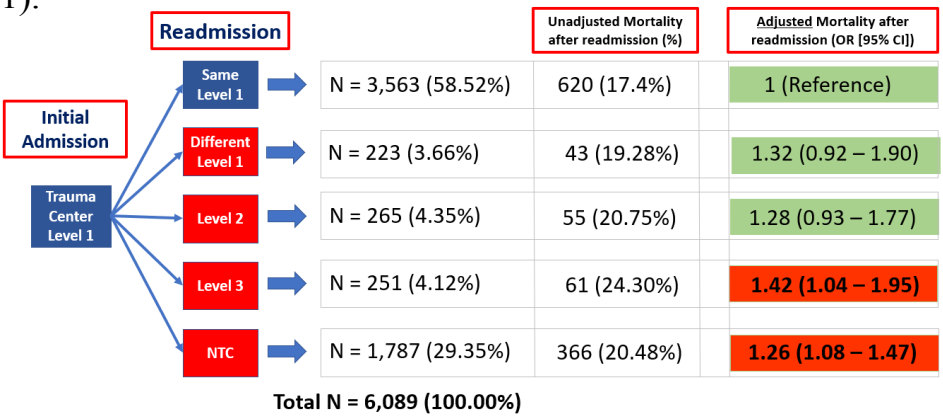
Manuel Castillo-Angeles MD, MPH, Cheryl Zogg MPH, Molly Jarman PhD, MPH, Stephanie Nitzschke MD, Reza Askari MD, Zara Cooper MD, MSc, Ali Salim MD, Joaquim Havens MD
Brigham and Women's Hospital

Invited Discussant: Daniel Margulies, MD

Introduction: Care discontinuity, readmission to a non-index hospital following surgery, has been shown to increase mortality in emergency general surgery. It is unknown if this effect exists in trauma patients. We hypothesize that the established systems and standards of care associated with trauma center designation would negate this effect. Our goal was to determine the effect of trauma center designation on mortality in the setting of care discontinuity.

Methods: This was a retrospective analysis of Medicare inpatient claims (2014-2015) of older adult trauma patients admitted to Level 1 trauma centers. Care discontinuity was defined as readmission within 30 days to a non-index hospital. Trauma center designation was categorized as Level 1, 2, 3, and Non-trauma centers (NTC). Multivariate logistic regression analysis was performed to determine the association of trauma center designation, care discontinuity and mortality.

Results: There were 188,734 patients admitted to a level 1 trauma center. Of these, 6,089 (20.22%) were readmitted within 30 days of discharge. Overall 30 day-mortality after readmission was 20.8%. After adjusted analysis, there was no difference in mortality between patients readmitted to the same level 1 (index), different level 1 (non-index), or level 2 trauma centers. Patients readmitted to level 3 or NTC had higher odds of mortality (Figure 1).



Conclusion: Mortality after readmission for trauma in the elderly is very high. Unlike emergency general surgery, care discontinuity within similarly designated trauma centers is not associated with increased mortality. Readmission to a less advanced or non trauma center is associated with increased mortality. It is likely the process measures and established standards of care associated with trauma center designation contribute to this outcome. This supports the use standardized processes of care in other at-risk patient groups, including emergency general surgery.

APHERESIS PLATELETS HAVE COMPROMISED AGGREGATION COMPARED TO POOLED PLATELETS

Christina Riojas MD, Michael Ekaney PhD, Juan Carillo-Garcia BS, Iain McKillop PhD, Susan Evans MD
Carolinas Medical Center, Atrium Health

Invited Discussant: Noelle Saillant, MD

BACKGROUND: Platelets, which are routinely used for the clinical correction of coagulopathy, have limited availability due to short shelf life (5 days). Previous studies have identified cold storage and cytochrome c (cyt c) supplementation as protective of ex vivo platelet function in pooled platelets and cold stored whole blood. Because apheresis platelets are the predominant source of stored platelets, we sought to determine the effect of storage temperature and cyt c on platelet aggregation function in apheresis platelets stored in platelet additive solutions (PAS). We hypothesized that cold storage and cyt c supplementation preserves function of apheresis platelets.

METHODS: Apheresed platelets (n=5) were collected into InterSol-PAS (Fresenius Kabi), and divided into 3 separate bags designated as control (vehicle), cyt c-d1 (100μM cyt c added day 1) and cyt c-d1/10 (100μM cyt c added day 1 and day 10). Platelets were stored at 4°C without agitation. Sequential aliquots (5 mL; days 1, 5, 10, and 15) were collected and platelet mapping thromboelastography (PM-TEG) assessing adenosine diphosphate (ADP) and arachidonic acid (AA) receptor platelet stimulation, oxygen consumption, and biochemical parameters were measured. In order to establish baseline function for comparison, platelet coagulation was determined on day 1 in pooled platelets from 5 donors.

RESULTS: Baseline ADP and AA induced aggregation were substantially impaired in apheresis platelets compared to pooled platelets, and this persisted throughout storage even with cyt c supplementation. Apheresis platelets also demonstrated a decline in oxygen consumption at day 5, 10 and 15 compared to day 1. Initial lactate concentration was similar for apheresis and pooled platelet aliquots, although pH was significantly lower in apheresis platelet aliquots. Lactate concentration rose significantly in the apheresis platelet aliquots throughout storage compared to baseline.

CONCLUSIONS: Apheresis platelets demonstrate markedly depressed aggregation function immediately after collection compared to pooled platelets which does not recover despite administration of cyt c. This dramatic aggregation suppression may be attributed to the mechanical nature of the apheresis collection process, which is fundamentally different than the process for collecting pooled platelets. The platelet additive solution may also have an impact on the decreased function. Subsequent studies to determine the impact of this suppressed ex vivo aggregation on in vivo bleeding are warranted. If decreased in vivo function is shown to correlate with poor effect from platelet transfusion, techniques to ameliorate or avoid this would help optimize use of platelets.

Session XI: Quickshot Session I 1-13
Quickshot 8: 9:42 AM - 9:48 AM

TRAUMA PATIENT TRANSPORT TIMES AND MORTALITY UNCHANGED DESPITE TRAUMA CENTER PROLIFERATION

Michael Jones MD, Jordan Paulus BS, Kristina Chapple PhD, James Bogert MD, Hahn Soe-Lin MD, Jordan Jacobs MD, Jordan A. Weinberg MD
Dignity Health, St. Joseph's Hospital and Medical Center

Invited Discussant: Nicholas Namias, MD, MBA

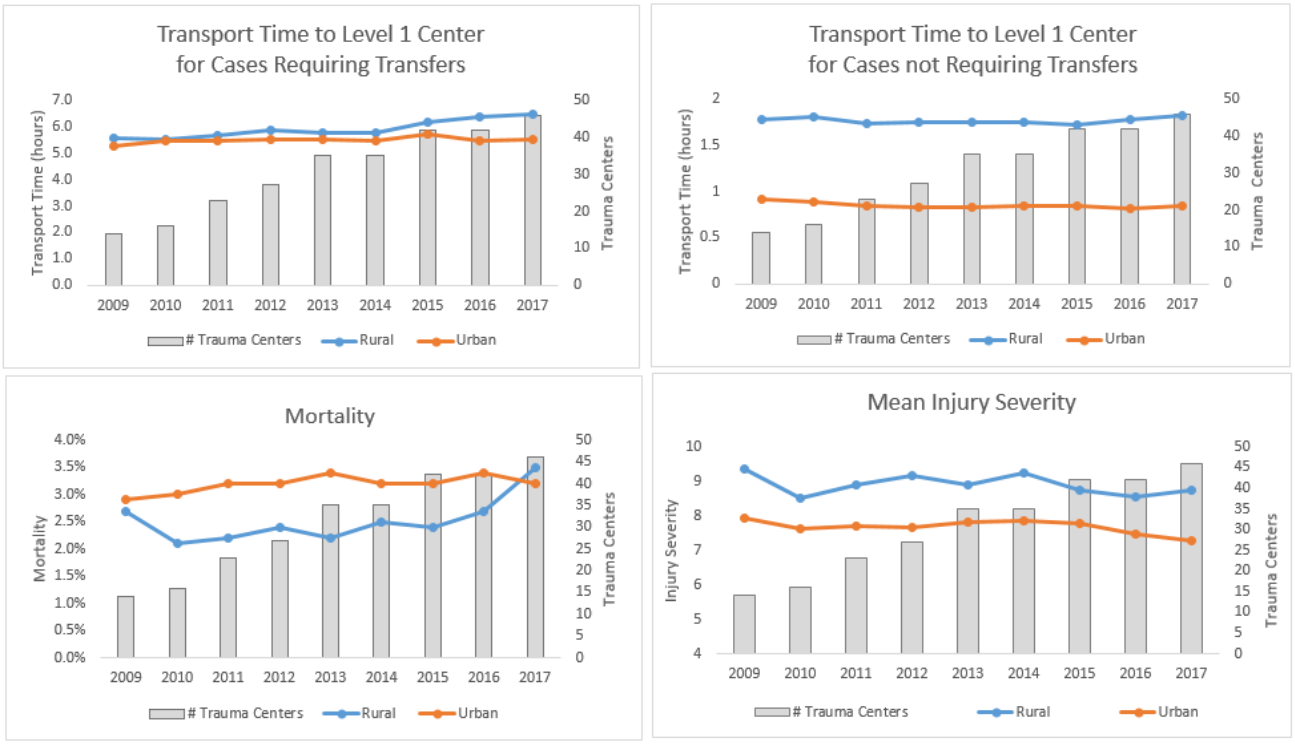
Introduction: In certain regions of the U.S. there has been a dramatic proliferation of trauma centers. The goal of our study was to evaluate transport times and patient mortality during this period of trauma center proliferation.

Methods: Aggregated data summarizing level 1 trauma center admissions in Arizona between 2009 and 2017 were provided to our institution by the Arizona Department of Health Services. We evaluated transport times, injury severity and mortality for both rural and urban injuries.

Results: Data included statistics summarizing 230,505 level 1 trauma admissions in the state of Arizona. The number of state-designated trauma centers during this time increased from 14 to 46, with level 1 centers increasing from 8 to 13. The median scene to level 1 transport time remained relatively unchanged in urban areas from 1.0 to 0.98 hours from 2009 to 2017. In rural areas, transport times were nearly three times longer with the median scene to facility time increasing from 2.59 to 3.56 hours. Figure 1 demonstrates median transport times to level 1 centers for urban and rural with (upper left) and without (upper right) interfacility transfers. From 2009 to 2017, there was an upward trend in both urban and rural mortality by 0.3% (2.9% vs 3.2%) and 0.8% (2.7% vs. 3.5%), respectively (Figure 1 – lower left); Slight decreases in mean ISS (rural 9.35 vs. 8.23; urban 7.94 vs 7.28) were observed over this period (Figure 1 – lower right).

Conclusion: Despite the 3-fold increase in the number of state-designated trauma centers, neither transport time nor mortality has decreased in both rural and urban areas. These findings highlight the need for regulatory oversight regarding the number and geographic placement of trauma centers.

Figure 1. Transport times, mortality and injury severity for level 1 trauma center admissions in rural and urban areas.



Session XI: Quickshot Session I 1-13
Quickshot 9: 9:48 AM - 9:54 AM

IMMUNE SIGNATURES CORRELATE WITH CLINICAL OUTCOME AFTER TRAUMA INJURY

April Mendoza MD, MPH, Susan Raju Paul MD, Majed El Hechi MD, Leon Naar MD, Charlie Nederpelt, Inge Van Erp, Sarah Mikdad, George Velmahos MD, PhD, Mark Poznansky MD, PhD, Patrick Reeves PhD
Massachusetts General Hospital

Invited Discussant: Jennifer Leonard, MD, PhD

Introduction: Major injury results in an early cascade of immunologic responses that can increase susceptibility to complications including infection. We propose that detailed immune profiling can identify immune signatures that correspond to patient outcomes.

Methods: Trauma patients were prospectively enrolled between Sept 2018 and December 2019. Serial whole blood samples were obtained from trauma patients (median ISS 24 [21-34]) at days 1 and 3 after injury, and from age- and sex-matched uninjured controls using a standardized protocol for fixation, storage, and staining. Samples were labeled for mass cytometry with a 38-marker panel. Computational clustering of immune cells and a Spearman's analysis was used to identify correlations between cell population frequencies, clinical measures, and patient outcomes (Figure). Strength of correlation was determined by R2 values and subsequent analysis of variance was calculated between groups to identify significant changes.

Results: Samples from 18 patients and 4 controls were collected. Analysis revealed 10 immune cell clusters having a R^2 >0.69 that correlated with one or more clinical outcomes. At day 3, neutrophil and other myeloid-origin epitope signatures had a positive correlation with increased ICU and hospital length of stay (LOS). Conversely, CD4 T-cell subtypes such as Th17 and effector T-cell subsets were associated with improved patient outcomes including: decreased ventilator-days (R^2 =-0.76), hospital-acquired pneumonia (R^2=-0.69), and organ dysfunction (R^2=-0.73). An elevation of myeloid dendritic cells by day 3 (p=0.02) was associated with an increased ICU and hospital LOS.

Conclusion: Computational analyses of deep immune profiling of trauma recovery demonstrate an association with specific immune populations and patient outcomes early after injury. Our results suggest that alterations in myeloid-origin cell types, namely neutrophils and other granulocytic subsets, likely contribute to immune dysfunction after injury. Preservation of effector-T cell functions correspond with decreased hospital LOS and less organ dysfunction. Overall, these data demonstrate the central role of innate immunity in the dysbiosis observed after severe injury and the importance of a competent adaptive response. Future studies will further characterize the myeloid subsets to better understand their role in adaptive immunity recovery and behavior.

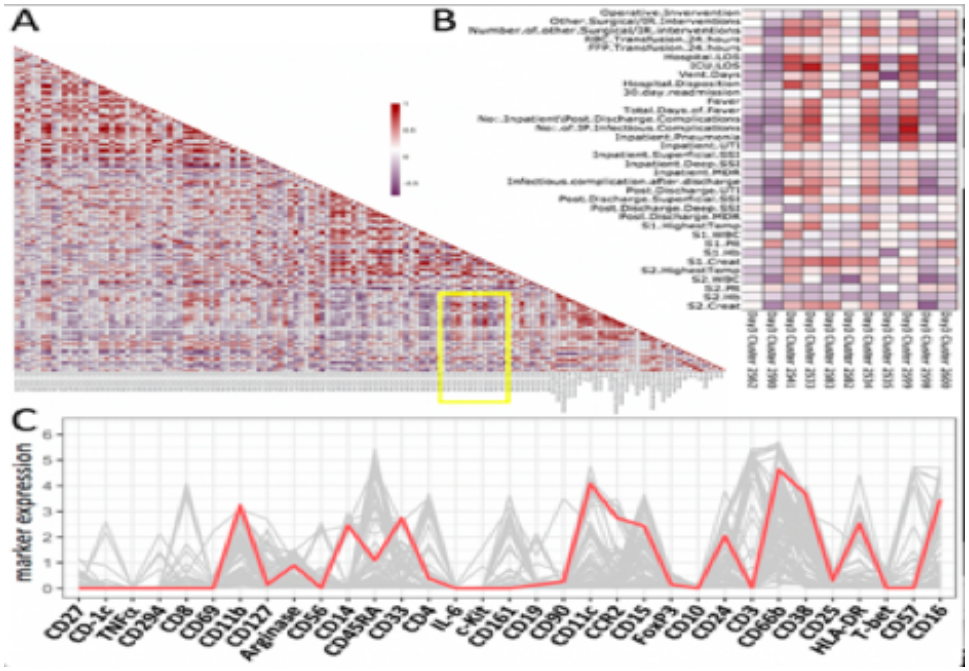


Figure. Correlation of immune clusters to clinical data. A. Color coded matrix of all clusters detected from 18 patients across day 1 and day 3, correlated to clinical measures on a scale of 1 to -1. Correlation values were determined based on cluster frequency relative to clinical measures for individual patients. B. Expanded view of yellow box from panel A. C. Parallel coordinate plot illustrating the phenotypic profile of a single cluster (red line), all other clusters mapped for context (grey lines).

THE EFFECT OF THE AFFORDABLE CARE ACT ON RATES OF INPATIENT REHABILITATION HOSPITAL ADMISSION IN A MATURE TRAUMA SYSTEM

Frederick Rogers MD, Tawnya Vernon, Madison Morgan BS, Mike Winter DO,
Alan D. Cook MD, Eric H. Bradburn DO
Penn Medicine Lancaster General Health

Invited Discussant: Edward Cornwell, III, MD

INTRODUCTION: The beneficial effects of acute rehabilitation for trauma patient are well documented but can be limited due to insurance coverage. The Patient Protection and Affordable Care Act (ACA) went into effect on March 23, 2010. We sought to analyze the likelihood of discharge to rehab for trauma patient before and after the implementation of the ACA. We hypothesized that there would be a higher rate of inpatient rehabilitation hospital (IRH) admission after the ACA was put into effect.

METHODS: The Pennsylvania Trauma Outcome Study (PTOS) database was retrospectively queried from 2003-2017 for all trauma patients admitted to accredited trauma centers in Pennsylvania who also had a Functional Status at Discharge (FSD). Admission to an IRH was determined using discharge destination. Two categories were created to represent periods before and after ACA was implemented: 2003-2009 (pre-ACA) and 2010-2017 (post-ACA). A multilevel mixed-effects logistic regression model controlling for age, injury severity, and FSD assessed the adjusted impact of ACA implementation on IRH admissions.

RESULTS: From the PTOS query, 341,254 patients had FSD scores and of these patients, 47,523 (13.9%) were admitted to IRH. Patients who were severely injured were more likely to be admitted to IRH. Compared to FSD scores signifying complete independence at discharge, those with lower FSD had significantly increased odds of IRH admission. The odds of IRH admission post-ACA implementation significantly increased when compared to pre-ACA years (AOR: 1.10; 95%CI: 1.08-1.13, $p < 0.001$, AUROC: 0.826).

CONCLUSION: The implementation of the ACA significantly increased the likelihood of discharge to IRH for trauma patients. This suggests that the ACA may have positively impacted access to inpatient rehabilitation centers.

Table 1. Multivariate analysis of ACA implementation on rehab admission rates from the PTOS database

		IRH Admission
Variable	**AOR** (95% CI)	*p*
ACA implementation	**1.10** [1.08-1.13]	**<0.001**
ISS		
Mild: 0-9	Reference	---
Moderate: 10-16	1.90 [1.85-1.96]	<0.001
Severe: 17-25	3.46 [3.36-3.56]	<0.001
Profound: 26-75	7.92 [7.63-8.23]	<0.001
FSD		
Complete Independence: 20	Reference	---
Independence with Device: 15-19	11.68 [11.25-12.14]	<0.001
Modified Dependence: 10-14	18.42 [17.61-19.27]	<0.001
Complete Dependence: 5-9	15.37 [14.47-16.33]	<0.001
		AUROC: 0.826

PREDICTORS OF SURVIVAL AFTER CRANIOTOMY IN GERIATRIC PATIENTS WITH TRAUMATIC BRAIN INJURY

Muhammad Zeeshan MD, Kartik Prabhakaran MD, Faisal Jehan MD, James Feeney MD, Muhammad Khan MD, Rifat Latifi MD, Peter Rhee MD, MPH
Westchester Medical Center

Invited Discussant: Jennifer Hubbard, MD

Introduction: As the population of trauma patients continues to age, traumatic brain injury (TBI) poses a high risk of morbidity and mortality amongst the elderly. While craniotomy can be a potentially life-saving intervention in patients with TBI, it is unclear as to how many and which type of geriatric trauma patient would benefit from craniotomy. The aim of our study was to assess the factors predictive of survival in geriatric TBI patients who underwent craniotomy.

Methods: We performed a 2-year analysis of ACS-TQIP database (2015-2016) and included all geriatric trauma patients (> 65y) with isolated severe TBI who underwent craniotomy. We excluded patients with concomitant severe injuries to other organs (i.e. any other body region AIS > 2), had penetrating mechanism of injury, who were transferred or dead on arrival. Patients were studied for demographic data, pre-hospital anticoagulant use, ISS, AIS-Head, and frailty. Frailty was calculated using the modified frailty index (mFI). Our principal outcome measure was in-hospital mortality. Multivariate regression analysis was performed to identify predictors of survival.

Results: We identified 46,359 geriatric patients with isolated severe TBI out of which 9.9% (n=4,621) patients underwent craniotomy and were included in our analysis. Mean age was 71+7y, 63% were male, and 80% were caucasian. Overall mortality was 27% (n=1247). On regression analysis, age < 84 (OR: 2.14[1.8-3.1]), mFI < 0.27 measured by modified frailty index (2.49[2.01-4.57]), ≤ 2 concomitant morphologies of TBI (3.24 [2.45 – 5.64]), and absence of pre-hospital anticoagulants (4.21 [3.21 – 8.210] were independently associated with survival.

Conclusion: One out of every 10 geriatric trauma patients with isolated severe TBI underwent craniotomy, and almost 1 out of every 4 patients who underwent craniotomy died. Younger age (< 84), low frailty index, single morphology of intracranial bleed, and absence of pre-hospital anticoagulant use are independently associated with a higher rate of survival. Identifying predictors of survival after craniotomy for TBI may improve resource utilization amongst geriatric trauma patients

Session XI: Quickshot Session I 1-13
Quickshot 12: 10:06 AM - 10:12 AM

ADMINISTRATION OF VALPROIC ACID IN CLINICALLY APPROVED DOSE IMPROVES NEUROLOGIC RECOVERY AND DECREASES BRAIN LESION SIZE IN SWINE SUBJECTED TO HEMORRHAGIC SHOCK AND TRAUMATIC BRAIN INJURY

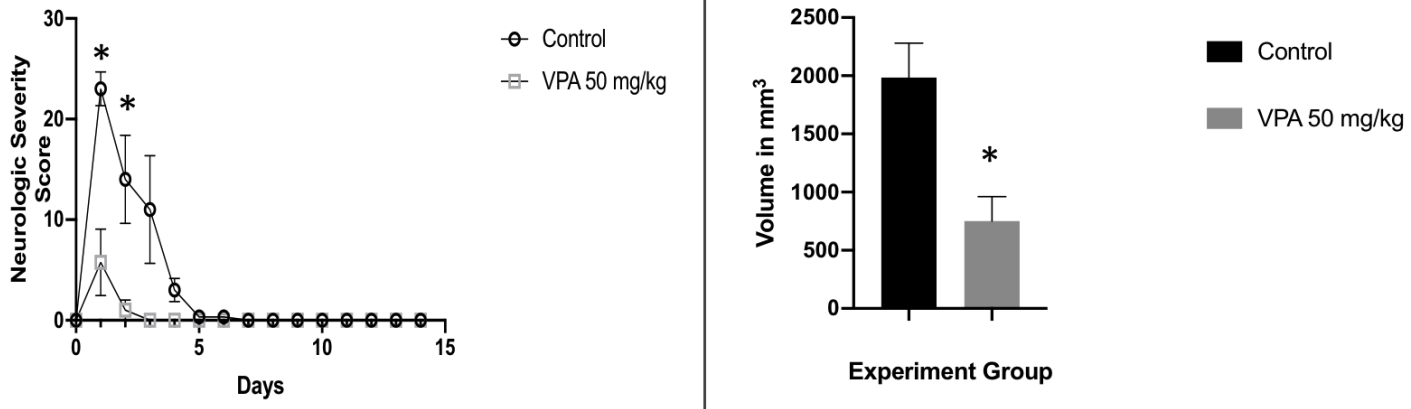
Glenn Wakam MD, Ben Biesterveld MD, Michael Kemp MD, Umar F. Bhatti MD, Rachel O'Connell BS, Alizeh Shamshad BS, Ali Siddiqui BS, Aaron Williams MD, Hasan B. Alam MD
University of Michigan

Invited Discussant: Ali Salim, MD

Background: Hemorrhagic shock and traumatic brain injury (TBI) continue to be the leading causes of morbidity and mortality in trauma. We have previously shown that treatment with valproic acid (VPA) at a dose of 150 mg/kg improves neurologic recovery and decreases brain lesion size in swine models of TBI and hemorrhage. However, 150 mg/kg is higher than the Food and Drug Administration (FDA) approved dose of 60 mg/kg, which raises concerns about dose related toxicity. In order to translate this treatment into clinical practice, validation of drug efficacy at a lower dose is necessary. In this large animal study, we evaluated neurologic outcomes, brain lesion size, and drug pharmacokinetics after administration of an FDA approved dose of VPA. We hypothesized that a dose of 50 mg/kg will improve neurologic outcomes and decrease brain lesion size in swine subjected to TBI and hemorrhagic shock

Methods: Yorkshire swine (n = 4/cohort) were subjected to TBI and hemorrhagic shock (40% of total blood volume). Animals remained in hypovolemic shock for 2 hours (simulating delayed medic response time in the battlefield) before resuscitation with normal saline (3x hemorrhage volume; control) or normal saline + single dose VPA (50 mg/kg). Neurologic severity scores [Range: 0 (no deficit)-32 (severe deficit)] were assessed daily for 14 days, and brain lesion size was measured using magnetic resonance imaging on postinjury day (PID) 3.

Results: Shock severity, response to resuscitation, and laboratory data were similar in both groups. VPA treated animals demonstrated significantly lower neurological severity scores (Figure) on PID 1 (23±4 versus 5.5±7 in control and VPA groups, respecively; p = 0.003) and PID 2 (14±6 versus 1±3 in the control and VPA groups, respectively; p=0.028). VPA treated animals had significantly smaller brain lesion sizes (1985.1±588.5mm^3 versus 751.3 ±364.7mm^3 in the control and VPA groups (figure), respectively; p=0.025).



Conclusion: In swine subjected to TBI and hemorrhagic shock, administraton of an FDA approved dose of VPA is safe, and associated with smaller brain lesion size and faster neurological recovery. These findings could facilitate earlier translation of VPA into clinical practice for the treatment of TBI.

Session XI: Quickshot Session I 1-13
Quickshot 13: 10:12 AM - 10:18 AM

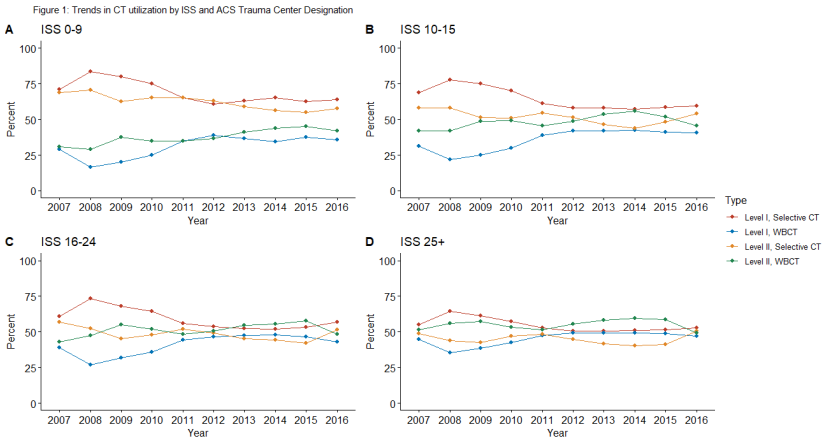
TRENDS IN UTILIZATION OF WHOLE-BODY COMPUTED TOMOGRAPHY IN BLUNT TRAUMA: A 9-YEAR RETROSPECTIVE STUDY USING TRAUMA QUALITY IMPROVEMENT PROJECT (TQIP) DATABASE

Corinne Bunn MD, Brendan Ringhouse MD, Purvi Patel MD, Fred A. Luchette MD, MSc, Richard Gonzalez MD, Marshall Baker MD, MBA
Loyola University Chicago

Invited Discussant: Sharmila Dissanaike, MD

Introduction: Advances in computed tomography (CT) have led to increasing implementation of whole-body CT (WBCT) protocols in blunt trauma. The use of WBCT in awake, clinically stable patients has sparked controversy regarding unnecessary radiation exposure and increase costs of care. We aim to evaluate national trends in the utilization of WBCT imaging in clinically stable, neurologically intact patients admitted to an American College of Surgeons (ACS) level I and II centers after blunt trauma.

Methods: We queried the ACS Trauma Quality Improvement Project (TQIP) database to identify patients aged 18-65 years presenting after MVC to a level I or II trauma center with initial systolic blood pressure (SBP) > 100mg, a Glasgow Coma Scale (GCS) of 15 and having had CT imaging within 2 hours of arrival. WBCT was defined as simultaneous CT of the head, chest and abdomen. A CT of only one or two regions was defined as selective CT. Annual percentages of WBCT vs selective CT for level I and II centers were calculated and stratified by Injury Severity Score (ISS). Univariate analysis was performed to identify variables associated with use of WBCT between trauma centers. Multivariable regression was use to evaluate significance of trend over time and overall risk adjusted odds for WBCT.



Results: A total of 333,559 patients were identified; 202,657 (60.8%) had selective CT and 218,040 (39.8%) had WBCT. In patients with low severity injury (ISS of 0-9), the rate of WBCT at level II centers consistently exceeded that of level I center. Univariate analysis of patients with ISS 0-9 revealed that WBCT was performed more commonly at level II than level I centers in patients discharged directly from the ED (22.0% vs 18.4% p

Conclusion: Over the last 9 years, there has been an increasing utilization of WBCT relative to selective CT in adults after MVC who arrive hemodynamically stable and neurologically intact. In patients with ISS of 0-9, level II trauma centers are utilizing WBCT in patients with no associated head, chest or abdominal injury and patients who do not require surgery more frequently when compared to level I trauma centers.

Session XII: Quickshot Session II 14-26
Quickshot 14: 10:30 AM - 10:36 AM

THE EXTENT TO WHICH GEOGRAPHY EXPLAINS ONE OF TRAUMA'S TROUBLING TRENDS: INSURANCE-BASED DIFFERENCES IN APPROPRIATE INTER-FACILITY TRANSFER

Cheryl K. Zogg PhD, MSc, MPH, Molly Jarman PhD, MPH, Kevin M. Schuster MD, MPH, Adrian A. Maung MD, Kimberly A. Davis MD, MBA
Yale University School of Medicine

Invited Discussant: Kristan Staudenmayer, MD, MSc

Introduction: Trauma systems were developed to facilitate the direct transport and transfer of patients with major and complex traumatic injuries to designated Trauma Centers (TC). Despite efforts to ensure equal access to high-quality trauma care, research suggests that when presenting to non-trauma centers (NTC), uninsured adults are more likely to be transferred, often resulting in more favorable outcomes compared to better-insured patients. Variations in geography have been suggested to explain the trend. The objective of this study was to determine the extent to which geography as measured by (1) clustering of hospitals within state-based emergency health services (EHS) and national trauma referral regions (TRR) and (2) distance/time by road to the nearest L1 or L2 TC account for insurance-based differences in appropriate inter-facility transfer.

Methods: Florida state inpatient (SID) and emergency department (SEDD) claims from 2008-2017 were used to identify adult trauma patients aged 18-64 years initially presenting to NTC Emergency Departments (EDs) with an overall Injury Severity Score (ISS) > 15. Sub-analyses considered adults with gunshot wounds, acetabular fractures, severe traumatic brain injuries, and hand amputations regardless of ISS. In each case, increasingly complex risk-adjusted multilevel (mixed-effects) logistic regression models were used to determine differences in the relative odds of direct admission-vs-transfer and subsequent outcome measures (30-day mortality, readmission, major morbidity).

Results: A total of 19,663 adults with ISS > 15 presenting to NTC EDs satisfied inclusion criteria. Of these, 3,952 adults were uninsured; 32.9% (1,300) of uninsured adults were transferred. In contrast, 18.1% of adults with private insurance (1,478/8,179), 17.2% with Medicaid (465/2,702), 19.1% with Medicare (*e.g.* Social Security Disability; 437/2,286), and 16.5% with other forms of insurance coverage (*e.g.* TRICARE; 416/2,514) were transferred. Corresponding risk-adjusted OR of direct admission-vs-transfer are presented as Model 1 in **Figure** (*e.g.* private-vs-uninsured OR[95%CI]: 2.22[2.04-2.42])**.** Accounting for clustering of hospitals within EHS regions reduced risk-adjusted OR by an average of 2.0% (Model 2; private-vs-uninsured: 2.17[1.98-2.36]]). Within national TRR it reduced risk-adjusted OR by an average of 6.5% (Model 3; private-vs-uninsured: 1.95[1.75-2.15]). Further risk-adjustment for time and distance by road to the nearest L1 or L2 TC explained up to 10.1% of differences in transfer status between patients but did not remove the insurance-based triage effect, nor did it account for resulting differences in outcomes (*e.g.* 30-day mortality admitted-vs-transferred OR[95%CI]: 1.85[1.13-3.04]). Stratification by distance to the nearest L1 or L2 TC further defied expectations, suggesting that the triage disparity actually became more pronounced among NTC EDs with more ready access to higher-level trauma care (lowest tertile: +0.6%, highest tertile -28.4%). Results among condition-specific sub-analyses were similar. No analyses pointed toward geographic clustering of regional insurance triage patterns.

Conclusion: Variations in geography explained part, but not all, of insurance-based differences in trauma system utilization and appropriate inter-facility transfer. The persistence of greater transfer rates and better outcomes among uninsured adult patients questions the success of transfer-guideline implementation and speaks to room for improvement in trauma system structure.

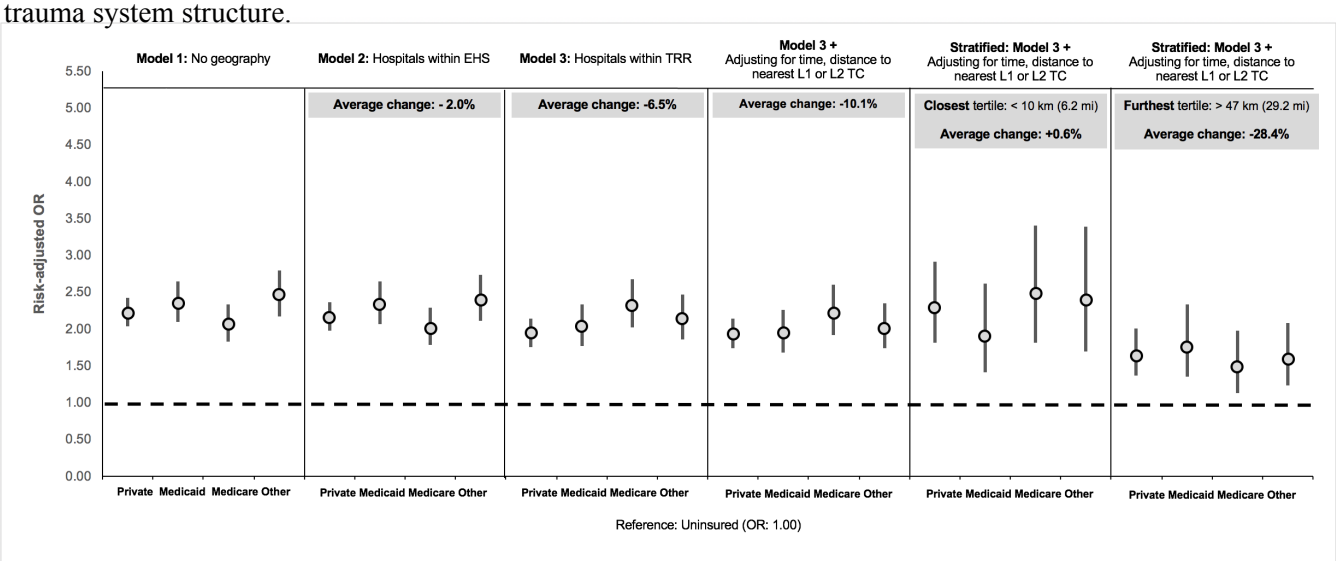


Figure. Results represent risk-adjusted odds ratios (OR; circle) and corresponding 95% confidence intervals (95%CI; black bar) taken from multilevel (mixed-effects) logistic regression models. All models accounted for clustering of patients within hospitals and were risk-adjusted for differences in patient age on index admission, gender, Elixhauser comorbidities, overall ISS, and head/neck AIS.

Session XII: Quickshot Session II 14-26
Quickshot 15: 10:36 AM - 10:42 AM

PERSISTENT INFLAMMATORY CATABOLIC SYNDROME AFTER HYPOTHERMIA IN TRAUMA PATIENTS

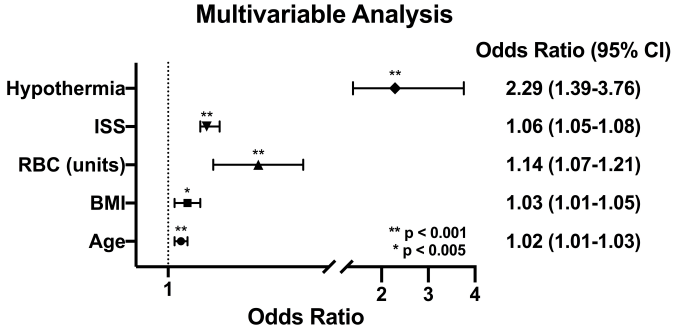
David Miranda MD, MSc, Rebecca Maine MD, MPH, Mackenzie Cook MD, Grant E. O'Keefe MD, MPH, Saman Arbabi MD, MPH, Eileen M. Bulger MD, Bryce R. Robinson MD, MSc, Joseph Cuschieri MD
Harborview Medical Center

Invited Discussant: Susan Evans, MD

Introduction: Persistent inflammatory catabolic syndrome (PICS) occurs frequently in patients who survive severe injury. However, the modifiable factors associated with developing PICS remain poorly elucidated. Previous work has suggested that hypothermia on presentation is associated with increased mortality, and rapid correction is associated with improved outcome. Given the reduction in early mortality due to improved care, we hypothesized that admission hypothermia (AH) is associated with the development of PICS, and that rapid intervention to correct AH would improve outcome.

Methods: To determine the association of AH and PICS, we analyzed prospectively collected data (Cohort 1) in the Inflammation and Host Response to Injury database. AH was defined as initial body temperature ≤ 34.5◦ C. PICS was defined as death or multi-organ failure > 14 days after injury. Univariable analyses involved Student's T-test and Pearson's Chi square. Logistic regression controlled for age, BMI, Injury Severity Score (ISS), blood product transfusion, and initial shock status. To assess the effect on PICS of intravascular rewarming (IVR), we analyzed prospectively collected data from a single center of hypothermic patients from 2013-2018 (Cohort 2) and performed similar statistical analyses.

Results: Of the 1675 patients in Cohort 1, there was no significant difference in age, BMI, or ISS between patients who had AH (n=254) and those who did not (n=1,421). On univariable analysis, 120/254 (47.2%) of patients with AH had PICS, compared to 134/1421 (9.4%) without AH who had PICS, $p < 0.001$. On multivariable logistic regression, AH was associated with increased risk of PICS, OR 2.29 (1.39-3.76) but not increased risk of death OR 1.3 (0.9-1.9). In 89 patients with AH in Cohort 2, univariable analysis revealed 45/68 (66.1%) without IVR had PICS, compared to 6/21(28.5%) with IVR who had PICS, $p < 0.001$. There was no effect of IVR on mortality. Multivariable logistic regression showed patients not receiving IVR had increased risk of PICS, OR 3.67 (1.21-8.98).



Conclusions: Hypothermia is associated with the development of PICS in severely blunt injured patients without an effect on mortality. Rapid correction of hypothermia with IVR is associated with a significant reduction in the development of PICS. Thus, prompt identification of patients with hypothermia should guide the clinician to rapidly rewarm injured patients to prevent the development of PICS and improve outcome.

RESUMPTION OF LONG TERM ANTICOAGULATION AFTER TRAUMATIC INTRACRANIAL HEMORRHAGE IN GERIATRIC PATIENTS -- A BAD IDEA?

Adrian W. Ong MD, Alison Muller, Pamela Jones, Anthony Martin, Forrest B. Fernandez M.D.
Reading Hospital

Invited Discussant: Jody DiGiacomo, MD

Background: Cessation of anticoagulation (AC) after traumatic intracranial hemorrhage (tICH) is necessary, but it is unclear if risk benefit analysis supports resumption of AC after discharge from hospital in geriatric patients at risk for recurrent tICH. We hypothesized that AC resumption after tICH is not associated with long term hemorrhagic complications.

Methods: We conducted a 4-year prospective observational study enrolling patients on AC admitted with tICH and surviving to discharge. Patients who had no follow up after discharge were excluded. Events of interest (major bleeding, arterial and venous thromboembolism [VTE], acute myocardial infarction [AMI], transient ischemic attack or stroke [TIA/S], new or worsened tICH and death) were recorded up to 24 months after discharge. Patients who had AC resumed within 3 months after tICH were compared to those without AC resumption at 3 months with univariable analyses. A p value of less than 0.05 was considered significant.

Results: 179 patients survived to discharge with 35 lost to follow up, leaving 144 patients with a median (interquartile range, [IQR]) age of 82 (75-86) for further analysis. Indications for AC were most commonly atrial fibrillation (AF) (78%) and VTE (17%). 114 (94%) had no tICH in the preceding 5 years. Median (IQR) follow-up period was 22 (7-24) months, with 50 (35%) resuming AC within 3 months of discharge. Compared to those without AC resumption, those with AC resumption were younger (median age 80.5 vs. 83 years, p=0.02), had similar Charlson Comorbidity Index scores (median, 5 vs 5, p=0.1), CHA_2DS_2-VASc scores (median, 4 vs 4), rates of TIA/S (8% vs 16%, p=0.1), VTE (6% vs 1%, p=0.1), AMI (0% vs 3%, p=0.6), arterial thromboembolism (0% vs 3%, p=0.6), major bleeding (10% vs 12%, p=0.8) and readmission for new or worsened tICH (8% vs 14%, p=0.2). The follow-up periods were similar in both groups (median, 24 vs 21 months, p-0.2), with equivalent mortality rates (24% vs 32%, p=0.3).

Conclusion: Over 90% of anticoagulated geriatric patients surviving to discharge after an episode of tICH had no tICH in the preceding 5 years, but mortality was substantial in the subsequent 24 months after discharge from an episode of tICH. AC resumption within 3 months was not associated with an increased risk of hemorrhagic or thrombotic complications. The risk benefit analysis for resumption of AC continues to be challenging in this cohort and should be further evaluated through large longitudinal cohort studies.

Session XII: Quickshot Session II 14-26
Quickshot 17: 10:48 AM - 10:54 AM

CAN VARIATIONS IN INSULIN REQUIREMENTS BE AN EARLY INDICATOR OF SEPSIS IN BURN PATIENTS?

Chathurika S. Dhanasekara PhD, Simran Singh MBA, Nadia Tello BS, Parker Southerland BS, Adel Alhaj Saleh MD, Jennifer Kesey, Sharmila Dissanaike MD
Texas Tech University Health Sciences Center

Invited Discussant: David Harrington, MD

Introduction: Early identification of sepsis is a key step in reducing morbidity and mortality. Burn patients pose an additional challenge to early identification, due to their hypermetabolic state, and loss of skin barrier to infection.[1] Thus, many sepsis studies have excluded burn patients, limiting evidence regarding sepsis recognition following burns.[2,3] The American Burn Association (ABA) diagnostic criteria includes an increase in insulin requirement > 25 % over 24 hours as an indication of possible sepsis.[4] However, there is no conclusive evidence as to the time point at which insulin requirements start to increase in sepsis. Therefore, we aimed to determine the exact time point at which the insulin requirements increase among non-diabetic burn patients with sepsis.

Methods: A retrospective chart review in non-diabetic burn patients ≥ 20% TBSA during 2010-2018 who received a blood culture for suspected sepsis according to 2007 ABA diagnostic criteria. Absolute insulin requirement at intervals (0, 24, 48, and 72, and 96 hours prior to a blood culture) were Box-Cox transformed and compared vs. -96 hours reference using mixed-effects models accounting for within-patient dependencies using the lmerTest package in R (version 3.5.3).

Results: Fifty-eight patients (84% men, age 44 ± 17 years, TBSA 49 ± 17.5%), were included in the study. Forty-two patients had positive blood cultures (72%) with 81% being positive for gram-negative organisms. When cube root of daily insulin requirement was regressed on each time point (24, 48, 72, and 96 hours prior to obtaining blood culture) in a mixed-effects model with -96 hours as the reference category, statistically significant positive effects were observed for -48, -24, and 0 hours (Table 1).

Conclusion: Daily insulin requirement seem to increase 48 hours prior to development of other clinical signs of sepsis, and can be used as a sensitive early marker.

Table 1. Summary of Regression cube root of insulin requirement vs. time points.

	Estimate (β)	SE	df	t-statistic	p-value
Intercept	3.130	0.262	275.994	11.966	
-72 hours	0.235	0.183	275.994	1.285	0.120
-48 hours	0.435	0.182	275.994	2.388	**0.018**
-24 hours	0.464	0.182	275.994	2.547	**0.011**
0 hours	0.485	0.182	275.994	2.665	**0.008**

References

1. Greenhalgh DG. Sepsis in the burn patient: a different problem than sepsis in the general population. *Burns & trauma* 2017;5:23.

2. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche J-D, Coopersmith CM. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *Jama* 2016;315:801-810.

3. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, Kumar A, Sevransky JE, Sprung CL, Nunnally ME. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Intensive care medicine* 2017;43:304-377.

4. Group ABACCoBSaI, Greenhalgh DG, Saffle JR, Holmes IV JH, Gamelli RL, Palmieri TL, Horton JW, Tompkins RG, Traber DL, Mozingo DW. American Burn Association consensus conference to define sepsis and infection in burns. *Journal of burn care & research* 2007;28:776-790.

CALCIUM SIGNALING DRIVES FEMALE-SPECIFIC PLATELET HYPERACTIVITY: A MECHANISTIC EXPLORATION OF SEX DIMORPHISMS IN PLATELET FUNCTION

Julia R. Coleman MD, MPH, Ernest E. Moore MD, Kenneth Jones PhD, Marguerite Kelher MSc, Sanchayita Mitra, Mitchell J. Cohen MD, Jason Samuels MD, Christopher Silliman MD, PhD
University of Colorado-Denver

Invited Discussant: Stephen Cohn, MD

Introduction: Females demonstrate hypercoagulability relative to males, which confers survival benefit in the setting of trauma-induced coagulopathy; however, the mechanism remains unknown. We have described that female platelets have increased activation with adenosine diphosphate (ADP) stimulation, whereas male platelets have increased activation with platelet-activating factor (PAF). PAF stimulates the P2Y1 receptor, which increases intracellular calcium, while ADP stimulates the P2Y12 receptor, which decreases intracellular cAMP. Platelet estradiol receptor signaling converges on these same pathways. We hypothesize that the sex-based differences in platelet activity are due to nongenomic effects of estradiol, as evidenced by sex dimorphisms in platelet RNA and cAMP signaling.

Methods: Apheresis platelets were collected from healthy volunteers. For cAMP, $1x10^8$ platelets/mL were activated with 10 μM of ADP or 2 μM of PAF, and intracellular cAMP levels were measured from the cell lysates by ELISA. For RNA sequencing, RNA was isolated using Qiagen RNeasy kit and sequenced on Illumina HiSeq2000. A custom computational pipeline was used for discovery of differential gene expression.

Results: Platelets from 12 healthy volunteers were assayed for intracellular cAMP (6 males, 6 females). There were no differences in cAMP levels by sex after ADP (3.0±0.4 pmol/mL in males versus 3.2±0.2 pmol/mL in females, p=0.49) or PAF stimulation (3.0±0.3 pmol/mL in both sexes, p=0.56). Platelets from 12 separate healthy volunteers were assayed for RNA (6 females, 6 males). There were significant differences by sex in RNA sequences related to calcium signaling. Specifically, TREML1 RNA, which encodes proteins that propagate platelet activation by enhancing calcium signaling, was 1.77-fold higher in females versus males (26.43 versus 14.91, p=0.007). Best1 RNA, which encodes proteins promoting intracellular calcium flux, was 1.38-fold higher in females versus males (225.32 versus 162.92, p=0.01).

Conclusion: Sex dimorphisms exist in platelet RNA transcripts involved in calcium signaling required for platelet activation, which may be affected by estradiol through nongenomic action.

MANAGING ACUTE UNCOMPLICATED APPENDICITIS IN FRAIL GERIATRIC PATIENTS: A SECOND HIT MAY BE TOO MUCH

Mohamad Chehab MD, Michael Ditillo DO, Lourdes Castanon MD, Letitia Bible MD, Molly Douglas MD, Samer Asmar MD, Narong Kulvatunyou MD, Lynn Gries MD, Bellal Joseph MD
The University of Arizona

Invited Discussant: Joseph Sakran, MD, MPA, MPH

Introduction: Some studies have proposed the use of antibiotics only in cases of acute uncomplicated appendicitis (AUA). However, there remains a paucity of data evaluating this nonoperative approach in the vulnerable frail geriatric population. The aim of this study is to examine long-term outcomes of frail geriatric patients with AUA treated with appendectomy compared to initial nonoperative management.

Methods: We conducted a one-year (2017) analysis of the Nationwide Readmissions Database and included all frail geriatric (age ≥65) patients with a diagnosis of AUA. Frailty was assessed using the 5-factor modified frailty index (mFI). Patients were stratified into those undergoing appendectomy at index admission (OP) vs. those receiving antibiotics only without operative intervention (NOP). Patients in the NOP group were excluded if they expired during their index admission. Primary outcome measure for the OP group was procedure-related complications. Primary outcome measure for the NOP group was 6-month failure of NOP (return with uncomplicated or complicated appendicitis; need for appendectomy at non-index admission; missed appendiceal neoplasm). Secondary outcome measures were mortality, overall hospital length of stay (LOS), and healthcare costs. Multivariate regression analysis was performed adjusting for demographics and comorbidities.

Results: A total of 5613 frail geriatric patients with AUA were identified: 4242 (75.6%) in the OP group and 1371 (24.4%) in the NOP group. Patients in the OP and NOP were comparable in terms of age (74±7 vs. 75±7 years; $p = 0.094$), sex (46 vs. 47% male; $p = 0.132$), and mFI (0.34 vs. 0.36; $p = 0.089$). 8.5% of patients in the OP group had procedure-related complications, while 16.8% of patients in the NOP group failed NOP within 6 months. 6-month mortality was significantly higher in the NOP group compared to the OP group (2.3 vs. 1.1%; $p < 0.001$). Also, patients in the NOP group had a significantly greater number of 6-month overall hospitalized days (5 [3,10] vs. 3 [2,6]; $p < 0.001$) and higher 6-month overall costs (16 [12,27] vs. 11 [8,19] $K; $p < 0.001$) and hospital charges (46 [22,89] vs. 32 [23,49] $K; $p < 0.001$). On multivariate analysis, NOP was independently associated with increased mortality (OR 2.1 [1.3-3.2]; $p = 0.003$).

Conclusion: NOP of frail geriatric patients presenting with AUA was associated with increased mortality. One in six patients failed NOP within 6 months and subsequently had longer hospital stays and higher healthcare costs. Appendectomy may offer better outcomes in managing AUA in the frail geriatric population.

Session XII: Quickshot Session II 14-26
Quickshot 20: 11:06 AM - 11:12 AM

DIFFERENCES IN RATE OF INTERVENTION FOR BLUNT SPLENIC INJURY IN ADOLESCENTS BETWEEN ADULT AND COMBINATION ADULT/PEDIATRIC CENTERS

Arthur D. Grimes MD, Alessandra Landmann MD, Kenneth Stewart PhD, Jeremy Johnson MD, Ryan Kennedy MD
University of Oklahoma

Invited Discussant: Mary Edwards, MD

Introduction: Pediatric Trauma Society (PTS) guidelines for management of blunt splenic injury (BSI) recommend aggressive non-operative management. This is divergent when compared to adult guidelines. Adolescent patients, age 13-17 years, while included in pediatric trauma guidelines, are often under-represented in studies of pediatric patients. Many adolescent patients are treated at adult or non-pediatric trauma centers. We hypothesize there is no difference in the adjusted odds of surgical/embolization splenic interventions by age group for patients age 6 to 24 years arriving at adult only or combination adult and pediatric trauma centers.

Methods: National 2017 Trauma Quality Improvement (TQIP) data were used to conduct a retrospective study of patients age 6 to 24 years who presented with BSI to an adult or adult/pediatric combination trauma center. Three age groups were defined (age 6-12, 13-17, 18-24). Covariates included sex, spleen organ injury scale (OIS), gender, > 40mL/Kg or > 4 units of blood transfused in first 24hrs, and final injury severity score (ISS). An intervention was defined as a spleen-specific surgical, angiography, or embolization procedure. Association of need for spleen intervention and age group was assessed using multivariable adjusted logistic regression. Area-under-curve (AUC) and Hosmer-Lemeshow goodness-of-fit (H-L) statistics were used to assess model discrimination and fit respectively.

Results: 579 patients age 6-12, 1283 age 13-17, and 3389 age 18-24 were included. At adult only centers, spleen interventions among 13-17 year olds (17.0%) were more similar to 18-24 year olds (19.6%) than to 6-12 year olds (6.9%). At combination centers, intervention among 13-17 year olds (10.1%) was closer to the 6-12 group (7.3%) than to the 18-24 group (20.7%). Interaction was present for age group and center type so separate models were developed. Adjusted odds for splenic intervention at adult only centers were 2.3 (95%CI 1.3, 4.1) and 3.1 (95%CI 1.8, 5.3) times higher for 13-17 year olds and 18-24 year olds respectively, when compared to those age 6-12 (AUC 0.84, H-L p=0.31). At combination centers, compared to ages 6-12, the adjusted odds of splenic intervention were higher for 18-24 year olds (OR 3.9 95%CI 2.3, 6.6) but no longer significant for 13-17 year olds (OR 1.7 95%CI 0.95, 3.0) (AUC 0.86, H-L p=0.40).

Conclusion: We demonstrate that adolescent patients, age 13-17, are more likely to undergo interventions for BSI when compared to patients age 6-12 at adult only trauma centers. The elevated OR persists, despite similarities in severity of organ injury and need for blood product transfusion. The incidence of splenectomy has not decreased in this age group over the past 18 years, despite recommendations from the PTS. Further efforts to selectively study this group and disseminate guidelines is warranted.

Session XII: Quickshot Session II 14-26
Quickshot 21: 11:12 AM - 11:18 AM

HOSPITAL COSTS FOR FIREARM INJURIES BY U.S. REGION, 2005-2015

Sarabeth Spitzer MD, Lakshika D. Tennakoon MD, MSc, Joseph Forrester MD, MSc,
David A. Spain MD, **Thomas G. Weiser MD, MPH**
Stanford University Medical Center

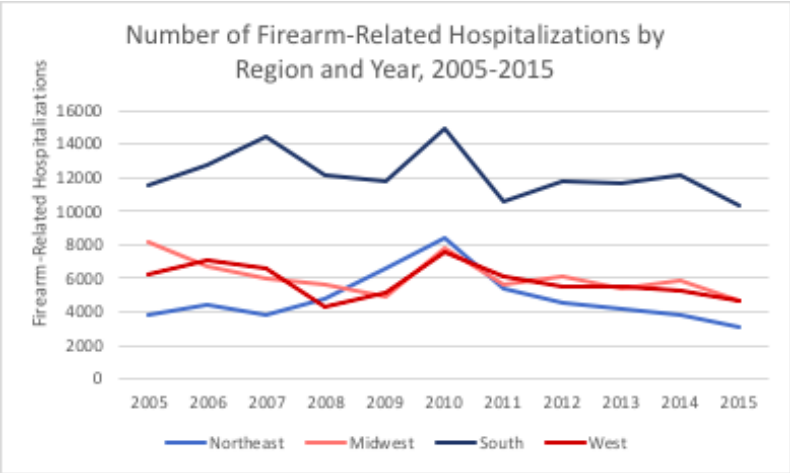
Invited Discussant: Sigrid Burruss, MD

Introduction: Firearm injuries are a costly public health challenge nationally. As payments for firearm injuries are frequently covered by government-sponsored programs, understanding regional differences may be useful to craft appropriate policies, especially since state gun laws vary widely. We estimated the number of hospitalizations and hospital costs for patients injured by firearms from 2005-2015 for each region of the United States and analyzed cost burden by payer status.

Methods: We used the Healthcare Cost and Utilization Project Nationwide Inpatient Sample to identify patients admitted for firearm injuries from 2005 to 2015. We converted hospitalization charges to costs, which were inflation-adjusted to 2015 dollars. We used survey weights to create regional estimates. We used the Nationwide Readmission Database 2010-2015 to assess the frequency of readmissions at 30 days and associated hospital costs for each region, applied them proportionally to the earlier years, and estimated the share borne by government insurance coverage.

Results: Firearm-related hospital admissions were highly variable within the US. It was highest in the South, which also had the highest proportion of injuries to total population (0.11%). Total regional admissions during the 11 years of this study were 52,797, 66,734, 134,008, and 64,004 for the Northeast, Midwest, South, and West respectively. In the Northeast, regional costs were $1.19 billion (13.8% of total), of which 55.7% was covered by a government payer; for the Midwest, costs were $1.71 billion (19.8% of total), 39.9% of which was covered by the government; in the South costs were highest at $3.59 billion (41.5% of total), but government plans only covered 33.8% ; and costs for the West were $2.15 billion (24.9%), with government programs covering 46.1% of the cost burden.

Conclusions: Hospital admissions and costs for firearm injuries demonstrated wide variation over the past decade. Injury control strategies have not been well applied to this national public health crisis. Costs per patient were also variable, suggesting opportunities for improvement. Government insurance programs cover 41.1% of costs, indicating that tax dollars heavily subsidize the financial burden of firearm injuries.



COMPARISON OF SURGICAL RIB FIXATION BETWEEN PATIENTS WITH AND WITHOUT FLAIL CHEST

Alice Piccinini MD, Thomas J Martin, Eric Benoit MD, Sean F. Monaghan MD, Andrew Stephen MD, Stephanie N. Lueckel MD, Charles A. Adams, Jr. MD, Tareq Kheirbek MD
Rhode Island Hospital

Invited Discussant: Raminder Nirula, MD, MPH

Introduction: Surgical rib fixation (SRF) has emerged as a valuable option for rib fractures associated with flail chest (FC), and was recently proposed for the management of non-flail chest (NFC) with improvement in pain scores and quality of life. We investigated the difference in outcomes of the procedure between flail and non-flail chest.

Methods: The Trauma Quality Improvement Program 2017 database was queried for rib fracture patients that underwent surgical fixation procedure using ICD-10 codes. We compared demographics, time to surgery, length of stay (LOS), ICU admission and duration, rate of intubation, ventilator days ventilator associated pneumonia (VAP), discharge disposition and mortality. Statistical analysis was performed using SPSS version 23.

Results: We identified 150,340 patients with rib fractures, of whom 6,578 (4.4%) had FC and 2,391 underwent SRF (1.6%). Surgical rib fixation was used more frequently in FC (1042/6,578, 15.8% vs NFC 1349/143,762, 0.9%, $P < 0.001$), and 1167 (49%) were performed at university hospitals (FC 50.1% vs NFC 47%, NS), and the majority were men (74.2%, no difference between the two groups). A higher proportion of patients with more than 3 fractured ribs in the NFC group who underwent fixation had (FC 77.4% vs NFC 85%, $p < 0.001$), There were no differences in age (FC 55.6±15.4 vs NFC 54.7±15.6, NS), time to surgery (*median* 4 days in both groups, NS), unplanned ICU admission (6.7% vs 5.6%, NS), respiratory failure (3.4% vs 2.4%, NS), or number of days on ventilator (median: 7 vs 8, NS) between the groups. Flail chest patients had higher ISS (median: 22 vs 17, $p < 0.001$), ICU LOS (8 vs 6 days, $p < 0.001$), Hospital LOS (13 vs 11 days, $p < 0.001$), need for intubation (57.8% vs 39.4%, $p < 0.001$), VAP (6.7% vs 3.6%, $p < 0.001$), and mortality (3.5% vs 1.7%, $p=0.006$). Of SRF patients who survived, 55.1% were discharged home (FC 51.3% vs NFC 58.1%, $p <0.001$). Adjusting for age, gender, ISS, hospital LOS, need for intubation, ICU admission, and VAP, surgical rib fixation was not associated with statistically higher odds of mortality in FC compared to NFC (OR:1.48, 95%CI: 0.82-2.66).

Conclusion: In our analysis of a recent national sample of patients with rib fractures, surgical rib fixation is still potentially under-utilized, especially among patients with non-flail chest, who fared comparably well. There was a low rate of reported complications and mortality. The observed higher mortality in patients with flail chest appears to be due to differences between the groups in injury severity and not directly related to rib fixation. Further investigation should be performed to properly identify patients who would benefit from surgical rib fixation.

LAPAROSCOPIC TRANSCYSTIC COMMON BILE DUCT EXPLORATION IMPROVES OUTCOMES IN EMERGENCY GENERAL SURGERY (EGS) PATIENTS WITH CHOLEDOCHOLITHIASIS

John A. Michel-Ruddy MD, Ashkan Moazzez MD, MBA, Matthew B. Bloom MD, Joseph R. Sirody MD, Sydney Read MD, Kwang Kim, Kelsey Luna BS, Alyson Morgan BS, Angela L. Neville MD, Brant Putnam MD, Dennis Y. Kim MD
Harbor-UCLA Medical Center

Invited Discussant: Edgardo Salcedo, MD

Introduction: Implementation of an acute care surgery (ACS) model improves outcomes including decreased time to surgery and length of stay (LOS) in patients with acute biliary diseases requiring laparoscopic cholecystectomy (LC). The impact of an ACS service on outcomes among patients with common bile duct (CBD) stones is less clear, as timing of ERCP is usually based on consultant availability. The objective of this study was to compare outcomes between single-stage laparoscopic transcystic CBD exploration (LCBDE) and two-stage LC+ERCP for CBD stones. We hypothesized that LCBDE results in decreased LOS and complications compared to LC+ERCP for EGS patients with CBD stones.

Methods: We performed a 2.5-year retrospective case-control analysis of adult patients admitted to an urban level 1 trauma center with a diagnosis of choledocholithiasis or acute mild gallstone pancreatitits (GP). LCBDE patients were compared to those who underwent LC+ERCP. Variables analyzed were patient demographics, operative details, and outcomes. The main outcome measure was hospital LOS. Secondary outcomes were time to surgery, operative case duration, and complications. Coarsened exact matching (CEM) was performed to compare LCBDE to LC+ERCP patients on a 1:1 basis to control for age, gender, BMI, and an admission diagnosis of choledocholithiasis.

Results: Of 1265 patients, 214 (16.9%) were diagnosed with choledocholithiasis and 52 (4.1%) with GP. LCBDE was performed in 75 patients (28.2%) and these patients were younger, with a lower BMI, and higher incidence of choledocholithiasis (all $p < .01$). On unadjusted analysis, time to surgery was shorter, procedural duration was longer, and there were no differences in LOS or complications between groups. On CEM, 48 LCBDE patients were matched to 48 LC+ERCP patients. Similar to the unmatched analysis, LCBDE resulted in a decreased time to LC and longer operative time (**Table**). However, LOS was decreased in patients undergoing LCBDE and the incidence of post-operative complications did not differ between groups.

	LCBDE (n = 48)	LC +ERCP (n = 48)	*p* value
LOS, days	3.0 ± 1.3	4.6 ± 1.7	<.001
Admission to OR, days	1.2 ± 0.9	2.7 ± 1.2	<.001
Total procedure time, min	203 ± 93	167 ± 54	.03
Unable to clear CBD	3 (6.3%)	3 (6.3%)	1.0
Pancreatitis	2 (4.2%)	1 (2.1%)	.56
Readmission	6 (12.5%)	3 (6.3%)	.29

Conclusion: When compared to LC+ERCP, single-stage LCBDE reduces time to surgery and LOS, with no difference in complications in patients with choledocholithiasis. Further study is required to identify potential barriers to the more widespread adoption and implementation of LCBDE in the EGS setting.

MULTICENTER VALIDATION OF THE BOWEL INJURY PREDICTION SCORE (BIPS) FFOR IDENTIFYING PATIENTS REQUIRING SURGERY

Michael Wandling MD, MSc, Joseph Cuschieri MD, Rosemary A. Kozar MD, PhD, Amanda Celii MD, Clay C. Burlew MD, Robert McIntyre MD, Walter L. Biffl MD, Lucy Kornblith MD, Julie A. Dunn MD, Kimberly A. Peck MD, Stefan Leichtle MD, S. Rob Todd MD, Daniel Lollar MD, Thomas J. Schroeppel MD, Michelle K. McNutt MD
University of Texas Health Science Center at Houston

Invited Discussant: Ruben Peralta, MD

Introduction: Identifying patients who require surgical intervention for blunt bowel and mesenteric injury (BBMI) remains a challenge, particularly in traumatic brain injury (TBI) where exam may be unreliable. A pilot trial showed the Bowel Injury Prediction Score (BIPS) could identify patients requiring therapeutic laparotomy. We hypothesize 1) that BIPS can be validated in a prospective multi-center study and 2) that BIPS remains accurate in the setting of TBI.

Methods: Patients were prospectively enrolled at 15 U.S. trauma centers following blunt trauma with suspicion of BBMI on CT scan between July 1, 2018 and July 31, 2019. BIPS was calculated by assigning one point each for: 1) WBC >= 17,000, 2) abdominal tenderness, and 3) injury grade >= 4 on CT scan. A total score >= 2 identifies BBMI requiring laparotomy. Risk-adjusted odds ratios for need for laparotomy for BIPS components were calculated. Sensitivity, specificity, PPV, NPV, and ROC curves were calculated to validate the predictive ability of BIPS. The accuracy of BIPS in TBI was similarly evaluated.

Results: Of 313 patients meeting enrollment criteria, 38% had BBMI requiring therapeutic laparotomy. There were no demographic differences between those requiring therapeutic laparotomy and those who did not. Logistic regression identified BIPS components of WBC >= 17,000 (OR=1.5, p=0.18), abdominal tenderness (OR=3.8, p < 0.01) and CT grade >= 4 (OR=11.1, p < 0.01) as independent predictors of need for laparotomy. Patients with BIPS >= 2 were 8.8 times more likely to have surgically significant BBMI vs. those with BIPS >= 2 as an accurate predictor of BBMI requiring therapeutic laparotomy including the subset of TBI patients.

	All Patients	Mild/Mod TBI (GCS 8-15)	Severe TBI (GCS <8)
Sensitivity	71.7%	72.0%	70.0%
Specificity	77.7%	73.9%	92.3%
PPV	66.7%	64.3%	82.3%
NPV	81.5%	80.1%	85.7%
AUROC	0.75	0.73	0.81

Conclusions: The easily calculated BIPS provides both positive and negative prediction of need for therapeutic laparotomy in patients with BBMI. In the setting of TBI with an unreliable abdominal exam, BIPS remains an accurate predictor. Calculation of BIPS during the initial management of patients with BBMI can be a useful adjunct in determining who should be taken to the operating room versus who can be safely managed non-operatively.

READY FOR PRIME TIME? PGY-5 RESIDENT AUTONOMY AND PERFORMANCE IN EMERGENCY GENERAL SURGERY USING SIMPL CASE EVALUATION DATA

Adam C. Nelson MD, Amy N. Hildreth MD
Wake Forest Baptist Health

Invited Discussant: Michael Cripps, MD

Introduction: There is a paucity of data regarding graduating general surgery resident experience with emergency general surgery (EGS), and case volume is not a surrogate for competence. As an alternative, the System for Improving and Measuring Procedural Learning (SIMPL) is an electronic, competency-based evaluation with qualitative assessments of surgical proficiency for varying case complexity. We sought to characterize chief resident experience with EGS using SIMPL evaluations. Since EGS cases are complex and often technically difficult, evaluations of cases with higher complexity may provide insight into residents' ability to independently perform EGS cases after graduation. We hypothesized that residents would have lower measures of autonomy and performance for EGS cases of the highest complexity.

Methods: SIMPL evaluations of PGY-5 surgery residents from 2015 to 2020 were queried for the seven most common laparoscopic and open EGS procedures. The relative frequency of each case type, rates of high case complexity, meaningful autonomy, and practice-ready or better performance were determined. Logistic regression was used to characterize resident autonomy and performance with respect to case complexity. Mixed-effects modeling was used to control for case complexity, time trends, multiple procedures, rater stringency, individual trainee and program characteristics, and procedure type.

Results: 3,818 evaluations were included. Laparoscopic cholecystectomy, laparoscopic appendectomy, open and laparoscopic colectomy accounted for 78% of EGS total case volume. Thirty-five percent of cases were high complexity. For these complex cases, 71% of evaluations characterized chiefs as having meaningful autonomy and 78% as having practice-ready or better performance. High case complexity versus low and moderate complexity was an independent predictor of both lower levels of autonomy (OR 0.25, $p = 0.001$) and performance (OR 0.44, $p = 0.001$).

Conclusions: The majority of chief resident EGS case volume is derived from exposure to only a minority of case types. Chief residents are not universally ready for independent performance of highly complex EGS procedures. Metrics are needed to better define resident exposure to emergency cases; our findings suggest a need for additional training in acute care surgery for those wishing to practice emergency surgery.

DO PATIENTS WITH MINIMAL BLUNT THORACIC AORTIC INJURY (BTAI) REQUIRE TEVAR?

Joseph J. DuBose MD, Kristofer Charlton-Ouw MD, Benjamin Starnes, Naveed Saqib MD, Elina Quiroga MD, Jonathan Morrison MD, PhD, Bruce Gewertz MD, Ali Azzizadeh
Uniformed Services University of the Health Sciences

Invited Discussant: Demetrios Demetriades, MD, PhD

Objective(s): The optimal management of "minimal" BTAI remains controversial, with experienced centers o!ering therapy ranging from medical management (MM) to TEVAR. We analyzed contemporary management and outcomes of BTAI.

Methods: The Aortic Trauma Foundation (ATF) registry was utilized to examine demographics, injury characteristics, management and outcomes of patients with BTAI.

Results: 296 patients from 28 international centers were analyzed; mean age 44.5 (SD 18); 76% (225/296) male; mean ISS 34 (SD 14). BTAI was classified as Grade I 22.6% [67/296]; Grade II 17.6% [52/296]; Grade III 47.3% [140/296]; Grade IV 12.5% [37/296]). Overall mortality was 14.2% (42/296); aortic related mortality (ARM) 4.7% (14/296). Among all deaths, 33%(14/42) were ARM. Open repair was required for only 2% [Table 1], with most undergoing TEVAR (58.4%) or MM (28.0%). TEVAR complications occurred in 3.4% (6/173), most commonly Type 1 endoleak (2.3%; 4/173). Among patients with minimal aortic injury (MAI, GI+GII), 78% (93/119) received MM, while 22% underwent TEVAR. No di!erence in overall or ARM between MM and TEVAR was noted for Grade I-II injuries; although 2 patients undergoing initial MM required intervention for injury progression (both by TEVAR).

Conclusions: Among trauma victims with BTAI, ARM occurs in 1/3. TEVAR has replaced open repair but remains equivalent in outcomes to MM forMAI. Our data supports modification of current BTAI practice guidelines.

SVS Grade	Aortic-related death prior to opportunity for repair	Medical Mgmt alone	Open repair	TEVAR	Aortic-related mortality
1 (N = 67)	0% (0/67)	91.0% (61/67)	0% (0/67)	9.0% (6/67)	1.5% (1/67)
2 (N = 52)	0% (0/52)	61.5% (32/52)	0% (0/52)	38.5% (20/52)	1.9% (1/52)
3 (N = 140)	0.7 (1/140)	11.4% (16/140)	1.4% (2/140)	86.4% (121/140)	1.4% (2/140)
4 (N = 37)	16.2% (6/37)	2.7% (1/37)	10.8% (4/37)	70.3% (26/37)	27.0% (10/37)
All BTAI (N =296)	2.4% (7/296)	28.0% (83/296)	2.0% (6/296)	58.4% (173/296)	4.7% (14/296)

Management type	All-cause mortality	Aortic-related mortality
Overall (N=296)	14.2% (42/296)	4.7% (14/296)
Medical management alone (N = 83)	8.4% (7/83)	0% (0/83)