

DISCRIMINATION OF PATHOPHYSIOLOGY IN SYSTEMIC INFLAMMATION BY CANONICAL DISCRIMINANT ANALYSIS BASED ON TRANSCRIPTOME ANALYSIS

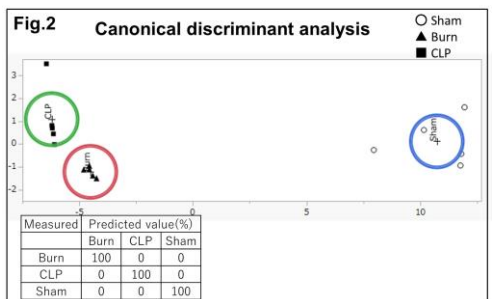
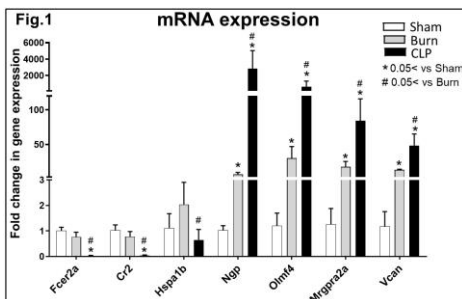
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Introduction: It is difficult to diagnose the pathophysiology of systemic inflammation by a single biomarker. We aimed to develop a novel method to discriminate pathophysiology by evaluating multiple gene expressions as a pattern using transcriptome analysis.

Methods: We employed cecal ligation and puncture (CLP) using 25G needle, and 20% full thickness burn injury model for systemic inflammation models. RNA was extracted from whole blood 24 hours after injury, and RNA sequencing was performed on a next-generation sequencer (NGS) (n=3 per group). qPCR was performed on genes (Cr2, Fcer2a, Hspa1b, Ngp, Olfm4, Mrgpra2, Vcan) that showed significant changes between groups in the statistical analysis after NGS (n=6 per group). The gene expression patterns were compared by canonical discriminant analysis (CDA).

Results: Statistical analysis after NGS showed significant difference in 1746 mRNAs among the 3 groups (ANOVA $p < 0.05$). The gene expression of Ngp, Olfm4, Mrgpra2, and Vcan was significantly upregulated in CLP and Burn compared to Sham, and Ngp and Olfm4 were significantly upregulated in CLP compared to Burn ($p < 0.05$). Cr2, Fcer2a was significantly lower in CLP compared to Sham and Burn ($p < 0.05$) (Fig.1). Each group showed a characteristic gene expression pattern, and CDA showed that each pathophysiology could be discriminated 100%, and, using only three parameters, it could be discriminated more than 90% for all specimens (Fig.2).

Conclusion: The results suggested the possibility of a novel method to discriminate pathophysiology based on gene expression patterns extracted by transcriptome analysis.



DO AS I SAY AND NOT AS I TEACH: SURGICAL CRITICAL CARE PROGRAM DIRECTORS AND DIPLOMATES SHAPE THE FUTURE OF SURGICAL CRITICAL CARE

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Introduction: In 1987, the Trauma, Burn, Surgical Critical Care Board (TBSCCB) began providing certification in surgical critical care through a certification examination (CE) process. The blueprint for the CE has remained largely unchanged since that time. In 2020, the TBSCC began to revise the CE, and wanted to evaluate the relevance of exam content to SCC training programs and diplomates. The purpose of the study was to evaluate whether the material being tested aligns with clinical practice.

Methods: SCC program directors (PDs) and diplomates were identified, and on-line surveys administered. A draft blueprint was vetted with SCC PDs and diplomates to determine how frequently each item should be tested. Respondents were asked to rank each item by how frequently they felt it should be tested on the exam (4 = each year, 3 = every other year, 2 = every few years, 1 = never). Diplomates were also asked to identify how frequently specific topics were encountered in their practice. Results were compared with both t-tests and Mann-Whitney U test. Cohen's *d* was calculated as a measure of effect size. Given the large sample size, we used a p-value of < 0.001 and at least a moderate effect size as an indication of relevant differences.

Results: Response rates were 42% (n=70) and 30% (n=1307), respectively. 188 topics were evaluated. Program directors requested more frequent assessment than diplomates in 28 categories. Obstetrical emergencies and ICU billing and coding were the most discordant. There were 17 topics for which diplomates expressed high discordance between the importance of the topic and everyday practice (Table). The most frequently performed procedures were ultrasound for trauma, central line, arterial line and tube thoracostomy. Transthoracic echocardiography was performed more frequently than pulmonary artery catheter placement.

Conclusions: SCC practice has evolved significantly since the CE began. PDs and diplomates identified notable differences in the importance of various topics for testing indicating a discrepancy in the training vs practice paradigms. Assessments used to measure knowledge should be aligned with practice but require a balance of topics that are infrequently encountered but exquisitely life-threatening and time sensitive.

Table. Ranking of various items by diplomates "for testing" vs. "see in practice."

Topic	For testing	See in practice
ICU coding	2.18	3.33
Thoracic esophageal injury	2.74	1.74
Tracheal and bronchial injuries	2.92	1.92
Cardiac tamponade	3.28	1.96
Rectal injury	3.11	2.09
Pancreatic injury	3.21	2.13
Duodenal injury	3.13	2.12
Malignant hyperthermia	2.58	1.39
Great vessel injury	3.13	2.13
Larynx/thyroid/airway injury	2.86	1.85
Abdominal compartment syndrome	3.45	2.35
Anaphylaxis	2.92	1.9
SIADH and cerebral salt wasting	3.38	2.37
Extremity compartment syndrome	3.55	2.49
Diabetes insipidus	3.38	2.34
Surgical airways	3.59	2.58

IS PHENOBARBITAL THE DRUG OF CHOICE FOR ALCOHOL WITHDRAWAL SYNDROME PROPHYLAXIS IN TRAUMA PATIENTS?

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Introduction: The development of alcohol withdrawal syndrome (AWS) poses significant risk to the hospitalized trauma patient irrespective of injury severity. Although diazepam is a commonly used agent to prevent or treat AWS, phenobarbital is being increasingly used as an alternative. The purpose of this study was to compare both the efficacy and adverse effects of these two drugs in preventing AWS. We hypothesized that phenobarbital would be associated with a lower incidence of AWS than diazepam.

Methods: Adult trauma patients from a level 1 trauma center who received either scheduled-dose diazepam or phenobarbital for AWS prevention between 2015 and 2022 were reviewed. Primary outcome was development of AWS, defined as dose or frequency increase of the prophylactic agent, high usage of prn CIWA protocol, and/or medication regimen changes. Secondary outcomes included development of somnolence or unplanned intubation.

Results: 172 patients (89% male) with an average age of 49.6 ± 14.5 years and median injury severity score of 12 (5-17) were identified. 54 (31.4%) patients were initiated on diazepam, at a median daily dose of 20mg (15 – 20) and 118 (68.6%) patients were initiated on phenobarbital, at a median daily dose of 130 mg (130 - 195). Overall, 14 (8.1%) patients developed AWS. Comparing groups, 10 (18.5%) patients in the diazepam group developed AWS vs. 4 (3.4%) in the phenobarbital group ($P < 0.001$). Median daily dose was not different between patients who developed AWS vs those who did not for diazepam (27.5 mg vs 20 mg, $P = 0.806$) or phenobarbital (162.5 mg vs 130 mg, $P = 0.841$). Rate of somnolence was significantly higher in the diazepam group (diazepam 20.4% vs phenobarbital 8.5%, $P = 0.024$). No patient with AWS required intubation secondary to development of withdrawal.

Conclusion: Among hospitalized trauma patients, those treated with prophylactic phenobarbital were significantly less likely to develop AWS and experience somnolence vs prophylactic diazepam. Phenobarbital should be considered as a first-line agent for AWS prevention.

MRSA NASAL SWABS PREDICT NEED FOR ANTIBIOTIC COVERAGE IN A TRAUMA POPULATION

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Introduction: Methicillin Resistant Staphylococcus Aureus (MRSA) nasal swab screening in a general intensive care unit (ICU) population has a high negative predictive value (NPV) and is used to guide antibiotic stewardship. The role of MRSA nasal swabs to de-escalate broad-spectrum antibiotics in trauma populations, known to be susceptible to hospital acquired pneumonia, has not been defined. The goal of this study was to assess the utility of the MRSA nasal swab in predicting MRSA pneumonia in a trauma population, hypothesizing that MRSA swabs would have a high NPV.

Methods: A retrospective review of trauma ICU patients at a Level 1 trauma center who received an MRSA nasal swab and respiratory culture from 2020-2023 was performed. Positive and negative MRSA nasal swab groups were compared and sensitivity, specificity, positive predictive value (PPV), and NPV for MRSA culture growth and pneumonia ($\geq 10^5$ colonies) were calculated. The area under the curve (AUC) of a receiver operating characteristic was measured.

Results: A total of 163 patients were screened and cultured, of these, 22 (13.5%) had positive MRSA nasal swabs, with 15 (9.2%) having MRSA growth and 5 (3.1%) diagnosed with MRSA pneumonia. There were no significant differences in age, BMI, smoking, or COPD between the positive and negative swab groups. Sensitivity and specificity were 66.7% and 91.9% respectively with a PPV 45.5% and NPV of 96.5% for any MRSA growth (Table). AUC for MRSA culture growth was calculated to be 0.79. Nasal swabs had an NPV of 100% for MRSA pneumonia.

Conclusion: This study, which is the largest to date on this topic, found MRSA nasal swabs to have a high NPV for MRSA growth and pneumonia and can help deescalate empiric antibiotic coverage in trauma patients. Further studies are needed to investigate the incidence of MRSA and role of routine nasal swabs in these high-risk trauma patients.

	Culture positive	Culture negative	Total
Swab positive	10 (6.1%)	12 (7.4%)	22 (13.5%)
Swab negative	5 (3.1%)	136 (83.4%)	141 (86.5%)
Total	15 (9.2%)	148 (90.8%)	163 (100%)

Table: Nasal swab as a predictor of MRSA culture growth

PREDICTING READMISSIONS FOLLOWING SEPSIS: AN INTERPRETABLE MACHINE LEARNING APPROACH

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Introduction: Sepsis survivors are a leading cause of hospital readmissions. We developed an interpretable machine learning (ML) model to predict 30-day readmissions for post-operative sepsis and septic shock survivors.

Methods: NSQIP (2018-2021) was queried for post-operative sepsis or septic shock during admission. Univariate analysis compared readmitted and non-readmitted patients. Using demographics, comorbidities, pre-operative labs, surgical specialty, diagnoses present at time of surgery (PATOS), operative time, length of stay, post-operative complications, and discharge destination, AutoML, LightGBM and XGBoost models were developed with Shapley Additive Explanations (SHAP) for interpretability. Models were validated with an 80/20 train-test split.

Results: The cohort had 52,025 patients (75% sepsis and 25% septic shock); 75% had sepsis or septic shock PATOS. 6,374 (12.5%) had an unplanned readmission. Readmitted patients had more comorbidities ($p<0.05$) and higher 30-day rates of surgical site infection (SSI), pneumonia, unplanned intubation, pulmonary embolism, renal failure, cardiac arrest, DVT, MI, UTI, and reoperation ($p<0.05$). During initial admission, readmitted patients had shorter average length of stay (12.7 vs 13.3 days, $p<0.01$) and lower rates of pneumonia, unplanned intubation, stroke, and cardiac arrest ($p<0.05$) with no significant differences in other complications. LightGBM (accuracy=0.81; AUC=0.71) was chosen. The F1 maximizing threshold (0.6) resulted in a readmission rate of 29% and captured 37% of all readmissions. Mean absolute SHAP values revealed organ space SSI PATOS (0.26), days from operation to discharge (0.2), and post-operative organ space SSI (0.18) as the most influential factors in predictions.

Conclusions: Interpretable ML accurately predicts risk of readmission after survival of sepsis. SHAP identifies the contributing factors for each patient. Early identification of high-risk patients could inform decisions on discharge timing, disposition, and follow-up.

SPONTANEOUS BREATHING TRIAL PARAMETERS (NIF AND RSBI) ARE NOT PREDICTORS OF TRAUMA PATIENT REINTUBATION

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Introduction: Reintubation in trauma patients is linked to increased morbidity and mortality. While spontaneous breathing trial (SBT) factors such as negative inspiratory force (NIF) and rapid shallow breathing index (RSBI) are recognized in general intensive care unit populations, their applicability to trauma patients is less clear. This study aims to identify clinical predictors of reintubation in trauma patients, thereby offering insights for better management and prognostication.

Methods: A single center, retrospective (1/2017-12/2023) study of trauma patients ≥ 18 years-old who underwent extubation from endotracheal mechanical ventilation was performed. Exclusion criteria included self-extubation, patients with a tracheostomy or comfort measures, and death before extubation. The study compared patients unexpectedly reintubated at any point during their admission versus those who weren't, using multivariable logistic regression to identify risk factors associated with reintubation.

Results: From 424 trauma patients, 51 (12.0%) underwent reintubation. Patients reintubated were older (55 vs 39 years-old, $p=0.016$) and more often had congestive heart failure (7.9% vs 1.6%, $p=0.023$), cirrhosis (7.8% vs 1.9%, $p=0.032$), and a higher injury severity score (ISS) (27 vs 18, $p<0.001$). Reintubated patients had lower NIF (-24.0 vs -27.0, $p=0.037$) but increased ventilator days (6 vs 2, $p<0.001$) prior to extubation, whereas RSBI was similar between cohorts (32.0 vs 36.5, $p=0.076$). Multivariable logistic regression revealed that neither RSBI <50 or <100 , nor NIF <-20 were associated with reintubation, whereas increased age (OR 1.024, CI 1.004-1.044, $p=0.017$), ISS (OR 1.040, CI 1.005-1.076, $p=0.026$), and ventilator days before extubation (OR 1.132, CI 1.041-1.231 $p=0.004$) were associated with increased risk of reintubation (Table 1).

Conclusion: Over 10% of extubated trauma patients underwent reintubation. SBT parameters like RSBI and NIF were not associated with reintubation, whereas age, ISS, and ventilator days before extubation were independently associated risk factors for reintubation. This suggests patient-specific factors, beyond SBT parameters, should help guide extubation decisions.

STRESS HYPERGLYCEMIA RATIO PREDICTS MORTALITY IN TRAUMA PATIENTS

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Introduction: The relationship between hyperglycemia and poor outcomes after injury, including mortality, is well-established. This effect has been observed in patients both with and without diabetes mellitus (DM). Admission glucose (AG) alone may be inferior to more global markers of glycemic status such as the stress hyperglycemia ratio (SHR). The SHR has been demonstrated to correlate with mortality in non-trauma, critically ill populations. The purpose of our study was to investigate the relationship between SHR and outcomes in a trauma population.

Methods: Using a single institution Level 1 trauma center registry, data from all trauma admissions with HbA1c (2017-23) were obtained. The SHR was calculated as admission glucose divided by HbA1c-derived average glucose. Individual cohorts were compared using Student's T-test and Chi-Squared. SHR was studied across the cohort using a cutoff value of 1.14, identified in previous literature. Lastly, logistic regression analyses were performed to identify the odds ratio for death associated with increased SHR.

Results: 10,038 patients were studied (1,764 diabetic). The DM cohort had significantly higher AG, HbA1c, lower SHR, and higher mortality (6.9 vs 5.3%, $p=0.009$). Using an SHR cutoff of 1.14 in the entire study population, the high SHR cohort (4,337) had a longer ICU and hospital LOS, and mortality (9.1 vs 2.9%, $p<0.001$). On regression analysis, $SHR > 1.14$ was predictive of mortality (OR 3.38, CI 2.8-4.1), as was $AG > 180$ (OR 4.4, CI 3.7-5.3). In subgroup analysis, AG and SHR were strongly predictive of mortality for both DM and non-DM patients. However, SHR was more sensitive than AG in the non-DM cohort. In quartile analysis, a significant increase was seen in the OR for death within the 4th quartile, at an SHR of 1.33 (OR 5.7, CI 4.3-7.6).

Conclusions: Similar to AG, SHR is strongly predictive of mortality in both DM and non-DM trauma patients. SHR is a more sensitive predictor of mortality than AG in the non-DM patient and is more sensitive in the non-DM patient versus the DM cohort. Utilization of SHR appears to identify a cohort of patients at risk for death at a lower threshold than conventional measures such as AG.

THE ASSOCIATION OF WHOLE BLOOD VERSUS COMPONENTS WITH EARLY LABORATORY VALUE CHANGES

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Introduction: Many studies compare whole blood (WB) to component only (CO) transfusions with respect to overall outcomes in trauma patients. These studies are plagued by shortcomings including small volume transfusions, whole blood groups with minimal volumes of WB delivered and CO groups with low ratios of plasma to platelets to red blood cells. We aimed to compare early laboratory value changes in trauma patients receiving massive transfusions with either large volumes of WB or CO.

Methods: Retrospective review from a single level-1 academic trauma center performed from 2016-2021. We included patients >15 years old who received a massive transfusion with a minimum of 3 units in the 1st hour of either WB or red blood cells. Low titer group O leukoreduced whole blood (LTOWB) was utilized. Our primary outcome measures were early laboratory value changes including hematologic, organ specific, perfusion and coagulation from baseline to 8-12 hours. Appropriate tests for categorical, normally and abnormally distributed data were performed. Significance was set at $p < 0.05$.

Results: The WB group received a median of 5 units of WB and 0 units of other components and CO received a median of 6 units of red blood cells, 5 units of plasma and 1 unit of apheresis platelets. The median time to the 2nd blood draw was 9.4 hours after admission. There was a larger change in baseline to early platelet counts in the CO group (114 vs $80 \times 10^3/\mu\text{L}$, $p < 0.048$). and lesser change in LY30 (0 vs 0.7% , $p = .037$). There were no significant changes in baseline to early values for lactate (0.3 vs 0.8 mmol/L, $p > 0.9$), potassium (-0.4 vs -0.2 mmol/L, $p = 0.9$), creatinine (0.13 vs 0.12 mg/dL, $p = 0.4$), aPTT (1.2 vs 0.1 sec, $p > 0.9$), INR (-0.05 vs -0.05 , $p > 0.9$), fibrinogen (-1 vs -25 mg/dL, $p = 0.7$), hemoglobin (1.4 vs 0.95 g/dL, $p = 0.2$), pH (-0.12 vs -0.11 , $p = 0.2$), or base excess (-2.3 vs -2.45 mmol/L, $p = 0.7$).

Conclusion: CO resuscitation with high ratios results in a greater increase in platelet count and no change in LY30 compared to resuscitation with leukoreduced LTOWB. Overall differences in laboratory values between the 2 resuscitation techniques are minimal.

ENHANCING TRAUMA PATIENT SAFETY: A RELATIONSHIP- FOCUSED FEEDBACK WORKSHOP IN THE INTENSIVE CARE UNIT

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Introduction: Communication skills amongst health care workers are essential to provide safe patient care. It can be uniquely challenging to provide considered, well-timed, respectful peer feedback in high-pressure settings such as a Surgical Trauma Intensive Care Unit (STICU). Formally training trauma nurse team members in providing relationship-focused feedback has the potential for improving patient safety.

Methods: In a large Level I trauma center, STICU RN quality committee and communication experts developed a simulation-based workshop for bedside nurses with practice scenarios drawn from STICU RN experiences. Workshop content was derived from nursing/medical education literature. The SPIKES protocol, most used for “breaking bad news” in medical education, was adapted as a framework for difficult peer-feedback discussions. Pre/post surveys captured previous training, attitudes, and confidence performing target skills. Observers, small group facilitators, and nurse-actors rated learners on simulation performances.

Results: STICU RNs (N=54) participated in half-day workshops. In pretests, 93% agreed they had recently avoided giving feedback due to being uncomfortable; only 19% had received previous training in and felt empowered giving/receiving peer feedback. “Years in profession,” “leadership role,” and “trauma certification” were not statistically significantly related to simulation performance. RNs <30 years scored significantly higher in simulation skills than older RNs. Importantly, RNs stating they “feel empowered to provide feedback” performed statistically significantly better in simulation. After training, median STICU RN confidence increased ($p<.001$) regarding 1) ability to offer useful feedback, 2) using a framework to guide feedback, 3) ability to listen and problem solve with peers struggling with clinical skills. Most (79%) follow up surveys indicated that STICU RNs felt empowered to and had recently offered feedback when observing an opportunity.

Conclusion: A simulation-based feedback workshop designed for and implemented by trauma RNs and communication specialists can improve RN confidence, willingness, and skill engaging in important feedback discussions with peers, and lead to increased patient safety.

GROWING TRENDS OF PREHOSPITAL KETAMINE USE IN SEVERELY INJURED PATIENTS

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Introduction: Our local EMS guidelines prioritize the use of ketamine for acute pain management in patients with hypotension and respiratory failure. We hypothesize that prehospital ketamine for pain has increased and is a safe option for prehospital pain control. The specific aim of this study was to compare patients who received prehospital ketamine vs. fentanyl for pain.

Methods: This was a retrospective study (2014-2022) of adult trauma patients transported by EMS to our trauma center at the highest level of activation. We compared patients who received only fentanyl vs. only ketamine for prehospital pain. The ketamine and fentanyl groups were compared by univariate and multivariate analysis.

Results: 878 patients were included, 27% received ketamine and 73% received fentanyl. Ketamine use increased significantly from 2014-2022, $p<0.001$. Ketamine patients were younger (39 vs. 42, $p=0.0008$), but there was no difference in white/non-Hispanic ethnicity (53% vs. 55%, $p=0.58$), male gender (74% vs. 70%, $p=0.31$), or blunt mechanism (69% vs. 63%, $p=0.15$). Ketamine patients had a higher prehospital heart rate (103 vs. 99, $p=0.02$) and a lower systolic blood pressure (119 vs. 128, $p=0.0002$) and lower GCS (12 vs. 15, $p<0.0001$). These physiologic derangements persisted in the ED. Ketamine patients had a higher ISS (18 vs. 14, $p<0.0001$) and more often required an emergent hemorrhage control procedure (22% vs. 15%, $p=0.02$). Ketamine patients had a higher ED mortality (3% vs. 0.2%, $p=0.003$), and double the hospital mortality (6% vs. 3%, $p=0.06$). Ketamine patients spent more days in the hospital, ICU, and on the ventilator (all $p<0.05$). On logistic regression, prehospital GCS (AOR: 0.79 [0.73-0.87], $p<0.0001$) and blood pressure (AOR: 0.99 [0.98-0.99], $p=0.008$) were independently associated with receiving ketamine. While ketamine patients had worse outcomes, ketamine was not independently associated with mortality (AOR: 0.32 [0.09-1.2], $p=0.09$).

Conclusion: Ketamine use for prehospital pain control is increasing. Ketamine is being given to more severely injured patients with more physiologic derangement. Though patients who receive ketamine have worse outcomes, ketamine is not independently associated with mortality.

We anticipate that due to its mechanism of action leading to pain control without further respiratory suppression, ketamine will continue to be used more commonly for acute pain in trauma patients in the pre-hospital setting.