Influence of time to transport on clinical outcomes following evacuation from theater (LRMC/CONUS)

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FINAL REPORT

Date: 29 December 2020

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NOTICE AND SIGNATURE PAGE

Influence of time to transport on clinical outcomes following evacuation from theater (LRMC/CONUS)

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
29 December 2020	Final Report	09 Nov 16 – 06 Jan 19

4. TITLE AND SUBTITLE: Influence of time to transport on clinical outcomes following evacuation from theater (LRMC/CONUS):
1) Influence of Time to Transport to a Higher Level Facility on the Clinical Outcomes of US Combat Casualties with TBI: A Multicenter 7-Year Study
2) Characterization of long-range aeromedical transport and its relationship to the development of traumatic extremity compartment syndrome: a seven-year, retrospective study.

5a. CONTRACT NUMBER
W8XWH-16-P-0250

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER
DM15023

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
United States Air Force, 59th Medical Wing (59MDW/ST)
1255 Wilford Hall Loop, Building 4430
Lackland Air Force Base, 78236-9980

8. PERFORMING ORGANIZATION REPORT NUMBER
FWH20150081H

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
JPC-6 Combat Casualty Care
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Fort Detrick,MD21702-5024
Phone: (301) 619-7071

10. SPONSOR/MONITOR'S ACRONYM(S)
AMC

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
N/A

12. DISTRIBUTION / AVAILABILITY STATEMENT
Distribution A: Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT-

Background: The survival of combat-related, traumatically injured patients has improved, in part, due to the use of aeromedical evacuation platforms. One of the military medical evacuation teams operating in the combat setting is the Critical Care Air Transport Team (CCATT). It is vital to identify the evacuation needs of all casualties but equally important to determine patient and injury-specific needs of those transported out of theater via CCATT. One patient population of interest is casualties who sustained traumatic brain injury (TBI) in combat. The incidence of TBI in combat is estimated to be upwards of 20% constituting a significant portion of combat injuries. The optimal time to transport patients with TBI and the influence of aeromedical evacuation on patient outcomes remains unknown and no clinical studies to date have addressed this question. Treatment of TBI may require unique surgical interventions as well as delaying transport out of theater. While expeditious patient transport is advantageous, it may be more prudent and beneficial to the patient to have a delay in transport following necessary procedures and stabilization in-theatre.

Blast injuries often cause damage to muscle tissue, bone, connective tissue, and vasculature. Consequently, traumatic compartment syndrome of extremities (tCSoE) is another common complication seen in combat casualties. As soon as the clinical diagnosis of tCSoE is made, it is well established that early intervention such as fasciotomy is necessary for optimal patient outcomes. However, other factors not well understood are the effect of altitude, pressure changes, and hypoxia during long transports out of theater.

Objective: The long-term objectives were to identify the optimal time to transport trauma patients who were at risk for or developed traumatic compartment syndrome of extremities (tCSoE) or who suffered TBI in combat who were evacuated from a Role III military treatment facility (MTF) to Landstuhl Regional Medical Center (LRMC) and evaluate their clinical outcomes.
Specific Aim 1: To determine optimal time to transport patients with moderate or severe TBI.
Hypothesis: A longer length of stay in a theater hospital will be associated with decreased adverse clinical outcomes at 30 days, 6 months, and 1 year.
Specific Aim 2: To determine optimal time to transport patients with tCSoE.
Hypothesis: A shorter length of stay in a theater hospital will be associated with decreased clinical complications at 30 days, 6 months, and 1 year.

Study Design: We performed a systematic retrospective review of CCATT medical records of traumatically injured patients transported out of theater between January 2007 and December 2014. Trained critical care research nurses reviewed all of the medical records beginning at arrival to the first military treatment facility (MTF) in-theater through discharge from Role IV or V MTF (Landstuhl Regional Medical Center (LRMC) or a CONUS facility). Data abstracted included demographics, injury descriptors, clinical and laboratory parameters, procedures, and complications. The Department of Defense Trauma Registry (DoDTR) was queried to obtain up to 30 day, 6 month, and 1 year outcomes. Statistical analysis provided descriptive summaries and quantitative analysis. Multivariate analytical techniques, including logistic regression and proportional hazards regression models were used for reporting adjusted results. Data limitations were taken into account when interpreting and reporting results.

Conclusions: In patients with moderate to severe TBI, a delay in aeromedical evacuation after brain injury via pressurized cabin fixed-wing aircraft was associated with improved mortality rates. Longer time to transport was also associated with a higher odds of being discharged home and returned to duty. We also found no association between the timing of tCSoE and time of aeromedical transport. Based on the incidence of tCSoE diagnosis in our Pre- and Post-Flight groups, the greatest risk period for developing tCSoE is 1-3 days following injury; aeromedical transport does not increase the incidence. We can infer that aeromedical transport may not pose additional risks to patients as risk for or with tCSoE.

15. SUBJECT TERMS- aeromedical transport, military, TBI, compartment syndrome, time to transport

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT:**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
U			UU	30	Lt Col Joseph K. Maddry
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
U	U	U			210-539-0938

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Influence of Time to Transport to a Higher Level Facility on the Clinical Outcomes of US Combat Casualties with TBI: A Multicenter 7-Year Study

Gaps Addressed: 2015 ICL: AFMS (AMC) 25 - Epidemiology and Clinical Evaluation of Outcomes; AFMS 61 (AMC) Clinical and Functional Outcomes of Patient Movement

2016 AE RDD: CCA – Clinical En Route Care - 2. Epidemiology and Clinical Evaluation of Outcomes; 5. Clinical/Functional Outcomes of Patient Movement

Modified Abstract

Background: Traumatic brain injury (TBI) is a leading cause of death and disability worldwide and is associated with mortality rates as high as 30%. Patients with TBI are at high risk for secondary injury and need to be transported to definitive care expeditiously. However, the physiologic effects of aeromedical evacuation are not well understood and may compound these risks. Combat TBI patients may benefit from delayed aeromedical evacuation.

The goal of this retrospective study was to evaluate the impact of transport timing out of theater via Critical Care Air Transport Teams (CCATT) on the clinical outcomes of combat casualties with TBI.

Methods: We performed a retrospective review of patients with TBI who were evacuated out of theater by CCATT from January 2007 to May 2014. Data abstractors collected flight information, vital signs, procedures, in-flight assessments, and outcomes. Time to transport was defined as the time from injury to CCATT evacuation out of combat theater.

Results:

- 3,867 patients with TBI were transported from an in-theater MTF to Landstuhl Regional Medical Center (LRMC) during the study time period.
- 438 who met inclusion criteria ($\geq$ 18yrs, CCATT transport, head/neck AIS $\geq$ 3, ICD-9-CM code for TBI) were included in this analysis.
- 93% were US AD and 97% were male, median age 25 (IQR 21-30).
- Blast was the most common (70%) mechanism of injury and 65% of patients had penetrating injuries; 39% had severe TBI & 59% had polytrauma.
- Median time to transport (time from injury to departure from a Role III MTF) was 2 days (IQR 1–3) with a range of 0 to 18 days; all but two patients were transported within 7 days.
- Patients were categorized into three groups: patients who were transported within 24 hours of injury (n = 165), those transported 24-72 hours after injury (n = 163), and those transported over 72 hours after the time of injury (n = 110).
- Patients transported over 72 hours after injury had higher Injury Severity Scores (ISSs) and were more likely to have polytrauma, have had additional flights in-theater; and have received pre-flight blood products.
- Compared to those transported within 24 hours of injury, patients who were evacuated from theater after 72 hours or more were 70% less likely to be ventilated at discharge, less likely to have a GCS of 8 or lower (OR 0.3, 95% CI 0.2–0.4) and had a 30% lower odds of mortality (OR 0.7, 95% CI 0.7–0.8).
- Those transported over 24 hours after injury were twice as likely to return to duty or be discharged home (OR 1.7, 95% CI 1.1–2.8 for 24-72 hours; OR 2.7, 95% CI 1.5–4.9 for $\geq$72 hours).
- The occurrence of in-flight events associated with potential secondary brain injury was similar among groups. The one day or less group had significantly higher incidence of PaO_2 > 180 mmHg.

Conclusions: In patients with moderate to severe TBI, a delay in aeromedical evacuation out of the combat theater was associated with improved mortality rates and a higher likelihood of discharge to home and return to duty dispositions. This study is correlational in nature and focused on CCATT transports from Role III to Role IV facilities; as such, care must be taken in interpreting our findings and future studies are needed to establish a causal link between delayed evacuation and improved discharge disposition.

Evidence Based Recommendations:

- Medical personnel to include surgeons, validating flight surgeons, and CCATTs should consider if delaying of medical transport may be beneficial to their patients.
- Given the retrospective nature of this study and the potential for survival bias, a blanket policy mandating a delay in evacuation for TBI patients should not be instated.
- Future research should further evaluate the potential impact of early evacuation of TBI patients.
- Future research should further evaluate how to provide neurological intensive care unit (ICU) capabilities during CCATT transport of TBI patients.

Characterization of long-range aeromedical transport and its relationship to the development of traumatic extremity compartment syndrome: a seven-year, retrospective study

Gaps Addressed: 2015 ICL: AFMS (AMC) 25 - Epidemiology and Clinical Evaluation of Outcomes; AFMS 61 (AMC) Clinical and Functional Outcomes of Patient Movement

2016 AE RDD: CCA – Clinical En Route Care - 2. Epidemiology and Clinical Evaluation of Outcomes; 5. Clinical/Functional Outcomes of Patient Movement

Modified Abstract

Background: Musculoskeletal related injuries account for 10 of the top 15 diagnoses transported by CCATT. Patients with traumatic injuries of the extremities are at risk for the development of traumatic compartment syndrome of the extremities (tCSoE)—a common but emergent complication of trauma in which increased pressure due to injury causes bleeding, edema, and/or decreased blood flow to an extremity. Once tCSoE is diagnosed, a fasciotomy should be performed as soon as possible. A delay in diagnosis and treatment may increase morbidity and mortality. Aeromedical evacuation is associated with stressors such as hypobaria, hypoxia, and vibrations that could, in theory, increase the likelihood of compartment syndrome, or exacerbate compartment pressures.

The goal of this retrospective study was to evaluate the impact of transport timing out of theater via Critical Care Air Transport Teams (CCATT) on the clinical outcomes of combat casualties with tCSoE.

Methods: We performed a retrospective record review of combat casualties who had documentation of traumatic compartment syndrome of the extremities (upper and/or lower) and were transferred via aeromedical transport from Iraq or Afghanistan to Landstuhl Regional Medical Center (LRMC) from January 2007 to May 2014. Data abstractors collected flight information, vital signs, procedures, in-flight assessments, and outcomes. Time to transport was defined as the time from injury to CCATT evacuation out of combat theater.

Results:

- 238 patients with confirmed tCSoE were identified. 216 (91%) had data available for the date and time of injury and, at least, an approximated date for tCSoE diagnosis, and were included in this analysis.

- 98% were male, median age 23 (IQR 21-28).
- 24.7% of subjects had fasciotomies performed prior to tCSoE diagnosis. Of these, 9.4% had fasciotomy revisions or extensions. The rate of documented fasciotomy revision was 4.9% in those without documentation of fasciotomy procedure prior to tCSoE diagnosis (p=0.3157).
- In 80% of the study sample, documentation indicated tCSoE diagnosis within 1 day of injury.
- Documentation for the platform of transport to LRMC was available for 222 records (n=129; 58%, AE and n=93; 42%, CCATT).
- While the majority of casualties arrived at LRMC two days following injury (45%, n=107); 23% (n=55) arrived one day, 24% (n=58) three days, and 8% (n=18) more than 3 days following injury.
- A total of 113 (47%) casualties had a tCSoE diagnosis Pre-Flight and 123 casualties had the diagnosis made Post-Flight.
- The time of tCSoE diagnosis (Pre- or Post-flight) was not associated with the number of hours following injury that the patients arrived at LRMC: both Pre- and Post-flight groups had a similar proportion of patients who arrived at LRMC within 24, 48, 72, or 96+ hours.
- The time of tCSoE diagnosis (Pre- or Post-flight) was not associated with the number of hours following injury that the patients arrived at LRMC: both Pre- and Post-flight groups had a similar proportion of patients who arrived at LRMC within 24, 48, 72, or 96+ hours.
- When comparing Pre-flight versus Post-Flight groups there were no differences in the outcome measures.

Conclusions: We found no association between the timing of tCSoE and time of aeromedical transport. Based on the incidence of tCSoE diagnosis in our Pre- and Post-Flight groups, the greatest risk period for developing tCSoE is 1-3 days following injury and aeromedical transport does not increase the incidence. We can infer that aeromedical transport may not pose additional risks to patients as risk for or with tCSoE.

Evidence Based Recommendation:

- While current evidence does not indicate that aeromedical evacuation increases the risk of compartment syndrome, military medical personnel should monitor closely for evidence of compartment syndrome prior to, during, and after aeromedical evacuation, particularly 1-3 days following injury.

Publication

Maddry JK, Mora AG, Perez CA, Reeves LK, Paciocco JA, Clemons MA, Sheean A, Kester NM, Bebarta VS. Characterization of long-range aeromedical transport and its relationship to the development of traumatic extremity compartment syndrome: a seven-year, retrospective study. Mil Med. 2021 Jan 12:usaa462.
doi: 10.1093/milmed/usaa462. Epub ahead of print. PMID: 33433584.

2.0 INTRODUCTION

The use of aeromedical evacuation platforms has increased the survival of patients who were traumatically injured in combat. Nearly 8,000 critically ill or injured patients have been transported via CCATT since the beginning of the wars in Iraq and Afghanistan. CCATT is a US Air Force asset tasked with transporting critically ill and injured patients within the theater of operations, and out of theater to more advanced medical facilities.

Traumatic brain injury (TBI) is a leading cause of death and disability worldwide and is associated with mortality rates as high as 30%. Patients with TBI are at high risk for secondary injury and need to be transported to definitive care expeditiously. However, the physiologic effects of aeromedical evacuation are not well understood and may compound these risks. Aeromedical evacuation is associated with stressors such as hypobaria, hypoxia, and vibrations that could, in theory, lead to secondary insult to the brain in TBI, and increase the likelihood of compartment syndrome or exacerbate compartment pressures. Therefore, combat TBI patients may benefit from delayed aeromedical evacuation.

Musculoskeletal related injuries account for 10 of the top 15 diagnoses transported by CCATT. Patients with traumatic injuries of the extremities are at risk for the development of traumatic compartment syndrome of the extremities (tCSoE)—a common but emergent complication of trauma in which increased pressure due to injury causes bleeding, edema, and/or decreased blood flow to an extremity. Once tCSoE is diagnosed, a fasciotomy should be performed as soon as possible; a delay in diagnosis and treatment increases morbidity and mortality.

The purpose of this study was to provide evidence based on clinical outcomes to inform decisions related to timing of casualty evacuation out of theater.

3.0 METHODS, ASSUMPTIONS AND PROCEDURES

We performed a systematic retrospective review of CCATT medical records of traumatically injured patients transported out of theater between January 2007 and December 2014. Trained critical care research nurses reviewed all of the medical records beginning at arrival to the first MTF in-theater through discharge from Role IV or V MTF (LRMC or CONUS facility). Data abstracted included; demographics, injury descriptors, clinical and laboratory parameters, procedures, and complications. The Department of Defense Trauma Registry (DoDTR) was queried to obtain up to 30 day, 6 month, and 1 year outcomes. Statistical analysis provided descriptive summaries and quantitative analysis. Multivariate analytical techniques, including logistic regression and proportional hazards regression models, were used for reporting adjusted results. Data limitations were taken into account when interpreting and reporting results.

4.0 MAJOR EVENTS/MILESTONES/SUCCESS

- Kick Off Meeting – 06/15
- IRB/IACUC Approval – 07/15
- All experimental procedures completed – 03/19
- Data Analysis – 08/18
- Poster presentation – MHSRS; Orlando, FL; 2018
- Manuscript submitted to – Mil Med – 2019; Mil Med - 2021
- Dissemination of Results – 08/18

5.0 RISK ASSESSMENT

5.1 Risk Analysis:

This study presented no greater than minimal risks to the subjects. There were no interventions and no changes to the standards of care. The risk involved potential breaches of privacy and patient confidentiality should the data set be acquired by a person or agency outside of this research team. This risk is similar to basic patient care that would otherwise normally be carried out. The likelihood of this occurrence was mitigated by password protection of electronic files and removal of patient PHI.

5.2 Technical Challenges

Due to the retrospective nature of this study, some medical records may have missing data elements. The ability to access TMDS and M2 allowed us to validate data collected and reconcile missing or inaccurate data. Multiple data abstractors were used which caused variability of data. Research nurses were trained on database management, and data extraction. A standardized process for data abstraction, as was implemented in our previous studies, was used in order to decrease subjectivity in data collection methods. Quality assurance (QA) measures were utilized for all ECRC studies. A sub-set of 10% of the records were reviewed by another research nurse and evaluated for consistency. This proposal required coordination of several data repositories. The En route Care Research Center has conducted multiple retrospective research projects involving evacuation of combat casualties. We maintain a collaborative working relationship with the Joint Trauma System (JTS), a MOA with the USAISR, and access to relevant government electronic medical record systems for the purposes of this and previous studies.

6.0 TRANSITION PLAN

6.1 Military Relevance

Evaluating evacuation outcomes provides military planners and medical leaders with the evidence to optimize the evacuation of critically ill service members. The two groups of patients included in this study make up a significant portion of combat casualties. Knowledge gained from the study improves evacuation decision-making and ultimately the outcomes of the war fighter.

6.2 Transition Strategy

The results of this study provided new knowledge about the influence of transport time on combat casualty care and ensures that providers are equipped and prepared for the challenges faced in the delivery of care during evacuation. Data collected was filtered into the database for Project Mercury, can be queried to conduct retrospective analysis to support and provide research to investigators, and allows for performance improvement initiatives. Lessons learned establish the ground work for CPG development and standardization of care.

The results were also disseminated to the following:

1. The research community through national civilian and military academic conferences and meetings to include the Military Health Science Research Symposium (MHSRS).
2. Completed manuscripts submitted to peer-reviewed journals for publication.
3. The Defense Technical Information Center (DTIC) for publishing on their website.
4. Appropriate military leadership and training agencies.

7.0 RESULTS

Combat casualties with TBI: Our initial query from DoDTR yielded 3867 patients with TBI who were transported from a combat theater hospital to LRMC between January 2007 and May 2014. Of these, 477 fit the study inclusion criteria (18 years of age or older, transported via CCATT, and a documented head/neck AIS severity score of 3 or greater with an ICD-9-CM code for TBI). As the primary goal of this study was to evaluate outcomes related to time to transport, we excluded 39 patients who had a catastrophic brain injury (i.e., were on the levothyroxine/T4 protocol for organ donors, were being flown for organ donation, or were being flown home for family visitation). The final sample for analysis included 438 patients. The majority of patients were U.S. active duty males with a median age of 25 (IQR 21–30) (Table I). The median time to transport (time from injury to discharge from a Role III MTF) was 2 days (IQR 1–3) with a range of 0 to 18 days; all but two patients were transported within seven days.

For analyses we categorized patients into three groups: those transported within one day (n = 165, 38% of the sample), two days (n = 163, 37%), and three days or more (n = 110, 25%). We also ran all analyses with the two outliers (who were transported to LRMC in 13 and 18 days) removed and found similar results in both the univariate comparisons and multivariable models. Blast was the most common mechanism of injury (70%) and most patients (65%) sustained penetrating injuries. Over half (59%) of the TBI patients had polytrauma, and 39% had severe TBI. Those who were transported in three days or more had higher ISS scores, were more likely to be polytrauma patients, and were more likely to have additional flights in-theater (Table I). Prior to transport, most patients (72%) were on a ventilator, 28% had an ICP monitor placed, and 50% received blood products (Table II). Those who were transported in three or more days were more likely to require pre-flight blood products. The most common in-flight interventions were intravenous sedation, mechanical ventilation, and anti-seizure medications (Table II). Patients transported within one day were more likely to receive vasopressors, paralytics, and blood products during flight. During transport, 61% of all patients had temperature over 37.5 °C, 49% had PCO2 higher than 40 mmHg, 44% experienced systolic blood pressure (SBP) lower than 110 mmHg, and 46% had sodium levels lower than 145 mmol/L (Fig. 1). Seventeen percent had SpO2 of 95% or lower, and 19% had an in-flight PaO2 less than 80 mmHg. Six percent had PaO2 higher than 180 mmHg; this was more common in the one day group compared to the others (10% vs. 4% vs. 3%, respectively; p = 0.0173). Three percent of all patients had in-flight intracranial pressure (ICP) greater

Combat casualties with traumatic compartment syndrome of the extremities (tCSoE): We identified 238 unique records with a confirmed diagnosis of tCSoE during our study window. Of those, 91% (n=216) had data available for the date and time of injury and, at least, an approximated date for tCSoE diagnosis. The remaining 43 records had provider documentation of tCSoE diagnosis, but did not have a date or timestamp associated with the diagnosis. We found that time of fasciotomy and time of diagnosis were correlated for those patients for whom the two time points were available (r=0.77), so for records that were missing the time of diagnosis, we used the time of fasciotomy as a substitute data point.

Table 1 describes the demographics of our study population. A total of 22 had traumatic compartment syndrome of the upper extremities only, three of both upper and lower extremities, and the remainder of the lower extremities alone. Of note, 24.7% of subjects had fasciotomies performed prior to tCSoE diagnosis. Of these, 9.4% had fasciotomy revisions or extensions. The rate of documented fasciotomy revision was 4.9% in those without documentation of fasciotomy procedure prior to tCSoE diagnosis (p=0.3157). For 80% of the study sample, documentation indicated tCSoE diagnosis within 1 day of injury (Table 1). Documentation for the platform of transport to LRMC was available for 222 records (n=129; 58%, AE and n=93; 42%, CCATT). While the majority of casualties arrived at LRMC two days following injury (45%, n=107), 23% (n=55) arrived one day, 24% (n=58) three days, and 8% (n=18) more than 3 days following injury.

Timing of transport as a function of Pre- or Post-Flight Diagnosis of tCSoE

Casualties transported by CCATT were more likely to have developed tCSoE within 1 day following injury. In our study sample, none of the casualties whom developed tCSoE longer than 2 days from the injury date were transported by CCATT. CCATT transported casualties with higher injury severity (median ISS=10 for AE versus 20 for CCATT; p<0.0001) and a higher proportion of polytrauma compared to AE (88% AE versus 97% CCATT; p=0.0158). In contrast, AE transported a higher proportion of casualties with blunt related injuries (72% for AE versus 28% for CCATT; p=0.0115). However, times to transport casualties to LRMC were similar for the two modes of transport (median of 2 days, p=0.9676). AE and CCATT were equally likely to transport casualties to LRMC one day (23% AE vs 25% CCATT, p=0.7994) and two days (67% AE vs 69% CCATT, p=0.9778) following injury. Comparison of cumulative incidence profiles of

than 20mmHg, though it should be noted that ICP was only recorded for 116 out of 121 patients with an ICP monitor. Patients evacuated from theater within one day of injury spent significantly less time in the ICU and hospital compared to patients in the other two groups ($p < 0.0055$) (Table III). The vast majority of patients survived (96%) and continued medical care (88%). Six percent returned to duty or were discharged home. Nearly a quarter of patients (24%) still required mechanical ventilation at discharge and 13% were discharged on a ventilator with a Glasgow coma scale (GCS) score of 8 or lower; patients transported within one day were more likely to experience these negative outcomes ($p < 0.0055$). There was a significant association between low discharge GCS scores and total hospital/ICU/ventilator days spent by the patient. Compared to patients who did not have a discharge GCS score of 8 or lower, those who had a discharge GCS score of 8 or lower spent more days on a ventilator (median 7 [IQR 5–10] days vs. 5 [2–10] days, $p = 0.0026$), fewer days in the ICU (7 [5–10] vs. 9 [6–15] days, $p = 0.0004$), and fewer days in a hospital (5 [3–9] days vs. 18 [7–37] days, $p < 0.0001$). In multivariable logistic regression models, longer times to transport (i.e., two days, or three or more days) generally conferred better outcomes than more immediate transports, even after adjusting for ISS, polytrauma, head/neck AIS severity score, blast injury, cranial fracture(s), intracranial hemorrhage, presence of bone fragments or foreign bodies, and need for pre-flight blood products and surgical procedures (see Supplemental Table S2 for full model results).

Although we did not include the composite variable for severe TBI in the models, we did include a component of it (head/neck AIS severity score). We previously ran these analyses with severe TBI as a covariate and found that the models fit better when only AIS severity score was included. We also adjusted our model for hospital days spent at the Role IV MTF to account for the influence of the hospital length of stay and time between subsequent air transports on our dichotomous outcomes. Compared to those transported in one day or less, patients who were evacuated from theater after three or more days were 70% less likely to be ventilated at discharge with a GCS of 8 or lower (OR 0.3, 95% CI 0.2–0.4) and had 30% lower odds of mortality (OR 0.7, 95% CI 0.7–0.8). Both delayed transport groups were twice as likely to return to duty or be discharged home (OR 1.7, 95% CI 1.1–2.8 for 2 days; OR 2.7, 95% CI 1.5–4.9 for ≥3 days) and 50% less likely to be ventilated at discharge (OR 0.5, 95%CI 0.4–0.6 for 2 days; OR 0.5, 95% CI 0.3–0.7 for ≥3 days) than the one day group.

compartment syndrome diagnoses relative to injury time between AE and CCATT platforms did not differ (Log-rank statistic, $\chi 2=1.7403$; $p=0.1871$).

For the 22 patients whom did not have available timestamps for time of tCSoE diagnosis, we were able to determine whether the diagnosis was made prior to (Pre-Flight, n=6) or after transport to LRMC (Post-Flight, n=16) based on the facility in which the compartment syndrome was diagnosed. We re-assessed all records using the binary distinction for the time of tCSoE diagnosis as Pre-Flight (if the tCSoE diagnosis was made in-theater) or Post-Flight (if the CSoE diagnosis was made at LRMC; Table 2). A total of 113 (47%) casualties had a tCSoE diagnosis Pre-Flight and 123 casualties had the diagnosis made Post-Flight. Casualties whom developed tCSoE Pre-Flight versus Post-Flight were of similar age and sustained similar injuries compared to the Post-Flight group; however, the Post-Flight group had higher average ISS. Both tCSoE diagnoses and fasciotomies were performed at similar times following injury; however, the Post-Flight group arrived at LRMC more quickly than the Pre-Flight group. Albeit small numbers, casualties in the Pre-Flight group were more likely to have a secondary compartment syndrome diagnosis of another extremity and so, were more likely to have additional fasciotomies performed.

To determine whether aeromedical transport influenced the development of tCSoE, we first established the timing for the development of tCSoE for the Pre- and Post-Flight groups. We compared patients based on the amount of time elapsed between sustaining their injury and being transported. We used the number of hours post-injury that the patients arrived at LRMC as a data point to represent the time of transport following injury, and compared the LRMC arrival times for patients who had Pre- and Post-Flight diagnosis of tCSoE (Figure 1). We found that the time of tCSoE diagnosis (Pre- or Post-Flight) was not associated with the number of hours following injury that the patients arrived at LRMC: both Pre- and Post-Flight groups had a similar proportion of patients who arrived at LRMC within 24, 48, 72, or 96+ hours.

Next, to determine whether aeromedical transport influenced the timing of tCSoE development, we compared the time of transport following injury with the timing of tCSoE diagnosis for the Post-Flight group only. Similarly to the distribution of the population as a whole (Figure 1), we found that the incidence of tCSoE was similar regardless of the length of the delay in transport following injury (Figure 2). Therefore, for those patients whom did not have tCSoE at the time of transport, time of tCSoE diagnosis did not differ based on LRMC arrival day.

	In an attempt to understand factors associated with time-to-LRMC arrival in casualties with confirmed tCSoE, we used Cox proportional hazard regression techniques. When considering age, sex, injury, country of military operation, procedures performed in-theater, disposition in-theater, and transport platform, we found that casualties with head injuries arrived at LRMC faster than those without a head injury (Odds Ratio 2.27 ; 1.26-4.11). We also evaluated whether specific factors in the presence of aeromedical transport contributed to the timing of the development of tCSoE accounting for factors similar to the time-to-LRMC analysis. We did not identify any factors to be associated with faster time-to-tCSoE development. When considering causalities who developed lower extremity, traumatic compartment syndrome, there were higher odds of compartment syndrome within 24 hours with a concomitant head injury (Odds Ratio 3.72, 1.08-12.8) regardless of tourniquet application, amount of fluids, or blood product administration in-theater. In this study, tourniquet application, crystalloids, colloids, and blood products were not associated with developing compartment syndrome within 24 hours. **Outcomes** Comparing outcomes among the groups, the 1-Day group was more likely to have documented coagulopathy and lung dysfunction (Supplemental Table 1). Likewise, the 1-Day group had more ventilator days (3.1□8.0 days), ICU (6.1□9.9 days), and hospital days (25.1□29.0 days). Conversely, when comparing Pre-Flight versus Post-Flight groups there were no differences in the outcome measures (Supplemental Table 2). We had a high survival rate in this study sample—only n=3 did not survive their injuries.

8.0 CONCLUSION/DISCUSSION

Combat casualties with TBI:

We found that a longer time to transport out of theater by fixed-wing pressurized cabin aircrafts was associated with lower odds of mortality even after adjusting for confounding variables reflective of the acuity of injury. Similarly, after adjusting for covariates, those aeromedically evacuated out of theater two or more days after the injury were less likely to be ventilated at discharge and more likely to return to duty or be discharged home. Unlike previous studies evaluating events occurring during aeromedical evacuation of TBI patients, our study evaluated patient outcomes. There are no published clinical studies that have described the most favorable time to transport with regard to patient outcomes. While expeditious patient transport is advantageous, it may be more prudent and beneficial to the patient if transport followed necessary procedures and stabilization rather than to immediately evacuate. Exposure to altitudes greater than 6500 feet have been known to result in symptoms of acute mountain sickness (AMS). While the etiology of AMS is unknown, it is frequently presumed to be a result of neuroinflammation secondary to hypoxia.[25] In our study, the rates of hypoxia and hypoxemia were not significantly different across the three groups. However, while in-flight hyperoxemia (PaO2 >180 mmHg) only occurred for 6% of patients in our sample, it was twice as common for those evacuated within one day compared to the other groups. Our previous publication evaluating ventilator management of CCATT casualties demonstrated hypoxia seldom occurring in CCATT ventilated patients while hyperoxia was a more frequent occurrence.[21] Animal TBI models have demonstrated worse neurologic outcome in subjects exposed to hyperoxia following TBI.[26] Hypobaria alone during aeromedical evacuation may exacerbate TBI. Previous animal studies have demonstrated hypobaria resulting in a decrease in subject mean arterial pressure, cerebral perfusion pressure, and brain tissue oxygen partial pressure despite supplemental oxygen provided via a ventilator.[28] Animal studies have also demonstrated both hypobaria induced exacerbation of histologic brain injury in a TBI model and a lack thereof.[27–30] Skovira, et al found hypobaric exposure up to seven days following TBI exacerbated resulting in worsened cognitive deficits and neuronal loss, while 100% oxygen exposure resulted in further exacerbation.[14] It remains unclear if cabin altitude restriction (maintaining a higher aircraft cabin barometric pressure) would prevent the increased morbidity demonstrated in our study in those TBI patients aeromedically evacuated within one to two days of injury. Cabin altitude restriction results in increased fuel consumption and mechanical stress

Combat casualties with traumatic compartment syndrome of the extremities:

From January 2007 to May 2014, we documented 238 casualties who developed tCSoE. If aeromedical evacuation accelerated the time to development of tCSoE we would have expected to discover an increased incidence of tCSoE diagnoses following aeromedical transport and so postulate an increased risk of compartment syndrome with aeromedical transport. However, the incidence rate of tCSoE diagnosis following flight was comparable to the incidence rate prior to flight. Based on the results of this study, we are not able to conclude that aeromedical transport is associated with the timing of the development tCSoE, nor can we infer that aeromedical transport poses additional risks to casualties at risk for or with tCSoE. To our knowledge, this is the first human study evaluating the impact of the hypobaric aeromedical transport environment on tCSoE and subsequent patient outcomes.

It has been postulated that the hypobaric environment of aeromedical evacuation could increase the risk of compartment syndrome.[13,18-20] McGill et al. found that a cabin altitude pressure of 10,000 feet resulted in a 2.7 mmHg increase in compartment pressures of healthy swine.[13] However, the clinical significance of this small increase is unknown. This is in part due to conflicting literature on what compartment pressure is necessary to induce compartment syndrome. Ouellette and Kelly report the occurrence of compartment syndrome with pressures as low as 15 mmHg.[18] Conversely, Allen et al. claim that the development of compartment syndrome occurred at pressures greater than 40 mmHg.[19] Still other authors have contended that compartment syndrome occurs when the diastolic pressure minus the compartment pressure is less than 30 mmHg[20] or have argued the mean arterial pressure minus compartment pressure is more accurate.[20,21] While the explicit, numeric measure of compartment pressure is not universally defined, the presentation of compartment syndrome is reliably identified by clinicians.

While our study could not corroborate compartment pressure measures, the clinical presentation of tCSoE results of our study are consistent with animal studies of compartment syndrome in that they have found no clinically significant impact of hypobaria. Rietnour et al. induced elevated compartment pressures in a rat model using limb ischemia and found no difference in compartment pressures when comparing animals at sea level versus 10,000 feet.[15] Similarly, Kalns et al. found no difference in compartment pressures when swine with elevated compartment pressure were exposed to

placed on the aircraft. Clinicians and aircrew will need to continue to use the current evidence and the patients' clinical status to determine when to use cabin altitude restriction. Our study indicates that delaying aeromedical evacuation of TBI patients when feasible may confer benefit. Given maximal brain edema typically occurs three to five days following traumatic brain injury, Fang et al advised avoidance of aeromedical evacuation during this timeframe.[18] An animal study found hypobaric hypoxia exposure three hours after TBI resulted in an increased neuroinflammatory response whereas exposure [24] hours after TBI did not. The 2012 JTS CPG for neurosurgical management recommends clinicians consider observation in-theater for patients with marginal intracranial pressures.[23] Our study implies further expansion of the consideration of observation to patients with moderate to severe TBI regardless of intracranial pressures; however, further evidence is needed before policy changes are considered. Commanders and medical personnel must consider multiple medical, logistical, and military variables when evacuating patients. Since critically ill patients are at a greater risk for complications during transport, the medical team must prepare and stabilize the patient prior to movement while simultaneously considering the risks versus potential benefits of transport.31 Other potential etiologies of worsening outcomes in rapidly evacuated TBI patients may result from noise, vibration, acceleration/deceleration forces, patient movement, interruption of sleep, and decreased monitoring capabilities. Further research to determine what aspects of AE exacerbate TBI are necessary. Continued research of mitigation strategies and therapies to prevent secondary brain injury, to include cabin altitude restriction, are also necessary. Finally, TBI encompasses a diverse group of injuries to include penetrating trauma, blunt trauma, foreign bodies, cerebral anatomy, and various forms of intracranial hemorrhage. Future research should evaluate the impact of aeromedical evacuation timing on different types of traumatic brain injury. Our study has several limitations. First, the study is retrospective in nature and therefore we are only able to determine associations, not causation. Second, several confounding variables may have impacted patient outcomes. While we attempted to control for these factors by including them as covariates in our regression models, there are variables that were not routinely collected in patient care records (such as provider gestalt regarding urgency of evacuation). Furthermore, the data was abstracted from the CCATT record, creating the potential for missing data due to a lack of documentation by the en route care teams. This missing data may have resulted in Type 2 errors, particularly regarding comparisons of ICP. While all data abstractors were trained and periodic quality

hypobaria, but did find that hypobaria resulted in reduced muscle degeneration and microvascular thrombi.[14] Our study of tCSoE and aeromedical evacuation is consistent with animal studies of compartment syndrome in that both fail to determine a negative impact of hypobaria on tCSoE.
In our study, prophylactic fasciotomies performed before tCSoE diagnosis were not associated with subsequent revisions of an existing fasciotomy. Given the retrospective nature of our study, it is unclear if our findings support the need to perform prophylactic fasciotomies, or if prophylactic fasciotomies were performed on individuals who would not have developed tCSoE. Of note, in order to avoid the morbidity and mortality associated with delayed tCSoE diagnosis, aggressive employment of fasciotomy was used during OIF/OEF in accordance with the clinical practice guideline.

Casualties who developed tCSoE at LRMC (Post-Flight) arrived at LRMC more quickly and had higher average ISS than the Pre-Flight group. These findings support our hypothesis that for patients vulnerable to the development of tCSoE, aeromedical evacuation is not associated and not an influencing factor. Aligned with orthopedic clinical education, the greatest risk period is one to three days following injury and our study implies that the risk period may be independent of aeromedical evacuation. In fact, in both the Pre- and Post- flight groups, tCSoE diagnoses spiked at 48 hours post-injury. This contrasts with our study evaluating the impact of time to transport patients with traumatic brain injury, which found an association between delayed evacuation and improved outcomes regardless of injury severity.[22]

Deployed clinicians must remain aware that the incidence of tCSoE remains to be one to three days following the time of injury.[9] A significant proportion of casualties are flown out of theater during this critical time; however, aeromedical evacuation of stabilized patients with diagnosed tCSoE may not confer greater risks and may not be contraindicated. Furthermore, given our study demonstrating a clinically significant rate of subsequent fasciotomy revision, efforts could be made to ensure combat surgeons are well versed in this surgery.

Limitations

Our study has several limitations. We found no association between time of aeromedical evacuation and the development of tCSoE relative to injury, but, as with any retrospective study, we are unable to determine causation or a lack thereof. Second, the data were abstracted from the medical records and were subject to the availability of records and documentation practices of clinicians. Granularity of care provided to

reviews occurred, there also remains the potential for subjectivity in data abstraction from the CCATT patient care records.[32,33] The mechanism of injury, severity of injury, young age of our population, and long transcontinental evacuation times may limit the generalizability of our findings to the civilian population. Finally, this study is focused on the leg of transport between Role III and Role IV facilities and did not analyze any data from patients who died prior to arriving at a Role III MTF or were not evacuated via CCATT. The outcome measures only capture data for the period from injury to discharge or transfer from the last MTF (Role IV or Role V) reported for each patient in DoDTR. As such, care must be taken in interpreting our findings and future studies are needed to establish a causal link between delayed evacuation and improved discharge disposition. **Conclusion** In patients with moderate to severe TBI, a delay in aeromedical evacuation after brain injury out of the combat theater via pressurized cabin fixed-wing aircraft was associated with improved mortality rates. Longer time to transport was also associated with a higher odds of being discharged home and returned to duty.	include timestamps and temporal order is limited; thus, we used surrogate data measures to best interpret care and outcomes. Third, there is the potential for subjectivity in data abstraction. However, to mitigate these risks, we incorporated abstractor training, adhered to periodic quality reviews per our center's protocol, and reconciled discrepancies with supplemental data. Finally, the ability to extrapolate our findings to civilian trauma may be limited given that our patient population consisted predominately of young male adults who suffered from mechanisms of injury uncommon outside of military conflict. However, information derived from this study provides insight regarding the influence of altitude and related factors on the pathophysiology of the critically injured patients. **Conclusion** We found no association between the timing of tCSoE and time of aeromedical transport. Based on the incidence of tCSoE diagnosis in our Pre- and Post-Flight groups, the greatest risk period for developing tCSoE is 1-3 days following injury and aeromedical transport does not increase the incidence. We can infer that aeromedical transport may not pose additional risks to patients as risk for or with tCSoE.

9.0 DELIVERABLES

9.1 Publications:

Maddry JK, Arana AA, Perez CA, Medellin KL, Paciocco JA, Mora AG, Holder WG, Davis WT, Herson P, Bebarta VS. Influence of Time to Transport to a Higher Level Facility on the Clinical Outcomes of US Combat Casualties with TBI: A Multicenter 7-Year Study. Mil Med. 2019;00(0/0):1.

https://academic.oup.com/milmed/advance-article-abstract/doi/10.1093/milmed/usz178/5537331

Maddry JK, Mora AG, Perez CA, Reeves LK, Paciocco JA, Clemons MA, Sheean A, Kester NM, Bebarta VS. Characterization of long-range aeromedical transport and its relationship to the development of traumatic extremity compartment syndrome: a seven-year, retrospective study. Mil Med. 2021 Jan 12:usaa462.

doi: 10.1093/milmed/usaa462. Epub ahead of print. PMID: 33433584.

9.2 Presentations:

Impact of Time to Transport on Clinical Outcomes of Patients with Traumatic Brain Injuries (TBI) Following Evacuation from Theater via Critical Care Air Transport Teams (CCATT)

- Military Health System Research Symposiums (MHSRS) 2018 – Poster
- San Antonio Military Health System and Universities Research Forum (SURF) 2018 – Poster
- TriService Nursing Research Program (TSNRP) 2018 – Podium
- Government Services Chapter of the American College of Emergency Physicians (GSACEP) 2018 - Poster
- Air Force Medical Research Advisory Committee (MRAC) Meeting - Podium
- GSACEP 2019 – Poster

Patients with Extremity Compartment Syndrome: A Descriptive Study of 238 Patients Aeromedically Evacuated From Theater

- MHSRS 2018 – Poster
- Air Force Medical Research Advisory Committee (MRAC) Meeting – Podium
- GSACEP 2019 (Projected) - Poster

10.0 COST

This work was funded by a JPC-6 award. Total funding awarded for this Project Code Number DM15023 in the amount of $358,000.00 were expended by 30 Sep 2017.

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FIGURES AND TABLES:

TBI - Table 1. Demographics, flight, and injury information

Variable	Overall (N=438)	≤1 day (n=165)	2 days (n=163)	≥3 days (n=110)	p
Age	25 [21-30]	25 [21-30]	25 [22-30]	24 [21-29]	0.3883
Gender, % male	428 (97%)	161 (97%)	159 (98%)	108 (98%)	0.9275
Service category					0.7515
US active duty	408 (93%)	156 (95%)	151 (93%)	101 (92%)	
US civilian	8 (2%)	2 (1%)	3 (2%)	3 (3%)	
US contractor	21 (5%)	7 (4%)	9 (6%)	5 (5%)	
Foreign	1 (<1%)	0	0	1 (1%)	
Altitude restriction	81 (19%)	35 (22%)	29 (18%)	17 (15%)	0.4161
Additional flights in-theater	242 (55%)	59 (36%)	103 (63%)	80 (73%)	<0.0001
Mechanism of injury					0.0074
GSW	61 (14%)	33 (20%)	16 (10%)	12 (11%)	
Explosive	307 (70%)	107 (65%)	127 (78%)	73 (66%)	
MVC/other	70 (16%)	25 (15%)	20 (12%)	25 (23%)	
Type of injury					0.3413
Blunt	150 (34%)	59 (36%)	48 (29%)	43 (39%)	
Burn	3 (<1%)	2 (1%)	1 (1%)	0	
Penetrating	286 (65%)	104 (63%)	114 (70%)	67 (61%)	
Polytrauma*	259 (59%)	81 (49%)	102 (63%)	76 (69%)	0.0022
ISS	27 [21-35]	26 [20-34]	29 [22-36]	29 [24-36]	0.0247
AIS severity score head/neck > 3	263 (60%)	100 (61%)	96 (60%)	67 (61%)	0.9298
Preflight GCS score	7 [3-14]	6 [3-14]	6 [3-14]	9 [3-15]	0.4376
Preflight GCS score ≤ 8	263 (60%)	109 (66%)	97 (60%)	57 (52%)	0.0605
Severe TBI†	168 (39%)	74 (45%)	60 (37%)	34 (31%)	0.0582
Any intracranial hemorrhage	207 (47%)	91 (55%)	68 (42%)	48 (44%)	0.0475
Intraparenchymal hemorrhage	118 (27%)	55 (33%)	40 (25%)	23 (21%)	0.0514
Subarachnoid hemorrhage	114 (26%)	50 (30%)	42 (26%)	22 (20%)	0.1614
Subdural hematoma	93 (21%)	42 (25%)	25 (15%)	26 (24%)	0.0631
Intraventricular hemorrhage	34 (8%)	15 (9%)	12 (7%)	7 (6%)	0.6894
Epidural hematoma	30 (7%)	13 (8%)	8 (5%)	9 (8%)	0.4623
Facial fractures	211 (48%)	78 (47%)	81 (50%)	52 (47%)	0.8868
Cranial fracture	174 (40%)	70 (42%)	68 (42%)	36 (33%)	0.2207
Contusion	77 (17%)	32 (19%)	25 (15%)	20 (18%)	0.6163
Foreign bodies present	76 (17%)	31 (19%)	32 (20%)	13 (12%)	0.2042
Bone fragments present	61 (14%)	29 (18%)	25 (15%)	7 (6%)	0.0253
Midline shift	51 (12%)	23 (14%)	16 (10%)	12 (11%)	0.4886
Mass effect	35 (8%)	13 (8%)	10 (6%)	12 (11%)	0.3605
Herniation	22 (5%)	12 (7%)	8 (5%)	2 (2%)	0.1272
Diffuse axonal injury	21 (5%)	11 (7%)	5 (3%)	5 (5%)	0.3093
Compressed fourth ventricle	16 (4%)	8 (5%)	7 (4%)	1 (1%)	0.2005
Compressed ambient cistern	12 (3%)	8 (5%)	2 (1%)	2 (2%)	0.1564

Values given are median [IQR] or count (column percentage). P-values are for one-way ANOVA/Kruskal-Wallis test or chi square/Fisher's exact test.

GSW, gunshot wound; MVC, motor vehicle crash; ISS, injury severity score; AIS, Abbreviated Injury Scale; TBI, traumatic brain injury

* Polytrauma = AIS > 2 in at least one body region (BR) other than head

† Severe TBI = AIS severity score of the head/neck > 3 and a preflight GCS score ≤ 8

TBI - Table 2. Pre-flight and in-flight interventions

Variable	Overall (N=438)	≤1 day (n=165)	2 days (n=163)	≥3 days (n=110)	p
Pre-flight					
SpO_2, %	99 [98-100]	100 [98-100]	100 [98-100]	99 [96-100]	0.0153
Supplementary oxygen	65 (15%)	20 (12%)	24 (15%)	21 (19%)	0.2809
Mechanical ventilation	315 (72%)	123 (74%)	118 (72%)	74 (67%)	0.4153
Surgery: abdomen	99 (23%)	26 (16%)	43 (26%)	30 (27%)	0.0284
Surgery: extremities	217 (50%)	64 (39%)	90 (55%)	63 (57%)	0.0021
Surgery: head	247 (56%)	103 (62%)	89 (55%)	55 (50%)	0.1064
ICP monitor	121 (28%)	54 (33%)	39 (24%)	28 (25%)	0.1718
Ventriculostomy	94 (22%)	36 (22%)	34 (21%)	24 (22%)	0.9724
Craniotomy	56 (13%)	22 (13%)	15 (9%)	19 (17%)	0.1417
Craniectomy	45 (10%)	22 (13%)	14 (9%)	9 (8%)	0.2593
Globe repair	37 (8%)	15 (9%)	15 (9%)	7 (6%)	0.6616
Hematoma evacuation	33 (8%)	14 (8%)	8 (5%)	11 (10%)	0.2481
Fragment removal	27 (6%)	7 (4%)	13 (8%)	7 (6%)	0.3706
Duraplasty	19 (4%)	7 (4%)	7 (4%)	5 (5%)	0.9921
Lobectomy	9 (2%)	4 (2%)	2 (1%)	3 (3%)	0.6966
Any blood products	219 (50%)	67 (40%)	88 (54%)	64 (58%)	0.0074
Packed red blood cells	198 (45%)	58 (35%)	81 (50%)	59 (54%)	0.0037
Fresh frozen plasma	189 (43%)	59 (36%)	78 (48%)	52 (47%)	0.0521
Platelets	109 (25%)	28 (17%)	41 (25%)	40 (36%)	0.0013
Cryoprecipitate	77 (18%)	16 (10%)	30 (18%)	31 (28%)	0.0004
Massive transfusion	37 (8%)	10 (6%)	16 (10%)	11 (10%)	0.3766
Factor VII	22 (5%)	11 (7%)	2 (1%)	9 (8%)	0.0169
Whole blood	24 (5%)	7 (4%)	7 (4%)	10 (9%)	0.1573
Tranexamic acid	14 (3%)	0	6 (4%)	8 (7%)	0.0011
In-flight					
SpO_2, %	99 [98-100]	100 [99-100]	99 [98-100]	99 [98-100]	0.0004
Supplementary oxygen	72 (16%)	21 (13%)	26 (16%)	25 (23%)	0.0885
Ongoing mechanical ventilation	304 (69%)	119 (72%)	115 (71%)	70 (64%)	0.3015
Sedatives (IV infusion)	316 (72%)	127 (77%)	119 (73%)	70 (64%)	0.0514
Anti-seizure medications	158 (36%)	58 (35%)	58 (36%)	42 (38%)	0.8651
Acetaminophen	124 (28%)	39 (24%)	50 (31%)	35 (32%)	0.2355
3% saline infusion	116 (26%)	54 (33%)	37 (23%)	25 (23%)	0.0707
Vasopressors	91 (21%)	49 (30%)	25 (15%)	17 (15%)	0.0017
Sedatives (IV bolus)	62 (14%)	28 (17%)	16 (10%)	18 (16%)	0.1325
Paralytics	39 (9%)	23 (14%)	6 (4%)	10 (9%)	0.0049
Mannitol	18 (4%)	5 (3%)	7 (4%)	6 (5%)	0.6045
Steroids	16 (4%)	9 (5%)	4 (2%)	3 (3%)	0.2930
Any blood products	70 (16%)	23 (14%)	35 (21%)	12 (11%)	0.0433
Packed red blood cells	61 (14%)	20 (12%)	30 (18%)	11 (10%)	0.1007
Fresh frozen plasma	32 (7%)	10 (6%)	17 (10%)	5 (5%)	0.1378

Values given are count (column percentage) or median [IQR]. P-values are for one-way ANOVA/Kruskal-Wallis test or chi square/Fisher's exact test.
ICP, intracranial pressure; IV, intravenous

TBI - Table 3. Univariate comparison of outcomes

Variable	Overall (N=438)	≤1 day (n=165)	2 days (n=163)	≥3 days (n=110)	p
Days at Role IV MTF	3 [1-4]	3 [1-4]	3 [1-4]	3 [2-5]	0.6101
Total ventilator days	6 [2-10]	5 [2-9]	6 [3-10]	7 [2-12]	0.1288
Total ICU days	9 [6-15]	8 [5-13]	9 [6-15]	10 [7-16]	0.0006*
Total hospital days	14 [5-32]	10 [5-23]	17 [6-36]	18 [7-41]	<0.0001*
Discharge disposition					0.2724
Died	17 (4%)	8 (5%)	6 (4%)	3 (3%)	
Continued medical care	386 (88%)	150 (91%)	143 (88%)	93 (85%)	
Return to duty/discharged home	28 (6%)	6 (4%)	11 (7%)	11 (10%)	
Not specified	7 (2%)	1 (<1%)	3 (2%)	3 (3%)	
Overall survival	421 (96%)	157 (95%)	157 (96%)	107 (97%)	0.6623
GCS score ≤ 8 at discharge	62 (14%)	33 (20%)	19 (12%)	10 (9%)	0.0042*
Ventilated at discharge	104 (24%)	49 (30%)	34 (21%)	21 (19%)	0.0082
GCS score ≤ 8 and ventilated at discharge	58 (13%)	32 (20%)	17 (10%)	9 (8%)	0.0019*

Values given are median [IQR] or count (column percentage). P-values are for Kruskal-Wallis test or chi-square/Fisher's exact test. P-values are significant at $p<0.0055$ ($\alpha=0.05/9$) after Bonferroni correction.
Asterisk (*) indicates that ≤1 day was significantly different from 2 days and ≥3 days.
MTF, medical treatment facility; GCS, Glasgow Coma Scale

TBI - Supplemental Table S1. ICD-9-CM Codes for traumatic brain injury

Code	Description
800.	Fracture of vault skull
801.	Fracture of base skull
803.	Other and unqualified skull fractures
804.	Multiple fractures involving skull or face with other bones
850.	Concussion
851.	Cerebral laceration and contusion
852.	Subarachnoid, subdural, and extradural hemorrhage following injury
853.	Other and unspecified intracranial hemorrhage following injury
854.	Intracranial injury of other and unspecified nature
907.	Late effect of intracranial injury without mention of skull fracture

Derived from the Barell Injury Diagnosis Matrix (CDC. The Barell injury diagnosis matrix, classification by body region and nature of injury. http://www.cdc.gov/nchs/data/ice/ final_matrix_post_ice.pdf.)

TBI – Supplemental Table 2. Results of multivariable logistic regression analyses

Covariates	Outcomes			
	Mortality	**Return to duty or discharged home**	**Ventilated at discharge**	**Ventilated and GCS ≤8 at discharge**
Time to transport				
2 days vs. ≤1 day	0.9 (0.3-2.6)	1.7 (1.1-2.8)*	0.5 (0.4-0.6)*	0.5 (0.2-1.1)
≥3 days vs. ≤1 day	0.7 (0.7-0.8)*	2.7 (1.5-4.9)*	0.5 (0.3-0.7)*	0.3 (0.2-0.4)*
Additional flights in-theater (yes vs. no)	0.7 (0.4-1.2)	1.7 (0.9-3.1)	0.9 (0.4-1.8)	0.7 (0.3-1.8)
Composite ISS	1.1 (1.0-1.1)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Polytrauma (yes vs. no)	0.3 (0.1-0.7)*	0.6 (0.3-1.4)	0.9 (0.7-1.2)	1.9 (1.3-2.7)*
AIS severity score head/neck > 3 (yes vs. no)	0.8 (0.1-8.4)	0.3 (0.2-0.5)*	1.9 (1.0-3.5)	3.1 (2.0-4.7)*
Blast injury (yes vs. no)	0.5 (0.4-0.7)*	1.2 (0.7-1.9)	0.7 (0.6-0.8)*	0.5 (0.3-0.7)*
Cranial fractures (yes vs. no)	1.6 (0.5-5.2)	1.1 (0.5-2.6)	1.3 (0.9-1.7)	1.3 (0.9-1.9)
Intracranial hemorrhage (yes vs. no)	0.9 (0.7-1.1)	0.8 (0.6-1.0)	1.0 (0.5-2.1)	1.3 (0.6-2.4)
Bone fragments/foreign bodies present (yes vs. no)	1.3 (1.2-1.5)*	0.3 (0.2-0.5)*	1.0 (0.6-1.8)	0.7 (0.5-1.1)
Days at Role IV MTF	0.8 (0.8-0.8)*	1.0 (1.0-1.0)	1.0 (1.0-1.1)	1.0 (1.0-1.1)
Pre-flight blood products (yes vs. no)	3.1 (1.7-5.6)*	0.7 (0.4-1.1)	1.5 (1.3-1.8)*	1.7 (1.4-2.1)*
Pre-flight abdominal surgery (yes vs. no)	4.0 (2.9-5.6)*	0.9 (0.6-1.3)	0.8 (0.4-1.7)	1.3 (0.9-2.0)
Pre-flight extremity surgery (yes vs. no)	0.6 (0.3-1.5)	1.3 (0.7-2.4)	1.0 (0.5-1.9)	0.7 (0.4-1.1)
Pre-flight head surgery (yes vs. no)	0.5 (0.4-0.7)*	1.1 (0.6-2.0)	1.9 (1.1-3.3)*	3.3 (2.4-4.7)*
Adjusted R^2 for model	0.20	0.12	0.17	0.27
χ^2 p-value	<0.0001	<0.0001	<0.0001	<0.0001
Concordance score/ROC AUC	0.84	0.74	0.71	0.80

Values are adjusted odds ratio (95% confidence interval). Fit statistics for each model are given at bottom of table.
Asterisk (*) indicates significant odds ratios.
ISS, injury severity score; MTF, medical treatment facility; ROC AUC, area under the curve of the receiver operating characteristic.

tCSoE - Table 1. Descriptive summary of the total study population

	Total Population Mean±SD; Median [IQR] N=238
Age	25±6.2; 23 [21-28]
Gender, % male	98 (96-99)
Injury Description	
ISS	16±11.5; 13 [9-18]
Max AIS of Extremity Injuries	3±0.8; 3 [2-3]
	Total Population % (95% CI) n=238
Polytrauma	91 (87-94)
Explosive Device	69 (63-74)
Gunshot Wound	18 (14-24)
Penetrating	72 (66-77)
Blunt	26 (21-32)
Burn	3 (1-5)
Compartment Syndrome	
Upper Extremity	14 (10-20)
Lower Extremity	88 (82-92)
Dx Within 24 hours	80 (74-84)
Transport	
Iraq	46 (40-53)
Afghanistan	54 (47-60)
CCATT Platform	42 (36-48)

AE Platform	58 (52-64)
Arrived to LRMC Within 2 Days	45 (39-52)

Penetrating, blunt, and burn are mutually exclusive. Unable to determine body region (upper/lower extremity) of compartment syndrome diagnosis for n=59 records. Transport platform was unknown for n=16.

ISS, injury severity score; AIS, abbreviated injury scale; Dx, diagnosis; AE, Aeromedical Evacuation platform; CCATT, Critical Care Air Transport Team; LRMC, Landstuhl Regional Medical Center; SD, standard deviation; IQR, interquartile range; CI, confidence interval

tCSoE - Table 2. **Comparison of Pre- and Post- Flight CS groups**

	Pre-flight CS mean±SD; median [IQR]	**Post-flight CS** mean±SD; median [IQR]	**p-value**
Age	25±6.1; 23 [21-28]	26±6.3; 24 [21-28]	0.6260
Gender (% male)	98 (94-100)	98 (94-100)	1.0000
Injury Description			
ISS	14±10.7; 11 [6-17]	17±12.0; 14 [10-20]	0.0144
Max AIS of Extremity Injuries	2.7±0.7; 3.0 [2.0-3.0]	2.9±0.8; 3.0 [2.0-3.0]	0.0173
	Pre-Flight CS % (95% CI) N=113	**Post-Flight CS** % (95% CI) N=123	
Polytrauma	90.3 (83.4-94.5)	92.0 (85.9-95.6)	0.6378
Explosive Device	68 (59-76)	70 (61-77)	0.7726
Gunshot Wounds	18 (12-26)	18 (12-26)	0.9138
Penetrating	72 (63-80)	71 (63-79)	0.8482
Blunt	27 (19-36)	25 (19-34)	0.7271

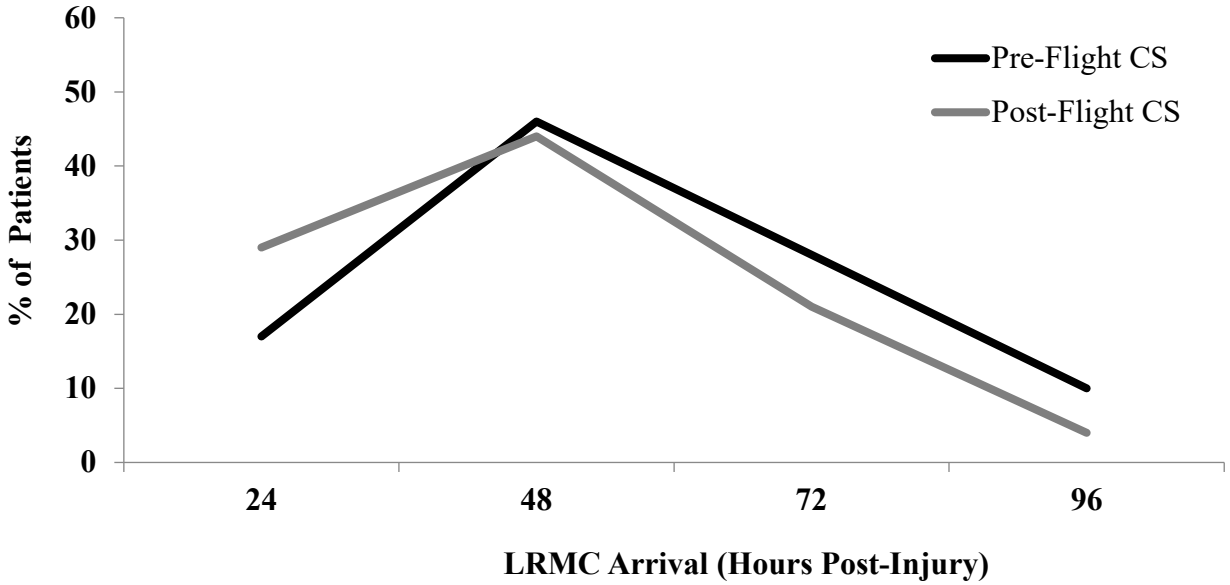
Burn	1 (0.2-5)	3 (1-8)	0.2170
In-Theater Interventions			
Tourniquet	38 (30-48); (43/113)	37 (29-46); (46/125)	0.8004
Direct Pressure	14 (9-22); (16/113)	12 (7-19); (15/112)	0.6027
Wound Vac	3 (1-8); (3/113)	1 (0.1-4); (1/125)	0.2543
Compartment Syndrome			
Upper Extremity	14 (7-25)	14 (10-22)	0.9121
Lower Extremity	88 (77-94)	88 (80-92)	0.9028
Dx Within 24 hours	84 (76-90)	72 (66-82)	0.9031
Dx Within 48 hours	12 (8-21)	19 (13-28)	0.9031
Time to 1st CS Dx (hours)	7.6±7.1; 4.6 [1.5-10.0]	8.0±7.4; 3.8 [2.1-15.3]	0.6496
In-Theater Fasciotomy (% yes)	96 (90-99)	92 (84-96)	0.2502
Fasciotomy (hours)	7.3±6.5; 4.8 [2.6-9.1]	7.1±6.4; 4.0 [3.0-8.8]	0.8455
Transport			
Iraq	37.5 (29.1-46.7)	54.4 (45.7-62.9)	0.0090
Afghanistan	62.5 (53.3-70.9)	45.6 (37.1-54.3)	0.0090
LRMC Arrival (days)	2.4±1.1; 2 [2-3]	2.1±1.0; 2 [1-3]	0.0156
% CCATT	36 (27-45)	48 (39-57)	0.0710
% AE	64 (55-73)	52 (43-61)	0.0710

Other			
Revision	6 (3-12)	5 (2-10)	0.7769
Additional CS Diagnoses (% yes)	5 (2-11)	0	0.0104
Additional Fasciotomies (% yes)	9 (5-17)	2 (1-7)	0.0411

*Lung dysfunction; atelectasis, pulmonary edema, acute respiratory distress syndrome, pneumonia

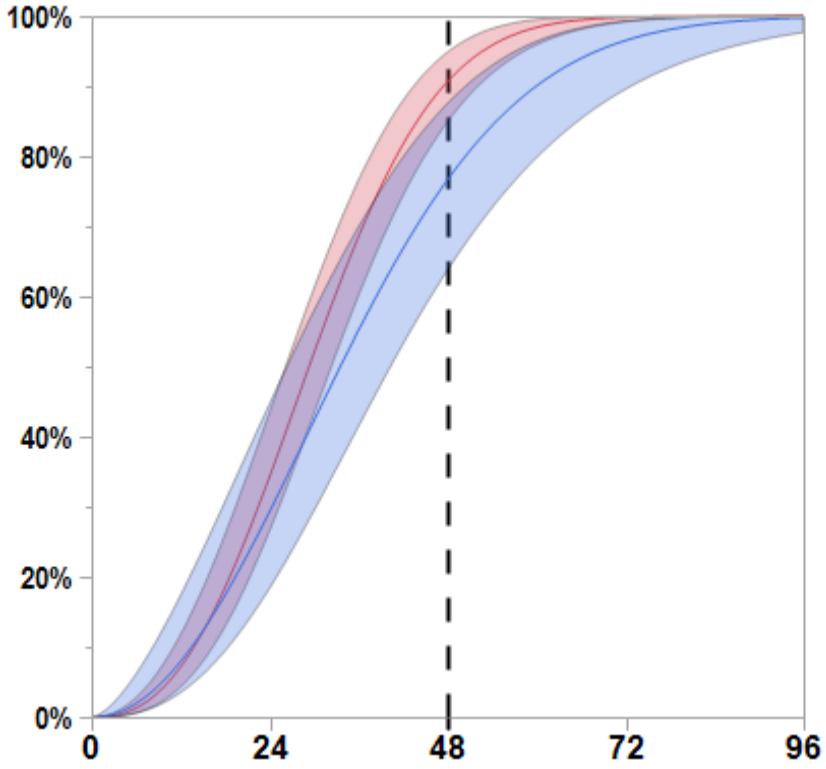
CS, compartment syndrome; ISS, injury severity score; AIS, Abbreviated Injury Scale; CS Dx, compartment syndrome diagnosis; LRMC, Landstuhl Regional Medical Center; AE, Aeromedical Evacuation platform; SD, standard deviation; IQR, interquartile range; CI, confidence interval

tCSoE - Figure 1: Percent of groups with compartment syndrome (CS) diagnosis based on LRMC Arrival in number of hours post-injury



tCSoE- Figure 1: Percent of patients transported who had compartment syndrome Pre-flight (black) or Post-Flight (grey) shown based on number of hours post-injury that they arrived at LRMC. Arrival time at LRMC used as a data point to represent the time of compartment syndrome diagnosis. There was no difference in time of arrival for the two groups.

tCSoE - Figure 2: Cumulative incidence of traumatic compartment syndrome of the extremities diagnosis following arrival to LRMC (Post-flight only)



tCSoE - Supplemental Table 1. Comparison of outcomes by day of compartment syndrome diagnosis groups.

	1-Day mean±SD; median [IQR] **OR** % (95% CI); (count/tot) n=172	**2-Day** mean±SD; median [IQR] **OR** % (95% CI); (count/tot) n=35	**3-Day** mean±SD; median [IQR] **OR** % (95% CI); (count/tot) n=7	**4-Day** mean±SD; median [IQR] **OR** % (95% CI); (count/tot) n=2	**p-value**
Abdominal CS	15.1 (10.5-21.2); (26/172)	14.3 (6.3-29.4); (5/35)	14.3 (2.6-51.3); (1/7)	0; (0/2)	0.6929
Infection/Sepsis	22.7 (17.0-29.5); (39/172)	17.1 (8.1-32.7); (6/35)	0; (0/7)	50.0 (9.5-90.5); (1/2)	0.4182
Coagulopathy	43.0 (35.9-50.5); (74/172)	22.9 (12.1-39.0); (8/35)	14.3 (2.6-51.3); (1/7)	50.0 (9.5-90.5); (1/2)	0.0355
Lung Dysfunction	23.8 (18.1-30.7); (41/172)	5.7 (1.6-18.6); (2/35)	0; (0/7)	0; (0/2)	0.0062
Ventilator Days	3.1±8.0; 0 [0-3]	0.8±2.0; 0 [0-1]	0±0; 0 [0-0]	0±0; 0 [0-0]	0.0233
ICU Days	6.1±9.9; 3 [0-7]	2.3±3.0; 1 [0-4]	0.6±1.0; 0 [0-2]	0±0; 0 [0-0]	0.0050
Hospital Days	25.1±29.0; 15 [5-34]	15.6±14.0; 10 [6-20]	18.4±13.9; 10 [7-29]	33.5±34.7; 34 [9-58]	0.5679
Mortality	1.2 (0.3-4.1) n=2	0; (0/35)	0; (0/7)	0; (0/2)	0.5148

*Lung dysfunction; atelectasis, pulmonary edema, acute respiratory distress syndrome, pneumonia

CS, compartment syndrome; ICU, intensive care unit; standard deviation; IQR, interquartile range; CI, confidence interval; tot, total

tCSoE - Supplemental Table 2. Comparison of outcomes (Pre-flight versus Post-flight groups)

	Pre-flight CS mean±SD; median [IQR] **OR** % (95% CI) n=113	**Post-flight CS** mean±SD; median [IQR] **OR** % (95% CI) n=125	**p-value**
Abdominal CS	14.0 (8.9-21.8)	13.6 (8.7-20.7)	0.9008
Infection/Sepsis	15.9 (10.3-23.8)	24.8 (18.0-33.0)	0.0891
Coagulopathy	39.8 (31.3-49.0)	36.8 (28.9-45.5)	0.6318
Lung Dysfunction*	20 (14.0-28.7)	20.8 (14.6-28.7)	0.9323
Ventilator Days	2.6±8.1; 0.0 [0.0-2.0]	4.5±17.6; 0.0 [0.0-3.0]	0.3174
ICU Days	4.9±9.5; 2.0 [0.0-6.0]	7.2±19.2; 3.0 [0.0-7.0]	0.6342
Hospital Days	21.7±24.1; 13.0 [6.0-29.0]	27.4±43.2; 15.0 [5.0-31.0]	0.7141
Mortality	0.9 (0.2-4.9) n=1	1.6 (0.4-5.6) n=2	1.0000

*Lung dysfunction; atelectasis, pulmonary edema, acute respiratory distress syndrome, pneumonia; CS, compartment syndrome; ICU, intensive care unit

12.0 LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

AE	Aeromedical Evacuation
AIS	Abbreviated Injury Scale
AMS	Acute Mountain Sickness
CCATT	Critical Care Air Transport Team
CONUS	Continental US
CPG	Clinical Practice Guidelines
DoDTR	Department of Defense Trauma Registry
DTIC	Defense Technical Information Center
ECRC	En route Care Research Center
GCS	Glasgow Coma Scale
GSACEP	Government Services Chapter of the American College of Emergency Physicians
ICP	In-Flight Intracranial Pressure
ICU	Intensive Care Unit
IACUC	Institutional Animal Care and Use Committee
IQR	Interquartile Range
IRB	Institutional Review Board
ISS	Injury Severity Score
IV	Intravenous
JPC-6	Joint Program Committee
JTS	Joint Trauma System
LRMC	Landstuhl Regional Medical Center
MHSRS	Military Health Science Research Symposium
MOA	Memorandum of Agreement
MRAC	Medical Research Advisory Committee
MTF	Medical Treatment Facility
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OND	Operation New Dawn
PHI	Protected Health Information

QA	Quality assurance
SBP	Systolic Blood Pressure
SURF	San Antonio Military Health System and Universities Research Forum
TBI	Traumatic Brain Injury
tCSoE	Traumatic Compartment Syndrome of Extremities
TSNRP	TriService Nursing Research Program
US AD	US Active Duty