

TALE OF TWO CITIES: PREHOSPITAL ENDOTRACHEAL INTUBATION WITH OR WITHOUT PARALYSING AGENTS IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY.

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Invited Discussant: Rochelle Dicker, MD

Introduction:

The role of prehospital endotracheal intubation (PETI) in patients with severe traumatic brain injury (STBI) is unclear. Prehospital airway management varies substantially across Australia: in Victoria paramedics use rapid sequence intubations drugs (RSI) to facilitate ETI, while in New South Wales (NSW), paramedics have no access to paralyzing agents and practice “cold ETI”. We hypothesised that RSI would increase PETI rate and improve in-hospital mortality rate.

Methods:

Four-year retrospective trauma registry based comparison of adult primary admissions [field Glasgow Coma Scale (GCS) <9 and Abbreviated Injury Scale of the head and neck (AIS H-N) >2] to either a Victorian or a NSW Trauma Center was performed. The cohorts were compared with univariate analysis followed by logistic regression to estimate the odds ratio for mortality and gamma regression to determine whether length of stay among survivors differed.

Results:

The Victorian cohort of 192 patients, when compared with the NSW cohort of 91 patients, did not differ in: demographics [77 vs. 76% males; 34 (IQR=28) vs. 33 (IQR=29) median age], first recorded field median GCS [3 (IQR=3) vs. 5 (IQR=3); $p=0.3$], median AIS H-N [5 (IQR=1) vs. 5 (IQR=1); $p=0.07$] and median ISS [38 (IQR=15) vs. 35 (IQR=19); $p=0.09$]. Victorian patients had more successful PETI (85 vs. 22%; $p<0.05$) with similar incidence of prehospital hypotension (27 vs. 10%; $p=0.5$) and prehospital desaturation (24 vs. 20%; $p=0.2$) events. On univariate and logistic regression analysis mortality did not differ among groups [31.7 vs 26.3%, $p=0.4$; OR=0.84 (CI:0.38-1.86, $p=0.67$)]. Among survivors, Victorian patients had longer median stay in ICU [364 (IQR=255) vs. 144 (IQR=276)] $189\pm$ SD hours; $p<0.05$), this difference persisted on gamma regression [effect= 1.58 (CI: 1.30-1.92, $p<0.0001$)].

Conclusion:

Paramedics using RSI to obtain PETI in patients with STBI show a higher success rate. This improvement did not reflect in a better mortality rate, nor a shorter ICU stay.

**SEVERE CEREBRAL HYPOPERFUSION IS FREQUENTLY DETECTED BY
EARLY PERFUSION-CT AND PREDICTS UNFAVOURABLE OUTCOME
FOLLOWING SEVERE TRAUMATIC BRAIN INJURY.**

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Invited Discussant: Juan Asensio, MD

Introduction:

In patients with severe traumatic brain injury (STBI) perfusion CT (PCT) provides additional information beyond the non-contrast CT (NCCT) and may alter clinical management. We hypothesized that this information may prognosticate functional outcome.

Methods:

Five-year prospective observational study was performed in a Level-1 Trauma Center on consecutive STBI who had CTP in conjunction with a follow-up NCCT within 48 hours from trauma. Additional findings (AdF) were defined as an area of altered perfusion larger than the abnormal area detected by the simultaneous NCCT. Severe hypoperfusion (SHy) were defined as a delayed transit of more than 2 seconds. Glasgow outcome scale-extended (GOSE) obtained 6 months post injury of less 5 was considered an unfavourable outcome.

Results:

Out of 85 patients with STBI, 50 were investigated with PCT, one patient was subsequently excluded due lack of STBI (hypoxic brain injury) [male: 80%, median age: 35 (IQR=30), prehospital intubation: 9 (18.3%); median worse GCS pre-intubation: 5 (IQR=3); median ISS: 29 (IQR=11); median head and neck AIS: 4 (IQR=1); median days in ICU: 10 (IQR=9)]. Intracranial pressure (ICP) monitored in 28 (57.1%). Twenty-nine (59.1%) patients had unfavourable outcome, of these 7 (14.2%) were deaths. There were 23 (46.9%) patients with AdF and 17 (34.6%) patients with SHy. Positive predict value (PPV) for unfavourable outcome of AdF was: 86.9%. PPV for unfavourable outcome of SHy was 88.2%. NPV of AdF and SHy was 57.6% and 50% respectively.

Conclusion:

PCT is a non-invasive valuable tool for early outcome prediction in patients who sustained STBI at the time of the first follow-up CT scan The potential impact on management and its cost effectiveness needs to be evaluated in larger scale studies.

TRAUMA PATIENTS WITH PREHOSPITAL GLASGOW COMA SCORE LESS THAN NINE: NOT A HOMOGENOUS GROUP.

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Invited Discussant: Michel Aboutanos, MD, MPH

Introduction:

Prehospital endotracheal intubation (PETI) is generally advocated for patients with both a traumatic brain injury (TBI) and prehospital Glasgow Coma Score (GCS) below nine. Most studies did not show a survival advantage following PETI. We hypothesized that patients with prehospital GCS below nine are inhomogenous in outcomes.

Methods:

All trauma activation patients (2005-2012) with prehospital GCS below nine and abbreviated injury scale head/neck above two were identified from trauma registry. Patients with isolated neck injuries, transfers and those who were extubated or died within 24 hours were excluded. Data collected on: prehospital and in-hospital vital signs, airway management, neurosurgical interventions, ICU length of stay and outcome. Patients were dichotomized based on a worse recorded prehospital GCS of 3-5 or 6-8, then statistically compared using Student t test and Mann Whitney U test.

Results:

The GCS 3-5 group (99 patients) when compared with the GCS 6-8 group (49 patients) had shorter prehospital times [63 (SD=28) vs. 79 (SD=26) minutes; $p<0.05$], more frequent episodes of both hypoxia (30.3% vs 7.7%; $p<0.05$) and hypotension (26.7% vs. 6.4%; $p<0.05$), had more neurosurgical procedures (15.1% vs. 4.0%; $p=0.05$) and higher mortality (33.3% vs. none; $p<0.05$). PETI was attempted more often in the GCS 3-5 group (57.5% vs. 28.6%, $p<0.05$) and was more often successful (39.3% vs. 12.2%; $p=0.05$). ICU stay did not differ among groups [14.2 (SD=26.5) vs. 11.9 (SD=12.6) days; $p=0.5$] even when only the survivors were included (SD 31.2) versus 11.9 days (SD 12.6); $p=0.1$).

Conclusion:

Severe TBI patients are fundamentally different based on their initial GCS falls into 3-5 or 6-8 category. Future trials should investigate and correct for this fundamental bias. Recommendations from trials investigating trauma patients with GCS less than nine should be translated with caution to clinical practice.

POSTINJURY MULTIPLE ORGAN FAILURE: MORE FREQUENT, MORE SEVERE BUT LESS DEADLY WITH LESS CRYSTALLOIDS.

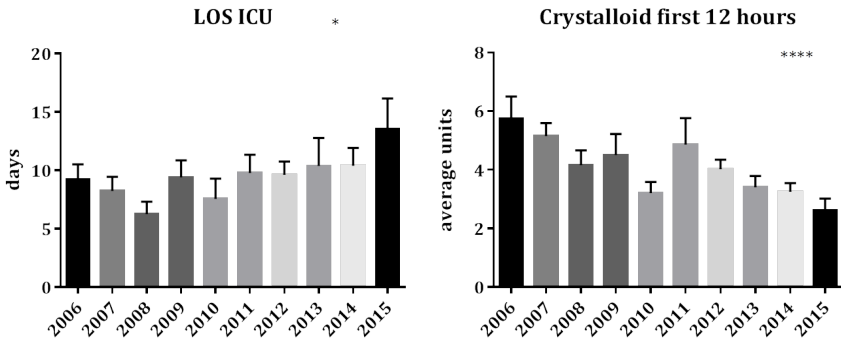
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Invited Discussant: Andrew Kirkpatrick, CD, MD

INTRODUCTION: Postinjury multiple organ failure (MOF) was recently reported to have decreasing incidence and mortality based on retrospective registry based studies. We aimed to describe the current epidemiology over the last ten years following the introduction of hemostatic resuscitation.

METHODS: A 10-year prospective inception cohort study was undertaken at a Level 1 Trauma Centre, ending in December 2015. Inclusion criteria: age ≥ 16 years, Injury Severity Score (ISS) > 15 , Abbreviated Injury Scale Head (AIS) < 3 and survived > 48 hours. Demographics, physiological and shock resuscitation parameters were collected. The primary outcome was MOF defined by the Denver Score > 3 . Secondary outcomes were ICU LOS and mortality. $* < 0.05$ based on ANOVA, Student-t and Fischer's exact test.

RESULTS: 347 patients met inclusion criteria (Age 47 ± 4 , ISS 29 ± 2 , Male 71%, BD 5 ± 0.8). 69 patients (19%) developed MOF. The average Denver score of MOF patients was 5 ± 0.8 with a mean duration of 4 ± 3 days. MOF patients had longer ICU LOS (19 ± 6 vs 7 ± 2 days*) and higher mortality (13% vs 5%). The incidence of MOF has increased from 17% to 30%* without change in demographics, ISS or shock severity. Over the 10-year period MOF database patients received less crystalloids, their ICU LOS increased (FIGURES 1 and 2), the Denver score increased from 1.6 ± 1 to 3.4 ± 1 * and MOF mortality decreased from 20% to 11%.



CONCLUSION: MOF still requires excessive healthcare resources. Our prospective purpose built database shows no change in demographics and injury/shock severity but MOF became more frequent and more severe with increased ICU LOS while patients are getting less crystalloids and more likely to survive.

**REDUCED DNASE ENZYME ACTIVITY IN RESPONSE TO HIGH
POST-INJURY MITOCHONDRIAL DNA CONCENTRATION PROVIDES A
THERAPEUTIC TARGET FOR SIRS**

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Invited Discussant: Ron Maier, MD

BACKGROUND: Cell free mitochondrial DNA (mtDNA) is pro-inflammatory and has been detected in high concentrations in trauma patients' plasma. Deoxyribonuclease (DNase) is the free plasma enzyme responsible for the digestion of extracellular DNA. The relationship between mtDNA and DNase after major trauma is unknown. We hypothesized that DNase activity would be elevated after injury and trauma surgery, and would be associated with high concentrations of extracellular DNA.

METHODS: 2-year prospective study was performed on 103 consecutive trauma patients (Male 81%, Age: 38 IQR 30-59 years; ISS: 18 IQR 12-26) who underwent standardised major orthopaedic trauma surgical interventions. Blood was collected at 5 peri-operative time points (pre-op, post-op, 7hrs, 24hrs and 3 days post-operatively). Healthy control subjects (n=20) were also sampled. Cell free mtDNA and nuclear DNA(nDNA) was measured using quantitative polymerase chain reaction. DNase was also assayed in the same plasma samples.

RESULTS: Increased levels of mtDNA (from Pre-op 89 ± 74 ng/ml to 3 days 205 ± 112 ng/ml $p < 0.0001$) and nDNA (from pre-op 28 ± 20 ng/ml to 3 days 37 ± 27 ng/ml $p < 0.05$) were present in trauma patients at all peri-operative time points compared to healthy controls (mtDNA: 4 ± 2 ng/ml; nDNA: 10 ± 5 ng/ml). DNase activity was lower in the trauma cohort (from Pre-op 0.06 ± 0.04 U/ml to 3 days 0.08 ± 0.04 U/ml $p < 0.0001$) compared to healthy controls (DNase: 0.17 ± 0.03 U/ml). There was no correlation between DNase and peri-operative DNA concentrations. Elevated mtDNA (but not nDNA) correlated with the development of SIRS ($p = 0.026$) but not MOF.

CONCLUSIONS: The significant perioperative elevation in plasma free MtDNA concentration is associated with the development of SIRS. The fact that increased cell free DNA concentrations present with significantly lower than healthy control DNase activity suggests a potential therapeutic opportunity with DNase administration to modulate post-injury severe SIRS

ELIXIR OF YOUTH, GDF11, IS INDUCED BY BLOOD LOSS IN TRAUMATIC INJURY

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Invited Discussant: Eric Ley, MD

Background: Recent ground-breaking work has shown that various organ/tissue functions in aged mice are rejuvenated when injected with the plasma of young mice or humans. In animal models, the rejuvenating effect of young plasma can be reproduced by a single factor found in young blood called growth and differentiation factor 11 (GDF11). Any factors that can increase erythroid progenitor cells are therefore of great relevance to acute and long-term trauma patient management. In this study, we investigated whether GDF11 expression responds to traumatic injury by measuring its concentration in the plasma of trauma patients up to 3 days over the perioperative period.

Methods: Plasma was collected from trauma patients requiring orthopedic surgical intervention at standardised time points: pre-operatively, post-operatively, 7 hrs, 24 hrs, 3 days and 5 post-operatively. Plasma GDF11 concentration was measured with western blotting alongside purified GDF11 standards for quantitation. Differences among GDF concentrations at perioperative time points were measured using a Friedman test. GDF11 concentrations were also correlated with a range of clinical data using the Spearman test.

Results: Plasma concentrations of GDF11 did not vary within perioperative time points, but did produce significant correlations with a number of patient parameters over the perioperative time points. GDF11 concentrations correlated negatively with red blood cell counts and positively with INR and PPT, as outlined in table 1 and figure1 (spearman r value and p values tabulated).

	GDF11									
	Preop		Post op		7hrs		24hrs		72hrs	
	r	p	r	p	r	p	r	p	r	p
RBC preop	-0.531	0.044	-0.643	0.011	-0.683	0.006		n.s		n.s
INR preop	0.574	0.02	0.647	0.007	0.627	0.009	0.747	0.001	0.591	0.016
PT preop	0.508	0.044	0.629	0.009		n.s	0.584	0.018	0.597	0.015

Conclusions: These results are consistent with the recently described role of GDF11 as a regulator of erythropoiesis in animal models and constitute the first evidence of this role in humans. Furthermore, GDF11 may serve as a potential therapy to complement cases where erythropoietin has been used, to replace erythroid progenitor-depleted bone marrow following trauma and prevent the chronic anaemia known to persist long after injury.