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Time is the enemy: Mortality in trauma patients with hemorrhage from torso injury occurs long before the "golden hour"

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ABSTRACT

Introduction: The concept of the "Golden Hour" has been a time-honored tenet of prehospital trauma care, despite a paucity of data to substantiate its validity. Non-compressible torso hemorrhage has been demonstrated to be a significant cause of mortality in both military and civilian settings. We sought to characterize the impact of prehospital time and torso injury severity on survival. Furthermore, we hypothesized that time would be a significant determinant of mortality in patients with higher Abbreviated Injury Scale (AIS) grades of torso injury (AIS $\geq$ 4) and field hypotension (prehospital SBP $\leq$ 110 mmHg) as these injuries are commonly associated with hemorrhage.

Methods: Data for this analysis was generated from a registry of 2,523,394 injured patients entered into the National Trauma Data Bank Research Data Set from 2012 to 2014. Patients with torso injury were identified utilizing Abbreviated Injury Scale (AIS) for body regions 4 (Thorax) and 5 (Abdomen). Specific inclusion criteria for this study included pre-hospital time, prehospital SBP $\leq$110 mmHg, torso injury qualified by AIS and mortality. Patients with non-survivable torso injury (AIS = 6), severe head injuries (AIS $\geq$ 3), no signs of life in the field (SBP = 0), interfacility transfers, or those with any missing data elements were excluded. This classification methodology identified a composite cohort of 42,135 adult patients for analysis.

Results: The overall mortality rate of the study population was 7.9% (3326/42,135); Torso AIS and prehospital time were noted to be strong independent predictors of patient mortality in all population strata of the analysis ($P < 0.05$). The data demonstrated a profound incremental increase in mortality in the early time course after injury associated with torso AIS $\geq$4.

Conclusion: In patients with high-grade torso injury, AIS grades $\geq$4, the degree anatomic disruption is associated with significant hemorrhage. In our study, a precipitous rise in patient mortality was exhibited in this high-grade injury group at prehospital times <30 min. Our data highlight the critical nature of prehospital time in patients with non-compressible torso hemorrhage. However, realizing that evacuation times $\leq$30 min may not be realistic, particularly in rural or austere environments, future efforts should be directed toward the development of therapies to increase the window of survival in the prehospital environment.

1. Background

In 1966, the National Academy of Sciences (NAS) published "Accidental Death and Disability: The Neglected Disease of Modern Society" perceiving injury to be one of the most significant public health problems faced by our nation.[1] At the same point in history, the surgical community was taking note of significant successes in trauma care on the battlefields of Vietnam such as advanced

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resuscitation practices and refined aeromedical evacuation capabilities.[2] The timely coevolution of these historical events generated the impetus to develop formal trauma systems to improve injury care across the nation. One pioneer in the genesis of the early trauma system concepts was Dr. R. Adams Cowley, who conceptualized the notion of the "golden hour ". In defining the emergency medical system for the State of Maryland, Dr. Cowley noted that " the first hour after injury will largely determine a critically injured persons chances for survival," an assertion which focused trauma care providers on the critical importance of time between injury and definitive care.[3–5] Whether driven by his prominence and authority in the field, the need to fill a critical void in trauma system development, to serve as a guiding principle to emergency medical systems providers or just a captivating marketing phrase, the concept of the "golden hour" has become firmly engrained in the lexicon of injury management for the last four decades. During the nascence of trauma systems in the US, achieving the 60-minute window to deliver the patient from point of injury to a hospital capable of managing severe trauma would have been a laudable objective. As trauma centers and systems have matured and become much more sophisticated within the last forty years, several have challenged the validity of the "golden hour" principle.

The development of structured trauma systems both in civilian settings and on the battlefield has been instrumental to decreasing delays in time to definitive care.[6] However, within the same context, the discrete relationship between prehospital time and its impact upon on survival has not been fully developed.[6] In addition, the impact of prehospital time intervals in injured civilians has not been consistently demonstrated, potentially secondary to heterogeneous populations and environments.[7,8,6,9,10] Even with the paucity of substantiating evidence to support the "golden hour", expedited response times continue to be utilized as surrogates for the quality of care provided to trauma patients.[11,12] Likewise, many contemporary EMS agencies have fostered the "scoop and run" paradigm, choosing to minimize time to definitive care while concurrently administering "treatment en route".[13]

Even with the inconsistent evidence to support a true "golden hour", the degree of cultural penetrance remains pervasive and was prominently evidenced by the 2009 mandate by then Secretary of Defense, Robert Gates, which obligated the aeromedical evacuation of critically injured combat casualties to a military treatment facility within 60 min.[14]

Ultimately however, there is little evidence to definitively support a true "golden hour", much less any ubiquitous prehospital time which improves trauma outcomes. However, intuitively, minimizing time to definitive care, particularly in patients with time sensitive pathology, should be effective in the context of survival benefit. The purpose of this study was to examine the mortality outcome association between prehospital time and torso injury severity. We hypothesized that patients with more severe torso injuries, particularly those manifest with non-compressible hemorrhage, that longer prehospital times would be associated with decreased survival.

2. Methods

This was a retrospective study of 2,523,394 patient records derived from the National Trauma Data Bank Research Datasets (NTDB-RDS) 2012 to 2014. The NTDB is compiled annually from participating trauma centers nationwide and is the largest aggregation of U.S. trauma registry data.

Patients with torso injury were identified utilizing Abbreviated Injury Scale (AIS) for body regions 4 (Thorax) and 5 (Abdomen). Torso injury morphology was ascribed utilizing the six digit pre dot AIS code. Injury severity was assessed utilizing the single digit post dot code. Patients with severe head injuries (AIS $\geq$ 3), non-survivable injuries (AIS = 6), no signs of life at the field (EMS SBP = 0), prehospital SBP greater than 110 mm Hg, transfers, or those with missing data elements were excluded. Specific inclusion criteria of pre-hospital time, torso injury and mortality identified a cohort of 42,135 adult patients for analysis.

We categorized prehospital times into 15 min intervals. Additional variables considered in the analysis included age, sex, mechanism of injury, field and emergency department vital signs, Abbreviated Injury Scale Score, and Injury Severity Score.

SPSS software, Version 22 (SPSS, Chicago, IL, USA) was used for all statistical analyses with a p value of <0.05 regarded as significant. Continuous numerical variables were analyzed by a two-sample *t*-test or one-way analysis of variance (one-way ANOVA). Categorical variables were analyzed by the $\chi 2$ test or Fischer's exact test. All numerical data were expressed as the mean $\pm$ standard deviation (SD).

3. Results

The mean age of our sample population was 37.4 years, median ISS was 14, 67.6% of the patients were male, and 73.3% of patients sustained blunt trauma. Motor vehicle collisions (MVC) accounted for 75.6% of blunt injuries, while firearm related injuries accounted for 55.2% of penetrating trauma.

The overall mortality in this analysis was 7.9% (3326/42,135); 7.4% (2371/32,077) with blunt mechanisms, 3.3% (143/4325) with stab wounds, and 14.2% (812/5733) with firearm injuries. Of the 3, 326 fatalities, 1022 (30.7%) of patients expired in the emergency department.

As expected, the risk of death was significantly influenced by the prehospital systolic blood pressure. Overall mortality in patients with mild hypotension (pSBP 90–110 mm Hg) was 5.0% (1364/27,241). The mortality in patients with moderate hypotension (pSBP 61–90 mm Hg) was 12.1% (1521/12,557), and 21.5% (502/2337) in those with severe hypotension (pSBP >0 but $\leq$ 60 mm Hg).

In patients with an Injury Severity Score (ISS) less than or equal to 15, 3.5% died. The mortality rate in patients with an ISS of 15–45 was 11.4%, and 34.2% in those with an ISS >45.

Overall median total prehospital time was 37 min, 40 min for blunt trauma and 28 min for penetrating injury.

The risk of death increased with longer prehospital times, and was most prominent within the first 30 min. The rise in mortality is

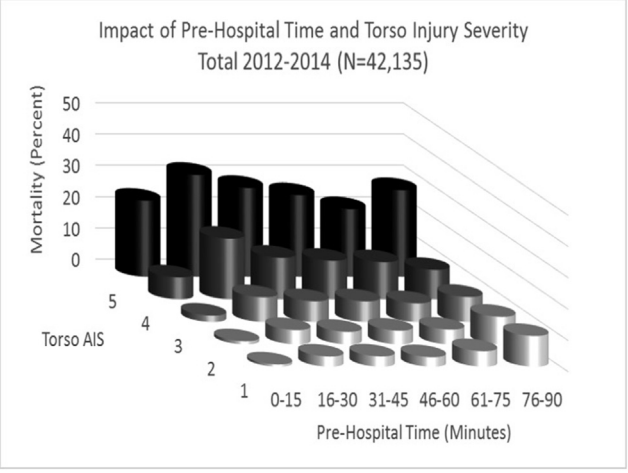

Fig. 1. Mortality Impact of prehospital time and torso injury severity for composite population 2012–2014 (N = 42,135).

Table 1
The impact of prehospital time and torso AIS in patients with prehospital SBP <110 (N = 42,135).

Time (Minutes)	AIS 1		AIS 2		AIS 3		AIS 4		AIS 5	
	Mortality	N	Mortality	N	Mortality	N	Mortality	N	Mortality	N
0–15	0.7	1489	1.0	811	2.0	2527	7.0	460	24.4	78
16–30	3.3	1623	4.6	1050	7.8	4737	19.3	1908	32.5	664
31–45	3.3	2278	4.0	1548	6.6	5810	13.2	2243	28.4	715
46–60	3.1	1339	4.4	1002	6.6	3578	12.3	1580	26.1	437
61–75	5.0	703	4.7	510	5.9	1973	11.8	838	21.6	245
76–90	9.9	281	8.8	215	7.9	946	9.4	417	27.7	130

also more notable in patients with higher Abbreviated Injury Scale (AIS) scores, with the most drastic increases in mortality occurring between AIS 3 to 4 and AIS 4 to 5. (Fig. 1 & Table 1). The data were subsequently stratified to evaluate the noted mortality effect of prehospital time and torso injury on population subsets including blunt injury (Fig. 2) and penetrating injury from GSW (Fig. 3). These subset analyses demonstrated similar observations of the profound impact of torso injury AIS ≥4 and time interval between injury and arrival at the hospital.

4. Discussion

The basic tenets of trauma care and trauma systems have highlighted the need for rapid transport of the trauma patient. Improving our ability to temporize or definitively control hemorrhage in a timely fashion before the onset of shock represents a perpetual major challenge in reducing trauma mortality.[15]

Mortality studies from conflicts in Iraq and Afghanistan by Eastridge et al. found non-compressible torso hemorrhage (NCTH) to account for the majority of potentially survivable deaths. The majority of these deaths occurred on the battlefield prior to reaching definitive surgical care.[16] Furthermore, military physicians demonstrated that following the aeromedical evacuation time mandate from Secretary of Defense Gates in 2009, there was a decrease in both killed in action (KIA), pre-military medical treatment facility mortality rates, from 16.0% to 9.9%, and overall case fatality rates (CFR) from 13.7% to 7.6%, with no associated increase in in-hospital mortality rates.[14]

This study is the first to our knowledge to analyze the association between prehospital times and torso injury severity, manifest by NCTH, on mortality outcomes in the civilian setting.

In the current analysis, torso injury morphology was ascribed utilizing the six-digit pre dot AIS code. Injury severity was assessed utilizing the single digit post dot code. The association of torso injury and non-compressible torso hemorrhage in the current study was predicated upon the assertion that the majority of high-grade torso injuries (AIS 4 & 5) have a significant hemorrhage component. This was based upon the predominance of relevant hemorrhage risk for visceral, vascular, and soft tissue injuries associated with AIS 4 and 5 severity codes for body regions 4 (Thorax) and 5 (Abdomen). In addition, less severe AIS injuries to the torso were upcoded to AIS 4 or 5 based upon >20% estimated blood loss, substantiating significant hemorrhage. In our study, we attempted to minimize the impact of confounders by selecting patients with torso injuries with a field SBP <110 mm Hg as a more clinically relevant definition of threshold of hypotension and associated metabolic hypoperfusion. Patients with severe traumatic brain injury (TBI) defined by (AIS ≥ 3) were excluded from analysis so as to exclude confounding effects from the known significant mortality outcomes associated with severe traumatic brain injury. Likewise, injuries classified with torso (thorax or abdomen) AIS 6 and those declared to have no signs of life (field SBP = 0 mm Hg) were excluded from the analysis in order to minimize bias in the study from expected non-survivors.

While it seems intuitive that rapid transport of critical trauma patients would positively impact survival, some patients may be in need of specialized care before transfer.[10] Contemporary prehospital care philosophy has fostered the concept of minimizing time to definitive care by administering “treatment en route”. Prehospital interventions can prolong transport times, and their benefit must ultimately be weighed against the possibility of delaying definitive hemorrhage control or other lifesaving

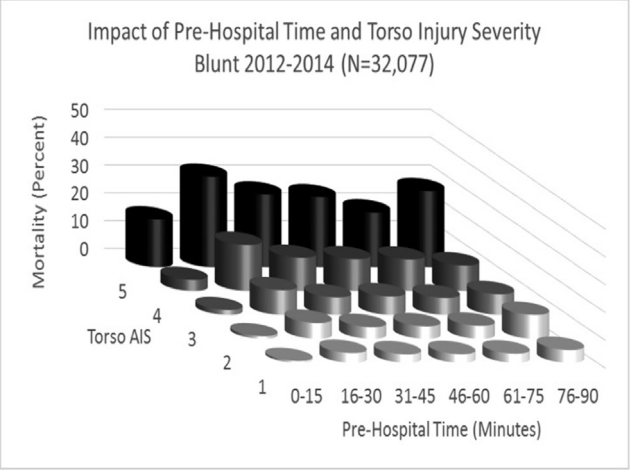

Fig. 2. Mortality Impact of prehospital time and torso injury severity for blunt injury 2012–2014 (N = 32,077).

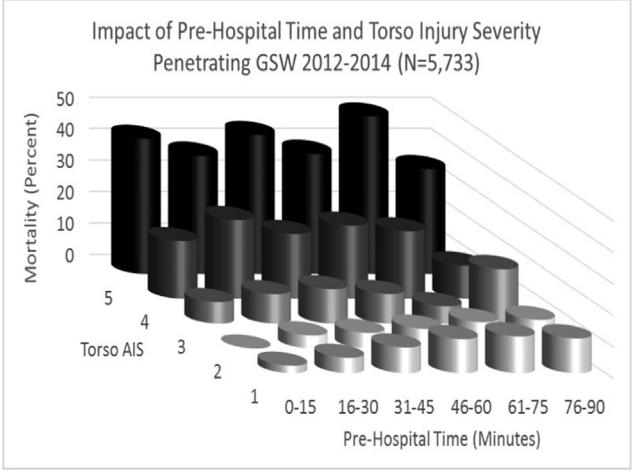

Fig. 3. Mortality Impact of prehospital time and torso injury severity for GSW penetrating injury 2012–2014 (N = 5733).

intervention.[17] The provision of medical interventions that do not delay the transfer of patients to definitive care centers provide an opportunity to control hemorrhage as proximate to the time of injury as possible. Several studies have investigated the effect of prehospital time intervals on patient outcome. McCoy et al. found that patients with penetrating trauma and ISS greater than 15, longer total prehospital transport times resulted in increased mortality.[18] Two studies by Sampalis et al. found that increased out-of-hospital times were associated with increased mortality among seriously injured trauma patients.[6,19] Kidher et al. reported that in patients with severe thoracic trauma (Median ISS of 35), prehospital times less than 65 min were associated with a lower possibility of death.[20]

There have been numerous studies however that have not found prehospital time to be a predictor of mortality. It is possible that heterogeneity in injury type and severity, as well as other confounders, precluded the ability to derive requisite associations of value.[8] The current analysis sought to overcome some of the vulnerabilities of previous studies by using a large sample (NTDB) across multiple years of review. The large sample allowed for the stratification of subpopulations for analysis maintaining enough power to derive meaningful conclusions. Likewise, since hemorrhage and traumatic brain injury are the most substantial effectors of injury mortality, we specifically chose to analyze the torso injury population since it has the inherent potential for non-compressible torso hemorrhage which represents one of the most prominent domains of current clinical trauma investigation.

In this analysis, we noted a precipitous incremental rise in patient mortality in patients with high-grade injuries at prehospital times 0–15 and 16–30 min, irrespective of mechanism. Interestingly, in patients with GSW and torso AIS 5, this mortality effect was at is maximum within the first 15 min window of the analysis, potentially alluding to the high risk for hemorrhage based upon mechanism.

Our study demonstrates the rapid potential for lethality of severe torso injury, many of which are likely associated with non-compressible torso hemorrhage. Evacuation times shorter than 30 min may not be realistic, particularly in rural or austere environments. This current work highlights the need for prehospital interventions that mitigate the harmful consequences of ongoing hemorrhage prior to the onset of "irreversible shock", during which patients become unresponsive to resuscitative efforts.[15,21] Tourniquets for example, when applied to injured extremities in the absence of shock, are associated with a 96% survival rate, compared to a 4% survival rate when applied after the development of shock.[22,23]

With torso hemorrhage accounting for the majority of fatalities secondary to exsanguination, the development of newer technologies that enhance our ability to establish effective hemorrhage control, not only in the operating room but throughout the trauma care system, would represent a revolution in injury care. Current products and technologies which are currently being developed to meet this need include topical hemostatic agents, junctional tourniquets, and retrograde endovascular balloon occlusion of the aorta (REBOA). Several novel investigations have demonstrated the value of EMS deployment of blood and blood products.[24,25] Future efforts will also likely yield shelf stable pathogen controlled lyophilized blood products to lengthen the window of survival for the bleeding trauma patient.[26,27]

Some authors have argued that not all trauma victims who are bleeding can be saved with improved care, and that reductions in transport times may simply move the location of death from the prehospital setting to the emergency department or the OR.[28]

Limitations to our analysis include inherent limitations of the NTDB Research Data Set including data quality, the data is a convenience sample denoted by a disproportionate representation of higher tier trauma centers with higher injury acuity, potential for sources of bias and missing data. To further qualify this liability, the NTDB has a vigorous data quality program to mitigate known limitations. In addition, we chose to exclude patients with any missing data elements rather than impute so as to minimize potential for bias. In addition, key assumption made with respect to the association of severe torso injury and NCTH are based upon empiric analysis of the AIS coding framework.

This analysis casts solid objective evidence disputing the dogma of the "golden hour", which now appears to be, at least a flawed clinical ideology. However, perhaps we should think twice before "throwing the baby out with the bath water." "Sometimes old dogmas help save lives, allowing people with diverse levels of knowledge to grasp a simple concept. The golden hour of trauma is (really about) the concept of timely care after injury; no need to reset your clocks.".[29]

5. Conclusion

In patients with high-grade torso injury, AIS grades $\geq$4, the degree anatomic disruption is often associated with significant hemorrhage. In our study, a precipitous rise in patient mortality was exhibited in this high-grade injury group at prehospital times <30 min. Our data highlight that the critical nature of prehospital time in patients with non-compressible torso hemorrhage. However, realizing that evacuation times <30 min may not be realistic, particularly in rural or austere environments, future efforts should be directed toward the development of therapies to increase the window of survival in the prehospital environment.

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