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"The Why & How Our Trauma Patients Die: A Prospective Multicenter Western Trauma Association Study."

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Abstract

Introduction: Historically, hemorrhage has been attributed as the leading cause (40%) of early death. However, a rigorous, real-time classification of the cause of death (COD) has not been performed. This study sought to prospectively adjudicate and classify COD to determine the epidemiology of trauma mortality.

Methods: 18 trauma centers prospectively enrolled all adult trauma patients at the time of death during 12/2015–8/2017. Immediately following death, attending providers adjudicated the primary and contributing secondary COD using standardized definitions. Data were confirmed by autopsies, if performed.

Results: 1536 patients were enrolled with a median age of 55 (IQR 32–75). 74.5% were male. Penetrating mechanism (n=412) patients were younger (32 vs 64, p<0.0001) and more likely male (86.7% vs. 69.9%, p<0.0001). Falls were the most common mechanism of injury (26.6%), with GSWs second (24.3%). The most common overall primary COD was TBI (45%), followed by exsanguination (23%). TBI was non-survivable in 82.2% of cases. Blunt patients were more likely to have TBI (47.8% vs. 37.4%, p<0.0001) and penetrating patients exsanguination (51.7% vs 12.5%, p<0.0001) as the primary COD. Exsanguination was the predominant prehospital (44.7%) and early COD (39.1%) with TBI most common later. Penetrating mechanism patients died earlier with 80.1% on day 0 (vs. 38.5%, p<0.0001). Most deaths were deemed disease related (69.3%), rather than by limitation of further aggressive care (30.7%). Hemorrhage was a contributing cause to 38.8% of deaths that occurred due to withdrawal of care.

Conclusions: Exsanguination remains the predominant early primary COD with TBI accounting for most deaths at later time points. Timing and primary COD vary significantly by mechanism. Contemporaneous adjudication of COD is essential to elucidate the true understanding of patient outcome, center performance, and future research.

Level of Evidence: II, Epidemiologic

Keywords

hemorrhage; cause of death; exsanguination

Introduction:

Trauma is the leading cause of death for trauma patients aged 1–44 years old and is expected to rise to the leading cause of death in older age groups as the Baby Boomers reach advanced age[1]. The trimodal distribution of trauma death was described initially by Trunkey in 1983 using epidemiologic data from the 1970s[2]. Immediate deaths were those occurring in the prehospital environment, early deaths up to 4 hours post-event, and late death days to weeks later. Immediate deaths were not felt to be preventable but early and late deaths potentially preventable. Since that time there has been significant changes to trauma care systems including prehospital advances, resuscitation practice changes, and improvement in critical care[3–8].

The most impactful of the improvements is the recognition of the role of acute traumatic coagulopathy (ATC) in poor outcome[4,9] and adoption of transfusion practices that favor more balanced resuscitation strategies designed to mitigate the effects of ATC. Hemorrhage related mortality is often attributed as the primary cause of preventable death comprising approximately 35–40% of all deaths and Traumatic Brain Injury (TBI) the most common cause of overall death[10]. For decades, these estimates have gone largely unchallenged despite the evolution of treatment advances in trauma care.

Although there have been a number of retrospective studies over the last 35 years since Trunkey's original trimodal distribution study disputing the pattern of death[7,11,12], there have been virtually no investigations in the last decade. Also, previous studies have lacked rigorous real-time classification of the cause of death (COD) and have relied upon registry based data or chart reviews to determine primary COD. This study sought to prospectively adjudicate COD following traumatic injury to determine if there has been a change in distribution of death with advances in trauma care.

Methods:

The study was approved by the Western Trauma Association Multicenter Trials Group and each enrolling trauma center's Internal Review Board. Eighteen centers prospectively enrolled all adult trauma patients at the time of death from December 1, 2015 to August 15, 2017. Deaths from drowning, hanging, burns, lightning strikes, and dog attacks were excluded from analysis. Basic demographic data (sex, age) and injury data (mechanism) were collected. All participating centers provided routine trauma care including adherence to Advanced Trauma Life Support (ATLS) principals and availability of massive transfusion protocols.

Prehospital arrest and need for Resuscitative Thoracotomy in the Emergency Department was recorded. The timing of death was determined with the date of arrival to the emergency department being considered day 0. Blood product consumption in the first 24 hours of care was provided. The location of death (Emergency Department, Operating Room, Intensive Care Unit, Interventional Radiology, or Ward) and circumstances of death were assessed including presence of a Do not resuscitate order, comfort care/withdrawal of care, pre-existing POLST, and family presence for decision making. Each death was also classified by the attending providers as disease related or secondary to withdrawal care.

Attending providers at the enrolling center adjudicated the primary and contributing secondary COD using standardized definitions immediately following death [eTable1]. Each patient death was attributed to a single primary COD. COD categories were adapted from prior work by Cripps et al.[13] and classified as exsanguination, early physiologic collapse (within 24 hours), late physiologic collapse (after 24 hours), Traumatic Brain Injury (TBI), sudden unexpected event, or due to a medical event that immediately preceded the trauma. TBI was further classified into imminently non-survivable or potentially survivable. Data were confirmed by autopsies for those who were coroner's cases, and at either Morbidity and Mortality conferences or Trauma Peer Review if no autopsy was available.

In addition to the primary COD, patients could have one or more Secondary contributing CODs. These were defined as hemorrhagic shock, obstructive shock, airway related, TBI, respiratory failure, pulmonary embolism (PE), sepsis, multiple organ failure (MOF), stroke, pre-existing medical disease, delayed/missed diagnosis, procedural complication, cardiopulmonary collapse (trauma related or non-trauma related), or other.

Data were grouped by mechanism of injury (blunt, penetrating) and timing of death (prehospital/emergency department, first 24 hours, and after 24 hours) for comparisons. Continuous variables were reported as medians with interquartile ranges (IQR) and compared with Wilcoxon Rank Sum. Categorical variables were compared with chi-squared and t-tests. Kaplan Meier curves were created based upon day of death. Statistical significance was determined at $p<0.05$ level.

Results:

Across the 18 centers, 1536 patients were prospectively enrolled with a median day of death of 1 (0–4). The cohort median age was 55 (IQR 32–75) and the majority (74.5%) were male [Table 1]. Blunt injury was present in 73.2% of the cohort. Penetrating mechanism (n=412) patients were younger (32 vs 64, p<0.0001) and more likely male (86.7% vs. 69.9%, p<0.0001). Overall, falls were the most common mechanism (26.6%, n=409) with gunshot wounds second (23.3%, n=358), and motor vehicle collisions (16.8%, n=258) next. Of the 358 patients suffering gunshot wounds (GSWs) 68.7% (n=246) sustained an isolated GSW and 31.3% (n=112) multiple GSWs. Traumatic Brain Injury (TBI) was present in 61.0% (686/1536) of the overall cohort and was present in 47.3% (532/1124) of the blunt injured patients [Table 1].

Primary cause and timing of Death

TBI was the most common overall primary COD (45%, 691 TBI deaths/1536 total deaths) with it being more common in blunt patients (47.8% vs. 37.4%, p<0.0001). The vast majority of TBIs were non-survivable based upon physician adjudication of the initial anatomic severity (82.2%). TBI resulting from penetrating trauma was significantly more likely to be non-survivable based on anatomic severity (98.1%, 151/154) compared with TBI from blunt injury (77.6%, 413/532; p<0.0001). TBI deaths occurred later than those from other causes [Figure 1].

The next most common primary COD was exsanguination (23%) [Table 2]. Exsanguination was more frequent in penetrating patients than blunt patients (51.7% vs 12.5%, p<0.0001). When considering the timing of death, exsanguination was the predominant prehospital (44.7%) and early COD (39.1%) [Figure 1]. Of those dying early (prehospital/emergency department) from exsanguination (n=205), nearly all (96%) died of truncal hemorrhage including 141 patients with penetrating truncal injury and 56 blunt truncal injury. An additional 7 patients died of isolated stab wounds to the neck and 6 patients suffered extensive extremity injuries resulting in hemorrhage. Only 1 of these 6 arrived with a tourniquet in place.

Prehospital arrest occurred in 35.7% (546/1536) and was most common in penetrating patients (n=247, p<0.0001). Overall, 14.7% (226/1536) underwent an Emergency Room resuscitative thoracotomy (EDT). REBOA (resuscitative endovascular balloon occlusion of the aorta) was attempted in 1.6% (25/1536 patients) with 22 of them being performed in the Emergency Department (ED) and 3 placed in the Operating Room. Of the attempted REBOAs, 3 were not able to be placed/deployed due to anatomic or technical reasons. Of the successfully deployed REBOAs in the ED, 78.9% (15/19) left the ED alive and later succumb to their injuries.

Although 1/3rd of deaths occurred in the emergency department, most deaths occurred in the intensive care unit (46.6%). Only 12.9% of patients died in the operating room. Less than 2% of patients were in a hospice unit at the time of their death [Table 3]. Penetrating mechanism patients died earlier (80.1% on day 0 vs. 38.5%, p<0.0001) [Figure 2] and were more likely to die in the ED than blunt patients (p<0.0001, Table 3). Late physiologic collapse occurred in 15.6% of the cohort and was present more often in the blunt patients (p<0.001). Most deaths following late physiologic collapse were attributed to limitation of further care (62.7%, 151/241).

Secondary cause of death

The most common secondary contributing causes of death were respiratory failure (13.7%), pre-existing conditions (9.2%), hemorrhagic shock (6.8%), and multi-organ failure (6.1%) [Table 4]. Respiratory failure and pre-existing conditions were more common in blunt patients (both p<0.0001, Table 4). There was no difference in hemorrhagic shock, obstructive shock, pulmonary embolism, sepsis, or procedural complications between blunt and penetrating mechanisms. Hemorrhage was a contributing cause to 38.8% of deaths that occurred due to withdrawal of care.

Blood product usage

Blood products were used in 33.5% (n=515) of the cohort. Amongst the 412 trauma patients suffering from penetrating mechanisms, 35% (145/412) received at least 1 unit of PRBCs and 17.5% (72/412) received massive transfusion (10 or more units of PRBCs in 24 hours). In blunt mechanism patients, 32.9% (370/1124) received at least 1 unit of PRBC and 11.7% received massive transfusion. The range of Packed Red Blood Cells (PRBCs) received was 1–133 units in penetrating mechanisms and 1–86 units in blunt mechanisms (eTable2). Plasma received ranged from 1–165 units (penetrating 1–165, blunt 1–84 units). Massive transfusion was more common in penetrating injury (p=0.003). For those receiving any blood products, the median ratio of PRBC:plasma was 1.21 (1.0–2.0) and was lower in the blunt patients (1.16 vs. 1.44, p=0.0003).

Role of Advanced Directives and Palliative Care

Most deaths were deemed disease related (69.3%), rather than from limitation of further care (30.7%). Pre-existing advanced directives or POLST forms were available in 135 patients (8.9%) and family available to participate in goal of care discussions in 60.0% [eTable3]. Half (50.9%) of the blunt mechanism patients had a DNR order in place at the time of their death compared with only 13.4% of the penetrating patients (p<0.0001). For patients dying following hospital admission (not in the Emergency Department), most (62.5%) were transitioned to comfort care including 69.9% of the blunt patients [eTable3]. Penetrating trauma patients were less likely to have comfort care orders at the time of death (25.7%) and were less likely (32.2%) to have family available for goal of care discussions (both p<0.0001).

Discussion:

For decades, the greatest burden of the loss of years of productive life have been attributed to traumatic injury for those aged 1–44 years old[1]. Strategies designed to mitigate the risk of death including prehospital, critical care, and resuscitation advances have been adopted. Although the field has had a general understanding of the timing of and causes of post-traumatic mortality, this current study represents a multicenter *prospective* investigation specifically designed to understand the how and why trauma patients succumb to injury using real-time cause of death adjudication.

Classic descriptions that are common in our literature suggest that approximately 35–40% of our patients die directly as a result of hemorrhagic causes and it has been argued that these represent the portion of poor outcomes that may be modifiable[10]. To date, few investigations have distilled apart the important components of mitigatable mortality risk. Indeed in all of these studies a patient dying from anatomically non-survivable exsanguination would be lumped together with a patient who bled to death as a result of suboptimal trauma care, and/or inadequate (but otherwise survivable) resuscitation[14]. In contrast to this older population level data, in the current study, less than a quarter of the overall cohort died of exsanguination. However, mechanism of injury was an important distinguishing feature for primary COD. Only 12.5% of blunt patients died of exsanguination compared with over half of the penetrating patients dying of hemorrhage.

One of the most important findings in this study is the factor of time of death. Most of the patients did not die in the emergency room and surprisingly, almost a third of patients died after limitation of further care. These are patients who had anatomically survivable injuries. This is the patient group that we feel may benefit from the ongoing work in trying to define better prehospital and very early interventions that may mitigate the outcome trajectory. Oyeniyi et al. recently found that in their center with efforts focused on hemorrhage control strategies, mortality fell. The rate dropped from a historic rate in their institution of 36% to 25% which was temporally related to the introduction of a bleeding control bundle[15]. Early blood product usage even in the prehospital environment has also shown promise for further reduction in mortality[6]. Others have reported that even a delay as short as 10 minutes to packed red blood cell transfusion increased the risk of death in hemorrhaging patients[16]. This further illustrates that investigating strategies such as prehospital blood product administration and hemorrhage control techniques like REBOA (resuscitative endovascular balloon occlusion of the aorta) aimed at very early intervention for those suffering exsanguination may play an important role in decreasing deaths from potentially preventable causes.

Although it could be argued that our data shows that perhaps there is less opportunity to intervene in exsanguination deaths, the vast majority of patients in this study died following admission to the inpatient unit, not in the Emergency Department/prehospital time period or in the operating room. Specifically, those who suffered blunt injury survived longer than the penetrating patients and interestingly, perhaps due to survival bias (lived longer), they received a more balanced ratio of PRBCs to plasma. Together these data support the hypothesis that better trauma care and resuscitation early, not only prevents early deaths but also establishes a trajectory that mitigates later death and improves overall long term survival.

Recent investigations of trauma resuscitation including the PROPPR trial have found that those who die of hemorrhage, die early[3–5]. Our study confirms these findings with exsanguination being the predominant cause of early deaths (prehospital/ED 44.7%; 1st 24 hours of hospitalization 39.1%). In addition, even when hemorrhage was not the primary cause of death, it was a factor in 38.8% of deaths that occurred following a decision to limit further aggressive care. The vast majority of these had concomitant TBI and over 80% of all TBIs were deemed non-survivable. A portion of the hemorrhage related deaths without question reflect anatomically non-survivable injuries especially for those dying in the prehospital/emergency department period, however, there does exist a narrow but important window to potentially impact outcome with further refinement of care[17, 18].

Although hemorrhage and TBI played important roles as the primary COD, there was a remarkable percentage (15.6%) of those suffering late physiologic collapse. Pro-inflammatory and infectious causes were the predominant etiologies of secondary COD including respiratory failure (13.7%), multi-organ failure (6.8%), and sepsis (4.2%). The combination of these factors most likely reflects a group of patients that survived their initial insult, but succumb to the late effects of critical injury. This is an important group of patients in which elements of mitigatable risk and failure to rescue play pivotal roles and should be the subject of further investigation.

Unique to our study, we collected goals of care data on patients to more fully understand the end of life events. Overall, less than a third of patient deaths were predominantly due to limitation of further care. There were significant and important difference by mechanism with almost all penetrating deaths secondary to disease. In contrast, nearly 40% of blunt patient deaths were due to withdrawal of care. Our data underscores the necessity of collecting the underlying etiology of death if mortality is to be used as a performance metric. Using retrospective data, Weireter et al. found similar findings in a single center study where those who had care withdrawn created a 23% increase in their overall mortality data[19].

Importantly, most (62.5%) of the cohort who survived to hospital admission were transitioned to comfort care prior to their deaths. Although more blunt mechanism patients had family available for discussion of goals of care and were more likely to have a DNR in place at the time of death, this likely reflects the longer length of time the blunt patients survived. Despite nearly 50% of the blunt patients having a DNR order at the time of their death, less than 2% of patients died in a hospice unit and most died in the ICU. This held true even for the blunt patients who were more likely to have care withdrawn, rather than die rapidly from disease. This study highlights that there is remaining uncaptured opportunities to maximize palliative care service and goals of care discussions for those highly likely to succumb to their injuries. Our ability to interpret the details of who was offered palliative care services is limited by lack of socioeconomic factors collected in the study.

There are a number of other potential limitations to this study. First, there was no standard protocol or treatment algorithm for patients leading to potential for wide spectrum of care across institutions that may have effected the COD. However, the participating centers all follow standard ATLS protocols for the initial care/stabilization of the patients, have massive transfusion protocols, and are accredited trauma centers. These criterion serve to help decrease the level of treatment bias that can exist. In addition, prehospital cardiac arrests that were transported to the participating centers were also included to reduce the bias of classification of ‘dead on arrival’ patients. Further, although the vast majority of the cases were coroners cases (72.8%, n=1113/1536), a consensus approach for cause of death was the best available method to determine primary cause of death in those lacking an autopsy. This approach was done to limit bias in the intrepretation of cause of death from a single attending provider by instead utilizing consensus amongst peers through the participating institution trauma peer review process as to the circumstances of the cause of death. In addition, there are no standard accepted definitions of cause of death. To standardize our categories, categories of cause of death were based on those from prior literature[13].

Conclusions:

Exsanguination remains the predominant early primary COD with TBI accounting for most deaths at later time points. Timing and primary COD vary significantly by mechanism. Contemporaneous adjudication of COD is essential to elucidate the true understanding of patient outcome, center performance, and future research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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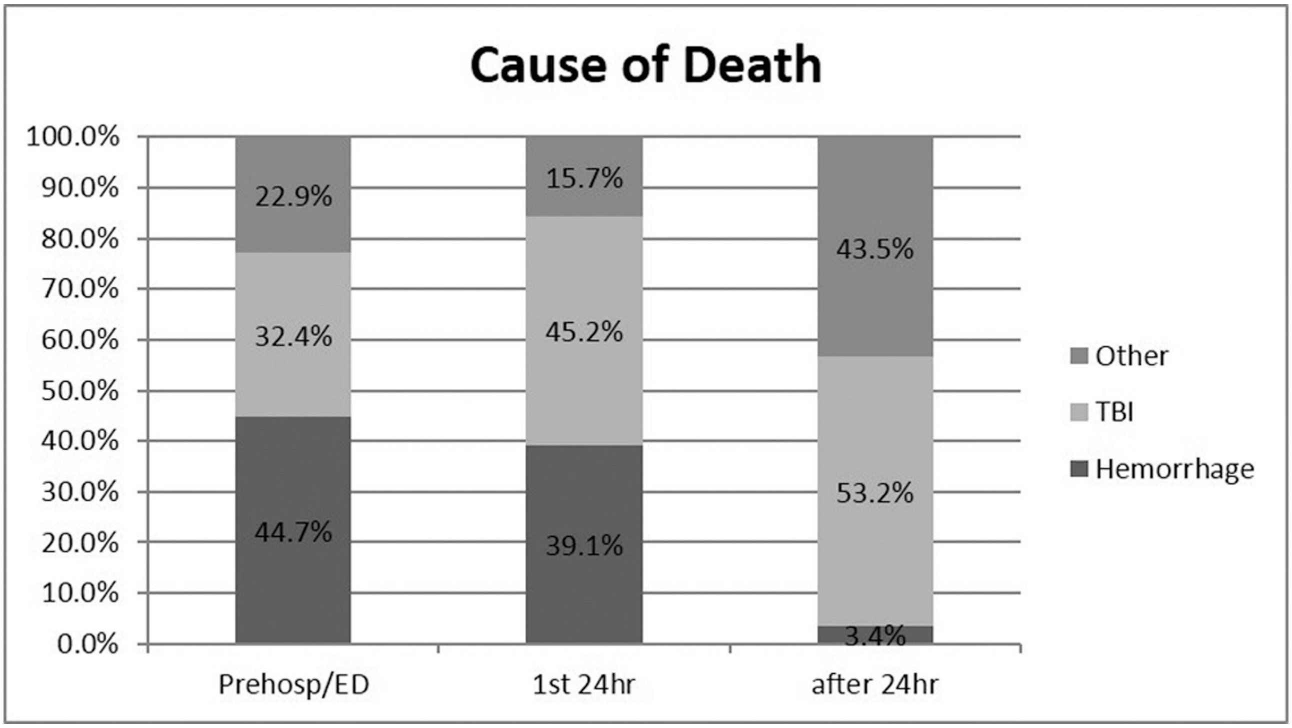

Figure 1 –.
Cause of Death by Time

Prehosp: prehospital; ED: emergency department; hr: hour; TBI: traumatic brain injury

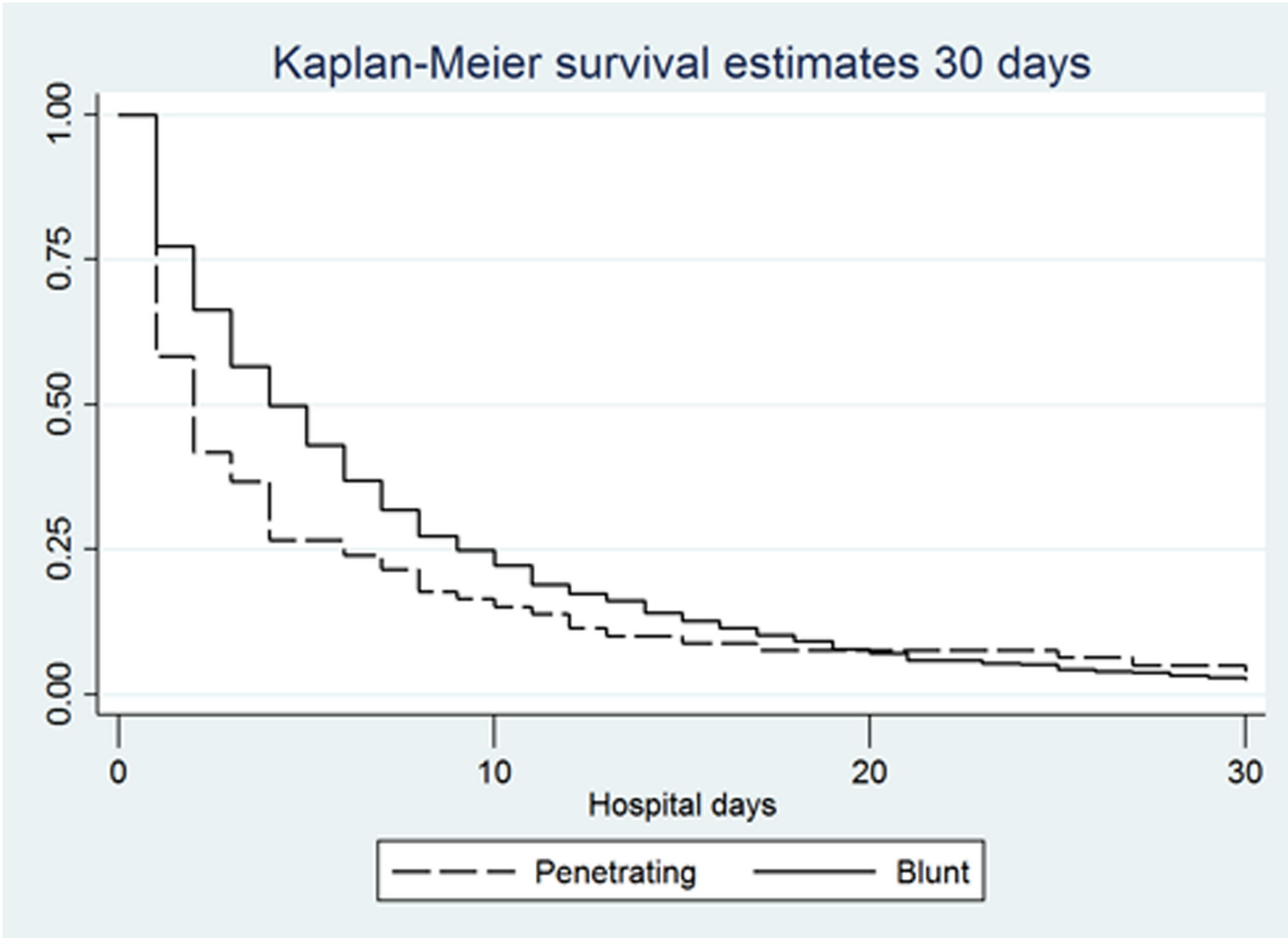

Figure 2 –.
Kaplan Meier Survival Estimates by Mechanism

Table 1:

Demographics

		Penetrating n=412	Blunt n=1124	Overall n=1536	p-value
Age (Median, IQR)		32 (25–43)	64 (43–80)	55 (32–75)	p<0.0001
Male		86.7%	69.9%	74.5%	p<0.0001
Mechanism	MVC		258	16.8%	
	MCC		105	6.8%	
	Fall		409	26.6%	
	Assault (Blunt)		20	1.3%	
	Crush		14	0.91%	
	Ped vs Auto		162	10.6%	
	Bike vs Auto		17	1.1%	
	Found Down		98	6.4%	
	Other Blunt		41	2.7%	
	SW	33		2.2%	
	Multiple SW	20		1.3%	
	GSW	246		16.0%	
	Multiple GSW	112		7.3%	
TBI		154 (37.4%)	532 (47.3%)	686 (61.0%)	
Median day of death		0 (0–0)	1 (0–6)	1 (0–4)	p<0.0001
Prehospital Arrest (N=411 pen, 1119 b)		247 (60.1%)	299 (26.7%)	546 (35.7%)	p<0.0001
ED Thoracotomy (n=412 pen, 1123b)		142 (34.5%)	84 (7.5%)	226 (14.7%)	p<0.0001
Death attributed to:					
	Disease Related	380 (92.2%)	684 (60.8%)	1064 (69.3%)	p<0.0001
	Withdrawal of Care	32 (7.8%)	440 (39.1%)	472 (30.7%)	p<0.0001

MVC: motor vehicle collision; MCC: motorcycle collision; Ped:pedestrian; Auto: automobile; SW: stab wound; GSW: gunshot wound; TBI: traumatic brain injury; pen: penetrating; b: blunt; ED: emergency department

Table 2:

Primary Cause of Death

	Penetrating	Blunt	Total	p-value
TBI	154 (37.4%)	537 (47.8%)	691 (45.0%)	p=0.0003
Exsanguination	213 (51.7%)	140 (12.5%)	353 (23.0%)	p<0.0001
Early Physiologic Collapse	24 (5.8%)	125 (11.1%)	149 (9.7%)	p=0.0019
Late Physiologic Collapse	17 (4.1%)	222 (19.8%)	239 (15.6%)	p<0.0001
Airway	3 (0.73%)	20 (1.8%)	23 (1.5%)	p=0.1329
Sudden Unexpected Event	1 (0.24%)	14 (1.3%)	15 (0.98%)	p=0.076
Pre-trauma Medical Event	0 (0%)	59 (5.2%)	59 (3.8%)	p<0.0001
Other	0 (0%)	7 (0.62%)	7 (0.49%)	p=0.1084
Total	412 (26.8%)	1124 (73.2%)	1536 (100%)	p<0.0001

TBI: Traumatic Brain Injury

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Table 3:

Death Location by Mechanism

	Penetrating N=411	Blunt N=1120	Total N=1531	p-value
ED	240 (58.4%)	275 (24.6%)	515 (33.6%)	p<0.001
OR	57 (13.9%)	87 (7.8%)	144 (12.9%)	p=0.003
ICU	112 (27.2%)	601 (53.7%)	713 (46.6%)	p<0.001
IR	0 (0%)	3 (0.27%)	3 (0.20%)	p=0.294
General Ward	2 (0.48%)	121 (10.8%)	123 (11.0%)	p<0.001
Hospice Unit	0 (0%)	31 (2.8%)	31 (2.0%)	p=0.007
Other	0 (0%)	2 (0.18%)	2 (0.13%)	p=0.391

ED: emergency department; OR: operating room; ICU: Intensive Care Unit; IR: interventional radiology

Table 4:

Secondary Causes Contributing to Death by Mechanism

	Penetrating N=412	Blunt N=1124	Total N=1536	p-value
Shock, Hemorrhagic	25 (6.1%)	79 (7.0%)	104 (6.8%)	p=0.510
Shock, Obstructive	2 (0.4%)	2 (0.1%)	4 (0.2%)	p=0.300
TBI	4 (0.97%)	84 (7.5%)	88 (5.7%)	p<0.0001
Airway	5 (1.2%)	34 (3.0%)	39 (2.5%)	p=0.046
Respiratory Failure	16 (3.9%)	195 (17.3%)	211 (13.7%)	p<0.0001
PE	2 (0.4%)	9 (0.8%)	11 (0.7%)	p=0.52
Sepsis	11 (2.7%)	53 (4.7%)	64 (4.2%)	p=0.076
Stroke	1 (0.2%)	27 (2.4%)	28 (1.8%)	p=0.005
MOF	9 (2.2%)	84 (7.5%)	93 (6.1%)	p<0.0001
Pre-existing Condition	5 (1.2%)	137 (12.2%)	142 (9.2%)	p<0.0001
Procedural Complication	1 (0.2%)	5 (0.4%)	6 (0.3%)	p=0.574
Other	0 (0%)	22 (2.0%)	22 (1.4%)	p=0.004

TBI: Traumatic Brain Injury; PE:pulmonary embolism; MOF: multi-organ failure