Title

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Surviving Traumatic Injury to Die of Acute Drug Poisoning: Do Trauma Centers need to be a Path for Intervention?

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Abstract

Background: Although death from drug overdose is a leading cause of injury-related death in the United States, its incidence after traumatic incident is unknown. Moreover, little is known about related risk factors. We sought to determine the incidence and characteristics of, and risk factors for, trauma patients suffering death by acute drug poisoning ("overdose") after hospitalization for a traumatic incident.

Methods: We conducted a retrospective chart review of all admitted trauma patients ≥18 years of age at the only level-1 trauma center in our region from 2012–2019, matched with unintentional overdose decedents from the California death registry. We assessed associations between demographic and clinical characteristics with risk of overdose death using cumulative incidence functions and Fine-Gray sub-distribution hazard models.

Results: Of 9,860 patients residing in San Francisco at the time of their trauma activation or admission during the study period, 1,418 died (4.3 per 100 person-years), 107 from unintentional overdose (0.3 per 100 person-years). Overdose decedents were 84% male, 50% white, with a mean age of 48 years at the time of presentation; 20% occurred within 3 months of hospitalization, and 40% were attributed to a prescription opioid. In multivariate analysis, younger age, male sex, white race, and having undergone a urine drug screening were all associated with subsequent death from overdose.

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Conflicts of interest: None

Conclusions: Over a mean 3.4 years follow-up, the mortality rate from overdose among adult patients with traumatic incidents was 0.3/100 person-years. Trauma hospitalization may serve as an opportunity to screen and initiate prevention, harm reduction, and treatment interventions.

Keywords

Substance use; Opioids; Trauma; Death from overdose

Introduction

Deaths from acute drug poisoning ("drug overdose") have risen precipitously for the past two decades and are now the leading cause of unintentional death nationwide.[1] Further, deaths have continued to rise in urban areas, such as San Francisco.[2–4] The opioid crisis, in particular, cost the U.S. economy an estimated $631 billion from 2015–2018, with 40% of that due to mortality, predominantly driven by lost lifetime earnings for those who died prematurely due to drug overdoses involving opioids.[5] Emergency department utilization for any reason has found to increase the risk of prescription drug overdose.[6] Additionally, the rate of preexisting substance use is significantly higher among trauma patients than in the general population, making these patients even more vulnerable to use disorders[7,8] and possibly death from overdose, although this phenomenon has not previously been studied.

Research on outcomes after traumatic injury has typically focused on in-hospital mortality or a brief follow-up period. These data are used as benchmarks to improve hospital care and quality. Recent studies have found that for trauma patients, long term survival is worse than predicted actuarial survival,[9] suggesting that the mortality of injury does not end at discharge. However, further investigation of mortality due to overdose after traumatic injury is hampered by several factors, including that trauma systems currently do not benchmark prescribing patterns, nor do they follow patients for substance use disorders, and only recently have other organizations taken steps to do so.[10,11] Furthermore, few data exist about risk factors for death from overdose after a traumatic injury and the incidence of death from overdose after a traumatic incident is unknown.

To begin to address these important gaps in understanding post-hospitalization mortality after traumatic injury, we sought to determine the incidence and characteristics of trauma patients suffering death by acute drug poisoning after hospitalization for a traumatic incident in San Francisco, CA. We also sought to identify risk factors for death from overdose in this group.

Methods

Study Design and Setting

We conducted a retrospective chart review at the only level one trauma center in the city and county of San Francisco, where deaths from drug overdose have recently risen steeply.[2–4] The trauma hospital catchment includes the city and county of San Francisco as well as patients from the next closest county. The study was approved by the Institutional Review

Board (#18–26422) at University of California San Francisco and Zuckerberg San Francisco General Hospital.

Study Participants

Patients were included in the study if they were residents of San Francisco County and age 18 or older at the time of presentation as a trauma activation resulting in admission to Zuckerberg San Francisco General Hospital (ZSFG), or when the trauma surgery team was subsequently consulted for a trauma injury (an upgraded or 'non-activated' trauma), between January 1, 2012, and July 30, 2019. For patients with multiple hospital admissions, the most recent hospitalization was included. Patients were excluded if they died prior to discharge (even if death was from a drug overdose), were discharged to hospice care, or if their address was outside of San Francisco county.

ZSFG has specific pre-defined criteria for trauma activations. These include noncritical or critical trauma activations determined by mechanism of injury, age, types and numbers of injuries, Glasgow coma score, hemodynamic status, and respiratory status in the field or upon arrival to the emergency department. Trained nurses with experience in emergency medicine and critical care review the patients' charts, identify injuries, and determine injury severity score. Once the data are abstracted, trauma registrars enter the data and perform the appropriate coding. Injury severity score (ISS), an established medical scoring system based on the squared sum of the three highest scores of each body region, is calculated to assess trauma severity within a range from 3 to 75, with increasing ISS associated with increasing mortality.[12] Both patient characteristics as well as variables collected in the trauma registry were used in the analysis.

Trauma patients meeting the above criteria were then matched to records from the California Electronic Death Registry, which includes San Francisco residents who died in another U.S. county. Patients were matched on date of birth and name, so that the final dataset represented actual patients and not merely a comparison of death incidence. We merged these two datasets at a fixed time point and accounted for varying length of follow up by using person-years in incidence rate calculations. Death from unintentional or undetermined overdose was considered a drug "overdose" death, our primary outcome.[13] Agents included prescription opioids, prescriptions benzodiazepines, heroin, fentanyl, cocaine, methamphetamine and alcohol. Known suicides were excluded from this group as these were deemed intentional deaths.

Measures

Measures collected from the index trauma-related medical care included urine drug screening and blood alcohol level testing and other variables as available in the trauma registry (i.e. age, sex, ISS, GCS in the emergency department, injury type (blunt, penetrating, burns), hospital length of stay, ICU length of stay, race and discharge disposition). In addition to determining overdose as the cause of death, we also coded the substance to which the death was attributed.

Statistical Analysis

Descriptive statistics, including mean and standard deviation (±SD) or median and interquartile range (IQR), were used to characterize the entire trauma population and the group of patients who died by overdose. We assessed associations between demographic and clinical characteristics and risk of overdose death using cumulative incidence functions and Fine-Gray sub-distribution hazard models, which account for the competing risk of death due to other causes. First, unadjusted regression for each independent variable was conducted and variables with $p \leq 0.10$ were then included in the multivariable model. Since a blood alcohol level was not checked for 40% of the study sample, we conducted a separate multivariable model including blood alcohol level. Similarly, since urine toxicology was not checked in 44% of patients, we conducted a separate multivariable model including urine toxicology positivity.

Results

From January 1, 2012 to July 30, 2019, there were 25,158 adult trauma activations and admissions, representing 23,751 unique patients, with 12,322 reportedly living outside of the study county. Of the 9,860 patients who met inclusion criteria, 1,418 died over 33,197 person-years of follow-up (median follow-up of 3.4 years, range of 0–7.9), for a mortality rate of 4.3 per 100 person-years; 107 (4.6%) of the deaths were due to drug overdose, for a rate of 0.3 per 100 person-years.

Over the full time period of the study, our patients represented 33,197 person-years of follow-up time. The included patients were 68% male and 39% white, with a mean age of 53 years at the time of presentation (Table 1). The mean ISS was 9.8± 8.2 and the average Glasgow Coma Score in the ED was 14± 2.3. A blood alcohol level was ordered for 60% of patients, and 28% underwent a drug screen, 55% of which were positive. The median blood alcohol level among those screened was 0 mg/dL (IQR 0–160) (Table 2). *Among those tested, 36.1% had a blood alcohol level >0. Of overdose decedents, 63.4% had a blood alcohol level >0 and of the group with deaths from other reasons, 25.8% had a blood alcohol level >0.*

Compared to the overall trauma population, overdose decedents were more likely to be male (84%) and white (50%), with a younger mean age (48 vs 53 years) at the time of trauma admission. The mean ISS for this group was 9.7± 9.1 and the average Glasgow Coma Score in the ED was 13.4 ± 3.2. Compared to the overall trauma population, patients who died of an overdose were more likely to have a blood alcohol level ordered (77%); and the median blood alcohol level was 118 (IQR 0–294). Forty-eight percent had a urine drug screen, 72% of which were positive.

The median time from trauma activation to death from overdose was 497 days (IQR 130–1,036), although 20% of overdose deaths occurred within the first 90 days. The three most common drugs to which death was attributed were methamphetamine (48%), cocaine (41%), and fentanyl (22%) (Table 3). Forty percent of deaths were due to prescription opioids, although 76% of those deaths were also attributed to an illicit substance. In fact, 40 decedents (37%) had two or more illicit substances causing death.

In the unadjusted Fine-Gray models, patients who died from drug overdose were more likely to be male (SHR 2.39, 95% CI 1.43–4.02, p=0.001), white vs all other races (SHR 1.49, 95% CI 1.01–2.21, p=0.045) (Fig 1), have received urine drug screen on admission (SHR 1.92, 95% CI 1.30–2.82, p=0.001) (Fig 2), be a younger age at the time of admission (SHR 0.99, 95% CI 0.98–0.99, p<0.001), have lower GCS in the ED (SHR 0.92, 95% CI 0.87–0.98, p=0.01), and have a longer length of hospital stay (SHR 1.01, 95% CI 1.00–1.01, p=0.004) (Table 4). Among those with a blood alcohol level checked, the level was higher among those who subsequently died from overdose. (p<0.001). Variables not significantly associated with risk of death from overdose included ISS, injury type (penetrating vs blunt), and disposition location (Appendix Fig 3). However, those who specifically left against medical advice had a higher risk of death (p-value = 0.10) (Table 4).

Multivariable analysis with all covariates with p<0.05 in the unadjusted Fine-Gray Models showed that in the subgroup of patients who had blood alcohol levels available, white race (SHR 1.74, 95% CI 1.08–2.80, p=0.02) and higher blood alcohol level (SHR 1.003, 95% CI 1.002–1.005, p<0.001) were significantly associated with death from overdose. In the subgroup of patients with urine toxicology checked, white race, having positive urine toxicology and having a blood alcohol level were significantly associated with death from overdose. In the multivariable model omitting blood alcohol level as a covariate, male sex (SHR 1.97, 95% CI 1.12–3.46, p=0.02), white race (SHR 1.57, 95% CI 1.05, 2.36, p=0.03), having had a urine drug screen checked (SHR 1.74, 95% CI 1.12–2.70, p=0.01), and younger age (SHR 0.99, 95% CI 0.99–1.00, p=0.02) were significantly associated with death from overdose.

The rate of overall death per 100 person-years increased as the age group increased. For patients aged 18–34 years the rate was 0.4 deaths/100 person-years; for ages 35–49 years, 2/100 person-years; for 50–69 years, 2/100 person-years; for 50–69 years, 3.7/100 person-years, and for patients 70 years old and greater was 13/100 person-years. This was different for patients who died of overdose for whom the rate of death first increased through the age groups with the highest rate being in the 35–49 year old group, but then decreased for our oldest patient cohort. Specifically, the rate for 18–34 years old was 0.1/100 person-years; for 35–49 years, 0.7/100 person-years; for 50–69 years, 0.5/100 person-years; and for patients 70 years and greater was 0.03/100 person-years.

Discussion

This is the first investigation to compare long-term mortality from drug overdose following traumatic injury in the United States. We found that 4.6% of all deaths after discharge from traumatic injury were due to overdose, corresponding to 0.3 drug overdose deaths per 100 person years over a mean 3.4 years of follow-up; in comparison, the rate of overdose death in California was 0.1 per 100 person years in 2018.[14] Patients who subsequently died of an overdose were more likely to be younger, white, and to have had urine drug screens ordered upon presentation, suggesting that providers recognized a risk of substance use.

Furthermore, our study adds to literature which demonstrates that mortality from overdose after admission for traumatic injury is high.[9] Callcut et al followed 908 highest level activation trauma patients for a median of 1.7 years, during which time 3% of post-discharge deaths were due to substance use or overdose. Our analysis, including a broader sample of trauma activations with many lower level activations, still found that 5% of post-discharge deaths were attributed to drug overdose. These results support a heightened risk of overdose death after a traumatic injury, though our results do not find an association between injury severity and risk of overdose.

Although recent reports focus on prescription opioids as a cause of death from drug overdose,[1] our study shows that non-prescription drugs contributed substantially. The majority of overdose deaths among trauma patients did not involve prescription opioids and more than half involved illicit substances, which is different from older studies in San Francisco showing a predominance of prescription opioids among overdose deaths[1] and more aligned with recent data in San Francisco showing rising rates of death from drugs like fentanyl and methamphetamine.[2] Other more recent studies have also suggested a predominance of illicit substances: in one state-wide study, 30% of opioid overdose decedents had not filled an opioid prescription in the six months preceding death.[15] Our finding that most overdose deaths involved a stimulant raises concerns about the association of stimulant use with traumatic events.[16] There are no FDA-approved treatments for any stimulant use disorders, thus involvement of addiction medicine consultation services may be essential to addressing this risk when patients present.

Our study has several public health implications. First, younger adults were more likely to die of overdose than older adults, an important societal impact of years of life lost. Second, as death from overdose involving opioids can be prevented if naloxone is administered promptly, our results support providing this medication to patients after a traumatic injury, particularly if they leave the hospital against medical advice, even if they do not receive an opioid prescription.[17] It is possible that the added support provided to patients who were transferred to acute care facilities and skilled nursing facilities is somehow protective. Third, we found that patients who later died from overdose were more likely than other patients to have had a blood alcohol level checked and to have had a urine drug screen. This may have been due to clinician concern about substance use and the role it may have played in hospital presentation. Such concern should prompt additional interventions addressing substance use. Finally, although we did not find a significant independent association with leaving against medical advice and subsequent overdose death, early patient-directed discharge has been associated with substance use disorders[18] and multiple other negative health outcomes.[19–22]

The limitations of our study include its retrospective design and limited geographic area. Importantly, variables that might be useful in further analyses did not reliably exist in our data set, such as linkage to outpatient substance use disorder treatment, prior hospitalizations or episodes of overdose or hospitalizations at other hospitals, or hospitalization for intimate partner violence or psychiatric disorders. However, a positive finding in any of these categories might only strengthen the case that traumatic injury and hospitalization is an important time to intervene. Further, we do not have prescribing data, so could not associate discharge prescribing of opioid analgesics with subsequent overdose death. Importantly, however, our geographic region is unique in that there is only a single level-1 trauma center, and the city and county are in fact the same geographic area. Further, we have a close partnership with the San Francisco Department of Public Health and a robust trauma registry program. While 98% of our trauma patients are screened for alcohol use, as is recommend by the American College of Surgeons, not all of this screening is done specifically with a blood alcohol level. Therefore, clinical judgment may have influenced the absence of this lab in some cases.

In summary, we found that patients who have suffered a traumatic injury are at risk of death from overdose post-discharge over several years of follow-up and identified associated demographic and clinical care characteristics. As overdose deaths continue to rise, it is critical to take advantage of points for potential interventions and application of the rapidly developing field of addiction medicine. These results, combined with the American College of Surgery recommendation for drug and alcohol use screening after trauma,[23] may help to identify people who can benefit from simple interventions such as discharge with naloxone to use in the event of unintentional opioid overdose.[19] Trauma hospitalization may confer opportunities to increase screening and initiate prevention, harm reduction, and treatment interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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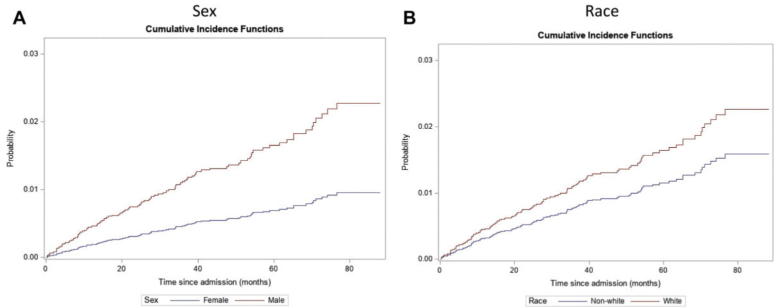

Figure 1.

Cumulative Incidence Function by Demographics for Death from Overdose with Competing Risk Death from Other Reasons

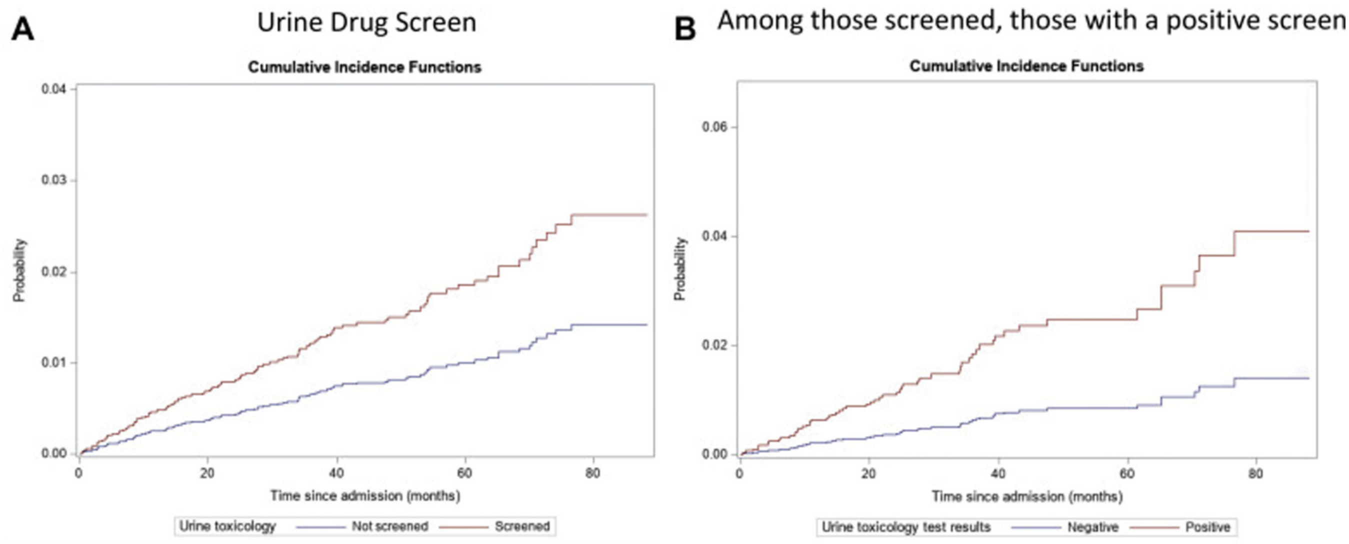

Figure 2.

Cumulative Incidence Function by Urine Drug Screen and Drug Screen Outcome in those Screened for Death from Overdose with Competing Risk Death from Other Reasons

Table 1:

Demographic Characteristics of Trauma Patients and those who died of Acute Drug Poisoning

	All Included Trauma Patients n=9,860	Acute Drug Poisoning Deaths (n=107)
Age in years at time of admission, mean (sd)	53 (22)	48 (11)
Sex		
Male	6,753 (68%)	90 (84%)
Injury Severity Score, mean (sd)	9.8 (8.2)	9.7 (9.1)
GCS in Emergency Department, mean (sd)	14.0 (2.3)	13.4 (3.2)
Injury Type		
Blunt	8515 (86%)	89 (83%)
Penetrating	1292 (13%)	17 (16%)
Burns	47 (<1%)	1 (<1%)
Hospital Length of stay in days, median (IQR)	4 (2–8)	5 (2–11)
ICU length of stay in days for those with ICU stays, n=3507, median (IQR)	3 (2–5)	3 (2–5.5)
Race		
White	3,864 (39%)	53 (50%)
Black	1,445 (15%)	24 (22%)
Asian	2080 (21%)	1 (1%)
LatinX	2,170 (22%)	24 (22%)
Native American/Hawaiian	79 (1%)	0 (0%)
Other/Unknown	222 (2%)	5 (5%)
Discharge disposition		
Home	5604 (57%)	67 (63%)
Home with services	1,031 (10%)	13 (12%)
Acute Care/Rehab	1,084 (11%)	5 (5%)
SNF/LTAC	1,547 (16%)	13 (12%)
AMA	280 (3%)	5 (5%)
Other	314 (3%)	4 (<1%)

Notes: *IQR = inter-quartile range, sd = standard deviation

Table 2:

Characteristics of Screening. (% is of column total, not overall total)

	All Included Trauma Patients n=9,860	Acute Drug Poisoning Deaths (n=107)
Urine Toxicology Ordered	3,767 (38%)	51 (48%)
Screened Positive (% of those performed)	1,507 (40%)	37 (72%)
Blood Alcohol Level Ordered	5891 (60%)	82 (77%)
Blood Alcohol Level of those performed, median (IQR)	0 (0–160)	118 (0–294)

Table 3:

Causal Agents in Acute Drug Poisoning Deaths

Drug	Patients, n (%)
Ethanol	37 (35%)
Prescription Opioids	
Codeine	1 (<1%)
Hydrocodone	7 (7%)
Oxycodone	8 (7%)
Morphine	18 (17%)
Methadone	11 (10%)
Benzodiazepines	
Alprazolam	1 (<1%)
Bromazepam	1 (<1%)
Chlordiazepoxide	3 (3%)
Diazepam	4 (4%)
Temazepam	1 (<1%)
Illicit Drugs	
Heroin	14 (13%)
Fentanyl	24 (22%)
Cocaine	44 (41%)
Methamphetamine	51 (48%)

Note: patients might have had more than one causal drug in their system, so the total does not add up to 107, however the %'s are of the total deaths (n=107)

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Table 4:

Sub-distribution hazard ratio (SHR) and 95% CI for SHR obtained from the Fine-Gray models for death from acute drug poisoning

	Unadjusted Model			Multivariable Model*		
Covariate	**SHR**	**95% CI of SHR**	**p-value**	**SHR**	**95% CI of SHR**	**p-value**
Age, years (at admission)	0.99	0.98–0.99	<0.001	0.99	0.99–1.00	0.02
Sex						
Male	2.39	1.43–4.02	0.001	1.97	1.12–3.46	0.02
Female	Reference group	*	*	Reference group	*	*
Injury Severity Score	1.00	0.97–1.03	0.99	*	*	*
GCS in Emergency Department	0.92	0.87–0.98	0.01	0.95	0.88–1.02	0.13
Injury Type						
Penetrating	1.20	0.72–2.02	0.48	*	*	*
Non-penetrating	Reference group	*	*	*	*	*
Hospital Length of stay, days	1.01	1.00–1.01	0.004	1.00	1.00–1.02	0.37
ICU length of stay, days	1.01	0.98–1.03	0.62	*	*	*
Race						
White	1.49	1.01–2.21	0.045	1.57	1.05–2.36	0.03
Non-White	Reference group	*	*	*	*	*
Urine toxicology screening						
Yes	1.92	1.30–2.82	0.001	1.74	1.12–2.70	0.01
No	Reference group	*	*	Reference group	*	*
Discharge disposition						
Home	1.45	0.80–2.62	0.22	*	*	*
Home with services	1.62	0.75–3.50	0.22	*	*	*
Acute Care/Rehab	0.53	0.19–1.50	0.23	*	*	*
AMA	2.39	0.85–6.72	0.10	*	*	*
Other	1.55	0.52–4.74	0.44	*	*	*
SNF/LTAC	Reference group	*	*	*	*	*

* Multivariable model included statistically significant ($p<0.05$) variables from the unadjusted model (gender, urine toxicology screening, age, GCS in ED).