The Effect of Illegal Drug Screening Results and Chronic Drug Use on Perioperative Complications in Trauma

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Abstract

Context: Illegal drug use and need for surgery are common in trauma. This allows examination of the effects of perioperative drug use. **Aim:** The aim was to study the effects of illegal drug use on perioperative complications in trauma. **Setting and Design:** Propensity-matched analysis of perioperative complications between drug screen-positive (DSP) and drug screen-negative (DSN) patients from the National Trauma Data Bank (NTDB). **Methods:** The NTDB reports drug screening as a composite. We compared complications for DSP, DSN, and specific chronic drug disorders. Time to first procedure was analyzed to determine whether delay to surgery was associated with reduced complications. **Statistics:** Logistic regression with 11 predictor variables was used to calculate propensity scores. Categorical and continuous variables were compared using Chi-square and Student's *t*-test, respectively. **Results:** 752,343 patients (21.9%) were tested for illegal drugs. DSP was protective for mortality-relative risk (RR) 0.84 ($P < 0.001$) and arrhythmia RR 0.87 ($P = 0.02$). All complications (AC) were higher for DSP with a RR of 1.08 ($P < 0.001$). Cocaine, cannabis, and opioids were associated with reduced mortality. Cocaine was associated with increased myocardial infarction (MI). All four chronic drug disorders were associated with markedly higher arrhythmia. All except cannabis were associated with higher AC. Mortality was significantly lower for DSP for every time interval until first procedure. Continuous-time until procedure was associated with increased MI and arrhythmia. **Conclusions:** DSP was protective of mortality and cardiac complications. Drug disorders were protective for mortality but increased arrhythmia and AC. Delay until the surgery does not diminish cardiac or overall risk.

Keywords: Cardiac, complication, illegal drugs, mortality, perioperative, trauma

Introduction

Drug screening is a routine although not a universal part of a trauma workup. It is also common before elective surgery. When a patient tests positive for methamphetamine or cocaine, elective surgery is typically canceled and delayed until the patient's drug screen is negative. The reasoning is that the sympathomimetic properties of these drugs could lead to cardiac complications. Other drugs such as narcotics and cannabis are generally not a contraindication for surgery; however, there are reports of increased cardiac morbidity among chronic users of these drugs.[1,2] In contrast to chronic use, there is little evidence that the results of drug screening affect the outcome.[3-5]

It is unlikely that anyone would approve a randomized trial for surgery for those positive for illegal drugs; however, there is a population in which drug-positive patients routinely undergo surgery. The National Trauma Data Bank (NTDB) contains a large number of patients who tested positive for illegal drugs and who subsequently had surgical procedures. The time to each procedure is recorded. In the trauma setting, a majority of procedures are urgent and emergent. They are typically done regardless of drug status. This represents an opportunity to see whether surgical procedures are associated with greater cardiac risk for the drug screen-positive (DSP) patients and whether delay to surgery improves the risk. Our hypothesis is that chronic drug use and DSP status are associated with increased cardiac risk in trauma and delaying surgery improves cardiac risk. The null hypothesis is that there is no association.

Access this article online

Quick Response Code:

Website: www.onlinejets.org

DOI: 10.4103/JETS.JETS_141_19

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How to cite this article: Culhane JT, Freeman CA. The Effect of illegal drug screening results and chronic drug use on perioperative complications in trauma. J Emerg Trauma Shock 2020;13:279-85.

Submitted: 25-Oct-2019. **Revised:** 27-Nov-2019. **Accepted:** 17-Feb-2020. **Published:** 07-Dec-2020.

Methods

Dataset

The National Trauma Data Bank is a registry of trauma data from multiple US trauma centers. Data from 2011 to 2015 were used. Patients 18 years and older were selected. Comparisons were done between patients who tested negative or positive for illegal drugs. Those not tested were excluded. The NTDB provides the following definition of drug use:

Drug use may be documented at any facility (or setting) treating this patient event. "Illegal use drug" includes illegal use of prescription drugs. If drug use is suspected, but not confirmed by test, record null value "Not Known/Not Recorded." This data element refers to drug use by the patient and does not include medical treatment. Data source hierarchy includes (1) laboratory results, (2) triage/trauma/hospital flow sheet, (3) nursing notes/flow sheet, and (4) history and physical.

A cardiac risk score was calculated based on the Revised Cardiac Risk Index (RCRI).[6] Where variables were not available, we used the closest approximation. Cardiac ischemia was considered positive if the patient had a history of myocardial infarction (MI) or angina. To calculate the RCRI, a point was assigned for cardiac ischemia, cerebrovascular infarction, chronic renal failure, congestive heart failure, and diabetes.

High-risk status of the procedure was based on a set of surgical procedures identified by Schwarze *et al*.[7] To select procedures which were likely to require general anesthesia, we reviewed the index of ICD9 procedure codes. We excluded nonsurgical procedures such as urinary catheter insertions and minor surgical procedures.

Table 1: Baseline characteristics of drug screen-positive and drug screen-negative patients

	No propensity match		After propensity match	
	Negative (%)	Positive (%)	Negative (%)	Positive (%)
Drug screen				
Positive blood alcohol	127,236 (32.3)	134,934 (38.3)	113,766 (37.9)	112,782 (37.6)
Female	125,727 (31.9)	85,881 (24.4)	78,575 (26.2)	77,772 (25.9)
Mean age	46.56	38.21	40.08	40.08
Median age (IQR)	47 (33)	35 (24)	38 (26)	38 (24)
Mean ISS	12.08	11.67	11.79	11.72
Mean cardiac risk score	0.16	0.078	0.089	0.089
Amphetamine disorder				
Positive blood alcohol	557,246 (16.3)	118 (18.8)	126 (19.8)	119 (18.7)
Female	1,268,152 (37.2)	165 (26.4)	168 (26.4)	168 (26.4)
Mean age	50.60	35.8	35.3	35.9
Median age (IQR)	50 (37)	34 (18)	33 (19)	34 (18)
Mean ISS	10.25	11.53	9.47	11.55
Mean cardiac risk score	0.19	0.07	0.061	0.067
Cocaine disorder				
Positive blood alcohol	556,346 (16.3)	1018 (35.5)	748 (30.3)	793 (32.2)
Female	1,267,692 (37.2)	625 (21.8)	541 (21.9)	569 (23.1)
Mean age	50.86	41.46	41.2	41.86
Median age (IQR)	50 (37)	42 (20)	40 (22)	43 (20)
Mean ISS	10.25	10.47	10.47	10.5
Mean cardiac risk score	0.19	0.14	0.11	0.14
Cannabis disorder				
Positive blood alcohol	555,936 (16.3)	1002 (42.3)	939 (28.3)	960 (29.0)
Female	1,267,380 (37.2)	468 (19.8)	635 (19.2)	607 (18.3)
Mean age	50.88	32.72	33.8	33.9
Median age (IQR)	50 (37)	29 (19)	30 (19)	30 (20)
Mean ISS	10.25	10.59	11.1	11.2
Mean cardiac risk score	0.19	0.07	0.08	0.09
Opioid disorder				
Positive blood alcohol	557,052 (16.3)	193 (24.8)	224 (10.5)	308 (14.5)
Female	1,267,689 (37.2)	231 (29.7)	606 (28.5)	621 (29.2)
Mean age	50.86	39.1	41.6	41.4
Median age (IQR)	50 (37)	41 (23)	40 (26)	41 (23)
Mean ISS	10.25	10.84	9.66	10.74
Mean cardiac risk score	0.19	0.136	0.16	0.16

IQR: Interquartile range, ISS: Injury severity score

Table 2: Effect of drugs on complications and mortality

Risk factor	Mortality					MI					Arrhythmia					All complications				
	Alive	Dead	Percentage	RR	*P*	Negative	Positive	Percentage	RR	*P*	Negative	Positive	Percentage	RR	*P*	Negative	Positive	Percentage	RR	*P*
DSP - All patients	291,497	8355	2.79	0.84	<0.001	299,400	452	0.15	0.95	0.47	299,354	498	0.17	0.87	0.02	212,905	86974	29.00	1.08	<0.001
DSP - Had surgery	102,222	3479	3.29	0.76	<0.001	105,463	238	0.23	0.79	0.01	105,536	165	0.16	0.99	0.930	66,986	38715	36.63	1.02	0.01
Amphetamine disorder	626	10	1.57	1.25	0.63	635	1	0.16	NA	0.32	605	31	4.87	3.10	<0.001	453	183	28.77	1.61	<0.001
Cocaine disorder	2435	29	1.18	0.40	<0.001	2454	10	0.41	3.33	0.05	2331	133	5.40	16.63	<0.001	1716	748	30.36	1.23	<0.001
Cannabis disorder	3270	39	1.18	0.37	<0.001	3305	4	0.12	4.00	0.18	3158	151	4.56	18.88	<0.001	2434	875	26.44	0.99	0.53
Opioid disorder	2092	33	1.55	0.55	0.005	2113	12	0.56	NA	0.001	2022	103	4.85	9.37	<0.001	1416	709	33.36	1.58	<0.001
Risk factor	**Mortality**					**MI**					**Arrhythmia**					**All complications**				
	Alive	**Dead**	**Percentage**			**Negative**	**Positive**	**Percentage**			**Negative**	**Positive**	**Percentage**			**Negative**	**Positive**	**Percentage**		
DSN - All patients	289,868	9984	3.33			299,378	474	0.16			299,278	574	0.19			219,558	80294	26.78		
DSN - Had surgery	84,981	3851	4.34			88,579	253	0.28			88,692	140	0.16			56,844	31998	36.02		
No amphetamine disorder	629	8	1.26			637	0	0.00			627	10	1.57			523	114	17.90		
No cocaine disorder	2392	73	2.96			2462	3	0.12			2457	8	0.32			1855	610	24.75		
No cannabis disorder	2322	77	3.21			3309	1	0.03			3302	8	0.24			2412	875	26.62		

RR is shown for DSP versus DSN patients for each risk factor. DSP: Drug screen positive, DSN: Drug screen negative, MI: Myocardial infarction, RR: Relative risk, NA: Not available

Table 3: Effect of time to the first procedure on complications and mortality

DSP	Day of the first procedure																			
	Mortality					MI					Arrhythmia					All complications				
	Alive	Dead	Percentage	RR	*P*	Negative	Positive	Percentage	RR	*P*	Negative	Positive	Percentage	RR	*P*	Negative	Positive	Percentage	RR	*P*
Day 1	55,728	2233	3.85	0.71	<0.001	57,837	124	0.21	0.90	0.006	57,810	151	0.26	0.74	0.005	36,693	21268	36.69	1.05	<0.001
Day 2	10,499	172	1.61	0.97	0.029	10,650	21	0.20	0.73	0.665	10,636	35	0.33	0.90	0.416	7084	3587	33.61	1.04	<0.001
Day 3	4954	76	1.51	0.70	0.003	5025	5	0.10	0.24	0.265	5015	15	0.30	0.82	0.387	3238	1792	35.63	0.99	0.159
Day 4 or Later	9630	292	2.94	0.86	<0.001	9872	50	0.50	0.75	0.042	9879	43	0.43	0.68	0.057	4776	5146	51.86	0.98	0.804
DSN	Day of the first procedure																			
	Mortality					MI					Arrhythmia					All complications				
	Alive	Dead	Percentage			Negative	Positive	Percentage			Negative	Positive	Percentage			Negative	Positive	Percentage		
Day 1	48,396	2760	5.40			51,034	122	0.24			50,977	179	0.35			33,194	17962	35.11		
Day 2	9179	155	1.66			9309	25	0.27			9300	34	0.36			6313	3021	32.37		
Day 3	4326	95	2.15			4403	18	0.41			4405	16	0.36			2823	1598	36.15		
Day 4 or later	8473	301	3.43			8715	59	0.67			8718	56	0.64			4125	4649	52.99		

RR is shown for DSP versus DSN patients in each time interval. DSP: Drug screen positive, DSN: Drug screen negative, MI: Myocardial infarction, RR: Relative risk

Analysis

The propensity for being drug positive was computed using a multivariate logistic regression with the variables such as age, sex, alcohol use, injury severity score, cardiac risk, and procedure under general anesthesia. Alcohol use was included because alcohol and drug use are often correlated, which could potentially introduce a bias. Including alcohol screening test results in the model allows us to select a control group with similar exposure to alcohol. The propensity score was used to match the drug-positive patients with a group of drug screen-negative (DSN) control patients with similar characteristics. According to the radius matching strategy, treatment and control cases are dropped if no within-caliper match is found. Therefore, there are fewer patients included in the propensity-matched comparison than that of the unmatched groups.

ICD9 codes were searched for diagnoses of abuse of four specific illegal drugs: amphetamine, cocaine, cannabis, and opioid. These include drugs commonly encountered and of greatest concern in the perioperative period. For each drug, we combined the codes into a category called a disorder. Relative risk (RR) of mortality, MI, arrhythmia, and the sum of all complications (AC) were calculated for DSP patients versus propensity-matched DSN patients. MI was reported directly. Arrhythmia is derived from ICD9 codes. The same comparison was made for the subgroup of patients who had surgery during their admission. We used Student's *t*-test for comparison of continuous variables and Chi Square for categorical variables.

Time to procedure

Patients who had surgery were divided into groups corresponding to the time until their first procedure. The time intervals analyzed were days 1, 2, and 3, and day 4 and later. The mortality rate of complications was calculated for each group. The RR was calculated for DSP patients versus propensity-matched DSN patients. Significance was tested with Chi–square test.

For DSP patients, the association of the continuous variable of time until a procedure with outcome variables was analyzed to examine whether the time for metabolism and elimination of illegal drugs was associated with greater safety. A multivariate logistic regression was performed using the time to first procedure as a predictor variable along with the same predictor variables used to calculate the propensity score. Adjusted odds ratios (ORs) were reported.

Statistics were performed with the IBM SPSS statistical package Version 24 (IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics [Table 1]

3,437,959 patients were analyzed. 752,343 patients (21.9%) were tested for illegal drugs. Propensity match resulted in 299,898 patients in each of the DSP and DSN groups. The overall risk of MI was 0.20%. 989,634 (23.2%) had at least one procedure typically done under general anesthesia. 164,135 (3.8%) had at least one high-risk procedure.

In general, DSP patients were younger and more likely to be male. They had a lower prevalence of chronic comorbidity. DSP patients showed greater alcohol abuse (38.3 vs. 32.3%). A similar pattern was seen for each specific drug disorder. Propensity-score matching resulted in more similar baseline characteristics.

Effect of drugs on complications and mortality for the entire cohort [Table 2]

For all screened patients, DSP status was protective for mortality and for arrhythmia. It predicted harm for AC. For patients who had at least one surgical procedure, DSP patients showed lower mortality and risk of MI. The rate of AC remained higher.

Mortality was lower for cocaine, cannabis, and opioid disorders. MI was higher for cocaine disorder. Arrhythmia was markedly higher for all defined drug disorders. For each drug, the most common arrhythmias were other specified cardiac dysrhythmias, atrial fibrillation, and cardiac arrest in that order. AC is greater for cocaine, amphetamine, and opioid disorders.

Outcome after delayed procedures [Table 3]

For patients who underwent surgery, mortality was lower for DSP for every time interval until first procedure. MI was lower for surgery on day 1 and day 4 or later. Arrhythmia was lower for day 1, and AC was higher for days 1 and 2.

For DSP patients, the multivariate analysis of the continuous variable of time until first procedure showed adjusted OR for mortality of 0.97 (P = 0.001) for each additional day. The adjusted OR for MI per additional day of delay was 1.07 (P < 0.001), for arrhythmia was 1.03 (P < 0.001), and for AC was 1.1 (P < 0.001). Thus, time until first procedure for DP patients is slightly protective for mortality and slightly harmful for MI, arrhythmia, and AC.

Discussion

The trauma population is known for both the frequent need for surgical intervention and a high prevalence of illegal drug use. The use of illegal drugs, particularly stimulant drugs such as amphetamine and cocaine, is often perceived as a perioperative cardiac risk factor.[8] When a patient tests positive for illegal drugs, surgery is typically delayed, often until a repeat of the patient's drug test is negative.[9] There is little evidence of benefit for this delay, but there is potential harm. Patients suffer longer exposure to untreated surgical problems, admissions may be longer, schedules are disrupted, and canceling and rescheduling cases consume resources.

Canceling surgery is not usually an option for trauma patients, but cardiac risk stratification remains an important part of their perioperative care. Identifying high-risk patients allows increased surveillance such as more intensive intraoperative cardiac monitoring or perioperative telemetry. If time permits, these patients might benefit from additional testing such as preoperative cardiac workup. Nonoperative management could be chosen over operative when both are reasonable therapeutic alternatives. If drug-positive status is shown to be harmful, surgeons could delay nonemergent procedures as long as possible until the drugs are eliminated from the body.

Effect of chronic drug disorders

In the studies that show harm, cardiac risk is generally due to chronic drug use, not acutely detectable levels of drugs on screening. This is consistent with our findings. We found that cocaine was significantly associated with MI, but methamphetamine was not. All individual drugs that we analyzed were associated with an increased risk of arrhythmia. This could be due to the effects of the drug itself or withdrawal from the drug. The effects of chronic drug use may be related to the cumulative effect on the heart associated with heavy use.[10]

Effect of positive drug screen

A positive screen for illegal drugs was associated with a lower mortality among trauma patients, including the subset who underwent surgery. Considering the body of evidence of harm due to illegal drug abuse, our findings seem counterintuitive. How could illegal drug use be protective when it is associated with so many adverse health consequences? One issue is that all illegal drugs are combined into one category. The NTDB includes a list of drugs that define a positive result. These include opioids, cannabis, stimulant, psychoactive drugs, and others.

Most of the concern for cardiac complications is related to the use of stimulant drugs. Abuse of stimulants, mainly cocaine and methamphetamine, is highly prevalent in the trauma population. A study in a level 1 trauma center in Philadelphia showed that 38% of trauma victims tested positive for cocaine in the serum or urine.[11] There is abundant evidence that cocaine and methamphetamine can be cardiotoxic;[5,12,13] however, this risk is not confined to stimulant drugs. Carman found that long-term opioid use was associated with an incidence rate ratio for MI of 2.6 versus nonopioid users.[1] Even cannabis is associated with some cardiac risk. In a multivariate analysis, Desai *et al*. found that a history of cannabis use was associated with a small but significant increased risk of MI (OR: 1.079).[2]

In contrast to evidence of harm, there are also reports of beneficial effects of drugs of abuse, including stimulant drugs in the trauma population. Duong *et al*. showed that amphetamine was associated with improved neurologic recovery in a group of trauma patients.[14] In a study from a single level 1 trauma center, Cheng showed a lower mortality rate in patients positive for amphetamine. When used alone, opiates and benzodiazepines were also predictive of reduced mortality.[15] In a rat model, Bania *et al*. demonstrated reduced hypotension in response to hemorrhage in cocaine-positive animals.

The results of screening tests, in contrast to a defined drug abuse disorder, do not correlate with clinically important morbidity or mortality. In an NTDB study, Cowperthwaite *et al*. found an increase in infectious complications for DSP patients but no other appreciable difference in clinical outcomes. They also noted a mortality of 3.4% for drug positive versus 4.5% for drug negative patients.[3] In a study from a level 1 trauma center in California, Fujii *et al*. found that a positive screen for marijuana, amphetamine, or cocaine is not significantly associated with increased mortality for trauma patients.[4] In an ER study of 378 episodes of amphetamine intoxication, Isoardi *et al*. found that the complications were mainly behavioral and renal. No cardiac complication was encountered.[5]

The protective effect of a positive drug screen may represent a genuine pharmacologic effect or it may be due to unmeasured baseline imbalance. Regardless of whether the protective effect is a genuine benefit or a marker of lower risk, these data show that a positive drug screen does not identify a higher risk subgroup in trauma.

Effect of time to surgery

Whether DSP status is a cause or a marker, the question that clinicians must answer as a part of perioperative risk stratification is whether drug screening results identify a population for whom general anesthesia is unsafe. The literature shows little evidence that a positive drug screen increases anesthetic risk.[8,16-18] However, because of the harm of chronic drug abuse, the presence of illegal drugs on a screening test has raised concerns for perioperative cardiac risk.[9,19] A survey study showed that 30% of providers believe that cocaine-positive patients should wait 7 days after a positive drug screen before undergoing an elective surgical procedure.[10]

Time to procedure is one of the few predictor variables that is potentially modifiable in the acute setting. Theoretically, by delaying procedures, one could operate at a time when the patient is less vulnerable to drug-related cardiac complications as the drugs are metabolized and eliminated. We can look at the rate of complications versus time to surgery to see if waiting longer is associated with lower risk.

The early increased risk is not surprising because procedures done within the first few hours typically address life-threatening conditions. However, when a procedure is classified as urgent rather than emergent, surgeons have more control over the timing. Surgery can often be delayed for a matter of days. There are some cases when polytraumatized patients may benefit from the delay of major surgical procedures. A model for deciding when cases should be delayed is damage control orthopedics.

There is evidence of better outcomes delaying orthopedic procedures for unstable patients. Early surgery may increase the systemic inflammatory response and lead to a "second hit", whereas an initial period of recovery may make surgery safer. Predictors of morbidity include physiologic variables such as temperature, base deficit, and lactate.[20-23]

If the patient is stable, early appropriate care leads to better outcomes.[24] There is even evidence that delay may increase cardiac complications. In a study of geriatric hip fracture patients, Smeets *et al*. found that preoperative cardiac evaluation in excess of ACC/AHA guidelines (overscreening) increased delay to surgery by 9.9 h. Delay to surgery of more than 48 h was associated with more postoperative cardiovascular complications and mortality.

While there is evidence of benefit from delaying cases according to the principles of damage control, there is little evidence that delaying cases due to drug screening results improve risk. Ryb and Cooper showed that among trauma patients undergoing surgery the 1st posttrauma day, cocaine status did not increase complications.[25] Our results are consistent with this study.

If it were beneficial to delay surgery until drugs of abuse are eliminated, we would expect an initial higher risk with DSP patients which would converge with DSN patients over time. Instead, our results show that the perioperative cardiac risk for DSP patients is lower than that for DSN patients for every time interval until first procedure. The multivariate analysis of time until procedure as a continuous variable shows that DSP patients experience greater cardiac risk with increasing time of delay.

Strengths of the study

A large database was used for greater statistical power. We stratified procedures according to the perioperative risk. We followed the time to the first procedure out for several days to examine the frequency of complications over time.

Limitations

The greatest weakness of this analysis is that the results of the toxicological screening are combined into one status: positive or negative. The effect of the more cardioactive drugs could be diluted or even counteracted by the others. A positive drug screen does not always indicate drug abuse. Many drugs with potential for abuse have therapeutic indications, for instance, opioids, benzodiazepines, and barbiturates may be prescribed. It is difficult to determine whether a drug was prescribed, given in the field or given by a transferring facility.

The majority of the population was not screened. This could potentially introduce a bias because facilities may have chosen which patients to screen based on characteristics that could affect outcome. Drug screens have inherent limitations. Typically, they do not include the levels of the drugs that are tested. We do not know how much the patient took or when. As with all retrospective analysis, cause and effect cannot be determined.

Conclusions

Perioperative cardiac risk is very low in the trauma population, <1%. Chronic abuse of the four selected drugs examined here is associated with increased risk of arrhythmia, not only sympathomimetic drugs but also opioids and cannabis. Increased cardiac monitoring should be considered for these patients.

A positive drug screen is not associated with increased perioperative cardiac morbidity or mortality. Thus, DSP status does not identify a high-risk subgroup. In fact, drug-positive status is actually a marker of lower risk. This group should not be targeted for increased surveillance or preoperative testing. Delay in performing surgery is not associated with improved cardiac morbidity for DSP patients. It does not make sense to delay a procedure to reduce cardiac risk due to drug status because cardiac risk does not diminish with greater delay. Illegal drugs are appropriately considered a health risk because they are associated with a higher rate of AC. The protective effect on mortality of DSP status and selected chronic drug disorders requires further investigation.

More detail in the trauma registry would allow us to gain a better understanding of the effect of illegal drug use in trauma. We recommend recording the specific drugs detected in the drug screen and providing more detail about who is selected for screening.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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