



Trauma patients with human immunodeficiency virus (HIV): a propensity matched analysis

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Abstract

Background Given the growing number of people worldwide living with human immunodeficiency virus (HIV), a larger subset of these patients are now susceptible to sustaining a traumatic injury. However, the impact of HIV on outcomes in trauma with modern antiretroviral treatment remains unclear. We hypothesized mortality and rates of infectious and inflammatory complications would be higher in HIV positive (HIV+) trauma patients.

Methods The Trauma Quality Improvement Program was queried to identify trauma patients ≥ 18 years of age with HIV. Due to the imbalance between HIV+ and HIV negative (HIV-) trauma patients, a 1:2 propensity-matched model was utilized. Matched variables included age, injury severity score, mechanism of injury, systolic blood pressure, pulse rate, Glasgow Coma Scale score, and patient comorbidities.

Results 84 HIV+ patients were matched to 168 HIV- patients. Compared to HIV- patients, HIV+ patients had no significant differences in mortality rate (9.5% vs. 4.8%, $p=0.144$) or infectious complications, including pneumonia (6.0% vs. 4.2%, $p=0.530$), urinary tract infection (1.2% vs. 1.2%, $p=1.000$), or severe sepsis (1.2% vs. 0.0%, $p=0.156$). However, higher rates of acute respiratory distress syndrome (ARDS) (9.5% vs. 0.6%, $p<0.001$) and acute kidney injury (AKI) (4.8% vs. 0.0%, $p=0.004$) were observed.

Conclusion HIV+ trauma patients are not at higher risk of mortality or infectious complications, likely due to the advent and prevalence of combination antiretroviral therapy. However, HIV positivity appears to increase the risk of AKI and ARDS in trauma patients. Further research is needed to confirm this finding to elucidate the etiology underlying this association.

Keywords Trauma · HIV · AIDS · Mortality · Complications · Outcomes

Introduction

As per the Joint United Nations Program on Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS), there were an estimated 36.9 million people worldwide living with HIV/AIDS in 2017 [1]. Within the United States, the Center for Disease Control and Prevention (CDC) estimates there were approximately 1.1 million

people aged ≥ 13 years living with HIV in 2015 [2]. Interestingly, most people with HIV are between the ages of 45–54, despite a much higher infection rate in younger individuals, indicating that people are surviving much longer with the disease [2]. In fact, since 2010, there has been a 34% decrease in AIDS-related deaths [3]. With fewer HIV positive (HIV+) patients succumbing to the progression of their disease, there is now a larger subset of these patients at risk for sustaining a traumatic injury. To optimize care for these patients, a keen understanding of the impact HIV has on outcomes in trauma is needed.

To date, the effects of HIV on trauma has been mixed in the literature. Martin et al. showed increased 30-day mortality in trauma patients [4] while other studies demonstrated no association with mortality [6–10]. Similarly, some studies have shown higher renal and pulmonary complications [5, 6] as well as higher infectious complications [5, 7, 8],

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whereas others have demonstrated no difference in renal [7, 8], pulmonary [7, 8], infectious [6], or overall complication rates [4, 9] in HIV+ trauma patients.

Furthermore, much of the existing literature evaluating the impact of HIV on clinical outcomes in trauma is nearing a decade old [5–8]. Since publication of these studies, the life expectancy in HIV+ patients has improved dramatically with the use of combination antiretroviral therapy (cART) such that the life expectancy gap relative to HIV negative (HIV–) patients is now as low as 8 years [10–12]. In addition, many of the available studies either analyze a small population and/or are conducted at a single center [4–6, 9]. Therefore, we sought to provide a large contemporary descriptive analysis of clinical outcomes in HIV+ trauma patients. We hypothesized that a HIV+ trauma cohort would have increased mortality rates, infectious complications (i.e., pneumonia, urinary tract infection (UTI), and sepsis), and inflammatory complications [i.e., acute respiratory distress syndrome (ARDS) and acute kidney injury (AKI)], compared to a propensity-matched HIV– group.

Methods

This study was approved by the Institutional Review Board at our institution. Furthermore, the study utilized a large national database with de-identified patients, thus no consent was required. The database used was the Trauma Quality Improvement Program (TQIP), a database comprised of a retrospective cohort of trauma patients from participating level I or level II trauma centers in the United States and Canada. TQIP patient inclusion criteria consists of age ≥ 16 , presence of at least one valid trauma International Statistical Classification of Diseases and Related Health Problems (ICD) diagnosis code, blunt or penetrating mechanisms of injury, Abbreviated Injury Scale (AIS) score ≥ 3 , and having data for hospital or emergency department disposition [13]. TQIP patient exclusion criteria consists of patients with advanced directives preventing life-sustaining care or age ≥ 65 with isolated hip fractures [13]. A retrospective analysis of the TQIP was performed from January 2010 to December 2016 to identify trauma patients who were ≥ 18 years of age with HIV. Patients considered HIV+ were those with an ICD-9 diagnosis code for HIV: 72 and 79.53. Patients considered HIV– were those without an ICD-9 diagnosis code for HIV.

Due to the observed imbalance between HIV+ and HIV– trauma patients, we elected to perform a propensity-matched analysis using a 1:2 model. This was derived from a logistic regression model in which the dependent variable was HIV. The variables utilized in our model included age, injury severity score (ISS), mechanism of injury, systolic blood pressure (SBP), pulse rate, Glasgow Coma Scale

(GCS) score on admission, and comorbidities such as history of hypertension, chronic obstructive pulmonary disease (COPD), cirrhosis, congestive heart failure (CHF), steroid use, end-stage renal disease (ESRD), and disseminated cancer. Patients with similar propensity scores were matched to compare outcomes among patients with and without HIV. Only cases that were within 0.001 of the estimated logit were selected. This technique of defining the closeness of a matched case is termed caliper matching and is a validated method of emulating randomization in observational studies [14]. Once propensity scores were calculated for each case, one HIV+ and two HIV– matched trauma patients were included for further analysis. If a close match was not available for a HIV+ trauma patient, they were excluded from analysis.

We performed bivariate analyses for all variables to confirm a successfully matched cohort. This was done with either a chi-square or Mann–Whitney-*U* test for categorical and continuous variables, respectively. The primary outcome was in-hospital mortality. Secondary outcomes included infectious and inflammatory complications such as AKI, ARDS, pneumonia, and UTI as well as other in-hospital complications. Other measured outcomes included total hospital length of stay (LOS), ventilator days and intensive care unit (ICU) LOS. All *p*-values were two-sided, with a statistical significance level of < 0.05 . All analyses were performed with IBM SPSS Statistics for Windows (Version 24, IBM Corp., Armonk, NY).

Results

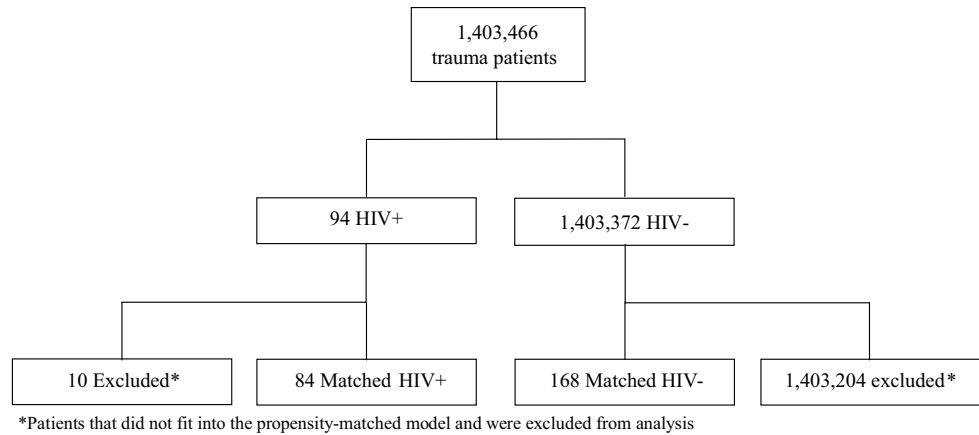
Demographics of HIV+ trauma patients

From 1,403,466 trauma patients, 94 (0.007%) patients were HIV+. After propensity-score matching, 84 HIV+ trauma patients were compared to a cohort of 168 HIV– trauma patients. There were 10 patients that did not fit into our propensity-matched model and were thus excluded from analysis (Fig. 1). Compared to a matched cohort of HIV– patients, the HIV+ patients had no differences in demographics, injury patterns, or vital signs upon hospital arrival. This confirmed successful matching between the two groups. Hypertension was the most common comorbid condition in both groups, followed by COPD, and diabetes. Traumatic brain injury (TBI) was the most common injury in both groups followed by injuries to the lower extremity (Table 1).

Clinical outcomes in HIV+ trauma patients

There was no difference observed in mortality rate (4.8% vs 9.5%, $p = 0.144$) or in the rate of infectious complications

Fig. 1 Selection of patients for the propensity matched analysis. *Patients that did not fit into the propensity-matched model and were excluded from analysis



including UTI (1.2% vs 1.2%, $p=1.000$), pneumonia (6.0% vs 4.2%, $p=0.530$), and sepsis (1.2% vs 0.0%, $p=0.156$) between the HIV+ and HIV- group. However, higher rates of ARDS (0.6% vs. 9.5%, $p<0.001$) and AKI (0.0% vs. 4.8%, $p=0.004$) were observed in the HIV+ group relative to the HIV- group. The LOS, ICU LOS, and median ventilator days did not differ between the two groups (Table 2).

Discussion

Though once considered a fatal disease, HIV/AIDS now more closely resembles a chronic disease with the advent and rise of cART medications [3, 15, 16]. In this study, we evaluated the clinical outcomes in this modern-day HIV+ trauma patient population and compared our findings to those reported in earlier studies. Using seven years of data derived from the TQIP database, we demonstrated no differences in mortality or rates of infectious complications between HIV+ and HIV- trauma patients. However, the HIV+ group was found to have higher rates of AKI and ARDS.

Prior literature generally has shown no association between HIV and mortality in trauma patients [5–8]. However, a recent study by Martin et al. evaluating trauma patients in Rwanda found HIV to be associated with increased 30-day mortality although no in-hospital mortality was reported [4]. Our study supports the findings of earlier domestic studies but appears to contrast the findings of the international study by Martin et al. It should be noted that direct comparisons between this study and the one by Martin et al. are difficult given the geographic disparities as well as the differing primary outcome of interest. However, their finding of no in-hospital mortality appears to support our results.

The association between HIV and development of infectious complications in trauma patients has been mixed, with some studies demonstrating higher [5, 7, 8] rates and others

demonstrating no difference [6] in the rate of infectious complications like pneumonia, UTI, bacteremia, and sepsis. However, these studies are relatively old with data ranging from 1989 to 2006, a time when treatment for HIV was not widely available. In fact, the CDC estimates only 28% of all HIV+ patients in the U.S. had achieved viral suppression by 2010 [17]. The only research addressing infectious complications in modern-day HIV+ trauma patients has been through relatively small single center or multi-center studies conducted outside of the U.S. Both, Martin et al., who evaluated adult HIV+ trauma patients in Rwanda, and McPherson et al., who evaluated adult HIV+ patients with penetrating abdominal trauma in South Africa, demonstrated no difference in infectious complications [4, 9]. Similarly, we did not find a difference in infectious complications when comparing U.S. HIV+ to HIV- trauma patients. This is likely reflective of the growing prevalence of cART and should thus be considered as physicians counsel patients and/or make decisions regarding management of HIV+ trauma patients.

The association between HIV and ARDS/AKI in trauma has varied in previous reports [5–8]. Here we reported a higher rate of ARDS and AKI in HIV+ trauma patients, a finding that supports the work by Stawicki et al. and Duane et al. [5, 6]. The mechanism for this might be related to the chronic inflammatory state that remains in HIV+ patients despite adequate viral suppression from cART [18]. As a known inducer of systemic inflammation [19], traumatic injury in HIV+ patients may serve to further augment the inflammatory state already present. This can amplify the activity of neutrophils known to be a component of the chronic inflammatory state observed in HIV [20]. Neutrophil activation is known to be key in the pathogenesis of ARDS [21] so additional neutrophil involvement may make HIV+ trauma patients susceptible for the development of ARDS. This augmented inflammatory state may also amplify pre-existing renal tissue injury and contribute to the development of AKI. However, the mechanism for higher rates of

Table 1 Demographics of HIV+trauma patients

Characteristic	Non-HIV (<i>n</i> = 168)	HIV (<i>n</i> = 84)	<i>p</i> value
Age, year, median (IQR)	50.0 (42)	50.0 (13)	0.824
Male, <i>n</i> (%)	131 (78.0%)	67 (79.8%)	0.745
ISS, median (IQR)	13.5 (13)	10.0 (13)	0.824
Blunt trauma, <i>n</i> (%)	152 (90.5%)	76 (90.5%)	1.000
Penetrating trauma, <i>n</i> (%)	16 (9.5%)	8 (9.5%)	1.000
Vitals/GCS			
Lowest SBP within 24 h, median (IQR)	138 (34)	132 (36)	0.755
Pulse rate, median (IQR)	88.5 (30)	88.0 (20)	0.964
GCS, median (IQR)	15 (0)	15 (1)	1.000
Comorbidities, <i>n</i> (%)			
Diabetes	27 (16.1%)	12 (14.3%)	0.712
Hypertension	50 (29.8%)	25 (29.8%)	1.000
COPD	31 (18.5%)	15 (17.9%)	0.908
Congestive heart failure	6 (3.6%)	3 (3.6%)	1.000
Cirrhosis	5 (3.0%)	3 (3.6%)	0.799
Steroid use	0 (0.0%)	0 (0.0%)	1.000
Chronic renal failure	8 (4.8%)	3 (3.6%)	0.663
Disseminated cancer	2 (1.2%)	1 (1.2%)	1.000
Injuries, <i>n</i> (%)			
Traumatic brain injury	78 (46.4%)	36 (42.9%)	0.591
Spine	42 (25.0%)	16 (19.0%)	0.290
Upper extremity	37 (22.0%)	14 (16.7%)	0.318
Lower extremity	56 (33.3%)	32 (38.1%)	0.455
Lung	38 (22.6%)	18 (21.4%)	0.830
Heart	0 (0.0%)	0 (0.0%)	1.000
Esophagus	1 (0.6%)	0 (0%)	0.479
Stomach	2 (1.2%)	1 (1.2%)	1.000
Small intestine	6 (3.6%)	2 (2.4%)	0.611
Colorectal	4 (2.4%)	0 (0.0%)	0.154
Pancreas	2 (1.2%)	0 (0.0%)	0.315
Liver	9 (5.4%)	6 (7.1%)	0.572
Spleen	11 (6.5%)	7 (8.3%)	0.604
Kidney	2 (1.2%)	1 (1.2%)	1.000

HIV human immunodeficiency virus, *IQR* interquartile range, *ISS* injury severity score, *SBP* systolic blood pressure, *GCS* Glasgow coma scale, *COPD* chronic obstructive pulmonary disease

AKI is likely multifactorial since AKI in HIV+ patients has typically been shown to have two or more contributing etiological factors such as infection, drug nephrotoxicity, and/or decreased renal perfusion [22]. The nephrotoxic effects of antiretroviral agents such as atazanavir, lopinavir, indinavir, and tenofovir are well documented [23–25] and may

occur insidiously [26]. It is possible that traumatic injury in HIV+ patients led to decreased renal perfusion from hypovolemia, exacerbating pre-existing renal injury and increasing the likelihood for AKI. More research is needed to evaluate the pathophysiology behind the increased rates of ARDS and AKI among HIV+ trauma patients. Clinicians should be aware of this finding to attempt to mitigate this through vigilant monitoring and/or targeted interventions.

As a large retrospective database study, there are inherent limitations to this work such as reporting bias and coding errors. The estimated prevalence of HIV in the US population in 2015 was 0.3%, which is much higher than the observed prevalence in this study. This could indicate a significant population of missed HIV+ patients in the cohort. Another limitation is in how HIV positivity was determined. To be considered HIV+ for this study, an ICD-9 diagnosis code for HIV must have been present. However, HIV is not a mandated comorbid condition. Therefore, it is possible HIV+ patients went unaccounted for, potentially further explaining the much lower prevalence of HIV in our study relative to the United States general population. Additionally, the TQIP database does not provide information on a patient's CD4 count, viral load, or treatment, which creates a non-homogenous population of HIV+ patients. Furthermore, we do not have any information regarding baseline renal function or prior history of infectious complications in our patient population, which may be serving as potential confounders. An additional important point to consider is the finding of no statistically significant difference in mortality rate between the two study groups despite the rate being nearly double in the HIV+ group. This may represent a type II error and should be investigated further with a larger multicenter study. Finally, as a retrospective study, our findings cannot be interpreted as causation. Our findings can only serve as markers of a correlation that merits future exploration.

Conclusion

HIV+ trauma patients had a similar rate of mortality and infectious complications compared to a matched population of HIV– trauma patients. This may be due to the advent of cART. However, HIV positivity is associated with an increased incidence of AKI and ARDS in trauma patients. Future clinical studies and basic science research investigating biochemical and/or physiological pathways that may predispose HIV+ patients to these inflammatory complications are warranted.

Table 2 Clinical outcomes in HIV+trauma patients

Outcome	Non-HIV (<i>n</i> = 168)	HIV (<i>n</i> = 84)	<i>p</i> value
LOS, days, median (IQR)	5.0 (7)	6.0 (9)	0.752
ICU, days, median (IQR)	3.0 (3)	3 (6)	0.952
Ventilator, days, median (IQR)	2.0 (6)	3.0 (5)	0.674
Complications, <i>n</i> (%)			
Myocardial infarction	0 (0.0%)	0 (0.0%)	1.000
Cardiac arrest	2 (1.2%)	1 (1.2%)	1.000
Cerebrovascular accident	2 (1.2%)	0 (0.0%)	0.315
Pneumonia	7 (4.2%)	5 (6.0%)	0.530
Ventilator associated pneumonia	0 (0.0%)	0 (0.0%)	1.000
Unplanned intubation	2 (1.2%)	1 (1.2%)	1.000
Acute respiratory distress syndrome	1 (0.6%)	8 (9.5%)	<0.001
Acute kidney injury	0 (0.0%)	4 (4.8%)	0.004
Deep venous thrombosis	4 (2.4%)	0 (0.0%)	0.154
Pulmonary embolism	1 (0.6%)	1 (1.2%)	0.616
Decubitus ulcer	2 (1.2%)	3 (3.6%)	0.201
Drug/alcohol withdrawal	5 (3.0%)	4 (4.8%)	0.471
Compartment syndrome, extremity	0 (0.0%)	1 (1.2%)	0.156
Graft/flap failure	0 (0.0%)	0 (0.0%)	1.000
Unplanned return to OR	1 (0.6%)	1 (1.2%)	0.616
Unplanned ICU	4 (2.4%)	1 (1.2%)	0.523
Superficial infection	0 (0.0%)	0 (0.0%)	1.000
Deep site infection	1 (0.6%)	0 (0.0%)	0.479
Urinary tract infection	2 (1.2%)	1 (1.2%)	1.000
Organ space infection	0 (0.0%)	(0.0%)	1.000
Osteomyelitis	0 (0.0%)	0 (0.0%)	1.000
CAUTI	0 (0.0%)	0 (0.0%)	1.000
CRBSI	0 (0.0%)	1 (1.2%)	0.156
CLABSI	0 (0.0%)	0 (0.0%)	1.000
Severe sepsis	0 (0.0%)	1 (1.2%)	0.156
Other	38 (22.6%)	12 (14.3%)	0.118
Mortality, <i>n</i> (%)	8 (4.8%)	8 (9.5%)	0.144

HIV human immunodeficiency virus, *LOS* length of stay, *IQR* interquartile range, *ICU* intensive care unit, *OR* operating room, *CAUTI* catheter-associated urinary tract infection, *CRBSI* catheter-related bloodstream infection, *CLABSI* central line-associated bloodstream infection

Author contributions JC, JN, AG were involved in the development of the study design as well as completion of the manuscript. AG compiled the necessary study statistics. All authors were involved in the analysis of data and critical revisions to the manuscript.

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Compliance with ethical standards

Conflict of interest The authors report no conflict of interest, financial or otherwise.

Informed consent This retrospective study involved humans but since a national database was used with de-identified patients, risk was minimal to participants. No consent was required.

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