

Epidemiology and Outcomes of Invasive Fungal Infections Following Civilian Trauma

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ABSTRACT # 748

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REVISED ABSTRACT

Background: Invasive fungal infections (IFI) following traumatic injury are devastating complications that threaten life and limb. In military combat wounds, post-traumatic IFI patients have up to 6 times higher mortality rates and 2.6-5.1 times higher rate of high-level amputations compared to non-IFI patients. No such data exists for the civilian population. This study is the first cohort to analyze a post-traumatic civilian population for IFI, its epidemiology and outcomes.

Methods: We conducted a single-center retrospective cohort study of all trauma patients over the age of 18 years admitted to a large tertiary referral hospital between 2004 to 2015 who required surgery for their injury and had operative cultures submitted from their wounds. Patient demographics, comorbid conditions, mechanisms of trauma, environmental exposures, and laboratory data were included for analysis. Patients with positive culture for fungus from a site compatible with IFI were considered IFI patients. Data was analyzed using descriptive statistics with $p < 0.05$ considered significant.

Results: 714 patients met inclusion criteria. Of these, 90 patients had a positive culture for fungus, 453 patients for bacteria; 80 had both fungus and bacteria present. 181 patients had no positive culture from a site of interest. Basic patient demographics, geographical setting of the trauma, and anatomical site of injury were not significantly associated with having a positive fungal culture. Necrosis was present in 19 (15.8%) IFI vs. 74 (7.5%) non-IFI patients ($p=0.014$). Soil contamination of a wound was present in 6 (6.7%) IFI vs. 11 (1.8%) non-IFI patients ($p=0.004$). 74.4% of 90 IFI wounds penetrated below fascial layers compared to 42.3% of 624 non-IFI wounds ($p < 0.001$). Presence of IFI increased likelihood of more surgical debridements (median(IQR) 1(2) vs. 3(7), $p < 0.001$) and longer hospitalization (16d vs. 28d, $p < 0.001$) compared to those without.

Conclusions: IFI significantly increased patient risk for more surgical procedures and prolonged hospital length-of-stay following traumatic injury in a civilian population. Presence of IFI was associated with wounds penetrating below the fascial layer, presence of wound necrosis, and soil contamination of a wound.

BACKGROUND

- Post-traumatic IFI are clinically complex infections with potentially serious patient outcomes.
- IFI have been systematically studied as complications of combat trauma in military populations. In this population, IFI increase mortality, time to wound closure, number of surgical procedures, and necessity of high-level amputations.
- IFI occur in traumatic injury in civilian populations, but there is no systematic study of IFI in patients suffering trauma from motor vehicle crashes, work injuries, recreational injuries, personal violence, and other violent traumatic injuries

METHODS

- Design:** Retrospective cohort from Barnes Jewish Hospital (BJH), a 1,368-bed academic hospital in St. Louis, MO.
 - Study cohort identified from the Trauma Registry Database maintained through BJH for trauma accreditation.
- Study Period:** January 1, 2004 to December 31, 2015
- Inclusion Criteria:** All patients age 18 or older with traumatic wounds requiring hospitalization, surgical intervention for management of trauma, and with cultures obtained during post trauma treatment.
- Exclusion Criteria:** All patients meeting the inclusion criteria were included in study
- Data Analysis and Statistical Analysis:**
 - Patients with positive culture for fungus from a site compatible with IFI were considered IFI patients.
 - Dichotomous variables were analyzed with Pearson chi-square or Fischer's exact test of independence.
 - Continuous variables analyzed by Mann-Whitney U Test for independent samples.
 - Values of $p \leq 0.05$ were considered significant.

RESULTS

Table 1: Baseline Characteristics by Presence of Invasive Fungal Infection (IFI)

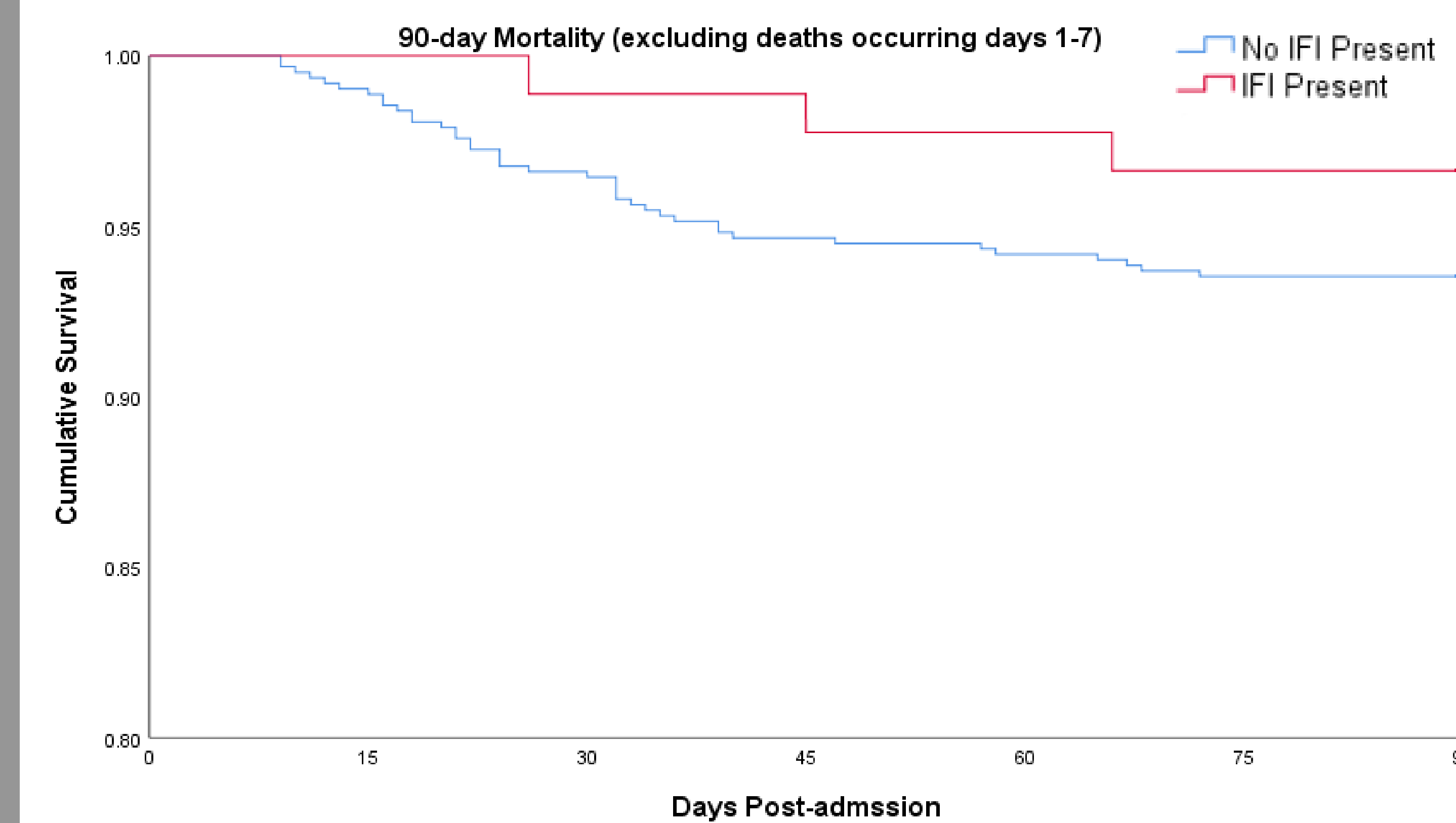
	No IFI Present=624 (87%)	IFI present= 90 (13%)	p Value
Age Median (range)	38 years (15-94)	33 years (14-80)	0.104
Sex			
Male	483 (77%)	77 (86%)	0.079
Race			
Black	283 (45%)	44 (49%)	0.629
Caucasian	325 (52%)	44 (49%)	
Other	16 (3%)	2 (2%)	
Injury Setting			
Urban	111 (18%)	14 (16%)	0.429
Suburban	8 (1%)	3 (3%)	
Agricultural	6 (1%)	1 (1%)	
Falls	66 (11%)	6 (7%)	
Gunshot/Stab wounds	147 (24%)	30 (33%)	
Industrial	19 (3%)	2 (2%)	
MVC	135 (22%)	19 (21%)	
Unknown	19 (3%)	2 (2%)	
Other	110 (18%)	13 (14%)	

Wound Characteristics

Wound Location	No IFI Present=624 (87%)	IFI present= 90 (13%)	p Value
Lower Extremity	182 (29%)	30 (33%)	0.419
Upper Extremity	218 (35%)	33 (37%)	0.748
Chest	56 (9%)	10 (11%)	0.513
Back	31 (5%)	6 (7%)	0.497
Abdomen	109 (17%)	42 (47%)	<0.001*
Pelvis	10 (2%)	1 (1%)	0.723
Perineum	5 (1%)	2 (2%)	0.201
Head	192 (31%)	17 (19%)	0.021*
Neck	18 (3%)	3 (3%)	0.814
Other	13 (2%)	1 (1%)	0.534
Wound Contamination			
Gross Contamination	53 (9%)	8 (9%)	0.925
Soil	11 (2%)	6 (7%)	0.004*
Plant matter	7 (1%)	1 (1%)	0.993
Fresh water	1 (<1%)	1 (1%)	0.111
Gravel	11 (2%)	3 (3%)	0.315
Other	28 (4%)	2 (2%)	0.317
Unknown	5 (1%)	1 (1%)	0.763
Wound Depth			
Superficial (skin/subcutaneous tissue)	168 (27%)	9 (10%)	<0.001*
Deep (extends to fascial/muscle layers)	187 (30%)	14 (16%)	
Penetrating fascial/muscle layers	264 (42%)	67 (74%)	
Presence of Wound Necrosis	74 (12%)	19 (21%)	0.014*

Table 2: Outcomes by Presence of Invasive Fungal Infection (IFI)

	No IFI Present=624 (87%)	IFI present= 90 (13%)	p Value
Hospital Length-of-Stay, median (IQR)	16 days (18)	28 days (27.5)	<0.001*
90-day Mortality (%)	46 (7.4%)	4 (4.4%)	0.383
Excludes deaths occurring days 1-7			
Debridement required of any wound	292 (47%)	46 (51%)	0.428
Total number of debridements required, median (IQR)	1 (2)	3 (7)	0.001*
Any complication of wound post-wound closure (%)	46 (7.4%)	19 (21.1%)	<0.001*
Post-wound closure return to the operating room (%)	39 (6.3%)	15 (16.7%)	<0.001*



- No significant difference in mortality between patients with IFI and without IFI ($p=0.249$)
- Deaths occurring <7 days were excluded from mortality analysis. IFI are unlikely to rapidly develop and subsequently contribute to mortality during this early time period.

ANALYSIS

- There were no significant differences in patient demographic information
- The cohort has a wide range of injury settings in which trauma occurred. There were no statistical differences in the presence or absence of IFI based on the injury setting. However, this cohort is likely representative of mechanisms of trauma for patients presenting to a large urban, academic hospital with a wide catchment area.
- There was a statistically significant association of abdominal wounds with IFI ($p < 0.001$). Our hypothesis for this observation is these wounds are likely to have bowel injury, increasing the likelihood of translocation of gastrointestinal fungal flora.
- Head wounds were less likely to have IFI.
- Soil was the sole contaminant with a statistically significant association ($p=0.004$) with presence of IFI. Soil is the natural habitat for many fungal organisms and this association has been identified in the literature previously.
- Patients with IFI had a significantly longer hospital LOS (median 28 vs 16 days, $p < 0.001$) compared to those without IFI. This increased duration is likely explained by the increased number of operations required for IFI wounds. The total number of debridement procedures was 3 (IQR=7) for IFI and 1 (IQR=2) for non-IFI wounds.
- IFI were associated with increased rate of wound complications following primary surgical closure ($p < 0.001$) and more likely to require a return trip to the operating room ($p < 0.001$)
- In contrast to military data and civilian case series/reports, there was no difference in mortality between patients with and without IFI ($p=0.383$)

CONCLUSIONS

- Presence of IFI significantly increased hospital length-of-stay, number of surgical debridements, risk for wound complications, and return visits to the operating room to manage complications following primary wound closure.
- The presence of wound necrosis, wound contamination with soil, and wound depth penetrating below the fascial/muscle layers are risk factors associated with the presence of IFI.
- Identification of risk factors for the development of IFI in civilian post-traumatic wounds could be used to identify high-risk patients that may benefit from early interventions such as anti-fungal prophylaxis.